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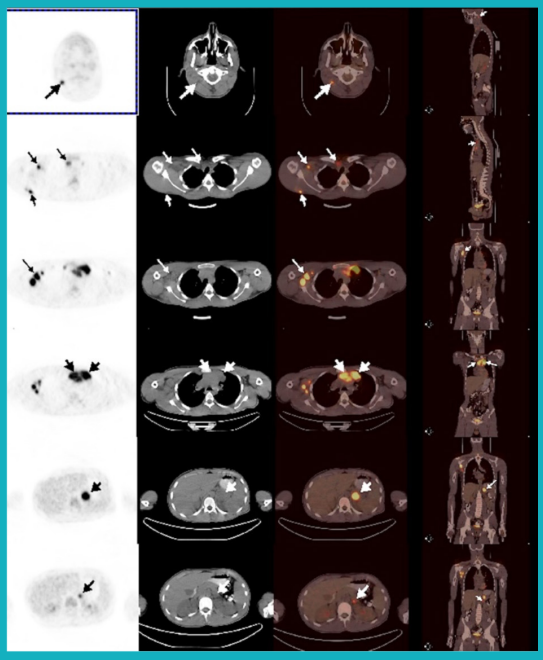

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Safe Laparoscopic Cholecystectomy Techniques in Difficult Cases

Zor Olgularda Güvenli Laparoskopik Kolesistektomi Teknikleri

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Cholecystectomy is one of the most frequently performed operations in general surgery practice. Its main indications are symptomatic gallstones, complications of gallstones and gallbladder polyps. In symptomatic patients, the gold standard today is laparoscopic cholecystectomy.

Although the number of bile duct injuries seen in laparoscopic cholecystectomy has decreased in recent publications, it is still twice as high as in open cholecystectomy (1). The most common cause of bile duct injuries in gallbladder surgeries is insufficient identification of tissues. Although the anatomical variations of the bile ducts up to 30% and the surgeon's experience are important factors, the most important reason for serious injury is the cut of the common bile duct, which is mistaken for the cystic duct. Previous attacks and dense adhesions are identified as another important factor. When the operation is started, if the situation is different from the standard expectations, it is important to prevent complications. Although many suggestions have been made about what we should do in this situation, the techniques we apply make things much easier. These are "critical view of safety", "triangle of safety technique", "fundus first" and "subtotal or partial laparoscopic cholecystectomy" techniques (2,3). If the anatomy cannot be understood, intraoperative cholangiography, intraoperative ultrasonography, fluorescence imaging methods may be guiding. In this article, I will talk about safe laparoscopic cholecystectomy techniques in difficult cases.

The generally applied method in laparoscopic cholecystectomy is the infundibular technique. Here, dissection is started from the neck of the bladder, the upward structures are clarified, the cystic artery and cystic duct are exposed, then clipped and cut (2). When laparoscopic cholecystectomy began to be widely used, some of the publications stated that biliary tract injuries increased. Injury is mostly caused by misidentification of anatomical tissues and technical difficulties. Inadequate surgical technique, inability to understand how the injury occurred, delay in conversion to open surgery, insufficient field of view, inflammation, aberrant anatomical structures, and male gender were defined as risk factors in some publications (1,4-6). Various opinions have been put forward in order to better determine the anatomical structures in laparoscopic cholecystectomy, and different perspectives have been tried to be put forward, especially when applying the dissection stage (3,4,6).

Critical View of Safety (CVS)

This method was defined by Strasberg in 1995 (7). There are 3 criteria in the CVS. The first is the cleansing of the elements in the Calot triangle from fat and fibrous tissues. The second criterion is the separation of the lowest part of the gallbladder from the cystic layer, where fibrous adhesions can be seen as the gallbladder is not peritonized. Sometimes this layer can be the liver bed. The third criterion is to make it clear that only two structures enter the gallbladder. The basic rationale of CVS is to apply the two-stage method used in open cholecystectomy to define the bile ducts. In the first, the cystic duct and artery are determined by dissection of Calot's triangle, then the gallbladder is completely separated from the bed and it is shown that there are only two structures connected to the gallbladder.

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Triangle of Safety Technique (TST)

This technique was described by Almutairi and Hussain (8). The aim of the TST technique is to define a new anatomical area different from Calot's triangle, which will create a safe dissection area away from the common bile duct in clarifying the tissues. While the gallbladder is pushed from the fundus to the right lobe of the liver by the assistant, the surgeon pushes the sac from the Hartman pouch laterally with his/her left hand. It is clarified in 4 basic steps using TST electro cautery hook. In the first step, the peritoneum on the gallbladder wall is dissected down from the midline parallel to the cystic artery and up to the junction of the cystic artery and cystic duct. In the second step, the branches of the cystic artery are determined one by one in accordance with the layers under the peritoneum and proceed to Calot's artery, where the cystic artery and cystic duct meet. In dissection, the place where the cystic duct enters the infundubulum and the posterior wall of the gallbladder are clarified. The third step is to separate the lateral peritoneal adhesions. The fourth step is to reach the lateral wall of the gallbladder by separating the tissues between the borders of the TST, while not injuring the branches of the posterior cystic artery.

"Fundus First" Laparoscopic Cholecystectomy

Here, unlike normal, the dissection is started from the fundus and progressed downwards to the liver hilum.[4] This technique is also called the "top-down" method. This method, which is frequently used in open cholecystectomy, is preferred in laparoscopic cholecystectomy when Calot's triangle is not prominent. In the anterograde approach, dissection is performed from the fundus to the infundibulum. The gallbladder is dissected from the liver bed. Some peritoneum is left in the liver bed to retract the liver. After making sure the cystic artery and cystic duct structures, these structures are clipped and cut.

Laparoscopic Subtotal or Partial Cholecystectomy

In this technique, dissection of Calot's triangle, of which anatomy cannot be clearly distinguished, is avoided. If access to Calot's triangle cannot be achieved safely due to fibrosis or inflammation with CVS and "first fundus" methods, a laparoscopic subtotal or partial cholecystectomy is performed by excising a portion of the gallbladder and its contents from a safe margin. All stones and bile contents should be safely aspirated and removed from the abdomen. Here, a partial cholecystectomy is performed and cut proximal to the cystic duct. In patients in whom the posterior wall of the gallbladder is very attached to the liver, partial cholecystectomy can be performed by leaving a part of the gallbladder in place. The mucosa of the remaining posterior wall should be cauterized (9,10).

In the presence of mild to moderate inflammation, the standard procedure can be applied. The first steps in the application of laparoscopic cholecystectomy are similar in most methods. Calot's triangle is cleared of fat and fibrous tissue. This can be done by a variety of techniques: tissue is separated with holders or gauze dissectors, cautery with hooks, or blunt-ended and curved dissectors. Dissection is usually done anterior and posterior to the Calot's triangle. There are two points to note for cautery. The first is the use of cautery at low power settings of 30W and below, and the second is to prevent unintentional damage to the surrounding tissues by pulling the cauterized tissue higher than the surrounding tissues. Cautery should be applied in shots of 2-3 seconds or less because thermal spread to surrounding tissues should be minimized. It is also important that the tissue is separated only in small pieces at one time. Because important biliary structures can be very small in diameter. With the application of these approaches, it is not difficult to clean the Calot's triangle from fat and fibrous tissue and to separate the gallbladder from under the cystic plaque in the presence of mild or moderate inflammation. When this is done, all structures are made visible before they are clipped and cut. If the tissues cannot be identified, the sac is separated from the bed until the right of the fundus. During separation of the cystic structures, the artery can be dissected first, because with the separation of the shorter artery from the cystic duct, the length of the cystic duct becomes more visible. Performing this intraoperative cholangiography also facilitates insertion of a catheter into the cystic duct if necessary. Each structure should then be clipped and cut to avoid damage. There are different methods in the literature on safe separation of the gallbladder laparoscopically. The surgeon should agree with his assistant in laying out the critical points during the dissection (5,6).

In severe inflammation, the ducts can be seen to cross the Calot's triangle and even merge with the cystic duct. However, the entrance to the gallbladder cannot be seen, sometimes the right hepatic duct directly entering the gallbladder can be seen. As in Mirizzi syndrome, the cystic duct may disappear due to a larger stone. In these conditions, the cystic duct terminates in the lower part of the right hepatic duct, and severe chronic inflammation may occur in all these patients. Surgeons are more likely to circumferentially dissect the common bile duct and consider it a cystic duct in the presence of severe acute and chronic inflammation. Because certain factors that occur in these conditions can hide the cystic duct and connect the main hepatic duct to the edge of the gallbladder. This can cause confusion between the main duct and the cystic duct and lead to bile duct damage. If the surgeon thinks that the main bile duct is the cystic duct, he/she should obtain a 360-degree view of the funnel-shaped structures similar to the fusion of the cystic duct and the gallbladder. If the cystic artery is not diagnosed, the Calot's triangle is not completely cleared, and the base of the cystic plaque is not visible, the surgeon will have difficulty continuing after isolating the common bile duct. This is actually acceptable and shows that there is a problem. It is important for the surgeon to understand this when this stage becomes more difficult during the operation. In addition, options such as intraoperative cholangiography, intraoperative ultrasonography, fluorescence imaging, conversion to open cholecystectomy, or seeking help from a colleague should be considered. The critical vision method may be superior to the infundibular technique in severe inflammatory conditions because it requires more care. The patient is definitely protected because the surgeon does not

usually refer to a wrong view. If there is severe adhesion and the anatomy cannot be differentiated, insistence on dissection should be avoided (2).

As a result, it is not possible to recommend a single method to prevent biliary tract injuries according to studies. Most of the surgeons firstly agree that CVS is the most appropriate dissection technique. If adequate vision is not achieved, "fundus first" technique is used and if this is not sufficient, "subtotal laparoscopic cholecystectomy" can be applied. In case of difficulties, it should not be avoided to resort to intraoperative cholangiography, intraoperative ultrasonography and fluorescence imaging methods. Recognition of dangerous situations and knowledge of alternative techniques will ensure that the surgery is completed with minimal risk of injury to the patient. In patients in whom exploration cannot be performed safely or in patients in whom open surgery is thought to be safer such as in patients with bleeding, open cholecystectomy should not be hesitated, and conversion to open should not be considered as a complication or failure. The request to complete the transaction should not prevent the transaction from being completed safely.

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Original Article

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The Role of Post-treatment FDG-PET/CT Scanning after the First-line Chemotherapy in Predicting Prognosis in Patients with Hodgkin Disease and High-grade Non-Hodgkin Lymphoma: A Comparative Study with Clinical Prognostic Risk Scoring Data

Hodgkin Hastalığı ve Yüksek Dereceli Non-Hodgkin lenfomalı Hastalarda Prognozu Tahmin Etmede Birinci Basamak Kemoterapiden Sonra Yapılan FDG PET/BT Taramasının Rolü: Klinik Prognostik Risk Skorlama Verileri ile Karşılaştırmalı Bir Çalışma

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ABSTRACT

Objective: We aimed to evaluate the role of fluorodeoxyglucose (FDG)-positron emission tomography/computed tomography (PET/CT) performed after the first-line therapy in predicting prognosis of lymphomas and compare the results with the pre-treatment prognostic risk scoring (PRS) indices.

Methods: One hundred three patients with histopathologically confirmed Hodgkin (HD) and high-grade non-Hodgkin lymphoma (NHL) were included in the study. All patients received FDG-PET/CT imaging after the end of primary treatment. After intraveneus application of FDG, whole body PET/CT from the upper thigh to the vertex was performed.

Results: The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of post-treatment FDG-PET/CT imaging in predicting remission status were 73.6%, 91.6%, 88%, 66.6%, and 94.0%, respectively. Those values were

ÖZ

Amaç: İlk basamak tedavi sonrası yapılan florodeoksiglukoz (FDG)-pozitron emisyon tomografi/bilgisayarlı tomografinin (PET/BT) lenfomaların prognozunu öngörmedeki rolünü değerlendirmeyi ve sonuçları, tedavi öncesi yapılan prognostik risk skorlama (PRS) indeksleri ile karşılaştırmayı amaçladık.

Yöntemler: Çalışmaya histopatolojik olarak doğrulanmış Hodgkin hastalığı (HH) ve yüksek dereceli non-Hodgkin lenfoma (NHL) tanısı alan ve FDG PET/BT taraması yapılan toplam 103 hasta dahil edildi. Tüm hastalara, birinci basamak tedavinin bitiminden sonra FDG PET/BT görüntüleme yapıldı. Hastalara FDG'nin intravenöz uygulamasından sonra üst uyluktan vertekse kadar tüm vücut PET/BT yapıldı.

Bulgular: Tedavi sonrası FDG PET/BT görüntülemenin duyarlılık, özgüllük, doğruluk, pozitif öngörü değeri (PPV) ve negatif öngörü değeri (NPV), remisyon durumunu öngörmede sırasıyla; %73,6,

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63.0%, 62.0%, 62.0%, 27%, and 88.0% respectively, for pre-treatment clinical risk scoring (p<0.001). Among the patients with positive PET scans after ending of the first-line therapy, 71.4% of those with only single lymph node station involvement stayed in remission, whereas 12.5% of the patients who had involvement of multiple lymph node stations and 16.7% of the patients who had extranodal disease could sustain in remission (p<0.05).

Conclusion: We found that FDG-PET performed after first-line therapy was superior to clinical PRS systems in predicting prognosis of HD and NHL disease as conclusions. Although it was more successful to predict patients who would stay in remission with its high NPV, FDG-PET/CT imaging had a lower PPV due to false positive results. However, persistent FDG uptake in multinodal lymphatic stations and/or in extranodal sites on the post-therapy PET/CT scanning was more suggestive in predicting risk for recurrence.

Keywords: Lymphoma, positron emission tomography/computed tomography, F-18 fluorodeoxyglucose, clinical prognostic risk scores

%91,6, %88 %66,6 ve %94,0 idi. Tedavi öncesi klinik risk skorlaması için bu değerler sırasıyla %63,0, %62,0, %62,0, %27 ve %88 olarak hesaplandı (p<0,001). Birinci basamak tedavisinin bitiminden sonra PET taraması pozitif olan hastalar arasında, yalnızca tek lenf nodu istasyonu tutulumu olanların %71,4'ü remisyonda kalırken, birden fazla lenf nodu istasyonu tutulumu veya ekstranodal hastalığı olan hastalarda remisyonda kalma oranı sırasıyla %12,5 ve %16,7 olarak hesaplandı (p<0,05).

Sonuç: Sonuç olarak, birinci basamak tedaviden sonra gerçekleştirilen FDG PET'nin, HH ve NHL'nin prognozunu öngörmede klinik PRS sistemlerinden daha üstün olduğunu bulduk. Yüksek NPV nedeniyle, remisyonda kalacak hastaları tahmin etmede daha başarılı olsa da, FDG PET/BT görüntülemenin yanlış pozitif sonuçlardan dolayı PPV daha düşüktür. Bununla birlikte, tedavi sonrası PET/BT taramasında multinodal lenfatik tutulumu olan ve/veya ekstranodal tutulumu olan hastalarda, tek lenf nodu tutulumu olanlara göre rekürrens olasılığının daha yüksek olduğu görüldü.

Anahtar Sözcükler: Lenfoma, pozitron emisyon tomografisi/bilgisayarlı tomografi, F-18 florodeoksiglukoz, klinik prognostik risk skorları

Introduction

Multislice computed tomography (CT) integrated positron emission tomography/CT (PET/CT) with Flourine (F)-18 labelled fluorodeoxyglucose (FDG) has been widely used in staging and follow-up of malignant lymphomas as happens in many other solid malignancies in recent years (1,2). Malignant tissues are capable of accumulating more FDG, a radiopharmaceutical of d-glucose analogue, compared to normal tissue due to their excess energy requirement, and represent themselves as highly contrasted foci on PET/CT imaging.

In curable lymphomas, i.e Hodgkin disease (HD) and aggressive non-Hodgkin lymphomas (NHL), the use of standart doxorubicin-containing chemotherapy regimens with or without involved field radiotherapy (IF-RT) has a high success rate. These standart therapy protocols are defined mainly according to histologic subtype and stage of the disease as well as prognostic prediction based on clinical prognostic risk scoring systems (PRS) (3,4). However, a complete long-term disease control can not be achieved in a substantial portion of patients with these standart chemotherapy regimens due to either resistant disease or early relapse. In this subgroup of patients with lymphoma, it is possible to get the disease under control by applying more aggressive chemotherapy protocols (5). However, this approach is required a more serious risk-benefit ratio calculation because of undesired toxic effects of such chemotherapy protocols for the patients (6). Therefore, an effective mid- or end-treatment evaluation is desired in patients with lymphoma and this is of particular importance to discriminate the subgroup of patients either who will have a resistant disease or be at higher risk for early relapse.

In this retrospective study we aimed to determine the efficacy of FDG-PET/CT imaging performed after the first-line treatment in predicting the prognosis of patients with lymphoma and we also compared the PET/CT results with the pretreatment prognostic scores.

Methods

Patients

A total of 103 patients with a diagnosis of histologically proven lymphoma, treated in the hematology clinic of the of the İstanbul University-Cerrahpaşa Hospital, and who underwent FDG-PET/CT scan after the completion of the first-line treatment, were analyzed retrospectively. Our study project was approved by the İstanbul University-Cerrahpaşa Clinical Research Ethics Committee (16.09.2008/27584). There were 56 (54.4%) patients with HD (32 nodular sclerosing, 21 mixed type, and 3 lymphocyte rich) and 47 (45.6%) patients with high-grade NHL (43 diffuse large B-cell lymphoma, 3 anaplastic T-cell lymphoma, and 1 Burkitt's lymphoma) (Table 1). The age ranged from 16 to 81 with an average of 41.6 ±17.1 (47 females and 56 males). The PET/CT studies were performed between 10 and 90 days after completing their first-line treatment. Thereafter, all patients were followed up in haematology outpatient clinic with an interval of 3-6 months and evaluated by physical examination and laboratory parameters as well as by imaging modalities when needed. Accordingly, their disease outcome status was classified in two groups as "remission" and "non-remission". The non-remission group was including those patients with partial remission or stable disease, and relapsed or progressed disease. The median follow-up duration was 31.8±7.5 months (ranged from 24 to 55 months). The patients who did not achieve remission were treated by further chemotherapy courses and/or stem cell transplantation with high dose chemotherapy (Table 2a, 2b).

Pretreatment Prognostic Risk Scoring

All patients were staged according to Ann Arbor classification from stage I to IV in the pretreatment evaluation (7). In HD

Table 1. Histological subtypes of patients with HD and NHL diagnosis

Hodgkin lymphoma			
Total	Nodular sclerosing 21 mixed type, and 3 lymphocyte rich	Mixed type sclerosing, 21 mixed type, and 3 lymphocyte rich	Lymphocyte rich
(n=56)	32 (57.1%)	21 (37.5%)	3 (5.3%)
Non-Hodgkin lymphoma			
Total	Diffuse large B-cell	Anaplastic T-cell	Burkitt's
(n=47)	43 (91.4%)	3 (6.3%)	1 (2.1%)

HD: Hodgkin disease, NHL: Non-Hodgkin lymphoma

group, stage I-IIA patients were classified as having "early (localised) stage" and stage IIB-IV patients were classified as having "late (advanced) stage. Then, early stage patients were classified in "favorable prognostic" and "unfavorable prognostic" groups according to German Hodgkin Lymphoma study group criteria (8). In NHL group, the patients were classified into low, low-medium, medium-high and high risk groups according to IPI (International Prognostic index) and age-adjucted (aa)-IPI criteria (4). Then, they were categorized within two groups as "low risk" (for low and low-medium groups) and "high risk" (for medium-high and high groups).

First-line Treatment Protocols

According to departmental protocols, patients with early stage HD were treated with ABVD regime from 2 to 4 courses followed by consolidation IF-RT and patients with advanced stage HD were treated with 6-8 courses of ABVD (a total of 10 patients). Nine patients with NHL were essentially treated with CHOP regime with rituximab (only in 9 patients without rituximab), from 3 to 8 courses followed by IF-RT. The indications for consolidation radiotherapy included (i) initial massive mediastinal disease; (ii) individual or confluent nodal masses; and (iii) macroscopic nodules in an intact spleen as determined by CT scan.

PET/CT Imaging and Evaluation Protocol

All patients underwent a post-therapy PET/CT scan, performed 10 to 90 days (median 36.7) after completion of the first-line treatment protocol. A dedicated high-resolution LSO based PET scanner that was integrated with 6 slice CT (Siemens Biograph 6 LSO HI-REZ PET/CT, Illinois, USA) was used for PET/CT imaging. All patients were given an iodine containing contrast agent (Telebrix 30 Meglumin, Guerbet, France or Urovist-angiografin 50, Bayer Türk Kimya, İstanbul, Turkey) diluted in 1.5 L of water and asked to drink it part by part starting 4-8 hrs before their appointment time. Patients were in at least 4 hr fasting at the time of their appointment. After ensuring the peripheral blood glucose level less than 180 mg/dL, 296-703 MBq (8-19 mCi) FDG was intravenously injected into the patient via an IV catheter and thereafter the patients were rested 1-1.5 hr in a semireclining chair in the waiting room. After that, the patients were lain down in supine position on the scanner table. First, a CT topogram image was obtained from the vertex to 1/3 proximal of thighs. Then a low-dose CT imaging (60-80 mAs) without IV contrast administration was performed followed by PET emission imaging in the guidance of the CT topogram. Total PET/CT imaging was generally completed in 7-8 bed positions within 20-25 minutes. Iterative algorithms were applied to both PET and CT data reconstruction using the vendor provided software and multiplanar (axial, sagittal, coronal) slices with approximately 0.5 mm thickness of both PET and CT images as well as maximum intensity projection (MIP) views were obtained. Attenuation correction based on CT data was applied to PET images. Attenuation corrected PET slices together with identically aligned CT slices and coregistered (fused) PET/CT slices as well as MIP images were projected onto high resolution LCD monitors for reviewing and reporting.

The PET/CT images were evaluated by an experienced nuclear medicine phycisian underguidance with all clinical information available. In visual evaluation of PET/CT images, any lymph node with an increased FDG accumulation more than mediastinal blood pool and/or any focus of increased FDG uptake within an extranodal organ was considered as positive finding for residual disease. Additionally, a semi-quantitative index of FDG uptake intensity normalized to the body weight, which was called maximum standart uptake value (SUV_{max}) was calculated according to standard formula using the vendor-software by drawing a region-of-interest from the most active part of the lesion for each PET-positive region. Additionally, PET-positive patients for residual disease were categorized into 3 groups according to disease sites and extension as follows: i. Single lymphatic station involvement, ii. Multiple lymphatic stations involvement, and iii. Extranodal disease with or without nodal involvement.

Statistical Analysis

The sensitivity, specifity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of post-treatment FDG-PET/CT imaging and pre-treatment PRS in predicting of disease outcome were calculated for both whole group and subgroups (HD and NHL). Chi-square test was used to compare the diagnostic accuracy rates between the methods, as well as

Table 2 a. Characteristics of patients with Hodgkin Disease

No	Age/sex	Follow-up duration	PRS	First-line treatment	Post-therapy PET/CT (extension)	SUV_{max}	Disease outcome
1	26/F	25 months	High	4 cyc-CT	Positive	4.0	Stable
2	26/M	38 months	High	8 cyc-CT	Negative	-	Remission
3	28/F	35 months	High	8 cyc-CT	Positive	6.3	Remission
4	18/M	24 months	High	4 cyc-CT	Negative	-	Remission
5	63/F	33 months	High	8 cyc-CT	Negative	-	Remission
6	33/M	20 months	Low	4 cyc-CT	Negative	-	Remission
7	17/M	29 months	High	4 cyc-CT	Negative	-	Remission
8	38/M	34 months	High	8 cyc-CT	Negative	-	Remission
9	16/M	32 months	Low	4 cyc-CT	Positive	18.2	Exitus
10	42/M	24 months	High	4 cyc-CT+RT	Negative	-	Remission
11	34/F	28 months	Low	4 cyc-CT	Negative	-	Remission
12	37/F	29 months	Low	2 cyc-CT	Negative	-	Remission
13	17/F	29 months	Low	4 cyc-CT	Negative	-	Remission
14	55/F	55 months	Low	4 cyc-CT+RT	Negative	-	Remission
15	54/M	34 months	High	4 cyc-CT	Negative	-	Remission
16	30/F	28 months	Low	4 cyc-CT	Negative	-	Remission
17	44/M	24 months	High	4 cyc-CT	Negative	-	Remission
18	16/F	32 months	Low	2 cyc-CT	Negative	-	Remission
19	60/M	24 months	High	4 cyc-CT	Negative	-	Remission
20	18/M	29 months	High	4 cyc-CT	Positive	3.3	Remission
21	24/F	28 months	Low	6 cyc-CT	Negative	-	Remission
22	30/F	24 months	Low	3 cyc-CT	Negative	-	Remission
23	28/F	28 months	Low	4 cyc-CT	Negative	-	Remission
24	24/F	36 months	Low	8 cyc-CT+RT	Negative	-	Remission
25	21/M	35 months	High	4 cyc-CT	Positive	3.2	Remission
26	23/M	26 months	Low	4 cyc-CT	Negative	-	Remission
27	56/M	26 months	High	4 cyc-CT	Negative	-	Remission
28	65/M	32 months	High	8 cyc-CT	Negative	-	Remission
29	16/M	26 months	High	4 cyc-CT	Negative	-	Remission
30	17/F	33 months	Low	8 cyc-CT	Positive	7.4	Remission
31	23/M	34 months	High	8 cyc-CT	Positive	11.8	Exitus
32	24/M	28 months	Low	2 cyc-CT+RT	Negative	-	Remission
33	24/F	28 months	Low	4 cyc-CT	Negative	-	Remission
34	26/F	28 months	Low	4 cyc-CT	Negative	-	Remission
35	68/F	28 months	High	4 cyc-CT	Negative	-	Remission
36	66/M	27 months	High	4 cyc-CT	Negative	-	Remission
37	25/M	52 months	Low	4 cyc-CT+RT	Negative	-	Remission
38	22/F	53 months	Low	6 cyc-CT+RT	Negative	-	Remission
39	59/M	40 months	High	4 cyc-CT+RT	Negative	-	Remission
40	47/M	39 months	High	6 cyc-CT	Negative	-	Remission
41	29/M	35 months	Low	6 cyc-CT	Positive	9.0	Exitus
42	61/M	39 months	High	4 cyc-CT	Negative	-	Remission
43	22/M	28 months	Low	6 cyc-CT+RT	Negative	-	Remission
44	46/M	29 months	Low	2 cyc-CT	Negative	-	Remission
45	32/F	35 months	Low	4 cyc-CT	Negative	-	Relapse

Table 2 a. Continued

No	Age/sex	Follow-up duration	PRS	First-line treatment	Post-therapy PET/CT (extension)	SUV_{max}	Disease outcome
46	29/M	43 months	High	6 cyc-CT	Negative	-	Remission
47	56/M	34 months	High	8 cyc-CT	Negative	-	Remission
48	36/F	39 months	High	8 cyc-CT	Positive	9.6	Remission
49	58/M	37 months	High	4 cyc-CT	Negative	-	Remission
50	21/M	39 months	High	4 cyc-CT	Negative	-	Remission
51	50/F	37 months	Low	4 cyc-CT	Negative	-	Remission
52	48/M	38 months	Low	4 cyc-CT	Positive	6.6	Relapse
53	26/F	30 months	Low	4 cyc-CT+RT	Negative	-	Remission
54	31/M	35 months	High	8 cyc-CT	Positive	8.3	Relapse
55	64/F	50 months	High	3 cyc-CT	Positive	12.6	Exitus
56	18/F	48 months	Low	6 cyc-CT+RT	Positive	16.3	Relapse

PRS: Pre-treatment clinical prognostic risk scoring, LOW: Low risk group, HIGH: High risk group, CYC: Cycles, CT: Chemotherapy, F: Female, M: Male, PET/CT: Positron emission tomography/computed tomography

to find out the differences between observed frequencies in the subgroups of the patient population. Kaplan-Meier analysis was used in calculating progression free survival (PFS) curves after first-line treatment for both group and the long-rank test was used for comparison between groups. PFS was defined as the time interval from the end of chemotherapy until progression, relapse, death or date of last follow-up or endpoint of our study. The compatibility between the PET and PRS was evaluated with kappa test. Moreover, the effect of different factors on remission was assessed by Cox regression analysis. SPSS statistical analysis package software (version 15.0) was used for statistical evaluation.

Results

Of the 56 patients with HD, 27 patients had favorable prognostic criteria and remaining 29 patients had unfavorable prognostic status on pre-treatment evaluation. On the other hand, there were 32 patients in low-risk and 15 patients in high-risk categories in the group of NHL patients. Post-treatment PET/CT was negative (no residual abnormality) in 82/103 (80%) patients, and positive in the remaining 21 (20%) patients (Table 3). Of the patients with negative post-treatment PET/CT study, 52 (63%) (22 HD; 30 NHL) had favorable/low-risk PRS, while 30 of them (21 HD; 9 NHL) (37%) had unfavorable/high-risk PRS. In 7 out of 21 (33%) patients (5 HD, 2 NHL) with positive post-treatment PET/CT, there was favorable/low-risk PRS versus unfavorable/high-risk PRS in 14 (67%) patients (8 HD; 6 NHL). There was a significant difference between the favorable/low-risk group and the unfavorable/high risk group in terms of post-treatment PET/CT imaging results (p=0.013). In PET-positive patients, SUV_{max} values of the lesions ranged from 2.5 to 18.2 (average 9.1).

At the end of follow-up period, 84 of 103 patients (81.6%) stayed in remission. Among these, 52 (61.9%) patients (22 HD; 30 NHL) had favorable/low-risk PRS versus 32 (38.1%) patients (25 HD;7 NHL) with unfavorable/high-risk PRS, while a big majority of the patients (91.6%) had negative PET/CT versus a minority of the patients (8.3%) with positive PET/CT study (Table 4) (Figure 1). Nineteen of 103 (18.4%) patients were in non-remission status, of whom 12 (63.1%) (4 HD; 8 NHL) had unfavorable/high-risk PRS and 7 (36.8%) patients

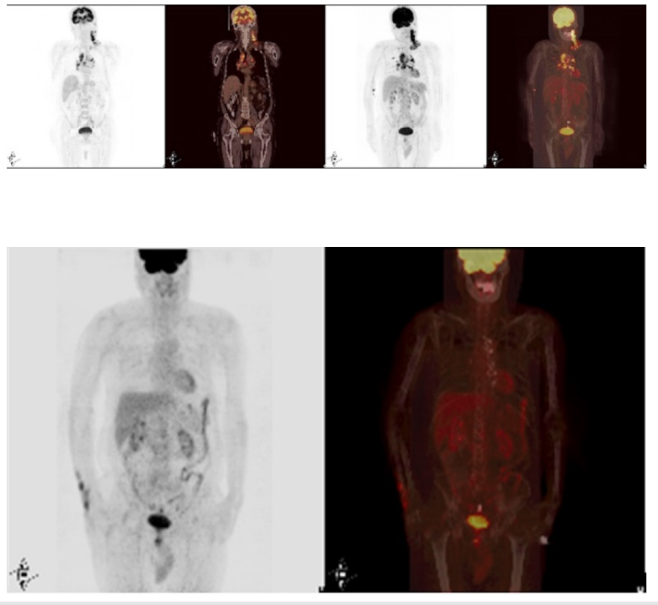

Figure 1. A) Top row: Initial (pre-treatment) FDG-PET/CT, B) Bottom row: Post-treatment FDG-PET/CT. Maximum intensity projection images of a patient with a mixed cell type of HD, who had unfavorable pre-treatment risk scoring. All hypermetabolic foci seen on the initial PET/CT study completely disappeared in the post-treatment study done after completion of chemotherapy. The patient stayed in remission during 29 months follow-up period

FDG-PET/CT: Fluorodeoxyglucose-positron emission tomography/computed tomography

Table 2b. Characteristics of patients with non-Hodgkin Lymphoma

No	Age/sex	Follow-up duration	PRS	First-line treatment	Post-therapy PET/CT (extension)	SUV_{max}	Disease outcome
1	54/F	29 months	Low	4 cyc-CT	Negative	-	Remission
2	24/M	29 months	High	8 cyc-CT	Positive	15.5	Exitus
3	70/M	28 months	Low	3 cyc-CT+RT	Negative	-	Remission
4	44/F	26 months	Low	6 cyc-CT	Positive	11.3	Remission
5	64/M	25 months	High	4 cyc-CT	Positive	3.5	Exitus
6	40/F	28 months	Low	3 cyc-CT	Negative	-	Remission
7	40/F	35 months	High	8 cyc-CT	Negative	-	Remission
8	53/M	34 months	Low	8 cyc-CT	Negative	-	Remission
9	24/M	32 months	Low	8 cyc-CT	Negative	-	Remission
10	64/M	33 months	High	8 cyc-CT	Negative	-	Exitus
11	51/M	38 months	Low	5 cyc-CT	Negative	-	Exitus
12	54/F	33 months	Low	3 cyc-CT+RT	Negative	-	Remission
13	59/F	32 months	Low	3 cyc-CT+RT	Negative	-	Remission
14	76/F	29 months	Low	5 cyc-CT	Negative	-	Remission
15	63/M	38 months	High	4 cyc-CT	Positive	7.7	Stable
16	38/M	29 months	Low	3 cyc-CT+RT	Negative	-	Remission
17	46/M	29 months	High	4 cyc-CT	Positive	8.1	Exitus
18	61/F	28 months	High	4 cyc-CT	Negative	-	Remission
19	70/F	31 months	Low	3 cyc-CT+RT	Negative	-	Remission
20	81/F	24 months	Low	8 cyc-CT	Negative	-	Remission
21	69/F	32 months	Low	3 cyc-CT+RT	Negative	-	Remission
22	24/F	48 months	Low	6 cyc-CT	Negative	-	Remission
23	50/F	24 months	Low	6 cyc-CT	Negative	-	Remission
24	57/F	36 months	Low	3 cyc-CT+RT	Negative	-	Remission
25	32/M	25 months	High	8 cyc-CT	Negative	-	Remission
26	46/M	49 months	High	8 cyc-CT	Negative	-	Remission
27	22/M	30 months	High	2 cyc-CT	Negative	-	Remission
28	62/F	24 months	High	5 cyc-CT	Negative	-	Relapse
29	72/M	24 months	Low	4 cyc-CT	Negative	-	Remission
30	47/M	24 months	Low	2 cyc-CT	Negative	-	Remission
31	35/M	24 months	Low	3 cyc-CT	Negative	-	Remission
32	45/F	24 months	Low	3 cyc-CT+RT	Negative	-	Remission
33	50/M	49 months	Low	8 cyc-CT	Negative	-	Remission
34	47/F	30 months	Low	3 cyc-CT	Negative	-	Remission
35	40/M	24 months	Low	4 cyc-CT	Negative	-	Remission
36	52/M	24 months	Low	4 cyc-CT	Negative	-	Remission
37	63/M	24 months	Low	4 cyc-CT	Positive	15.0	Stable
38	33/F	24 months	Low	8 cyc-CT	Negative	-	Remission
39	27/F	24 months	High	5 cyc-CT	Positive	2.5	Remission
40	50/F	30 months	High	8 cyc-CT	Positive	10.8	Exitus
41	30/M	40 months	High	8 cyc-CT	Negative	-	Relapse
42	62/F	48 months	Low	8 cyc-CT	Negative	-	Remission
43	55/M	25 months	High	4 cyc-CT	Negative	-	Remission
44	41/M	25 months	Low	4 cyc-CT	Negative	-	Remission
45	20/M	24 months	Low	4 cyc-CT	Negative	-	Remission
46	44/F	24 months	Low	4 cyc-CT	Negative	-	Remission
47	48/F	25 months	Low	6 cyc-CT+RT	Negative	-	Remission

PRS: Pre-treatment clinical prognostic risk scoring, LOW: Low risk group, HIGH: High risk group, CYC: Cycles, CT: Chemotherapy, F: Female, M: Male, PET/CT: Positron emission tomography/computed tomography

(5 HD; 2 NHL) had favorable/low-risk PRS. In this group, PET/CT was positive in 14 (73.7%) patients versus negative in only 5 (26.3%) patients (Figures 2, 3). Although both PRS and PET/CT imaging had statistically significant capability in terms of estimating remission status of the patients, the statistical power of PET/CT imaging was much stroger than that of PRS (p<0.001 versus p =0.046).

Post-treatment PET/CT imaging demonstrated 74% sensitivity, 92% specificity, 94% NPV, and 67% PPV and 88% accuracy in predicting remission status, whereas for PRS the same values were 63% and 62%, 88%, 27%, and 62%, respectively (p<0.001) (Tablo 5).

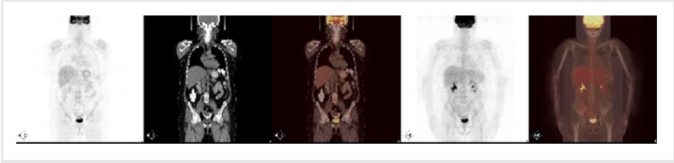

Figure 2. A patient with a diagnosis of DLBCL with a high-risk pre-treatment clinical scoring. The post-treatment PET/CT study done after 5 cycles of R-CHOP regime, revealed no residual disease. However, several trecurrences were diagnosed during 24 months follow-up period

PET/CT: Positron emission tomography/computed tomography, DLBCL: Diffuse large B-cell lymphoma

Kaplan-Meier survival analysis demonstrated a significant difference for assesment of PFS between PET positive and PET negative patients. (log-rank =2.1 p<0.05), while there was no significant difference between favorable prognostic/low-risk and unfavorable prognostic/high-risk groups for PRS (Figure 4).

There was a compatibility between PET result and remission (kappa =0.62), while no compatibility was available between PRS and remission (kappa =0.17).

On the Cox regression analysis, PET results and disease type were the most significant indices affecting final remission status. When the PET was negative, the remission more likely occurred (p<0.001). The patients with positive PET results have four times more risk to stay in non-remission status. There was also 2.3 fold less remission in the group with NHL comparing to HD group (p<0.05). Those patients with local residual disease on post-treatment PET studies had a more likelihood of staying in remission comparing to those with multifocal lymphatic and/or organ involvement (71% versus 29%; p<0.05).

Table 3. Relationships between post-treatment PET results and pre-treatment risk scoring

Hodgkin lymphoma	PET negative	PET positive	SUV_{max} (mean)
Fvr prog (n=27)	22 (81.5%)	5 (18.5%)	11.5
Unfvr prog (n=29)	21 (72.4%)	8 (27.6%)	7.4
Non-Hodgkin lymphoma			
Low-risk (n=32)	30 (93.7%)	2 (6.3%)	13.1
High-risk (n=15)	9 (60.0%)	6 (40.0%)	8.0
Overall			
Fvr prog/low-risk (n=59)	52 (88.1%)	7 (11.9%)	11.9
Unfvr prog /high-risk (n=44)	30 (68.2%)	14 (31.8%)	7.6
Total (n=103)	82	21	

Fvr prog: Favorable prognostic, Unfvr prog: Unfavorable prognostic, PET: Positron emission tomography

Table 4. Remission status related to post-treatment PET results and pre-treatment PRS

Hodgkin lymphoma	Fvr prog/low-risk	Unfvr prog/high-risk	PET positive	PET negative
Remission (n=47)	22 (46.8%)	25 (53.2%)	5 (10.6%)	42 (89.4%)
Non-remission (n=9)	5 (55.6%)	4 (44.4%)	8 (88.9%)	1 (11.1%)
Non-Hodgkin lymphoma				
Remission (n=37)	30 (81.1%)	7 (18.9%)	2 (5.4%)	35 (94.6%)
Non-remission (n=10)	2 (20.0%)	8 (80.0%)	6 (60.0%)	4 (40.0%)
Overall				
Remission (n=84)	52 (61.9%)	32 (38.1%)	7 (8.3%)	77 (91.7%)
Non-remission (n=19)	7 (36.8%)	12 (63.2%)	14 (73.7%)	5 (26.3%)
Total (n=103)	59	44	21	82

Fvr prog: Favorable prognostic, Unfvr prog: Unfavorable prognostic, PET: Positron emission tomography

Discussion

There are numerous reports available in the literature recommending the routine use of FDG-PET imaging to assess the post-therapy response in patients with HD and NHL (9-15). However, there are a considerable variation between the studies in terms of diagnostic accuracy and predictive values most probably due to heterogeneous population studied, difference of treatment protocols, and difference of PET timing etc.

Mid-treatment (interim) FDG-PET/CT scanning performed after 2-4 cycles of chemotherapy appears to have prognostic significance and may have a potential for earlier identification of chemoresistant disease in lymphomas, prior to treatment completion, leading to facilitate an individualized risk-adapted strategy. However, the importance of PET/CT at the end of the first line treatment continues (16-18).

In this retrospective study including a patient population referred from a single clinic, a new generation of hybrid PET/CT scanner was used. We found that post-treatment FDG imaging had 74% sensitivity, 92% specifity, 88% accuracy, 67% PPV and 94% NPV in predicting of long-term remission. These values were significantly better than those of obtained with the pre-treatment PRS, which were 63%, 62%, 62%, 27% and 88%, respectively (Table 5).

Despite PET's superiority comparing to PRS systems, our study revealed that the FDG-PET/CT was not excellent imaging modality for predicting disease outcome. There were 5 patients with HD and 2 patients with NHL who were were sustained in remission status at the end of follow-up period, despite positive PET results (false-postive rate =33%). This finding was most probably related to inflammatory changes occurring secondary to chemotherapy. Additionally, a sensitive reading of PET images might lead to false-positive results. We used mediastinal blood pool activity as the threshold for the lymph node uptake to define the post-therapeutical PET study as positive. There has been a great effort ongoing to find out what will be the best threshold activity, i.e mediastinum, liver or nearby background to determine positivity on the post therapeutic FDG-PET studies (19). In addition, there are reports available based on a SUVmax threshold or SUVmax difference between the initial study and post-therapeutic studies (20-22). Nevertheless, there has not been defined a well validated interpretation criteria to provide an excellent accuracy for post-treatment FDG-PET studies so far. Nevertheless, there has not been defined a well validated interpretation criteria to provide an excellent accuracy for post-treatment FDG-PET studies so far. Therefore, any ambiguous finding in FDG-PET/CT report that is not supported with clinical-laboratory data or other imaging modalities should be confirmed with biopsy if needed. Particularly, the new lesions that are not available in the pre-treatment PET/CT scan must be evaluated in caution.

On the other hand, negative post-treatment PET/CT scan could not completely predict long term remission, although it had higher NPV. In our group, there were 5 out of 82 (6%) patients

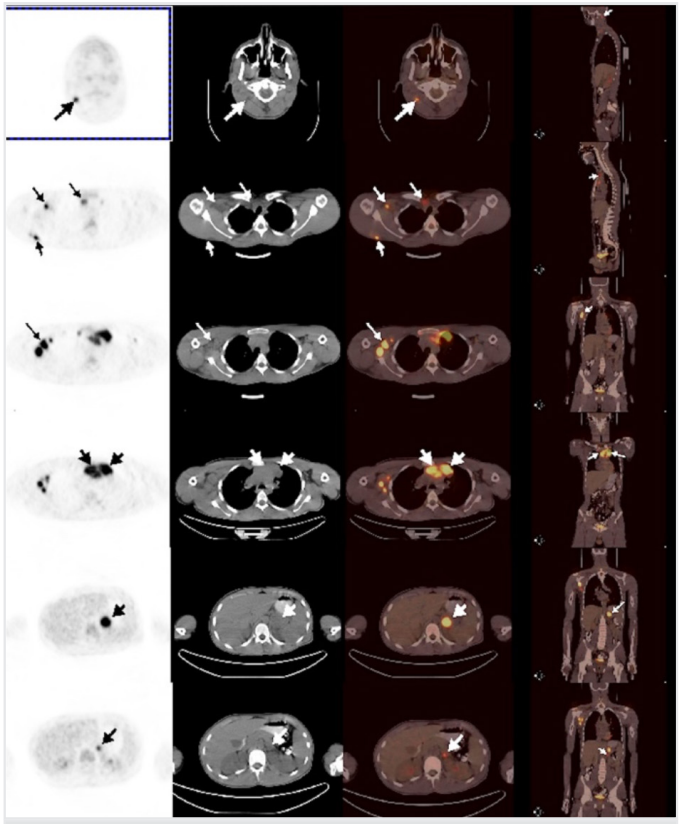

Figure 3. A 16-year-old patient with nodular sclerosing type HD with favorable prognostic factors on pre-treatment evaluation. Following 4 cycles of ABVD regime, the post-treatment PET/CT study demonstrated residive disease in multiple supradiaphragmatic and infradiaphragmatic lymphatic regions as well as in the left adrenal gland and in soft tissue of the left arm as shown on the selected slices above. Despite of further agressive chemotherapy applications, a remission status could not be managed and the patient died after 31 months

PET/CT: Positron emission tomography/computed tomography, HD: Hodgkin disease, ABVD: Adriamycin, bleomycin, vinblastine, dacarbazine

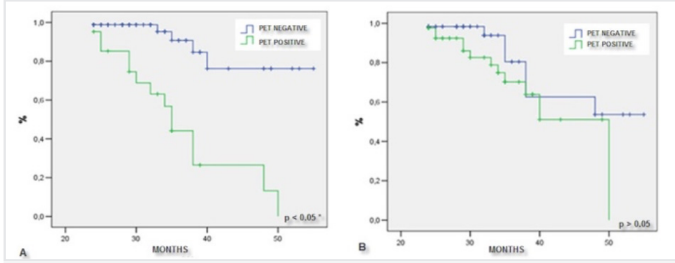

Figure 4. Kaplan-Meier plots of progression free survival in all patients: A) in relation to the post-treatment PET result; B) in relation to pre-treatment prognostic risc scoring

PET: Positron emission tomography

Table 5. Efficiacy of the post-treatment PET and pre-treatment prognostic risk scoring in assessment of remission status

	Sensitivity	Specifity	Accuracy	PPV	NPV	TP	TN	FP	FN
Hodgkin lymphoma									
PET	88.8%	89.3%	89%	61.5%	97.6%	8	42	5	1
PRS	44.4%	46.8%	46.4%	13.7%	81.4%	4	22	25	5
Non-Hodgkin lymphoma									
PET	60%	94.5%	87.2%	75%	89.7%	6	35	2	4
PRS	80%	81%	80.8%	53.3%	93.7%	8	30	7	2
Overall									
PET	73.6%	91.6%	88.0%	66.6%	94.0%	14	77	7	5
PRS	63.0%	62.0%	62.0%	27.0%	88.0%	12	52	32	7

PRS: Prognostic risk scoring, PPV: Positive predictive value, NPV: Negative predictive value, TP: True positive, TN: True negative, FP: False positive, FN: False negative, PET: Positron emission tomography

(1 HD, 4 NHL) with false-negative PET results, despitesensitive reading. This was most probably due to insufficient spatial resolution of PET imaging technology to detect microscopic residual disease. Therefore, we suggest that the patients in high risk group should be monitored closely even if their post-treatment PET/CT scans are negative.

There was a clear relationship between the disease extention on post-treatment PET scans and relaps rate in our study. The frequency of disease recurrence was significantly higher in the patients with involvement of multiple lymphatic stations or extranodal sites comparing to those with single lymphatic station involvement (Table 5).

Our results are generally compatible with the literature and the values of NPV and PPV are within the limits in published meta-analysis in this field (11,22). There is relatively few studies comparing the prognostic values between post-treatment PET and clinical risk scoring system. In Haioun study, including 90 patients with aggressive NHL, they performed PET studies before treatment, after 2 cycles of chemotherapy and at the end of treatment as well, and prospectively evaluated the predictive value of PET in the prediction of prognosis (23). In this study, 83% of post-treatment PET negative patients, and 58% of post-treatment PET positive patients stayed in complete remission. Two-year PFS was 90% in post-treatment PET negative group and 58% in post-treatment PET positive group. Accordingly, post-treatment PET was an independent prognostic marker in estimating PFS regardless the chemotherapy protocol.

Study Limitations

There are differences in treatment approaches and management of HD and NHL. The main limitation of our study was that it was not performed with a more standard patient group consisting of HD or high-grade NHL. Therefore, we presented both the general data and the data of both groups separately. In addition, the number of patients in both groups was relatively limited and the study was designed retrospectively.

Conclusion

In conclusion, our study confirmed that FDG-PET/CT scanning at the completion of the first-line therapy estimated the disease outcome of the patients with HD and aggressive NHL, better than population based pretreatment clinical risk scoring systems. However, particularly PPV of the end-treatment FDG-PET/CT imaging was still far away from the desired levels as to estimating disease recurrence, due to a relatively high false-positive rate. Nevertheless, our study demonstrated that the patients with persistent FDG uptake in multinodal lymphatic stations and in extranodal sites on the post-therapy PET/CT scanning were under more risk for recurrence. On the other hand, despite higher NPV, there might be some false-negative results with the post-treatment PET/CT imaging for estimation of permanent remission, most probably due to microscopic residual disease available at the end of therapy.

Ethics

Ethics Committee Approval: Our study project was approved by the İstanbul University-Cerrahpaşa Clinical Research Ethics Committee (16.09.2008/27584).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: E.B.E., Ş.G., K.S., Design: E.B.E., Ş.G., K.S., Data Collection or Processing: E.B.E., Ş.G., K.S., Analysis or Interpretation: E.B.E., Ş.G., K.S., Literature Search: E.B.E., Ş.G., K.S., Writing: E.B.E., Ş.G., K.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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Original Article

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Bezmialem Science 2022;10(3):274-80

The Validation and Reliability Study of Turkish Versions of Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder and Body Image Disturbance Questionnaire

Yale-Brown Obsesif Kompulsif Ölçeğinin Beden Dismorfik Bozukluğu Modifikasyonu ve Beden Görünüşü Rahatsızlığı Testinin Türkçe Versiyonlarının Güvenirlik ve Geçerlik Çalışması

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ABSTRACT

Objective: Body dysmorphic disorder (BDD) is a relatively common disorder and accepted as one of the obsessive-compulsive spectrum disorders group. No tests for BDD have been translated into Turkish yet. This study aimed to perform validity and reliability tests on the Turkish version of the Yale-Brown Obsessive-Compulsive scale Modified for BDD (T-YBOCS-BDD) and the Body Image Disturbance Questionnaire (T-BIDQ).

Methods: The patients who were admitted to the clinics of the dentistry faculty with the aesthetic problems were selected as the study group (n=80) and the control group was designed with the patients with non-aesthetic problems (n=81). The tests were administered to the patients within one week with the test and re-test method. Factor analysis was performed, and the statistical significance was accepted as p<0.05.

Results: In the evaluation of reliability, Cronbach's alpha was 0.808 for the T-YBOCS-BDD and it was 0.780 for the T-BIDQ. The factor analysis scores were 0.705 and 0.736, whereas and the values

ÖZ

Amaç: Beden dismorfik bozukluk (BDB) nispeten yaygındır ve obsesif kompulsif spektrum bozuklukları gruplarından biri olarak kabul edilmektedir. Literatürde henüz Türkçe'ye çevrilmiş BDB testi bulunmamaktadır. Bu çalışmada, Yale-Brown Obsesif Kompulsif ölçeği BDB modifikasyonunun (YBOKB-BDB) ve beden görünüşü rahatsızlığı testinin (BGRT) Türkçe versiyonları üzerinde geçerlik ve güvenirlik testleri gerçekleştirilmesi amaçlanmıştır.

Yöntemler: Diş hekimliği fakültesi kliniklerine estetik problemler ile başvuran hastalar çalışma grubu (n=80) olarak seçilmiş olup kontrol grubu ise estetik problemi olmayan hastalar (n=81) arasından seçilmiştir. Testler, bir hafta ara ile tekrarlanarak hastalara uygulanmıştır. Veriler faktör analizi ile değerlendirilmiş olup istatistiksel anlamlılık p<0,05 olarak kabul edilmiştir.

Bulgular: Türkçeye çevrilmiş YBOKB-BDB ölçeği ve BGRT için skorların sonuçlarının güvenirlik yönünden değerlendirmesinde Cronbach alfa değeri sırasıyla; 0,808 ve 0,780 olarak bulunmuştur. Faktör analizi puanları 0,705 ve 0,736 iken, Bartlett'in küresellik testi sırasıyla; 677.296 (df=66, p<0,001) ve 336.069 (df=21,

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of the Bartlett's test of sphericity were 677,296 (df=66, p<0.001) and 336,069 (df=21, p<0.001), respectively. Total mean scores of T-YBOCS-BDD revealed statistically significant results (p=0.006).

Conclusion: The tests resulted in high validity and reliability, therefore the results of this study highly recommended clinicians to perform these tests in the Turkish language-speaking countries.

Keywords: Body dysmorphic disorder, body image, obsession, reliability, validity

p<0,001) olarak saptanmıştır. T-YBOKB-BDB ölçeğinin ortalama puanları istatistiksel olarak anlamlı sonuçlar ortaya çıkmıştır (p=0,006).

Sonuç: Testler yüksek geçerlik ve güvenirlik ile sonuçlanmıştır. Bu nedenle bu çalışmanın sonuçlarına göre klinisyenlerin Türkçe konuşulan ülkelerde bu testleri yapmaları şiddetle önerilmektedir.

Anahtar Sözcükler: Vücut dismorfik bozukluğu, beden imajı, obsesyon, güvenilirlik, geçerlilik

Introduction

The appearance of most individuals would not be satisfactory according to them whereas some of them could be worried about a slight or imaginary flaw about how they look alike. These people might have physically & psychiatric problems simultaneously. Body dysmorphic disorder (BDD) is characterized with an excessive and persistent preoccupation with perceived defects or flaws in the appearance, which are unnoticeable to others, and associated repetitive behaviors (1). This disorder is a severe illness and relatively common and these patients are generally admitted to both psychiatric and non-psychiatric physicians and they have significant unrest or impaired functionality (2). BDD is currently accepted as a disorder of the obsessive-compulsive spectrum disorders (OCD) according to DSM-5 (3). Moreover, BDD is also engaged with eating, social anxiety and mood disorders (4).

Patients with BDD are often admitted to non-psychiatric physicians, especially aesthetic surgeons, to eliminate the perceived physical defects even though they are expected to consult with psychiatrists (2). Dealing with a mild/imaginary physical defect that is leading them to serious clinical stress or functionality loss in social, work and private life is considered as the major problem in BDD. Moreover, the worries about more than one body regions are reported in 68-98% of patients with BDD and the suicidality rates are significantly higher in them (5).

The Yale-Brown Obsessive-Compulsive scale Modified for BDD (YBOCS-BDD) is a 12-item, semi-structured, rater-administered measure that evaluates BDD severity in one-week-time (6). This likert-scale (0-4) aims to measure the severity of BDD in different factors such as; time & activity stress; defect; resistance & control; thoughts, interference, and avoidance. It was adapted from the Y-BOCS, which was the most widely used measure of OCD severity (7). Body Image Disorder Questionnaire (BIDQ) aims to diagnose the BDD with specific questions and includes a likert-scaled items (1-5) that are associated to resultant impairment in social, occupational, or other important areas of functioning, appearance-related concerns, associated experiences of emotional distress, interference with social life or with school, job, or role functioning, consequential behavioral avoidance and corresponding mental preoccupation (8). The evidence was provided in the validity and reliability of the BIDQ in a healthy sample and the BIDQ was reported as accurate questionnaire to evaluate the impairment in functioning and appearance-related anxiety (9).

The study aims to perform validity and reliability tests on the Turkish version of the YBOCS-BDD (T-YBOCS-BDD) and BIDQ (T-BIDQ), which are the most preferred on evaluation and measuring the severity of BDD, and to make these versions possible for use for the clinicians and academicians who study in countries where the Turkish language is spoken.

Methods

Ethical Statement

The study was approved by the research Ethics Committee of Bezmialem Vakıf University (22.10.2019 & 20/375). Written informed consent was obtained from all participants after the procedures were fully explained and before their inclusion in the study, anonymity was assured.

Turkish Translation

The original versions of BIDQ and YBOCS-BDD were translated from English into Turkish by two authors of this study who were fluent in English. Both translations were evaluated by a multidisciplinary committee composed of an orthodontist, an oral maxillofacial surgeon and two psychiatrists. During the translation phase, semantic, idiomatic, conceptual and cultural equivalences were provided. Translation errors were checked for all items and they were evaluated for content validity. Then, the back-translation into English by two independent translators. The back-translated versions of YBOCS-BDD and BIDQ were checked and compared with the original instrument by the same committee to perform the corrections for possible errors made during back-translation. A pilot study was carried out with 35 patients. The outcomes were satisfactory, therefore, the final versions of both tests were decided.

Subject Selection and Administration Methods

Power analysis in this study showed that 76 patients were needed in each group. Thus, 161 patients who were aged between 18 and 65 years were included in the study. Exclusion criteria were the inability to understand the interview questions, having severe physical deformities resulting from tumors or other conditions, and being previously diagnosed as having BDD or another psychiatric disease. The patients in study groups were obtained among the individuals who were admitted to the university hospital, faculty of dentistry with the complaint of dental anterior region aesthetics (n=80). The patients who were admitted to the same clinic without any esthetic considerations (such as pain, wisdom teeth, bleeding in the mouth, etc.) were selected

for the control group (n=81). T-BIDQ and T-YBOCS-BDD were performed to all patients with the face-to-face interview method. Within the first week, the scale and questionnaire were re-administered to individuals for reliability study (test-retest) because YBOCS-BDD was used to measure the BDD status within one week. Retesting of T-BIDQ and T-YBOCS-BDD was also performed.

In this study, the validity and reliability of the T-BIDQ and T-YBOCS-BDDwere compared in both control and study groups. The content validity analysis was applied to show the extent to each item in the scale and its contribution to the measurement of the phenomenon together with other items.

Statistical Analysis

The internal consistency of the scale was evaluated using the Cronbach's alpha coefficient, the additivity was evaluated using the Tukey additivity test, the sufficiency of the sample size was evaluated with the Kaiser-Meyer-Olkin test, factorability was evaluated with the Bartlett test, and the determination of the factor structures was through the Principal Component Factor Analysis. The Varimax method was used as the factor rotation method. The reliability of the scale was determined using the test-retest method, intragroup correlation coefficients, and the t-test for the matched subjects. The comparisons between groups with normal distribution were performed using for Mann-Whitney U test. The relationships between numerical data were analyzed with the Pearson or Spearman correlation analysis tests. A $p<0.05$ was considered as statistically significant. Distribution of the variable data was evaluated using the Shapiro-Wilk normality test and the Q-Q graphs. The threshold of statistical significance was set at $p<0.05$. Analyzes were conducted using TURCOSA (Turcosa Analytics Ltd Co, Turkey, www.turcosa.com.tr) statistical software.

Results

Validity

Content Validity

Content validity analysis of T-BIDQ and T-YBOCS-BDD was performed and conformity contents were arranged by adhering to the original version.

It was found that the total score of T-BIDQ did not differ between the patient and the control groups according to the median value. (p=0.059). The median value of the patient group was 10.00 and the 25th percentile value was 8.75 and the 75th percentile value was 12.00. The median of the control group was 10.00 and 25th percentile value was 10.00 and the 75th percentile value was -12.00. There was a difference between the patient and control groups according to the median T-YBOCS-BDD total score (p=0.006). The median of the patient group was 8.00 and the 25th percentile value was 3.50 and 75th percentile value was -15.00. The median of the patient group was 11.50 and the 25th percentile value was 6.25 and the 75th percentile value was -18.00 (Table 1).

The Results of Factor Analysis for T-BIDQ

The scores obtained from the sub-areas of the BIDQ were analyzed with the Principal Componet Factor Analysis. According to the analysis results, two factors which corresponded to 63.037% of the total variance and having an eigenvalue above 1.00 were determined. The cumulative explanation rates of the total variance were explained by the first component for 44.271%, and the second component for 63.037%. While the eigenvalue was 3,099 for the first component, this value was found to be 1,314 for the second component. Factor loadings for scale questions in each sub-area of these factors are included in Table 2. Varimax rotation was used to present results on factoring items. According to the results of the axis rotation analysis, the Factor 1 contained items 1, 2 and 7, while Factor 2 included items 3, 4, 5 and 6. The items were collected in 2 factors. The factor analysis score was 0.736, and Bartlett's test of sphericity was measured as 336,069 (df=21, $p<0.001$) for BIDQ in the KMO test. A sufficient significant correlation to perform a factor analysis for the assessment of the construct validity was demonstrated and shown in Table 2. Factor loadings for all items were noted above 0.40.

The results of factor analysis for T-YBOCS-BDD Scale

The scores obtained from the sub-areas of the T-YBOCS-BDD were analyzed by using the Principal Component Factor Analysis. According to the results of the analysis, four factors which corresponded to 67.816% of the total variance and had an Eigenvalue above 1.00 were determined. The cumulative explanation rates of the total variance were explained by the first component for 34.153% the second component for 47.973%, the third component for 58.419%, and the fourth component for 67.816%. While the Eigenvalue was 4,098 for the first component, this value was 1,658 for the second component, 1.254 for the third component, and 1,128 for the fourth component. Factor loads for scale questions in each sub-area of these factors are included in Table 3. Varimax rotation was used to present results on factoring items. According to the results of the rotation analysis, the first factor had items 3, 4 and 11, while the second factor had items 2, 7, and 12, the third factors had items 5,6,8 and 9, and the fourth factors had items 1 and 10. Articles were included. The items were collected in 4 factors. The factor analysis score was0.705 and Bartlett's test of sphericity was measured as 677.296 (df=66, $p<0.001$) for T-YBOCS-BDD in the KMO test. A sufficient significant correlation to perform a factor analysis for the assessment of the construct validity was demonstrated and shown in Table 3. Factor loadings for all items were noted above 0.40.

Table 1. Total mean scores of T-BIDQ and T-YBOCS-BDD

Tests (total scale)	Group: Control median (25p-75p)	Patients median (25p-75p)	p
T-BIDQ	10.00 (10.00-12.0)	10.00 (8.75-12.00)	**0.059**
T-YBOCS-BDD	11.50 (6.25-18.00)	8.00 (3.50-15.00)	**0.006**

Reliability

Internal Consistency Analysis- Cronbach's Alpha

A proof of construct validity in scale studies is the high internal consistency coefficient (Cronbach's alpha) of the scale. After the factor analysis results of this study, the factored items were found to have internal consistency coefficient as 0.780 for the T-BIDQ and 0.808 for the T-YBOCS-BDD, providing the evidence for the construct validity. The scores of ICC analysis for both tests are shown in Tables 4, 5.

The internal consistency coefficients (Cronbach's alpha) of items 1, 2 and 3 for the sub-factor groups formed for the T-BIDQ were determined as 0.735 and 0.730.

Discussion

The diagnosis of BDD could be challenging in clinical settings even though the incidence and severity of BDD were relatively common. Generally, patients with BDD consult dermatologists, dentists, oral & maxillofacial surgeons and more often plastic surgeons, rather than psychiatrists. For that, the determination of the prevalence of BDD in the psychiatric clinics is difficult and the aesthetic clinicians must be aware and have knowledge about this disease (10). In the literature, the prevalence of BDD in the general population is reported as 0.7-5.3% (11). Clinical studies have revealed higher rates such as, 8.8-12% in dermatology patients (12), 7% in cosmetic surgery patients (13), 14-42% in patients with atypical major depression (14), 11-13% in patients with social anxiety (15,16), 8-37% in patients with OCD (16), and 39% in patients with anorexia nervosa (17).

Moreover, the patients with aesthetic complaints are not only admitted to the plastic surgery and dermatology departments but also the dentistry faculty. Furthermore, they are usually admitted to almost all departments of the dentistry, but the maxillofacial

Table 2. Factor analysis results for T-BIDQ

Item	Mean	SD	Corrrected item-total correlation	Croncbach's alpha if item deleted	Factor loading
Factor 1 (concern)					
Q1	1.987	0.874	0.567	0.731	0.870
Q2	1.696	0.850	0.409	0.768	0.826
Q7	1.575	0.670	0.612	0.724	0.558
Factor 2 (defect)					
Q3	1.607	0.694	0.468	0.751	0.651
Q4	1.424	0.742	0.668	0.709	0.729
Q5	1.322	0.544	0.545	0.742	0.747
Q6	1.310	0.627	0.264	0.786	0.744

Table 3. Factor analysis results for T-YBOCS-BDD scale

Item	Mean	SD	Corrrected item-total correlation	Croncbach's alpha if item deleted	Factor loading
Factor 1 (time & activity distress)					
Q3	0.764	0.685	0.561	0.789	0.668
Q4	1.024	1.279	0.584	0.780	0.685
Q11	1.310	1.256	0.667	0.770	0.769
Factor 2 (time & insight)					
Q2	0.379	0.591	0.452	0.797	0.590
Q7	1.149	0.624	0.324	0.804	0.461
Q12	0.420	0.739	0.361	0.801	0.508
Factor 3 (resistance & control) **Q5**	0.925	1.087	0.508	0.788	0.619
Q6	0.341	0.798	0.516	0.790	0.559
Q8	1.546	1.014	0.384	0.800	0.468
Q9	0.695	1.593	0.506	0.797	0.595
Factor 4 (thoughts & interference/avoidance)					
Q1	1.229	0.584	0.397	0.800	0.702
Q10	1.310	0.895	0.379	0.800	0.492

surgery, orthodontics, prosthetic and restorative dentistry departments are the most preferred ones by patients with BDD.

In a study, Hepburn et al. (18) reported that patients with BDD who were admitted to the department of orthodontics revealed high requisition for the orthodontic treatment. Moreover, another study reported the rate of whitening and orthodontic treatment of those who had BDD was nine times higher (19). Therefore, the clinicians should keep in mind the situation of these patients and get knowledge about evaluating and managing the patients suspected from BDD (20).

Due to nature of the difficulties on detecting the patients with BDD, it is generally emphasized that the satisfaction of the treatment is negatively and adversely affected. Besides, the prevalence of BDD patients who are admitted to dental clinics still remains unknown. Because the rates of suicide attempts range from 3% to63% and the reported rates of suicidal ideation range from 17% to77%, high rates of suicidality have also been associated with BDD (5).

Table 4. Test-retest reliability and ICC between the T-BIDQ and 2 subscales (n=161)

Factors	Item	Croncbach's alpha	ICC	95 %CI
Factor 1 (concern)	**Q1**	0.735	0.735	(0.655-0.800)
	Q2			
	Q7			
Factor 2 (defect)	**Q3**	0.730	0.725	(0.648-0.789)
	Q4			
	Q5			
	Q6			

ICC: Intraclass correlation coefficient,

Table 5. Test-retest reliability and ICC between the T-YBOCS-BDD and 4 subscales (n=161)

Factors	Item	Croncbach's alpha	ICC	95% CI
Factor 1 (time & activity distress)	**Q3**	0.763	0.733	(0.652-0.797)
	Q4			
	Q11			
Factor 2 (time & insight)	**Q2**	0.648	0.533	(0.393-0.645)
	Q7			
	Q12			
Factor 3 (resistance & control)	**Q5**	0.681	0.681	(0.593-0.755)
	Q6			
	Q8			
	Q9			
Factor 4 (thoughts & interference/ avoidance)	**Q1**	0.492	0.460	(0.263-0.604)
	Q10			

ICC: Intraclass Correlation Coefficient, CI: Confidence interval,

The YBOCS-BDD and BIDQ-S (a modification for scoliosis disease) were translated into different languages such as Brazilian, Portuguese, Persian, Greek, Spanish, German and Chinese and these studies revealed successful outcomes (21-27). To our knowledge, the YBOCS-BDD was translated more times than the BIDQ. BIDQ was able to be found only in English, however, the BIDQ-S was translated into German and Chinese.

When it came to the evaluation of the reliability, Brito et al. (25) reported a YBOCS-BDD translation in Brazilian Portuguese. It was carried out with 93 patients who underwent rhinoplasty operation and the outcomes were highly satisfactory. Also, the test-retest method was applied for reliability at one-week intervals. In their study, they performed statistical analysis using correlation coefficient and ICC as well as the same statistical analysis were performed in the present study (25). On the other hand, Wetterkamp et al. (27) performed the German translated version of BIDQ-S in 259 patients with idiopathic scoliosis and revealed successful outcomes. In our study, the validity and reliability tests on the Turkish version of the BIDQ were performed with a translated version of the YBOCS-BDD simultaneously, and the results were also promising (Tables 1-5).

While evaluating the validity, in the original validation of the YBOCS-BDD study by Phillips et al. (28) three factors were accounted for 60% of the total variance: Factor-1 as core symptoms (time, interference and distress due to thoughts, interference due to compulsions, insight, and avoidance), Factor-2 as compulsions and Factor-3 as resistance and control of thoughts. The Turkish translated version of YBOCS-BDD and BIDQ demonstrated successful outcomes in which both tests revealed a sufficient significant correlation to perform a factor analysis, allowing the evaluation of the construct validity. Significant correlations could be established between T-YBOCS-BDD and global question as indicated by total and subscale scores of the corrected item-total correlations. These outcomes were indicative of a fair to excellent convergent validity. Factor loadings were noted for all items as above 0.60.

Four factors were extracted from the factor analysis and were accountable for a total of 67.816% of the variance.

On the other hand, the same factor analysis procedures were also performed for the T-BIDQ. Similar to the present study, Collison et al. (29) reported that the KMO test was excellent (i.e.,0.95), and Bartlett's test was significant ($p<0.001$), indicating suitability for factor analysis. According to their results, the factor loadings ranged from 0.53 to 0.87 whereas the parallel analysis identified a single latent component accounting for 67.14% of the variance. In the present study, factor loadings were noted as above 0.40 for all items. Two factors were extracted from the factor analysis and were accountable for a total of 63.037% of the variance. Significant correlations were shown between T-BIDQ and global question as indicated by total and subscale scores of the corrected item-total correlations. These outcomes were also indicative

of a fair to excellent convergent validity and the outcomes for the validity and reliability (Cronbach's alpha, ICC and 95% confidence interval) for the translated versions of YBOCS-BDD and BIDQ were reported similar to the literature (21-27).

There are no empirically derived cut off scores for YBOCS-BDD, however, a score of 20 or above generally indicates moderate BDD (30). Moreover, a cut off score for T-BIDQ was found as 11 in our study, but only one patient scored more than 20 in T-YBOCS-BDD and 11 in T-BIDQ, so as one of the limitations of the study, the ROC-curve for both tests would not be given despite the satisfactory outcomes. Therefore, it is highly recommended that higher numbers of patients should be included in further studies, even though numbers of the groups will be adequate in each group according to the power analysis.

Study Limitations

As one of the limitations of the study, divergent validity, which was one of the methods to evaluate the factorability of the scale, was not evaluated.

Conclusion

In conclusion, the T-YBOCS-BDD and T-BIDQ resulted in high validity and reliability. Therefore, the clinicians and academicians are encouraged to perform the translated forms of these scales and questionnaires in the population who speaks the Turkish language.

It is crucial to inform the patients preoperatively in general dentistry, especially during the aesthetical operations not to perform unsatisfactory treatments due to the nature of the patients with BDD who have perceptional problems on their appearance.

Further studies in dentistry field are recommended to be performed to assess the prevalence of BDD and the clinicians should be encouraged for performing these tests in dentistry for determining the real epidemiology of BDD.

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Ethics

Ethics Committee Approval: This study was approved by the Local Ethics Committee (22.10.2019/20/375).

Informed Consent: Written informed consent was obtained from all participants after the procedures were fully explained and before their inclusion in the study, anonymity was assured.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: T.Y., E.D.Ş., Ç.D.Ş., Design: T.Y., E.D.Ş., Ç.D.Ş., Data Collection or Processing: T.Y., E.D.Ş., M.K., G.E.Z., Analysis or Interpretation: T.Y., E.D.Ş., M.K., G.E.Z., Ç.D.Ş., Literature Search: T.Y., E.D.Ş., M.K., G.E.Z., Ç.D.Ş., Writing: T.Y., G.E.Z., M.K.

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Original Article

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The Importance of Osmolarity in the Prognosis Prediction of ST-elevation and Depression in aVR Derivation of Patients with Acute Coronary Syndrome

Akut Koroner Sendrom Hastalarının aVR Derivasyonunda ST-elevasyonu ve Depresyonunun Prognoz Öngörüsünde Osmolaritenin Önemi

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ABSTRACT

Objective: ST-elevation and depression in augmented voltage right (aVR) are associated with high mortality and prolonged coronary artery disease in patients with the acute coronary syndrome. It was aimed to compare the patients in terms of cardiac troponin, three-vessel disease, serum osmolarity and mortality.

Methods: The study was performed through retrospective scanning of the files of 372 (162 females, mean age 64±10 years) patients who were admitted to the emergency department due to chest pain between January 2014 and December 2016 and who were admitted to the cardiology clinic with the diagnosis of the acute coronary syndrome. Patients with ST-elevation in aVR were included in Group I and patients with ST-depression in aVR were included in Group II.

Results: Osmolarity was 295.8±16 in Group I and 291.7±8.1 in Group II. Troponin values in Group I was higher than Group II (p=0.002). The Gensini score was 40±2.7 in Group I and 28.6±2.3 in Group II (p=0.001). In Group I, unstable angina was found in 32 (18.1%) patient, ST-elevated myocardial infarction (MI) in 135 (76.3%) and non-ST-elevated MI in 10 (5.6%), whereas these numbers and percentages were 62 (31.8%), 106 (54.4%) and 27 (13.8%) in Group II, respectively (p=0.001). The three-

ÖZ

Amaç: Augmented voltage right'daki (aVR) ST-elevasyonu ve depresyonu akut koroner sendrom hastalarında yüksek mortalite ve uzamış koroner arter hastalığıyla ilişkilidir. Hastaların, kardiyak troponin, üç damar hastalığı, serum osmolarite ve mortalite açısından karşılaştırılması amaçlanmıştır.

Yöntemler: Çalışmaya Ocak 2014-Aralık 2016 tarihleri arasında acil servise göğüs ağrısı nedeniyle başvuran, akut koroner sendrom tanısıyla kardiyoloji kliniğine yatırılan, 372 (162 kadın, yaş ortalaması 64±10 yıl) hastanın dosyası retrospektif olarak taranarak dahil edildi. aVR'de ST-elevasyonu olan hastalar Grup 1 ve ST-depresyonu olan hastalar Grup 2 olarak ayrıldı. Hastaların prognozu, yaş, cinsiyet, lipid profili ve Gensini skoru, osmolarite ve mortalite açısından karşılaştırıldı.

Bulgular: Grup 1'de osmolarite 295,8±16, Grup 2'de 291,7±8,1 idi (p=0,003). Grup 1'in troponin değerleri Grup 2'den yüksekti. Gensini skoru Grup 1'de 40±2,7, Grup 2'de 28,6±2,3 idi (p=0,001). Grup 1'de unstabil angina 32 (%18,1), ST-elevasyonlu miyokard infarktüsü (MI) 135 (%76,3) ve non-ST-elevasyonlu MI 10 (%5,6) hastada görülürken; Grup 2'de sırasıyla; 62 (%31,8), 106 (%54,4) ve 27(138) hastada görüldü (p=0,001). Üç damar hastalığı Grup 1'de 56 (%31,6), Grup 2'de 29 (%14,9) hastada tespit edildi (p=0,001).

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vessel disease was found in 56 (31.6%) patients in Group I and 29 (14.9%) patients in Group II (p=0.001). The most common complication in both groups was ischemic heart failure. Mortality was observed in 36 (20.3%) patients in Group I and 14 (7.2%) in Group II. Osmolarity was lowest in unstable angina, highest in non-ST-elevation MI, and was also higher in three-vessel disease, men, and patients with mortality.

Conclusion: In patients with acute coronary syndrome, osmolarity may predict ST-elevation and depression in aVR, three-vessel disease, and mortality.

Keywords: Acute coronary syndrome, three-vessel disease, mortality, osmolarity

Her iki grupta en sık komplikasyon iskemik kalp yetmezliğiydi. Mortalite Grup 1'de 36 (%20,3) ve Grup 2'de 14 (%7,2) hastada görüldü. Osmolarite en düşük unstabil anginada, en yüksek non-ST-elevasyonlu MI'da tespit edildi ve ayrıca üç damar hastalığında, erkeklerde ve mortal seyreden hastalarda yüksek bulundu.

Sonuç: Akut koroner sendrom hastalarında osmolarite; aVR'de ST-elevasyonu ve depresyonu, üç damar hastalığı ve mortalite açısından öngörücü bir değer olabilir.

Anahtar Sözcükler: Akut koroner sendrom, üç damar hastalığı, mortalite, osmolarite

Introduction

In patients with acute coronary syndrome (ACS), early diagnosis and treatment planning are of great importance. Myocardial necrosis has been shown to develop after 30-min coronary artery occlusion in studies (1). Accordingly, mortality increases in every 30-min delay between the onset of symptoms and reperfusion therapy (2). Electrocardiography (ECG) is significant in determining the size of the myocardial area at risk and the severity of ischemia in these patients. In addition to diagnosis, ECG can provide precious information on the determination of coronary reperfusion therapy type, lesion localization, and prognosis in these patients. Despite the increasing prevalence of coronary artery disease (CAD), medical technologies, new developments in etiopathogenesis and treatment, ACS including ST-elevated and non-ST-elevated myocardial infarction (MI) has been remaining as the main cause of morbidity and mortality in the world (3).

How important is augmented voltage right (aVR) in electrocardiography? As is known, aVR provides specific information about the upper right part of the heart. If ST-segment elevation in V1 in ECG exceeds aVR, the proximal left anterior descending (LAD) occlusion is interpreted as the left main coronary artery (LMCA) occlusion, where ST-segment elevation in aVR exceeds V1 (4). It was found that 1 mm or more ST-segment elevation in aVR was associated with higher mortality in patients with acute "anterior and inferior" myocardial infarction. It was shown that ST-segment depression in lead aVR had higher mortality in patients with "anterior" MI (5). ST-segment depression in lead aVR in anterolateral acute MI has been stated to be useful in predicting larger infarct area and left ventricular dysfunction despite successful reperfusion (6). Also, except for myocardial infarctions, it has been associated with serious conditions such as ST-segment elevation in aVR, shock, cardiac tamponade in patients with Type A aortic dissection (7). Again, in ventricular tachycardia and supraventricular tachycardia studies, the long R wave at the beginning of the aVR lead confirmed the diagnosis in favor of ventricular tachycardia (8). aVR ST-segment elevation highlights atrioventricular re-entry tachycardia in differentiating the supraventricular tachycardia mechanism (9). PR depression seen in all other derivations with PR elevation in aVR suggests the diagnosis of pericarditis (10). Pulmonary embolism is associated with an increased risk of shock and death with ST elevation in aVR (11). One of the electrocardiographic changes encountered in cases of tricyclic antidepressant toxicity is the R wave >3 mm in aVR and an R/S ratio of >0.7 in aVR, all of which indicated that aVR has a high predictive value in terms of seizures and cardiac arrhythmias (12).

The specific and sensitive indicator of myocardial damage is cardiac troponins. Increasing cardiac troponin (cTn) level in ACS is important in terms of prognosis and treatment management. Therefore, the cTn level is frequently used in the differential diagnosis of ACS (13-16). In most patients with high-risk ACS, if myocardial necrosis is absent, these patients cannot be identified since serum troponins do not increase. Therefore, new cardiac biomarkers are needed to assist in providing a rapid and accurate diagnosis for ACS risk assessment in patients in whom markers showing myocardial cell damage are not elevated.

Apart from cardiac troponins, many studies may show marker properties. Serum osmolarity measurement is an easily calculated and non-invasive method. A normal value is 280-295 mOsm/kg H_2O, and this value is measured by an osmometer. Simple calculation is as follows "Osmolality (mOsm/kg H_2O)=2[Na^+]+Glucose/18+ blood urea nitrogen (BUN)/2.8" (17). The main components of osmolarity are; plasma glucose, BUN, and sodium (Na). Nutrition rich in Na, glucose, and protein forms the basis of atherosclerosis. These compounds cause metabolic activity resulting in increased heat in the body, then disrupt the coronary arteries. It is important to remove or limit the foods that increase the patient's osmolarity burden to protect the patient from CAD or to delay the development of the disease (18). Therefore, calculated osmolarity is an important indicator of CAD and mortality (19).

In the literature, we did not find studies of serum osmolarity levels with ST-elevation and depression in AVR. Therefore, we aimed to show the association of ACS subtypes with serum osmolarity level, three vascular diseases, morbidity, and mortality.

Method

Study Design and Population

The study was performed through scanning the clinical data and files of 372 (210 males, 162 females, mean age 64.25±10.81 years; range 39-87 years) patients who were admitted to the emergency department due to chest pain between January 2014 and December 2016, and who were admitted to the cardiology clinic with the diagnosis of the ACS.

Patients with normal ST segment in aVR, patients in whom blood glucose and lipid profile were not examined within the first 24 hours, patients in whom angiographies and echocardiography were not performed, patients with cerebrovascular disease, psychiatric diseases, chronic liver diseases, chronic inflammatory disease, malignancy or hematological diseases, and patients undergoing dialysis due to chronic renal failure were excluded.

The patients were divided into two groups as ST-elevation (Group I: 0.5mm and above elevation in aVR derivation) and ST-depression (Group II: 0.5mm and above depression in aVR derivation) in aVR derivation. These two groups were investigated in terms of age, gender, lipid profile, troponins, blood glucose, osmolarity, and Gensini score.

Patients with ACS were divided into three groups as high risk unstable, STEMI and NSTEMI. The acute STEMI was subdivided into inferior, posterior, anterior, lateral, diffuse anterior and high lateral myocardial infarction.

Three-vessel disease (TVD); was defined as stenosis of at least 50% and above in all of the LAD coronary artery, circumflex artery, and right coronary artery.

Complications following ACS are divided into six groups including ischemic heart failure, ventricular tachycardia, atrioventricular block, cardiac tamponade and effusion, acute pulmonary edema, and no complications.

Hemogram was measured using a Sysmex DI-60 CBC Analyzer (İstanbul, Turkey).

Biochemistry blood was analyzed with the Beckman Coulter Automated AU-680 (Beckman Coulter, Inc., Fullerton, CA, USA).

The demographic, clinical, and reference laboratory data of the patients who were admitted to the emergency department due to ACS were evaluated by reviewing the medical records of the hospital.

Cardiac biomarker analysis; cTn I values of patients were obtained using STAT Elecsys Cobas e-411 (Hitachi, Roche, USA) analyzers. Troponin levels were measured at the clinic where the patients were hospitalized at 0 hours, 6, and 12 hours at the time of admission to the emergency room. The reference range of troponin I was 0-0.05 ng/dL, and a value above this value was considered positive.

Acute coronary syndrome; patients who had chest pain and/or discomfort lasting at least 30 minutes and who were diagnosed as having STEMI with ECG according to the 2013 American College of Cardiology Foundation/American Heart Association guidelines were included in the study (20). UA/NSTEMI was defined according to the criteria of the 2014 American Heart Association/American College of Cardiology Guide for Management of NSTE-ACS Patients (20). Transthoracic echocardiography (TTE) was applied to all patients to determine whether there were motion abnormalities in the focal wall. In this study, Philips Epiq 7 Ultrasound Machine was used for TTE.

Angiographic analysis; all angiographies were evaluated by two experienced cardiologists blinded to the study. Inconsistencies were resolved in consensus.

Gensini score; is an important scale for coronary artery prevalence. The degree and severity of CAD were evaluated with the Gensini score (21).

Statistical Analysis

The study data were analyzed with SPSS v20.0 (SPSS Inc, Chicago, IL, USA) software package. Shapiro Wilk's test was used while investigating if the variables had a normal distribution. The Mann-Whitney U test and the Kruskal-Wallis H test were used to examine the differences between the groups as the variables did not have normal distribution. Friedman's Two-Way ANOVA was performed in the analysis of more than two dependent variables because they did not have normal distribution. In case of significant differences, variables that differed from each other were determined by using Multiple Comparison Tests. When analyzing the intergroup correlations of nominal variables, the chi-square analysis was performed. If the predicted values in the cells of 2X2 tables did not have enough volume, Fisher's Exact Test was used, and the Spearman's chi-square test was used with the help of Monte Carlo Simulation to analyze RxC tables. When interpreting the results, 0.05 was used as the level of significance, and P values below 0.05 were considered statistically significant.

Results

The mean Gensini score was 31.20±36.73 in all patientsand it was significantly higher in Group I (p=0.001). Triglyceride level was 140.39±91.65 mg/dL, high density lipoprotein 35.35±13.95 mg/dL, low density lipoprotein 106.52±47.01 mg/dL, low density lipoprotein 26.97±17.25 mg/dL, and blood glucose 139.27±69.01 mg/dL in all patients. No difference was found in terms of those markers between groups. However, cholesterol levels were found to be significantly higher in Group I (p=0.030). Osmolarity was measured as 293.38±13.46 mOsm/L and was higher in Group I (p=0.003). Among cardiac biomarkers of patients; cTn I level was 1.83±2.24 ng/dL, cTn II 5.15±7.21 ng/dL, and cTn III 12.24±17.78 ng/dL in all patients and their levels were statistically significantly higher in Group I. Osmolarity was higher, TVD was more, and prognosis was worse in patients with a Gensini score of more than 20 points (Table 1).

Table 1. Baseline characteristics of study patients

	All patients n=372 mean ± SD	**aVR (+) n=177** mean ± SD	**aVR(-) n=195** mean ± SD	p-value
Age, yr	64.40±10.68	64.25±10.81	64.61±10.51	0.745
Famale	162 (43.5%)	116 (51.8%)	46 (31.1%)	**0.001**
Male	210 (56.5%)	108 (48.2%)	102 (68.9%)	
TG, mg/dL	140.38±91.65	140.87±85.53	139.66±99.18	0.298
Cho, mg/dL	172.39±61.92	178.67±67.54	162.87±51.03	**0.030**
HDL, mg/dL	35.35±13.95	34.88±12.18	36.07±16.28	0.927
LDL, mg/dL	106.52±47.01	109.50±50.03	102.00±41.78	0.211
VLDL, mg/dL	26.98±17.25	8,93±0,86	8,24±1,03	**0.001**
Tn I, ng/dL	1.83±2.25	2.02±2.32	1.53±2.09	**0.002**
Tn II	5.15±7.21	5.73±7.73	4.27±6.26	0.013
Tn III	12.42±17.78	13.11±18.12	10.93±17.23	**0.016**
Osmolarity, mOsm/kg	293.38±13.46	295.85±16.01	291.67±8.10	**0.003**
LVEF, %	51.34±11.13	52.55±11.43	49.61±10.48	**0.012**
BS, mg/dL	139.27±69.01	142.07±73.28	135.02±61.98	0.350
Gensini score	31.20±36.73	40.04±2.71	28.62±2.30	**0.001**

Yr: Year, aVR: Augmented voltage right arm, +: ST elevation, -: ST depression, TG: Triglyceride, Cho: Cholesterol, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, Tn: Cardiac troponin, LVEF: Left ventricular ejection fraction, BS: Blood sugar, SD: Standard deviation

There was a significant difference between groups in terms of diagnosis (p=0.001), TVD (p=0.001), complication (p=0.001), and mortality (p=0.002). When the distribution of the diagnoses by groups was examined, 33 (14.7%) of 224 patients in Group I had UA, 61 (27.2%) inferior MI, 4 (1.8%) posterior MI, 66 (29.5%) anterior MI, 8 (3.6%) lateral MI, 36 (16.1%) common anterior MI, 5 (2.2%) high lateral MI and, 11 (4.9%) NSTEMI. Sixty six (41.2%) of the 148 patients in group II had UA, 22 (14.9%) inferior MI, 3 (2%) posterior MI, 26 (17.6%) anterior MI, 1 (0.7%) lateral MI, 7 (4.7%) diffuse anterior MI, 2 (1.4%) high lateral MI, and 26 (17.6%) NSTEMI. Inferior MI, posterior MI, anterior MI, lateral MI, diffuse anterior MI, high lateral MI were more common in Group I; UA and NSTEMI were more common in Group II (p=0.001, Table 2).

There was a statistically significant difference in terms of osmolarity between diagnoses (p=0.001, Table 3).

When osmolarity was compared in terms of gender (p=0.001), TVD (p=0.009), and mortality (p=0.011), there were statistically significant differences. However, no difference was found in terms of complications developed (Table 4).

There was no correlations between osmolarity and complications, but there were correlations between osmolarity and other variables (Table 5).

Discussion

Sudden occlusion or severe stenosis in the coronary artery causes acute coronary syndromes. Ischemic changes in ECG and increased serum cardiac markers play an important role in the diagnosis and treatment of patients with ACS. In electrocardiographic evaluation, aVR derivation is generally ignored, whereas ECG changes in aVR derivation are important in the prognosis of patients with ACS. In literature, studies on serum osmolarity levels and aVR derivation, TVD, and mortality are rare or absent. We planned the study to identify correlations between them.

The diagnosis and treatment of ACS should be done as soon as possible. With the delay of treatment, mortality increases and 63% of deaths due to MI occur within the first hour. The patient's history, ECG, and cardiac markers are important for the diagnosis of the ACS (22). Twelve-derivation ECG which is commonly used in diagnosis is fast, cheap, and easy. In emergency departments, ECG should be done within the first 10 minutes. Many findings can be detected with ECG. With these findings, it is possible to predict myocardial ischemia and its severity, and reperfusion treatment options can be decided. Also, ECG can provide information about ST-depression, ST-elevation and secondary developing reciprocal ST-depression, ischemic T negativity, emerging left bundle branch block, left anterior and posterior hemiblock (23,24).

Male gender is considered a risk factor alone in CAD in many studies and this is present in 60% of the patients. Atherosclerotic heart diseases, which do not occur 10-20 years earlier, are 3-6 times higher in males than in females (25). In the study, 56.5% of the patients were male and 43.5% were female. The mean age in Group I was 64 years and 48.2% of Group I were women, while the mean age in Group II was 64 years and 68.9% of Groups II were women. According to the data, the male gender was found a little bit low, and we thought that the reason might be a low number of patients included in the study. In two similar studies by Aygul et al. (26) and Wong et al. (5), the mean age was 61 and 60 years, and 32% and 29% were female, respectively,

Table 2. Test results regarding the difference between variables in terms of aVR Lead

		aVR (+) n (%)	aVR (-) n (%)	p-value
Diagnosis	**Unstable angina**	32 (18.1)	62 (31.8)	**0.001**
	Inferior MI	21 (11.9)	62 (31.8)	
	Posterior MI	1 (0.6)	6 (3.1)	
	Anterior MI	65 (36.7)	27 (13.8)	
	Lateral MI	8 (4.5)	1 (0.5)	
	Common anterior MI	35 (19.8)	8 (4.1)	
	High lateral MI	5 (2.8)	2 (1)	
	NSTEMI	10 (5.6)	27 (13.8)	
	Total	177 (100)	195 (100)	
TVD	**No**	121 (68.4)	166 (85.1)	**0.001**
	Yes	56 (31.6)	29 (14.9)	
	Total	177 (100)	195 (100)	
Complication	**No**	43 (24.3)	125 (64.1)	**0.001**
	Ischemic heart failure	83 (46.9)	30 (15.4)	
	Ventricular tachycardia	19 (10.7)	12 (6.2)	
	Atrioventricular block	8 (4.5)	17 (8.7)	
	Cardiac T/E	8 (4.5)	0 (0)	
	Acute pulmonary edema	16 (9)	11 (5.6)	
	Total	177 (100)	195 (100)	
Mortality	**No**	141 (79.7)	181 (92.8)	**0.002**
	Yes	36 (20.3)	14 (7.2)	
	Total	177 (100)	195 (100)	

MI: Myocardial infarction, NSTEMI: Non-ST-elevated MI, TVD: Three-vessel disease, T/E: Cardiac tamponade/effusion

in the group with ST-elevation in aVR. In the group with ST depression, the mean age was 58 and 61 years, and 16.8% and 28% were female, respectively.

Osmolarity has an important place in many systemic diseases, especially CAD. The study by Fauci (27) was one of the important studies that revealed the relationship between osmolarity and CAD. In another study, hyperosmolarity was shown to increase by 4.3 times and the risk of cardiovascular mortality by 3.9 times even after a moderate follow-up for cardiovascular mortality risk (28). Arbel et al. (29) found a significant difference between the calculated osmolarity values of patients with CAD and healthy individuals. In their study, in which Çiçek et al. (30) investigated the effect of hyperosmolarity on prognosis in patients undergoing primary angioplasty for STEMI, they predicted that, regardless of Na, blood glucose, and blood urea nitrogen, hyperosmolarity could lead to some important cardiac complications in the long-term follow-up of patients with STEMI undergoing primary percutaneous coronary intervention.

Serum osmolarity values in Group I were higher than Group II in the study. Greater detection of osmolarity in male gender may be a cause of CAD, thus mortality and poor prognosis. Mortality was significantly higher in Group I in which osmolarity was higher. Gensini score, which indicated the prevalence of CAD,

Table 3. Test results regarding the difference between osmolarity and diagnosis

Diagnosis	n	Mean ± SD	Min-max	p-value
Unstable angina	94	280.62±14.20	184-296	**0.001**
Inferior MI	83	285.89±5.95	273-294	
Posterior MI	7	290.57±4.96	280-294	
Anterior MI	92	296.30±2.39	278-299	
Lateral MI	9	299.77±0.44	299-300	
Common anterior MI	43	303.16±1.92	300-306	
High lateral MI	7	307.00±0.0	307-307	
NSTEMI	37	315.00±6.96	308-346	
Total	372	293.38±13.46	184-346	

SD: Standard deviation, Min: Minimum, Max: Maximum

also showed a positive strong correlation with cardiac troponin, STEMI, TVD, mortality, and osmolarity. Besides, it was found that it decreased the left ventricular ejection fraction and caused ischemic heart failure after showing negative correlation with STEMI. Osmolarity which could be examined with a simple method, might be predictive for mortality and ischemic heart failure in patients with ACS who were admitted to emergency

Table 4. Test results regarding the difference between variables in terms of osmolarity

Osmolarity			
		Mean ± SD	**p-value**
Gender	**Female**	290.05±15.02	**0.001**
	Male	295.00±11.86	
TVD	**No**	291.85±14.50	**0.009**
	Yes	296.25±8.75	
Complication	**No**	291.63±13.95	0.152
	Ischemic heart failure	295.46±11.36	
	Ventricular tachycardia	295.83±14.85	
	Atrioventricular block	295.00±12.54	
	Cardiac T/E	297.00±15.93	
	Acute pulmonary edema	295.90±15.13	
Mortality	**No**	292.20±13.31	**0.011**
	Yes	297.76±14.37	

Table 5. Correlation coefficients for osmolarity

	Osmolarity	
	r	p-value
LVEF	**-0.171**	**<0.001**
Complication	0.093	>0.075
cTn I	**0.110**	**<0.034**
cTn II	**0.119**	**<0.022**
cTn III	**0.125**	**<0.008**
Diagnosis	**0.169**	**<0.001**
aVR+/-	**0.141**	**<0.006**
Gensini score	**0.124**	**<0.017**
TVD	**0.120**	**<0.021**
Mortality	**0.153**	**<0.003**

departments due to chest pain, in whom ST-elevation and depression in aVR were detected on ECG.

In the study of Gorgels et al. (31), they reported left main CAD and TVD following detection of ST-elevation in aVR and ST depression in other derivations. Kosuge et al. (32) found that more than 0.5 mm ST elevation in aVR derivation was a strong marker of the occlusion of LMCA, or the presence of TVD. Patients were followed up for 90 days; and LMCA disease, TVD, and complications were observed more frequently in those with elevated troponin, and ST-elevation in aVR at the end of follow-up. As a result, they found that ST-elevation in aVR and troponin increase were simple and inexpensive tools for early risk assessment of ACS without ST-elevation. In another study, it was associated with TVD in 32% of patients with ST depression and with left main stenosis in 13% (33).

In our study, TVD was detected in 85 (22.58%) of 372 patients. TVD was detected in 4 (4.8%) patients with UA and 7 (8.3%) patients with NSTEMI among patients with ACS without ST-elevation. TVD was found in 36 (42.9%) of 92 patients with anterior MI and 17 (20.2%) of 83 patients with inferior MI. TVD was found in 56 (65.9%) patients in group I and 29 (34.1%) patients in Group II. We thought this was due to excess number of anterior, lateral, diffuse anterior, and high lateral MIs in Group I. Also, troponin was measured when the patients were admitted. Troponin values at 0^{th}, 6^{th} and 12^{nd} hours were higher in Group I. In patients with the ACS, elevated osmolarity and troponin in those with ST-elevation and depression in aVR might have predictive importance for TVD and mortality. Therefore, the presence of ST-elevation in aVR suggests that it is a better indicator for common and severe myocardial ischemia than ST-depression in other derivations.

Information about aVR derivation in MI with ST-elevation is more limited. In a study evaluating 100 patients who had acute anterior MI, it was shown that ST-segment elevation in aVR indicated a proximal lesion in the LAD with 95% specificity and 43% sensitivity (34). Yamaji et al. (4) compared changes in aVR derivation in acute occlusions of LMCA, LAD proximal and right coronary artery, and they found 88% sensitivity of ST-elevation in aVR in demonstrating acute LMCA occlusion. There are also studies evaluating the importance of ST-elevation in aVR lead in anterior MI and ST-depression in inferior MI (35,36). There was no study in which ST-segment change in aVR was evaluated in all MIs. In the study of Nair and Glancy (37) in 30 patients with acute inferior MI, 0.1 mV or more depression was observed in aVR derivation. In this study, aVR depression was found 80% specific and 96% sensitive in determining circumflex artery occlusion. In our study, among 177 patients in Group I; UA was seen in 32 (18.1%), NSTEMI in 10 (0.6%), and STEMI in 135 (81.8%). In Group II, 62 of 195 (31.8%) patients had UA, 27 of 195 (13.8%) had NSTEMI and 106 of 195 (54.4%) had STEMI. Accordingly, MIs due to LAD occlusion and anterior group MIs due to circumflex artery occlusion were common in Group I, while more MIs due to occlusion of the right coronary artery and its branches and lessinferior group MIs due to circumflex

artery involvement were detected in Group II. Unstable angina and NSTEMIs were more common in Group II. Accordingly, the Gensini score, TVD, mortality, and development of ischemic hearth failure were higher in Group I than in Group II.

In some studies, mortality and prognosis were compared with patients with normal ST segment. Therefore, mortality was found higher in patients with ST-elevation or depression. Hebbal et al. (38) showed that ST-depression in aVR was more mortal than elevation. It was stated that this was because depression affected wider myocardial area. Again, mortality was found higher in patients with ST-depression in aVR than in those with normal ST segment in aVR. On the other hand, Wong et al. (5) found a two-times increase in 30-day mortality in patients with aVR elevation. In our study, the mortality rate was higher in the group with ST-elevation in aVR. In similar studies, Antman et al. (39) and GRACE study (40) reported that ST-elevation in aVR was highly associated with in-hospital mortality, ischemic events, and heart failure, and was more effective than ST depressions. In our study, mortality was detected in 43 of 372 patients (11.55%). Mortality was seen in 36 of 177 (20.3%) patients in the group with ST-elevation in aVR and 14 of 195 (7.2%) patients with ST depression. In the ST-elevation group, it was found that mortality was higher because TVD was frequent, Gensini score, troponin level, and osmolarity were higher, and left ventricular ejection fraction were lower. This situation might increase the need for patients to have a coronary bypass and contribute to the worsening of their prognosis. The reason for elevated osmolarity in the ST-elevation group in aVR might be due to the fact that larger myocardial area such as in anterior MIs was affected.

We found that troponin and osmolarity were higher in the group with ST-elevation in aVR than in the group with depression. Serum osmolarity was found to be higher in patients with TVD and patients with mortality. In UA, where myocardial involvement was low, serum osmolarity level was low when compared to other acute coronary syndromes. We think that osmolarity increases due to more inflammatory events that occur when myocardial necrosis is wide, such as coronary artery disease, ST-elevated MI and NSTEMI.

Study Limitations

The most important limitation was that the study was retrospective and single-centered. Also, the difficulty in accessing the drugs used by the patients, difficulty in completion of the deficiencies in the registration system, and difficulty in accessing echocardiography and angiography reports were other important limitations. Moreover, other known risk factors of patients were not evaluated, so the multivariate analysis could not be performed to define the independent factor.

Conclusion

Serum osmolarity level was higher in the group with ST elevation in aVR derivations than in the ST depression group. Also, serum osmolarity was found to be higher in males, patients with TVD and patients with mortality. We think that osmolarity, just like troponin, can predict morbidity and mortality, and its effects in patients with CAD are open to investigation.

Ethics

Ethics Committee Approval: The study was approved by the institutional review board.

Informed Consent: Written informed consent was not necessary because the study was performed retrospectively by screening patient files.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.C., Ş.H.E., Concept: A.C., Ş.Ö.H., Design: Ş.Ö.H., Ş.H.E., Data Collection or Processing: A.C., Ş.Ö.H., Ş.H.E., Analysis or Interpretation: A.C., Ş.H.E., Literature Search: Ş.Ö.H., Ş.H.E., Writing: A.C.

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Original Article

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Research of Nutritional Behavior in Patients with Gastroesophageal Reflux

Gastroözofageal Reflü Hastalarında Beslenme Davranışının Araştırılması

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ABSTRACT

Objective: Gastroesophageal reflux (GER) is the migration of stomach contents to the lower part of the oesophagus, which is a physiological phenomenon that can usually be detected 10-15 times a day. It can occur after meals and during sleep. This study was conducted to investigate the nutritional behaviour of patients diagnosed as having GER disease (GERD).

Methods: In this research, among patients who were admitted to the gastroenterology outpatient clinic in a training and research hospital in İstanbul between June and December 2019, 104 patients aged 18-65 and diagnosed as having GERD as the study group, and 104 individuals not diagnosed as having GERD as the control group were included.

Results: Of both patient and control groups, 49% were male and 51% were female. It was determined that those diagnosed as having the disease frequently experienced pyrosis and regurgitation with acidity. The average body mass index (BMI) of the patient group was 30.40 kg/m^2, and of the control group, it was 25.41 kg/m^2 ($p<0.05$). In this study, nutritional habits were assessed, and statistically significant variations were found in the number of meals, meal skipping, eating speeds, and food temperatures. It was determined that most people with GERD symptoms ate more chocolate, fatty foods, acidic foods, spicy foods, and sodas than the control group. It was found that most individuals diagnosed as having GERD were overweight and their physical activities were significantly lower than the control group ($p<0.05$).

ÖZ

Amaç: Gastroözofageal reflü (GÖR), mide içeriğinin özefagusun alt kısmına doğru hareketi olup normalde günde 10-15 kez gözlenebilen fizyolojik bir olaydır. Bu durum yemekten sonra ve uyku sırasında oluşabilmektedir. Bu çalışma GÖR hastalığı (GÖRH) tanısı almış hastaların beslenme davranışının araştırılması amacıyla yapılmıştır.

Yöntemler: Bu çalışmada İstanbul'da bir eğitim ve araştırma hastanesinde gastroenteroloji polikliniğine Haziran-Aralık 2019 tarihleri arasında başvuran hastalardan GÖRH tanısı alan, yaşları 18-65 arasında değişen 104 hasta ve kontrol grubu olarak GÖRH tanısı almayan 104 birey seçilmiştir.

Bulgular: Hasta ve kontrol grubunun %49'u erkek ve %51'i kadındır. Hastalık tanısı alanların sıklıkla pirozis ve asit regürjitasyonu yaşadıkları belirlenmiştir. GÖRH tanısı konulan bireylerin beden kitle indeksi (BKİ) ortalamasının 30,40 kg/m^2, kontrol grubundaki bireylerin BKİ ortalamasının 25,41 kg/m^2 olduğu tespit edilmiştir ($p<0,05$). Bu çalışmada bireylerin beslenme alışkanlıkları değerlendirilmiş ve öğün sayısı, öğün atlama durumu, yemek yeme hızları, yemek ısıları açısından istatistiksel olarak anlamlı farklılıklar bulunmuştur. GÖRH semptomları yaşayan bireylerin büyük çoğunluğunun reflüjenik besinler olan çikolata, yağlı besinler, asitli besinler, baharatlar ve kolalı içecekleri kontrol grubuna göre daha çok tükettikleri saptanmıştır. GÖRH tanısı alan bireylerin çoğunluğunun fazla kilolu olduğu, fiziksel aktivitelerinin kontrol grubuna göre anlamlı derecede düşük olduğu tespit edilmiştir ($p<0,05$).

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Conclusion: As a result, the improvement in feeding behaviour and reducing the BMI level to acceptable limits would minimize the incidence of GER.

Keywords: Gastroesophageal reflux, nutritional behaviour, nutritional assessment

Sonuç: Sonuç olarak, beslenme alışkanlıklarındaki değişimin ve BKİ düzeyinin normal sınırlara getirilmesinin GÖR oluşumunu azaltacağı kanaatine varılmıştır.

Anahtar Sözcükler: Gastroözofageal reflü, beslenme davranışı, beslenme değerlendirmesi

Introduction

Gastroesophageal reflux (GER) is a physiological phenomenon which is the migration of stomach contents to the lower part of the esophagus, that can usually be detected 10-15 times a day (1). This physiological condition is short-lived and does not give any symptoms. However, if there is a more severe and prolonged reflux, then there are different signs. In this case, GER disease (GERD) is mentioned (2,3). The most common symptoms of GERD are pyrosis and regurgitation (4). Other symptoms are bloating, feeling of fullness in the stomach, chest pain, difficulty swallowing, cough, and hoarseness (2). In endoscopy, pathological findings are seen in just 30-40% of patients with GER, and no pathological findings are seen in the endoscopy of the remaining (5). Complications such as erosive esophagitis, esophageal stricture, Barrett's esophagus and cancer of the esophagus can be seen in endoscopy, depending on the duration and intensity of the symptoms (2,5).

The prevalence of GERD in the world varies between 7-25%. While it is between 10-20% in Europe and America, it is 2.5-7.8% in East Asian countries and 11.6% in Australia. In our country, GERD frequency is between 10-20%, as in Western countries (1,6). The prevalences of Obesity and GERD have dramatically increased in western societies over the last 40 years. Obesity is an important factor in the occurrence of GERD (7). Obesity promotes GERD development by increasing the intragastric pressure and reducing the lower esophageal sphincter (LES) pressure (8,9).

The gradual increase of GERD symptoms in the population shows that it is important to determine the risk factors for this disease. Studies have shown that reducing obesity, maintaining a healthy diet, and avoiding pests such as smoking, and alcohol are important for GERD development and treatment (10). The purpose of this study is to determine the anthropometric measurements and general features and nutritional status of GERD-diagnosed individuals.

Methods

This study was conducted between June and December 2019 in patients diagnosed as having GERD among those who presented to the İstanbul Okan University Gastroenterology Outpatient Clinic and Nutrition and Dietetics. A total of 104 patients, 53 females and 51 males, diagnosed as having GERD, aged between 18-65 were included in the study. In addition, 104 patients without GERD symptoms were taken as the control group. The survey form used for patients (study group) and control group in the study was prepared by the researchers from a literature review for similar studies (10).

The "Ethics Committee Approval" dated 13 March 2019, numbered 104, was obtained from the İstanbul Okan University Ethics Committee for the survey study. The research was launched with the approval of İstanbul Okan University on May 28, 2019, with the permission of Nutrition and Dietetics. The individuals included in the study read and signed the informed volunteer consent form which was signed by the researcher, and a copy was delivered to them.

Questionnaire Form

Descriptive information (age, education level, occupation, and bad habits such as smoking and alcohol) was asked in the first part of the questionnaire applied to the participants. Additionally, participants were asked whether there were signs of GERD, the length and frequency of symptoms in patients with symptoms, and whether their families had GERD. The nutritional habits of the patients were questioned in the survey. The daily physical activity status of the patients was questioned.

Anthropometric Measurements

The body mass index (BMI) is determined by calculating the body weight and height of all the questionnaire participants. BMI is calculated as kg/m^2 using the body weight (kg)/height (m^2) formula. It is graded according to World Health Organization's BMI classification data (11).

Statistical Analysis

All data were evaluated using the SPSS 22.0 Statistics Program. First, during the evaluation of the study results, descriptive statistics (mean, standard deviation, minimum, maximum) were clarified for the numerical variables. To settle on the required form of analysis, it was then evaluated whether the data met the usual requirements of distribution. Since the collected data provided the normal distribution conditions, it was decided to apply parametric analysis methods. In this context, two independent samples t-test was used to show whether there was a difference between the two groups (e.g., study and control groups). Significance in the analysis was evaluated at the level of $p<0.05$ (12).

Results

Demographic variables of the individuals participating in the study are given in Table 1. When the gender distribution was analysed, it was shown that roughly half of the sample consisted of women and the other half consisted of men, and the study and control groups had similar distribution.

When analysing the educational status of the individuals taking part in the study, it was shown that 43.75% of them were high school graduates, 29.33% were university graduates, and

Table 1. Distribution by demographic variables

		Study n=104		Control n=104		Total n=104	
		n	%	n	%	n	%
Age	18-24	8	7.69	6	5.77	14	6.73
	25-32	18	17.31	23	22.12	41	19.71
	33-40	16	15.38	29	27.88	45	21.63
	41-48	27	25.96	23	22.12	50	24.04
	48-65	35	33.65	23	22.12	58	27.88
Gender	Male	51	49.04	51	49.04	102	49.04
	Female	53	50.96	53	50.96	106	50.96
Educational status	Illiterate	7	6.73	0.00	0.00	7	3.37
	Primary school	24	23.08	1	0.96	25	12.02
	Secondary school	16	15.38	6	5.77	22	10.58
	High school	26	25.00	65	62.50	91	43.75
	University	29	27.88	32	30.77	61	29.33
	Master's degree	2	1.92	0.00	0.00	2	0.96
Occupational status	Housewife	34	32.69	8	7.69	42	20.19
	Officer	11	10.58	18	17.31	29	13.94
	Worker	25	24.04	74	71.15	99	47.60
	Self-employment	11	10.58	1	0.96	12	5.77
	Other	23	22.12	3	2.88	26	12.50
	Total	104	100	104	100	104	100

the remaining part did not attend secondary or primary school or kindergarten. It was seen that 47.6% of the individuals participating in the study were workers. Looking at the study population directly, it was shown that 32.69% of refluxed patients were housewives and 24.04% were workers. In the control group, the rate of housewives was 7.69% and the rate of workers was 71.15%.

While the individuals in the study group involved in the study had an average BMI of 30.40, the individuals in the control group had an average BMI of 25.41, and a statistically significant difference was observed between the experimental and control groups ($p<0.05$).

In this study, the smoking rate in the experimental group was 49.04%, while it was 36.54% in the control group. While in the study group, the smoking period was 13.9 years, in the control group it was 12.1 years ($p>0.05$). The alcohol intake rate in the study group was 20.19%, while in the control group it was 1.92% ($p<0.05$). While the duration of alcohol consumption of individuals in the study group was 7.1 years, the duration of alcohol consumption of individuals in the control group was 6 years ($p>0.05$).

It was investigated whether there was a substantial difference in terms of the family history between the individuals in the study and control groups, and it was found that 57 of the individuals in the study group had reflux symptoms in the family, and that 5 of those in the control group had reflux symptoms in the family ($p<0.05$). Although only 29.81% of the individuals in the study group reported engaging in physical activity, this figure was 67.31% for the control group ($p<0.05$).

In this study, it was found that the control group had more main and snack meals than the study group. While the number of people fed with 4 meals a day in the study group was 35.58%, this rate was 63.46% in the control group, and the number of people fed with 5 meals a day was 7.69% in the study group and 19.23% in the control group ($p<0.05$). When the eating style was questioned, it was determined that 62.50% of the individuals in the study group and 12.5% of the individuals in the control group ate fast/very fast ($p<0.05$). Of the individuals in the study group 60.58% and 28.85% of the individuals in the control group ate hot/very hot food ($p<0.05$).

In this study, it was found that 31.73% of the individuals in the study group ate before going to bed at night, and this rate was 5.77% in the control group ($p<0.05$).

The t-test results regarding the frequency of consuming fatty foods of the individuals participating in the study are given in Table 2. The consumption of whole milk, creamy yoghurt and kashar cheese from the fatty food group was examined. It was found that 22.1% of the individuals in the study group drank whole milk, 27.9% ate creamy yogurt and 30.8% ate kashar cheese every day. It was determined in the control group that these foods were not eaten regularly, 9.6% drank whole milk 4-5 days a week, 13.5% consumed creamed yogurt and 1% consumed kashar ($p<0.05$).

Table 2. Results by frequency of eating fatty foods

	The frequency of consumption of foods	Never		Once a month		Once in every 15 days		Once per week		2-3 times per week		4-5 times per week		Every day		t-value*	p-value
	Food & drink	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
Study group	Milk (whole milk)	24	23.1	3	2.9	1	1.0	5	4.8	19	18.3	29	27.9	23	22.1	11.651	0.000
	Yoghurt (with cream)	4	3.8	2	1.9	1	1.0	6	5.8	19	18.3	43	41.3	29	27.9		
	Kashar cheese	22	21.2	7	6.7	2	1.9	12	11.5	8	7.7	21	20.2	32	30.8		
	Margarine	81	77.9	7	6.7	0.00	0.0	4	3.8	3	2.9	6	5.8	3	2.9		
	Butter	9	8.7	3	2.9	2	1.9	9	8.7	11	10.6	7	6.7	63	60.6		
Control group	Milk (whole milk)	11	10.6	23	22.1	17	16.3	31	29.8	12	11.5	10	9.6	0.00	0.0		
	Yoghurt (with cream)	4	3.8	9	8.7	20	19.2	36	34.6	21	20.2	14	13.5	0.00	0.0		
	Kashar cheese	95	91.3	2	1.9	2	1.9	0.00	0.0	3	2.9	1	1.0	1	1.0		
	Margarine	101	97.1	1	1.0	0.00	0.0	1	1.0	0.00	0.0	0.00	0.0	1	1.0		
	Butter	19	18.3%	3	2.9	0.00	0.0	4	3.8	8	7.7	2	1.9	68	65.4		

p<0.05 is statistically significant.
*t-test

Table 3. Results of the frequency of consuming acidic foods

		Never		Once a month		Once in every 15 days		Once per week		2-3 times per week		4 - 5 times per week		Every day		t-value*	p-value
	Food & drink	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
Study group	Tomato	1	1.0	0.00	0.0	0.00	0.0	2	1.9	7	6.7	11	10.6	83	79.8	19.569	0.000
	Onion	2	1.9	0.00	0.0	1	1.0	2	1.9	6	5.8	10	9.6	83	79.8		
	Garlic	9	8.7	4	3.8	4	3.8	18	17.3	26	25.0	20	19.2	23	22.1		
	Pickle	16	15.4	14	13.5	8	7.7	11	10.6	28	26.9	22	21.2	5	4.8		
	Citrus fruits	17	16.3	4	3.8	5	4.8	14	13.5	16	15.4	18	17.3	30	28.8		
	Tomato paste	3	2.9	0.00	0.0	1	1.0	5	4.8	10	9.6	10	9.6	75	72.1		
Control group	Tomato	0.00	0.0	0.00	0.0	2	1.9	90	86.5	12	11.5	0.00	0.0	0.00	0.0		
	Onion	3	2.9	0.00	0.0	5	4.8	90	86.5	6	5.8	0.00	0.0	0.00	0.0		
	Garlic	64	61.5	10	9.6	17	16.3	10	9.6	3	2.9	0.00	0.0	0.00	0.0		
	Pickle	60	57.7	14	13.5	10	9.6	17	16.3	2	1.9	0.00	0.0	1	1.0		
	Citrus fruits	11	10.6	1	1.0	8	7.7	62	59.6	20	19.2	0.00	0.0	2	1.9		
	Tomato paste	12	11.5	1	1.0	2	1.9	4	3.8	4	3.8	1	1.0	80	76.9		

p<0.05 is statistically significant.
*t-test

Table 4. Results of the frequency of eating sugar group foods

		Never		Once a month		Once in every 15 days		Once per week		2-3 times per week		4 - 5 times per week		Every day		t-value*	p-value
	Food & drink	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
Study group	Sugar	25	24.0	5	4.8	4	3.8	2	1.9	5	4.8	10	9.6	53	51.0	7.991	0.000
	Honey/jam/molasses	12	11.5	8	7.7	7	6.7	8	7.7	22	21.2	12	11.5	35	33.7		
	Chocolate	12	11.5	6	5.8	3	2.9	14	13.5	16	15.4	22	21.2	31	29.8		
	Deserts with syrup	20	19.2	18	17.3	13	12.5	19	18.3	29	27.9	4	3.8	1	1.0		
	Milky desserts	20	19.2	16	15.4	10	9.6	29	27.9	25	24.0	3	2.9	1	1.0		
Control group	Sugar	23	22.1	20	19.2	20	19.2	15	14.4	3	2.9	1	1.0	22	21.2		
	Honey/jam/molasses	14	13.5	30	28.8	17	16.3	31	29.8	3	2.9	2	1.9	7	6.7		
	Chocolate	11	10.6	5	4.8	14	13.5	45	43.3	25	24.0	1	1.0	3	2.9		
	Deserts with syrup	25	24.0	58	55.8	14	13.5	7	6.7	0.00	0.0	0.00	0.0	0.00	0.0		
	Milky desserts	12	11.5	36	34.6	45	43.3	10	9.6	1	1.0	0.00	0.0	0.00	0.0		

p<0.05 is statistically significant.
*t-test

Table 5. Results on the frequency of consuming acidic and non-acidic beverage group foods

		Never		Once a month		Once in every 15 days		Once per week		2-3 times per week		4 - 5 times per week		Every day		t-value*	p-value
	Food & drink	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
Study group	Water	1	1.0	0.00	0.0	0.00	0.0	0.00	0.0	1	1.0	0.00	0.0	102	98.1	8.576	0.000
	Tea	4	3.8	1	1.0	0.00	0.0	0.00	0.0	3	2.9	2	1.9	94	90.4		
	Herbal teas	69	66.3	7	6.7	2	1.9	4	3.8	6	5.8	4	3.8	12	11.5		
	Turkish coffee	19	18.3	2	1.9	0.00	0.0	3	2.9	9	8.7	5	4.8	66	63.5		
	Nescafe	67	64.4	4	3.8	4	3.8	5	4.8	8	7.7	4	3.8	12	11.5		
	Sodas	40	38.5	8	7.7	3	2.9	9	8.7	11	10.6	19	18.3	14	13.5		
	Mineral water	28	26.9	3	2.9	6	5.8	4	3.8	20	19.2	26	25.0	17	16.3		
Control group	Water	1	1.0	0.00	0.0	0.00	0.0	0.00	0.0	0.00	0.0	0.00	0.0	103	99.0		
	Tea	2	1.9	0.00	0.0	0.00	0.0	0.00	0.0	1	1.0	1	1.0	100	96.2		
	Herbal teas	86	82.7	0.00	0.0	0.00	0.0	4	3.8	6	5.8	2	1.9	6	5.8		
	Turkish coffee	9	8.7	1	1.0	4	3.8	39	37.5	17	16.3	4	3.8	30	28.8		
	Nescafe	88	84.6	2	1.9	0.00	0.0	4	3.8	1	1.0	0.00	0.0	9	8.7		
	Sodas	26	25.0	16	15.4	42	40.4	17	16.3	1	1.0	1	1.0	1	1.0		
	Mineral water	39	37.5	19	18.3	33	31.7	8	7.7	2	1.9	1	1.0	2	1.9		

p<0.05 is statistically significant.
*t-test

The t-test results regarding the frequency of consuming fatty foods of the individuals participating in the study are given in Table 3. In the study group, tomato and onion were eaten daily at a rate of 79.8%, garlic 22.1%, pickle 4.8% and citrus 28.8%. In the control group, the daily consumption of these foods was 0% or was close to 0% and taking into account consumption rates 2-3 times a week, the rates were as follows: tomatoes 11.5%, onion 5.8%, garlic 2.9%, pickle 1.9%, and citrus fruits 19.2% ($p<0.05$).

In this study, eating frequency and spice consumption of fried foods were examined. Although 23.1% of the study group consumed French fries 2-3 times a week and 14.4% of the study group consumed other fried vegetables, these amounts were 3.8% and 2.9% respectively in the control group ($p<0.05$). While the daily consumption of peppermint/red pepper/black pepper in the study group was 67.3%, it was 0% in the control group. It was determined that 2-3 times a week the control group consumed the spice group at a rate of 11.5% ($p<0.05$).

The t-test results regarding the frequency of consuming fatty foods of the individuals participating in the study are given in Table 4. It was found that daily sugar consumption was 51%, daily honey/jam/syrup consumption was %33.7, daily chocolate consumption was %29.8, the consumption of desserts with syrup 2-3 times per week was 27.9 %, milky dessert eating percentage was 24%; whereas in the control group daily sugar consumption rate was 21%, honey/jam/syrup consumption was 6.7%, chocolate consumption was 2.9%, the consumption of desserts with syrup 2-3 times was 0%, and the consumption of milky sweet was 1% ($p<0.05$).

The t-test results regarding the frequency of consuming fatty foods of the individuals participating in the study are given in Table 5. While the rates of daily consumption of Turkish coffee, soda and mineral water were found 63.5%, 13.5% and 16.3%, respectively in the study group; these rates were 28.8%, 1% and 1.9%, respectively in the control group.

Discussion

The GERD is an important health problem in the world. In the world, this disease is seen between 7-25% and in western countries this prevalence is between 10-20% (13). In Turkey, frequency of GERD is observed similar with the frequency in the West (1).

If GERD is not treated, complications such as esophagitis, esophageal stricture, Barett's esophagus and adenocarcinoma of the esophagus may develop. As a result of studies, it is thought that factors such as eating habits and lifestyle play an important role in the etiology of the disease (3,10).

The best determined risk factors for GERD are malnutrition, obesity and advanced age (1). It is known that the age factor is effective in the frequency of GERD (14). In that analysis, the average age of GER patients was estimated to be older than control group. In a study conducted to examine the incidence of GERD in Taiwan, it was found that the risk of developing GERD was higher in the 40-49 and 50-59 age groups (15). In their research, Moshkowitz et al. (16) noted that GERD symptoms were more frequent over the age of 35, and GERD was more frequent at an average age of 44±14 years. In this study, it was found that GERD was more common in the 41-48 and 49-60 age groups.

Eco-factors such as physical activity and obesity are known to play a role in GERD. It has been reported in studies that moderate physical activity has a protective effect against GERD (17,18). In this study, in the control group, the rate of moderate activity (brisk walking) was 67.31% , while in the study group, this rate was 29.81% ($p<0.05$).

The prevalence of obesity increases significantly in many parts of the world, and this situation leads to many diseases. Obesity facilitates the formation of GERD by causing an increase in intraabdominal pressure, delay in gastric emptying and a decrease in LES pressure (19). In Korea, Song et al. (20) examined the relationship between BMI and GERD. They found that the risk of obese individuals for GERD increased 2.5 times compared to healthy individuals. Murray et al. (21) reported that the frequency of heartburn increased 2.91 times and acid regurgitation increased 2.23 times in obese individuals compared to normal weight individuals. Ayazi et al. (22) reported that the rate of regurgitation was higher in people with higher BMI values than with normal BMI values. In a study conducted in Sweden, it was stated that individuals with BMI >30 kg/m^2 had a higher risk of GERD compared to individuals with normal weight (BMI: 20-25 kg/m^2) (23). In this study, the mean BMI of individuals diagnosed as having GERD was found to be 30.40, and the mean BMI of the control group was found to be 25.41. This result shows that the increase in BMI increases the risk of developing GERD.

It was stated that smoking, the number of cigarettes smoked, and the duration of smoking were important risk factors for GERD, and in a study, the risk of developing GERD increased by 1.7 times in individuals who smoked compared to non-smokers (24). In this study, the smoking rates between the two groups were not statistically significant due to the high rate of smoking in both the study group and the control group ($p>0.05$). For this reason, we cannot express an opinion on the relationship between smoking and GERD according to our study.

Alcohol use is a risk factor for GERD as it damages the gastric mucosal barrier. The incidence of GERD was found 2.5 times higher in 2,000 alcohol users in Poland compared to the control group (25). Mohammed et al. (26) conducted a survey in 1,533 people and reported that the risk of GERD symptoms in men with excessive alcohol use (30 units/week) increased 2.96 times. In this study, the rate of alcohol consumption in the study group was found to be higher than the control group ($p<0.05$). As a result, we can say that GERD symptoms are more common in people who use alcohol.

It has been stated that genetic factors play a role in the etiopathogenesis of GERD (1). This situation was also observed

in this study. It was found that the rate of reflux symptoms in the family of individuals in the study group was higher than the control group ($p<0.05$).

Number of meals reflects the size of the portion of the food eaten at a meal. The excess amount of food taken in a meal causes distension in the stomach and prolongs the time of food leaving the stomach. As a result, the delay in gastric emptying rate facilitates the relaxation of the LES and leads to reflux. This situation will lead to the GERD. If snacks are included between 3 main meals, the portion in the meal will decrease. This will reduce the incidence of GERD symptoms (27). In this study, it was observed that the individuals in the control group had more main and snack meals compared to the study group ($p<0.05$).

In this study, it was found that the individuals in the experimental group skipped more meals. According to these results, it is understood that the number of meals of the individuals in the study group is lower and their portions in a meal are larger.

In this study, it was determined that 62.50% of the individuals in the study group and 12.5% of the individuals in the control group ate food fast / very fast. If food is eaten fast / very fast, the stomach fills up quickly and the pressure in the stomach increases by stretching, thus causing reflux (28). In a study conducted by Wildi et al. (29), 20 healthy individuals were asked to consume a meal in 5 minutes, and it was found that reflux was experienced 14 times in two hours after the meal consumed in 5 minutes. This suggests that eating food fast may pose a risk for GERD.

In this study, it was determined that 60.58% of the individuals in the study group and 28.85% of the individuals in the control group ate hot/very hot food. Very hot meals cause erosion in the stomach and increase the acid secretion, thus facilitating the formation of GERD (30).

In this study, it was determined that 31.73% of the individuals in the study group ate before going to bed at night, while 5.77% of the individuals in the control group ate before going to bed at night. In a study conducted in İzmir, this situation was found to be 45.3% in the patient group (10). We can say that eating before going to bed at night facilitates the formation of GERD.

In this study, we compared the foods frequently consumed by the study group with the control group. As a result, it was found that the individuals in the study group consumed more fatty foods than the individuals in the control group ($p<0.05$). Studies have found that the frequency of GERD increases after high-fat meals (31,32). In another study, it was found that the total fat in the diets of GERD patients was high (33). Dibley et al. (34) reported that fatty milk and dairy products increased GERD symptoms.

In this study, the frequency of eating acidic foods was investigated. It was found that the individuals in the study group consumed these foods more frequently than the control group ($p<0.05$). Allen et al. (35) reported that onion consumption increased pyrosis. Dibley et al. (34) found that raw tomato and citrus consumption increased the symptoms of reflux.

In this study, the frequency of eating fried foods was examined and it was concluded that the individuals in the experimental group consumed more fried foods than the individuals in the control group ($p<0.05$). El Serag et al. (36) reported that eating fried foods increased GERD symptoms.

Study Limitations

In this study, the frequency of eating sugary foods was examined, and the rate of consuming sugary foods in the study group was significantly higher than the control group ($p<0.05$). Sweets are frequently consumed foods in our country and are high energy sources (37). Studies have reported that sugary foods and chocolate are reflugenic foods (33,38).

In this study, the consumption frequency of acidic and non-acidic beverages group was examined, and the consumption of Turkish coffee, cola drinks and soda was found to be significantly higher in the individuals in the study group compared to the individuals in the control group ($p<0.05$). It has been reported that soda consumption increases distention and acid secretion in the stomach, which leads to reflux (39). Fass et al. (40) reported that carbonated drinks increased pyrosis. Cola drinks have been reported to increase GERD symptoms in studies (10,20).

It was reported in the study conducted by Boekema et al. (41) that coffee consumption did not cause reflux. In a study conducted in 2014, it was reported that there was no significant relationship between coffee intake and GERD (42).

Conclusion

Dietary habits and lifestyle are the leading risk factors that can be changed in the prevention of this disease. The results obtained in our study and the related literature publications we reviewed show similar results, and it is very important to regulate proper nutrition and lifestyle in the prevention of GERD. In order to prevent GERD, 3 main meals should be eaten, and the stomach must not be filled out with the main meals. In order not to eat too much during these meals, snacks should be eaten. Food intake should be stopped at least 2-3 hours before going to bed. In our meals, fatty and carbohydrate foods should be less, and protein content should be higher. Foods such as spices, tomatoes, onions, garlic and citrus fruits, cola and carbonated drinks that increase the irritation of the esophagus should be minimized. It is important to do the necessary physical activity to keep the BMI levels of individuals within normal limits. Harmful habits such as smoking, and alcohol use should be avoided.

Ethics

Ethics Committee Approval: The "Ethics Committee Approval" dated 13 March 2019, numbered 104, was obtained from the İstanbul Okan University Ethics Committee for the survey study.

Informed Consent: The individuals included in the study read and signed the informed volunteer consent form which was signed by the researcher, and a copy was delivered to them.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: B.Y., H.F.A., Design: B.Y., H.F.A., Data Collection or Processing: B.Y., H.F.A., Analysis or Interpretation: B.Y., H.F.A., Literature Search: B.Y., H.F.A., Writing: B.Y., H.F.A.

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Original Article

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Determination of Interobserver Correlation in the Evaluation of Liver Histopathology of Chronic Hepatitis B Patients and the Reflections on Treatment

Kronik Hepatit B Hastalarının Karaciğer Histopatolojisinin Değerlendirilmesinde Gözlemciler Arası Uyumun Saptanması ve Tedaviye Yansımaları

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ABSTRACT

Objective: Histopathological examination of the liver is the gold standard in the follow-up and treatment of chronic hepatit B vius (HBV) disease. Ishak's Modified histological activity index (HAI) and fibrosis staging system are usually used in Turkey. Although a common scoring system is used, the same sample can be interpreted differently between different pathologists due to various variables. In this study, the evaluation of liver histopathologies of chronic HBV patients by pathologists in different hospitals and the correlation of the results with each other and the effect on the treatment decision were investigated.

Methods: Pathology slides of liver biopsy materials of 10 patients were evaluated by pathologists in 5 different tertiary care hospitals. Using non-parametric statistical methods, the coefficient of agreement between pathologists was determined. Also, descriptive statistics were used to determine the percentage of receiving treatment.

Results: Agreement between pathologists was calculated the most in total HAI and Fibrosis score (k=0.8186, k=0.8217). The Kuder-

ÖZ

Amaç: Kronik hepatit B virüsü (HBV) hastalığında takip ve tedavide karaciğerin histopatolojik incelemesi altın standarttır. Türkiye'de histopatolojik değerlendirmede genellikle İshak'ın Modifiye histolojik aktivite indeksi (HAİ) ve fibroz evreleme sistemi kullanılmaktadır. Ortak bir skorlama sistemi kullanılmasına rağmen çeşitli değişkenlerden dolayı aynı örnek farklı patologlar arasında farklı yorumlanabilmektedir. Bu çalışmada kronik HBV hastalarının karaciğer histopatolojilerinin farklı hastanelerdeki patologlarca değerlendirilmesi ve çıkan sonuçların birbirleri ile uyumu ve tedavi kararı üzerindeki etkisi araştırılmıştır.

Yöntemler: Tedavi endikasyonu olup karaciğer biyopsisi yapılan 10 hastaya ait preparatlar 5 farklı 3. basamak hastanesindeki patologlar tarafından değerlendirilmiştir. Non-parametrik istatistiksel yöntemler kullanılarak patologlar arası uyum katsayısı belirlenmiştir. Ayrıca tedavi alabilme yüzdelerinin belirlenmesi için tanımlayıcı istatistiklere de başvurulmuştur.

Bulgular: Patologlar arası uyum en fazla toplam HAİ ve Fibroz skorunda hesaplandı (k=0,8186, k=0,8217). Tedavi kararında

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Richardson reliability coefficient among centres was found to be high in the treatment decision (k=0.8207). Although all patients were indicated for treatment according to The European Association for the Study of the Liver 2017 guideline, it was calculated that an average of 58% of the patients could receive treatment according to liver histopathology.

Conclusion: Differences in the pathological diagnosis between pathologists in centres may cause delays in chronic hepatitis B patients' access to treatment.

Keywords: Liver biopsy, liver histopathology, interobserver agreement, Modified Ishak scoring system

merkezler arasındaki Kuder-Richardson Güvenirlik katsayısı yüksek bulundu (k=0,8207). Hastaların hepsinin The European Association for the Study of the Liver 2017 kılavuzuna göre tedavi endikasyonu olmasına rağmen, karaciğer histopatolojisine göre ortalama %58 tedavi alabileceği hesaplandı.

Sonuç: Merkezlerdeki patologlar arasındaki uyum farklılıkları, kronik HBV hastaların tedaviye ulaşabilmesinde gecikmelere sebep olabilmektedir.

Anahtar Sözcükler: Karaciğer biyopsisi, karaciğer histopatolojisi, gözlemciler arası uyum, Modifiye İshak skorlama sistemi

Introduction

Hepatitis B virus (HBV) is a hepatotropic DNA virus that can cause acute and chronic hepatitis. As a result of chronic diseases caused by HBV, fatal complications such as liver failure, hepatocellular cancer and liver cirrhosis may develop (1). Liver biopsy has an important place in the diagnosis of these complications due to HBV and in deciding the treatment. Many scoring and staging systems have been established in order to increase agreement among pathologists and to establish a standard in the histopathological examination of the liver. While deciding to start treatment in patients with chronic hepatitis B in Turkey, İshak's Modified Histological Activity index (HAI) and İshak's fibrosis staging system (FSS) are generally used (2).

Histopathological examination of the liver is affected by many variables. At the beginning of these variables, there are features related to the biopsy application such as the size of the tissue examined, whether it is fragmented or not, and whether it is taken under the capsule. In addition, errors in the preparation stages, the experience of the pathologist and the scoring systems used can also affect the histopathological examination (3-8).

Modified Ishak scoring examines in detail the main lesions such as interphase hepatitis, confluent necrosis, apoptosis and inflammation. It also makes a detailed evaluation by using 7 different scores in fibrosis staging (Table 1). The fact that Ishak's Modified HAI and fibrosis staging are so detailed increases its distinguishing and descriptive feature, while decreasing its reproducibility (6).

The conditions and rules for providing health services by the state in Turkey are specified in the Health Implementation Communiqué (SUT). According to this communiqué, liver biopsy is mandatory in order to start antiviral therapy in patients with khronic HBV, unless there are contraindications, except for a few exceptional cases (9). In patients with HBV DNA level above 2,000 IU/mL according to SUT, treatment can be started in patients with liver biopsy score of HAI ≥6 or FSS ≥2 according to Ishak. Scoring systems are important for the standardization of the evaluation of patients, but we can still witness different results reported in the same sample among pathologists in daily practice. One-point differences in the interpretation of scoring among pathologists can be critical in whether patients receive treatment or not.

Our aim in this study is to determine the consistency of the histopathological examinations of liver biopsy samples obtained from patients with HBV according to the Modified Ishak scoring system among different pathologists in different hospitals and to examine the reflections of the differences in treatment.

Method

Ethics Committee

The ethics committee approval of our study was obtained from the Clinical Research Ethics Committee of Bakırköy Dr Sadi Konuk Training and Research Hospital with the decision number 2019/94.

Material

In our study, 10 patients who were admitted to the infectious diseases outpatient clinics in March 2019 and underwent liver biopsy were included in the study. The histopathological preparations of 10 patients who were planned to be treated for chronic HBV disease and underwent liver biopsy were evaluated by pathologists in five different tertiary care hospitals. A total of 20 preparations stained with Hematoxylin & Eosin and Mason Trichrome stains were evaluated by five different pathologists according to Ishak's Modified HAI and FSS. The results were processed into Excel spreadsheets.

Inclusion/Exclusion Criteria

Patients older than 18 years of age who were followed up for chronic HBV and had phase 2 and phase 4 characteristics according to the EASL (The European Association for the Study of the Liver) 2017 guideline and had liver biopsy indication were included in the study (10). Patients with non-HBV liver disease were excluded from the study. Likewise, patients with contraindications for liver biopsy, pregnant women, and patients whose biopsy material contained less than 5 portal areas were excluded from the study.

Statistical Analysis

Goodness of agreement between pathologists (inter-observer) was evaluated with Kendall's W Coefficient of Agreement,

Table 1. Ishak scoring system

Ishak's Modified histological activity index (grading)	Score
A. Periportal or periseptal interphase hepatitis (piecemeal necrosis)	
None	**0**
Mild (focal, in the area of several portals)	**1**
Mild/Moderate (focal, in most of the portal areas)	**2**
Moderate (in less than 50% of the tracts or septa, with continuity around them)	**3**
Severe (in more than 50% of tracts or septa, with continuity around them)	**4**
B. Confluent necrosis	
None	**0**
Focal confluent necrosis	**1**
Zone 3 necrosis (in some areas)	**2**
Zone 3 necrosis (in most areas)	**3**
Zone 3 necrosis and infrequent portal-central bridging	**4**
Zone 3 necrosis and numerous portal-central bridging	**5**
Panacinar or multiacinar necrosis	**6**
C. Focal (spotty) lytic necrosis, apoptosis and focal inflammation (per 100 magnification)	
None	**0**
1 or less focus	**1**
2-4 foci	**2**
5-10 foci	**3**
More than 10 foci	**4**
D. Portal inflammation	
None	**0**
Mild (in some or all portal areas)	**1**
Moderate (in some or all portal areas)	**2**
Moderate/prominent (in all portal areas)	**3**
Distinct (in all portal areas)	**4**
Ishak's Fibrosis staging system	**Stage**
No fibrosis	**0**
Fibrous enlargement in some portal areas and +/- short fibrous septa	**1**
Fibrous enlargement of most of the portal areas and +/- short fibrous septa	**2**
Fibrous expansion and sparse porto-portal bridging (P-P) in most portal areas	**3**
Fibrous expansion and pronounced bridging of the portal areas [(P-P), as well as Porto-central (P-C) bridging]	**4**
Rare nodules with pronounced bridging (P-P and/or P-S) (incomplete cirrhosis)	**5**
Cirrhosis (possible or certain)	**6**
*Modified from references 2 and 8	

which was one of the non-parametric statistical methods. For this purpose, separate coefficients were calculated for the A, B, C and D categories of the Modified HAI grading system detailed in Table 1. The same was calculated for fibrosis staging and HAI Total score. For treatment, HAI 6 and above and/or fibrosis 2 and above were accepted (according to SUT 2018). However, Kuder-Richardson Confidence coefficient (K-R 20) was calculated because whether or not to receive treatment was yes/no and 0/1 according to binary system. Descriptive statistics were also used when necessary. IBM SPSS 23 package program was used for statistical calculations.

Results

Half of the 10 patients participating in the study were male and half were female, and their ages ranged between 22 and 61. The average age of women was 47 (35-61) and the average age of men was 36.6 (22-57). The data of the patients are given in Table 2.

The histopathological examination results of the centers are summarized in Table 3. HAI results were first given, and then categorical details were given, and FSS was shown in the same table. Inter-observer agreement was high for category A and D scores in HAI grading (k=0.8186, k=0.8217), but there was no agreement between observers for category B scores in HAI grading (Kendall's W k<0.5), and observer-observer agreement for category C scores. Although there was agreement between them, it was not high. The agreement between observers was high in the total score of HAI grading and FSS. In the treatment decision, K-R 20 coefficient was considered reliable because it was above 0.8.

The closer Kendall's coefficient of agreement is to one, the more consistent the scores given by the pathologists are, the closer it is to zero, the more inconsistent the scores are, and it means there is no similarity. The Kuder-Richardson Reliability coefficient (K-R 20) is a value between zero and one, but the closer it is to one, the higher the reliability. The calculated coefficients are given in Table 4.

While all of the current patients (100%) had a treatment indication according to the 2017 EASL guidelines, an average of 58±38% had treatment indications considering the histopathology criteria determined by the SUT. Although patients vary according to the centers they go to, the percentage of treatment also varies, and the percentage of receiving treatment according to the centers is 58±15% on average. The percentages of receiving treatment are shown in Table 5.

Discussion

Liver histopathology in patients with chronic HBV is still the gold standard for demonstrating liver status. There are several scoring systems developed to create a standard approach in this regard (2). Although these scoring systems were created to ensure harmony between observers, various differences may occur due to the subjective perspective of the observers in the evaluation. While these differences decrease among intracentral

Table 2. Demographic and biochemical characteristics of the patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Gender	Male	Female	Male	Female	Female	Male	Male	Female	Male	Female
Age (year)	44	35	57	40	61	28	22	41	32	58
HBeAg	Positive	Positive	Negative	Positive	Negative	Negative	Positive	Negative	Negative	Positive
HBV DNA IU/mL	32,857,266	204,764	14,516	263,113729	64,8241	28,515	180,685,412	25,279	6,664,000	23,764,512
ALT IU/ mL	311	215	94	26	44	45	64	28	67	118
AST IU/ mL	652	162	59	22	51	33	34	28	41	83
WBC mL	5,420	4,700	7,570	6,500	5,320	8,300	7,700	6,700	10,420	6,270
Hgb g/dL	15.1	9.9	14.6	11.7	13.4	12.3	13.4	12.8	14.4	12.1
PLT 10^3/mL	158	323	179	242	149	302	208	201	353	145
MPV fL	11.3	8.8	9.7	10.6	9.3	9.3	10	9.2	11.2	9.8
INR	1.2	0.9	1.04	1.09	1.04	0.9	1.2	0.96	1.1	1.1
GGT IU/L	107	95	15	16	20	25	15	12	22	127
ALP IU/L	92	127	76	29	127	75	68	91	81	157
Alb g/dL	4.3	4.4	3.7	4.5	3.7	3.8	5.1	3.6	3.8	3.8
Glob g/dL	3.5	2.8	4	3	4	2.9	2.4	3.2	3.7	3.9

Table 3. Scores of the patients according to the centers HAI total [categories (A+B+C+D)]/fibrosis

	Center 1	Center 2	Center 3	Center 4	Center 5
Patient 1	3 (1+0+1+1)/1	4 (2+0+1+1)/1	6 (1+1+2+2)/1	4 (1+0+1+2)/1	7 (2+0+2+3)/3
Patient 2	6 (1+0+2+3)/1	6 (2+0+2+2)/2	7 (2+1+1+3)/2	7 (2+1+1+3)/2	7 (2+0+2+3)/4
Patient 3	5 (1+2+1+1)/2	3 (1+0+1+1)/1	4 (1+1+1+1)/1	1 (0+0+1+0)/1	3 (1+0+1+1)/1
Patient 4	6 (1+0+3+2)/0	5 (1+0+2+2)/0	5 (1+0+2+2)/0	3 (1+0+1+1)/1	7 (2+0+2+3)/2
Patient 5	6 (2+0+3+1)/3	6 (1+1+2+2)/3	8 (2+1+3+2)/3	4 (1+0+2+1)/3	10 (3+2+2+3)/5
Patient 6	3 (0+0+2+1)/1	4 (1+0+2+1)/1	4 (1+0+2+1)/1	3 (1+0+1+1)/1	3 (1+0+1+1)/2
Patient 7	2 (0+0+1+1)/2	3 (1+0+1+1)/1	2 (0+0+1+1)/1	3 (1+0+1+1)/2	5 (1+0+2+2)/2
Patient 8	3 (0+0+2+1)/1	4 (0+1+2+1)/0	2 (0+0+1+1)/0	1 (0+0+1+0)/1	3 (1+0+1+1)/1
Patient 9	12 (2+4+3+3)/3	7 (2+1+2+2)/3	10 (3+1+3+3)/3	9 (3+0+3+3)/2	9 (3+0+3+3)/5
Patient 10	10 (4+0+3+3)/6	7 (3+0+2+2)/5	15 (4+4+3+4)/5	6 (3+0+1+2)/4	13 (3+2+4+4)/5

observers, they increase among intercentral observers (4). This situation was also stated in a study published in the Journal of Hepatology, the publication organ of EASL, in 2020 (11).

Today, the most commonly used liver histopathological examination score in patients with chronic HBV is the Modified Isaac scoring system (8). In our study, fibrosis, HAI category A (Interphase hepatitis) and D (portal inflammation) results were found to be highly compatible in the interobserver evaluations in different centers. However, HAI category C (focal necrosis) was found to be acceptable at an acceptable level among observers, while HAI category B (confluent necrosis) was found to be inconsistent. In a study conducted in our country, fibrosis was

Table 4. Calculated coefficients

	Coefficient (*,**)
Category A	0.8186*
Category B	0.3147*
Category C	0.6309*
Category D	0.8217*
HAI total	0.8753*
Fibrosis staging	0.8635*
Treatment decision	0.8207**

*Kendall's coefficient of agreement W, **Kuder-Richardson Confidence coefficient (K-R 20), HAI: Histological activity index

Table 5. Percentages and details of receiving treatment by patients and centers

Can the patient get treatment? (Yes/no)

	Center 1	Center 2	Center 3	Center 4	Center 5	Percentage of receiving treatment
Patient 1	No	No	Yes	No	Yes	40%
Patient 2	Yes	Yes	Yes	Yes	Yes	100%
Patient 3	Yes	No	No	No	No	20%
Patient 4	Yes	No	No	No	Yes	40%
Patient 5	Yes	Yes	Yes	Yes	Yes	100%
Patient 6	No	No	Yes	No	Yes	40%
Patient 7	No	No	No	Yes	Yes	40%
Patient 8	No	No	No	No	No	0%
Patient 9	Yes	Yes	Yes	Yes	Yes	100%
Patient 10	Yes	Yes	Yes	Yes	Yes	100%
Percentage of receiving treatment	60%	40%	60%	50%	80%	

found to be compatible between observers, category D was moderate, and category A and C were weakly compatible. In their study, Westin et al. (4) found the interobserver category C assessment to be of low agreement.

In the presence of cirrhosis, it is common to obtain fragmented tissue during liver biopsy. The presence of fragmentation in the tissue may also cause the fibrosis value to be scored lower (12). The liver lobe where the biopsy is performed may also cause differences in fibrosis scoring. However, even if the lobes from which the biopsy is taken are different, the fibrosis scoring may be consistent between the observers, while the HAI evaluation may be inconsistent between the observers (13).

The ultimate goal in many liver diseases is to prevent liver fibrosis, failure, cirrhosis and hepatocellular carcinoma (14). In studies, it is emphasized that the samples taken by biopsy may not show the pathology in the liver completely due to the fact that liver biopsy samples only 50 thousandths of the liver and that the heterogeneous distribution of chronic viral hepatitis in the liver (14). Nowadays, various serum biomarkers or radiological evaluation methods, in which the elasticity of the liver is measured, are more preferred instead of an invasive method such as biopsy in evaluating the status of the liver in chronic viral HBV infections (1,14).

As far as we can research, there is no study in the literature on how the interobserver agreement, which is another aim of our study, is reflected in the treatment. While all of the patients included in the study had an indication for initiation of treatment according to the 2017 EASL guideline (10), it was found that only 58% of the patients met the indication for initiation of treatment according to the histopathological criteria determined by the SUT. These indication rates vary considerably between centers. This situation may cause delay in initiation of treatment in patients and may cause progression of liver damage.

Study Limitations

The fact that the length of the biopsy specimens and whether they were fragmented were not taken into account was a limitation of the study. The small number of samples was another limiting factor.

Conclusion

In our country, where histopathological evaluations are accepted as criteria for starting treatment in patients with chronic HBV, incompatibility between observers in different centers may cause differences in treatment initiation rates. This situation needs to be investigated in larger studies.

Ethics

Ethics Committee Approval: The ethics committee approval of our study was obtained from the Clinical Research Ethics Committee of Bakırköy Dr Sadi Konuk Training and Research Hospital with the decision number 2019/94.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: Z.S.K., A.N.T.Y., A.G.S., G.Ç., M.C., Concept: Y.D., Z.S.K., M.C., Design: Y.D., Z.S.K., A.N.T.Y., A.G.S., G.Ç., M.C., Data Collection or Processing: Y.D., Z.S.K., A.N.T.Y., A.G.S., G.Ç., M.C., Analysis or Interpretation: Y.D., Literature Search: Y.D., Z.S.K., M.C., Writing: Z.S.K.

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Original Article

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Prevalence of Electrolyte Impairments Among Outpatient Elderly Subjects

Ayaktan Takip Edilen Yaşlı Bireylerde Elektrolit İmbalanslarının Prevalansı

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ABSTRACT

Objective: To determine the prevalence of different electrolyte imbalances in a cohort of elderly subjects aged ≥65 years, and evaluate associations between each electrolyte imbalance and functional dependence.

Methods: We reviewed medical records of consecutive outpatient elderly subjects. Frequency of hyponatremia (serum sodium of <136 mmol/L), hypernatremia (serum sodium of >145 mmol/L), hypokalemia (serum potassium of <3.5 mEq/L), hyperkalemia (serum potassium of >5.3 mEq/L), hypocalcemia (serum calcium of <8.5 mg/dL), hypercalcemia (serum calcium of >10.5 g/dL), hypophosphatemia (serum phosphorus of <2.5 mg/dL), hyperphosphatemia (serum phosphorus of >4.5 mg/dL), hypomagnesemia (serum magnesium of <1.6 mg/dL), and hypermagnesemia (serum magnesium of >2.3 mg/dL) were assessed. Associations between each electrolyte disorder and Barthel and Lawton-Brody activities of daily living (BADL and IADL) were analyzed.

Results: Among the 464 subjects, hyponatremia (11.2%) hypomagnesemia (9.1%) and hypermagnesemia (8.8%) were the most common disorders. Patients with one electrolyte imbalance constituted 30.2% (140 patients) of the cohort, while 44 (9.5%) had two, and 7 (1.5%) patients had ≥2 electrolyte imbalances, concurrently. Calcium, phosphorus, and magnesium disorders were more common among subjects who were 80 years of age or more, compared to those aged 65-79 years, while the frequency of potassium disorders was lower in the former group. Hyponatremia

ÖZ

Amaç: Yaşlı bireylerden (≥65 yaş) oluşan bir kohortta farklı elektrolit bozukluklarının sıklığının belirlenmesi ve her bir bozukluğun fonksiyonel bağımlılık ile ilişkisinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Ardışık olarak ayaktan takip edilen yaşlı bireylerin tıbbi kayıtları geriye dönük incelendi. Hiponatremi (serum sodyum <136 mmol/L), hipernatremi (serum sodyum >145 mmol/L), hipokalemi (serum potasyum <3,5 mEq/L), hiperkalemi (serum potasyum >5,3 mEq/L), hipokalsemi (serum kalsiyum <8,5 mg/dL), hiperkalsemi (serum kalsiyum >10,5 g/dL), hipofosfatemi (serum fosfor <2,5 mg/dL), hiperfosfatemi (serum fosfor >4,5 mg/dL), hipomagnezemi (serum magnezyum <1,6 mg/dL) ve hipermagnezemi (serum magnezyum >2,3 mg/dL) sıklıkları değerlendirildi. Her bir elektrolit bozukluğunun Barthel ve Lawton-Brody günlük yaşam aktiviteleri skorları (BADL and IADL) ile ilişkileri analiz edildi.

Bulgular: Dahil edilen 464 bireyde, hiponatremi (%11,2) hipomagnezemi (%9,1) ve hipermagnezemi (%8,8) en sık bozukluklar olarak dikkati çekti. Bir elektrolit bozukluğu olan hastalar kohortun %30,2'sini (140 hasta) oluştururken, 44 (%9,5) hastada iki ve 7 (%1,5) hastada 2 ve üzeri elektrolit imbalansı saptandı. Kalsiyum, fosfor, ve magnezyum bozuklukları 80 yaş ve üzeri bireylerde 65-79 yaş aralığı bireylere kıyasla daha sık görülürken, potasyum bozuklukları ilk grupta daha az sıklıkta idi. Hiponatremi ve hipokalseminin BADL ve IADL skorlarına göre fonksiyonel bağımlılıkla anlamlı derecede birlikte görüldüğü

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and hypocalcemia were associated with functional dependence based on BADL and IADL scores. Patients with multiple electrolyte abnormalities had a higher risk of functional dependence.

Conclusion: Hypomagnesemia was as common as hyponatremia, especially among patients with an age of 80 years or more. Hyponatremia and hypocalcemia appeared to be associated with functional dependence. The higher number of electrolyte abnormality the higher risk of functional dependence. Our results should be confirmed by studies with larger sample sizes.

Keywords: Elderly, electrolyte, magnesium

saptandı. Eş zamanda çok sayıda elektrolit bozukluğu olan kişilerin fonksiyonel bağımlık riskinin arttığı gözlendi.

Sonuç: Hipomagnezemi hiponatremi kadar sık olup, özellikle 80 yaş ve üzeri bireylerde daha sıktır. Hiponatremi ve hipokalsemi fonksiyonel bağımlılık ile ilişkili görünmektedir. Elektrolit bozukluklarının sayısı arttıkça fonksiyonel bağımlılık riski de artmaktadır. Sonuçlarımız daha büyük çalışmalarca doğrulanmalıdır.

Anahtar Sözcükler: Yaşlı, elektrolit, magnezyum

Introduction

Electrolyte imbalances are common in the elderly and prevalences are increased by age (1,2). Elderly patients may be more prone to develop electrolyte abnormalities due to physiological changes of the kidney (3). Electrolyte abnormalities may be associated with a longer hospital stay or mortality among subjects who are admitted to hospital (4). Many previous studies have shown that hyponatremia is the most common electrolyte disorder in the elderly (3). Although the current literature suggests that hyponatremia is the most prevailing electrolyte abnormality, the prevalence of various electrolyte abnormalities has rarely been studied in the same cohort. Liamis et al. (1) recruited subjects who were aged 55 years or more from the general population and assessed electrolyte abnormalities and risk factors for these disorders. However, they mainly focused on hyponatremia, hypernatremia, hypokalemia, hyperkalemia, and hypomagnesemia. Another study investigated the frequency of electrolyte disorders (4), but the age cut-off for inclusion criteria was 18 years or older. Moreover, the study sample comprised of subjects who were admitted to emergency department. Several electrolyte disorders in these studies were associated with mortality, longer hospital stay and/or readmission.

Despite the wide range of studies, no study has evaluated frequency of all electrolyte abnormalities in an elderly outpatient setting. In this paper, we aimed to evaluate the frequency of sodium, potassium, calcium, phosphorus, and magnesium abnormalities in serum of elderly subjects who were admitted to a single outpatient geriatric clinic in Turkey.

Methods

This study was approved by the Institutional Review Board of our institution (IRB code: 54022451-050.05.04-; 25.08.2020). Patients who presented to out patient geriatric clinics between July 2016 through April 2020 were included. All participants were ≥65 years of age. Their demographic data were recruited from patient files.

The definitions for each electrolyte abnormality were as follows:

- Hyponatremia: serum sodium concentration of <136 mmol/L (5).
- Hypernatremia: serum sodium concentration of >145 mmol/L (6).
- Hypokalemia: serum potassium concentration of <3.5 mmol/L (7).
- Hyperkalemia: serum potassium concentration of >5.3 mmol/L (7).
- Hypocalcemia: serum calcium (total) concentration of <8.5 mg/dL (8).
- Hypercalcemia: serum calcium (total) concentration of >10.5 mg/dL (8).
- Hypophosphatemia: serum phosphorus concentration of <2.5 mg/dL (9).
- Hyperphosphatemia: serum phosphorus concentration of >4.5 mg/dL (9).
- Hypomagnesemia: serum magnesium concentration of <1.6 mg/dL (10).
- Hypermagnesemia: serum magnesium concentration of >2.3 mg/dL (9).

Sodium and calcium concentrations were corrected for blood glucose and serum albumin levels. All of the measurements were performed as a part of the comprehensive geriatric assessment.

Associations between each of electrolyte imbalance with basic activities of daily living (BADL) and instrumental activities of daily living (IADL) were assessed. The BADL is a scale that includes 10 questions about the ability to provide self-care, use toilet, get dressed, eat, urinary and fecal continence, use the stairs, move from bed to chair, and mobility (11). Scoring is as follows:

- 0-20 points, completely dependent
- 21-61 points, severely dependent
- 62-90 points, moderately dependent
- 91-99 points, mildly dependent
- 100 points, independent

The Lawton-Brody IADL index has been proposed as a means to determine the instrumental activities of daily living of

subjects, which includes 8 questions about telephone usage, preparing meals, shopping, doing daily house works, laundry, transportation, taking pills, and money management (12).

The scoring is as follows:

• 0-8 points, dependent

• 9-16 points, semi-dependent

• 17-24 points, independent

The Mini Nutritional Assessment (MNA) was used for nutritional evaluation. A total MNA score of <17 was accepted as malnutrition (13).

Statistical Analysis

Quantitative variables were expressed as median with the interquartile range (25-75%). Qualitative variables were expressed as proportions. Groups were compared for means using the Mann-Whitney U test or the Kruskal-Wallis test, as appropriate. Chi-squared tests were used for comparisons between proportions. Associations between each electrolyte abnormality and ADL indexes were assessed by logistic regression analysis. Results were expressed as odds ratios and 95% confidence intervals for logistic regression. Statistical analysis was performed using SPSS 22.0 version (IBM SPSS, Chicago, IL). A P value of 0.05 or lower was considered to be statistically significant.

Results

Among the 1,802 consecutively evaluated elderly subjects, 1,310 lacking electrolyte measurements and 28 with no ADL evaluation were excluded. Finally, the cohort included 464 patients. The median age was 78 (72-83) years and 321 (69.2%) were women. Hypertension (HT), diabetes mellitus (DM), and chronic kidney disease (CKD) were present in 69%, 36%, and 39% of the subjects, respectively. Overall, 195 (41.2%) patients had at least one electrolyte imbalance. The frequency of each disorder was as follows: hyponatremia, 11.2%; hypernatremia, 1.7%; hypokalemia, 1.7%; hyperkalemia, 6.7%; hypocalcemia, 4.7%; hypercalcemia, 2.6%; hypophosphatemia, 5.0%; hyperphosphatemia, 2.6%; hypomagnesemia, 9.1%; and hypermagnesemia, 8.8%.

Hyponatremia

A total of 52 patients (11.2%) had hyponatremia . The median sodium level was 140 (138-142) mmol/L. Median glomerular filtration rate among patients with hyponatremia was lower than patients with normonatremia, but this was not statistically significant (median 63 versus 69 mL/min/1.73 m^2, p=0.064). Median BADL and IADL scores were 76 versus 85 and 8 versus 14 among patients with hyponatremia and normonatremia, respectively (p values 0.001 and 0.016, respectively). The median age and sex distribution were comparable between hyponatremia and normonatremia groups.

For the BADL, dependence was more commonly observed among patients with hyponatremia (p=0.005, Table 2). This was also the case based on the IADL scores (p=0.027). The association between hyponatremia and the grade of dependency based on BADL remained significant in patients with an age of 80 years or older, while the significance was lost in patients with an age of 65 to 79 years. In the contrary, the association between hyponatremia and the grade of dependency based on the IADL was significant for patients with an age of 65 to 79 years, but not for those who were ≥80 years of age. Although more commonly seen in subjects with chronic kidney disease, and those who were exposed to thiazide diuretics and overall anti-hypertensives, we could not observe a significant association between hyponatremia and any of these factors.

Hypernatremia

Only 8 (1.7%) patients had hypernatremia by definition. All of the patients had a serum sodium of 146 mmol/L. In this group with a quite low sample size, we could not find a significant association between age, sex, drug exposures, and BADL/IADL scores with hypernatremia.

Hypokalemia

Only 8 (1.7%) patients had hypokalemia, with a median potassium level of 3.2 (2.9-3.4) mEq/L. Similar to the hypernatremia group, we could not find a significant association between age, sex, drug exposures, and BADL/IADL scores and hypernatremia. None of the 8 patients with hypokalemia had chronic kidney disease.

Hyperkalemia

Thirty-one (6.7%) patients had hyperkalemia, with a median serum potassium of 5.6 (5.5-5.9) mEq/L. The median estimated glomerular filtration rate (eGFR) of patients with hyperkalemia was significantly lower in comparison to patients with normokalemia (53 vs 69 mL/min/1.73 m^2, p<0.001). Age and sex distribution were comparable across groups. Patients with hyperkalemia were more likely to have dependence based on BADL and IADL total scores, and there was trend toward significance for each comparison (p=0.059 for both comparisons). Significances were lost when hyperkalemia versus normokalemia were compared for different categorizations of BADL and IADL indexes.

Hypocalcemia

Twenty-two (4.7%) patients had hypocalcemia, with a median serum total calcium of 8.3 (8.1-8.4) mg/dL. Similar to patients with hyperkalemia, patients with hypocalcemia had a lower median eGFR compared to patients with normal serum calcium levels (48 vs 68 mL/min/1.73 m^2, p=0.035). In addition to a lower median eGFR value, patients with hypocalcemia had a higher median serum magnesium level (2.1 versus 1.9 mg/dL, p=0.04). Age and sex distributions were comparable, but patients with hypocalcemia were significantly more dependent based on BADL and IADL scores (p values 0.004 and <0.001, respectively). This was also significant when BADL and IADL categorizations were assessed for associations with hypocalcemia.

Hypercalcemia

Of the 12 (2.6%) patients with hypercalcemia, the median serum calcium level was 10.9 (10.7-10.9) mg/dL. The highest serum calcium was 11.0 mg/dL. No significant association was found in terms of age, sex, drug exposures, kidney functions, and BADL/IADL scores in comparisons between hypercalcemia versus normocalcemia groups.

Hypophosphatemia

Of the 23 patients with hypophosphatemia, the median serum phosphate was 2.3 (2.1-2.4) mg/dL. DM was recorded in 37% of patients with normophosphatemia versus 13.6% of patients with hypophosphatemia. Similarly, CKD was also more common in the latter group, although not significant. Patients with normophosphatemia were more likely to be dependent based on BADL scores, but not IADL scores.

Hyperphosphatemia

Median phosphorus level of 12 subjects with hyperphosphatemia was 5.0 (4.7-5.3) mg/dL. According to IADL scores, patients with hyperphosphatemia were more likely to be dependent (p=0.065).

Table 1. General characteristics of the total cohort.

Variable	
Age, years	78 (72-83)
Female sex	69.2%
Comorbidities	
Diabetes mellitus	36%
Hypertension	69%
Chronic kidney disease	39%
Heart failure	11%
Ischaemic heart disease	15%
Cerebrovascular disease	13%
Drug exposures	
Insulin	15%
ACEi/ARB	58%
Beta-blockers	24%
Loop diuretics	5%
Thiazides	48%
Spironolactone	2%
Polypharmacy	43%
Hemoglobin, g/dL	12.6 (11.4-13.8)
Serum creatinine, mg/dL	0.89 (0.75-1.15)
Glomerular filtration rate, ml/min/1.73 m^2	68 (50-83)
Serum sodium, mmol/L	140 (138-142)
Serum potassium, mmol/L	4.4 (4.1-4.8)
Serum magnesium, mmol/L	2.0 (1.8-2.1)
Serum calcium, mmol/L	9.4 (9.1-9.8)
Serum phosphorus, mmol/L	3.3 (3.0-3.7)

Numerical variables are presented as median with the interquartile range (25-75%). ACEi/ARB: Angiotensin converting enzyme inhibitor/angiotensin receptor blocker

Table 2. Associations of electrolyte abnormalities with instrumental activities of daily living scores.

The Barthel BADL	$HypoNa^+$ versus $NormoNa^+$	$HyperNa^+$ versus $NormoNa^+$	$HypoK^+$ versus $NormoK^+$	$HyperK^+$ versus $NormoK^+$	$HypoCa^{++}$ versus $NormoCa^{++}$	$HyperCa^{++}$ versus $NormoCa^{++}$	$HypoPO_4^-$ versus $NormoPO_4^-$	$HyperPO_4^-$ versus $NormoPO_4^-$	$HypoMg^{++}$ versus $NormoMg^{++}$	$HyperMg^{++}$ versus $NormoMg^{++}$
Complete Dependence	11.5%/4.2%	0.0%/4.2%	0.0%/4.9%	6.5%/4.9%	27.3%/4.0%	0.0%/4.0%	0.0%/5.1%	8.3%/5.1%	2.4% / 4.5%	12.2% / 4.5%
severe Dependence	25.0%/15.8%	0.0%/15.8%	25.0%/16.0%	22.6%/16.0%	27.3%/16.3%	8.3%/16.3%	8.7%/17.2%	8.3%/17.2%	31.0% / 15.0%	17.1% / 15.0%
moderate Dependence	44.2%/44.1%	37.5%/44.1%	37.5%/43.5%	51.6%/43.5%	31.8%/43.7%	75.0%/43.7%	47.8%/44.1%	33.3%/44.1%	45.2% / 44.9%	34.1% / 44.9%
Mild dependence	17.3%/17.3%	37.5%/17.3%	25.0%/17.9%	12.9%/17.9%	9.1%/18.1%	16.7%/18.1%	4.3%/18.4%	16.7%/18.4%	9.5% / 18.6%	17.1% / 18.6%
Independence	1.9%/18.6%	25.0%/18.6%	12.5%/17.6%	6.5%/17.6%	4.5%/17.9%	0.0%/17.9%	39.1%/15.2%	33.3%/15.2%	11.9% / 17.1%	19.5% / 17.1%
p-value	0.005	0.454	0.879	0.424	<0.001	0.226	0.015	0.468	0.072	0.239
The Lawton-Brody IADL	$HypoNa^+$ versus $NormoNa^+$	$HyperNa^+$ versus $NormoNa^+$	$HypoK^+$ versus $NormoK^+$	$HyperK^+$ versus $NormoK^+$	$HypoCa^{++}$ versus $NormoCa^{++}$	$HyperCa^{++}$ versus $NormoCa^{++}$	$HypoPO_4^-$ versus $NormoPO_4^-$	$HyperPO_4^-$ versus $NormoPO_4^-$	$HypoMg^{++}$ versus $NormoMg^{++}$	$HyperMg^{++}$ versus $NormoMg^{++}$
Dependent	53.8%/35.1%	0.0%/35.1%	37.5%/35.8%	48.4%/35.8%	59.1%/35.8%	25.0%/35.8%	30.4%/37.5%	16.7%/37.5%	47.6% / 34.4%	46.3% / 34.4%
semi-dependent	19.2%/22.8%	50.0%/22.8%	12.5%/22.6%	29.0%/22.6%	18.2%/22.8%	33.3%/22.8%	21.7%/22.1%	50.0%/22.1%	26.2% / 22.8%	19.5% / 22.8%
Independent	26.9%/42.1%	50.0%/42.1%	50.0%/41.6%	22.6%/41.6%	22.7%/41.4%	41.7%/41.4%	47.8%/40.3%	33.3%/40.3%	26.2% / 42.8%	34.1% / 42.8%
p-value	0.027	0.066	0.781	0.112	0.079	0.623	0.741	0.065	0.102	0.312

BADL: basic activities of daily living. IADL: instrumental activities daily of living.

Table 3. Frequency of electrolyte disorders according to different age groups.

Electrolyte impairment	Overall	65-79 years (n=269)	≥80 years (n=195)
Hyponatremia	52 (11.2%)	30 (11.2%)	22 (11.3%)
Hypernatremia	8 (1.7%)	5 (1.9%)	3 (1.5%)
Hypokalemia	8 (1.7%)	6 (2.2%)	2 (1.0%)
Hyperkalemia	31 (6.7%)	22 (8.2%)	9 (4.6%)
Hypocalcemia	22 (4.7%)	12 (4.5%)	10 (5.1%)
Hypercalcemia	12 (2.6%)	6 (2.2%)	6 (3.1%)
Hypophosphatemia	23 (5.0%)	10 (3.7%)	13 (6.7%)
Hyperphosphatemia	12 (2.6%)	5 (1.9%)	7 (3.6%)
Hypomagnesemia	42 (9.1%)	20 (7.5%)	22 (11.3%)
Hypermagnesemia	41 (8.8%)	21 (7.9%)	20 (10.3%)

Hypomagnesemia

Forty-two patients had hypomagnesemia, and the median serum magnesium level was 1.5 (1.4-1.6) mg/dL. The frequency of hypomagnesemia was higher in patients with an age of >79 years compared to those with an age of 65 to 79 years. However, the severity of hypomagnesemia was similar. Hypomagnesemia was associated with dependency based on BADL and IADL scores (p=0.072 and 0.102, respectively). Patients with hypomagnesemia were older than patients with normomagnesemia, although not significant (median 81 vs 78, p=0.114).

Hypermagnesemia

Forty-one patients had hypermagnesemia, and they had a median serum magnesium of 2.4 (2.3-2.8) mg/dL. Similar to hypomagnesemia, hypermagnesemia was more common in ages over 79, but the severity of the disorder was comparable across age groups. The frequency of dependency was not significantly higher among subjects with hypermagnesemia.

Interrelationships Between Electrolyte Abnormalities

There was no significant association between hypernatremia, hypokalemia, hypophosphatemia and other electrolyte disorders. The following associations were noted:

Hyponatremia: Patients with hyponatremia were more likely to have hypokalemia compared to patients without hyponatremia (15.4% versus 5.6%, p=0.008). Similarly, hypocalcemia was also more commonly observed among patients with hyponatremia (11.5% versus 3.9%, p=0.014). Patients with hyperkalemia more commonly had hyperphosphatemia compared to non-hyperkalemia (p<0.001).

Hyperphosphatemia was present in 12.9% of patients with hyperkalemia while in 1.8% of those without hyperkalemia had hyperphosphatemia (p<0.001).

Hypocalcemia: Hyperphosphatemia was more common in patients with hypocalcemia versus normocalcemia (9.1% vs 2.3%, p=0.049). Hypermagnesemia was seen in 31.8% of patients with hypocalcemia versus 7.7% of patients with normocalcemia (p<0.001).

Hypercalcemia: Twenty-five percent of patients with hypercalcemia had hypermagnesemia versus 8.4% of those without hypercalcemia had hypermagnesemia (p=0.080).

Hyperphosphatemia: Of the patients with hyperphosphatemia, 25.0% had hypermagnesemia, while 8.2% of without hyperphosphatemia had hypermagnesemia (p=0.015). Similarly, hyperkalemia (25.0% versus 6.0%, p<0.001) was more common in patients with hyperphosphatemia.

Hypomagnesemia: Hyperkalemia was more common in patients with hypomagnesemia versus non-hypomagnesemia (14.3% versus 5.9%, p=0.005). The majority of patients with hypomagnesemia plus hyperkalemia had DM (5 of 6 patients) versus 35.2% of the remaining (p=0.024).

Hypermagnesemia: Of the 41 patients with hypermagnesemia 17% had hypocalcemia versus 3.5% of those without hypermagnesemia had hypocalcemia (p<0.001). In the former group, 9.8% had hyperphosphatemia while 1.9% of the latter had hyperphosphatemia (p=0.015).

Associations with Age

Patients were divided into 2 groups in terms of age: 65-79 years and >79 years. The former group more commonly had DM (4.1% vs 28.0%, p=0.003) and less frequently had CKD (32.0% vs 48.7%, p<0.001). Calcium, phosphorus, and magnesium disorders were more common among subjects who were aged 80 years or more, compared to those aged 65-79 years, while frequency of potassium disorders were lower in the former group (Table 3).

Associations with Comorbidities

The CKD comprised 91.7% of patients with hyperphosphatemia while 37.6% of patients without hyperphosphatemia had CKD (p<0.001). Similarly, CKD was more common among patients with hyperkalemia versus non-hyperkalemia group (71% versus 36.7%, p<0.001). None of the 8 patients with hypokalemia had CKD, in comparison, 39.7% of patients with non-hypokalemia had CKD (p=0.018).

The DM was present in 70.7% of patients with hypomagnesemia and 32.4% of those without hypomagnesemia (p<0.001). This was in contrast to hypermagnesemia, 21.4% of whom had DM versus 36.9% in patients with non-hypermagnesemia (p=0.111). Similarly, patients with hypophosphatemia less frequently had DM than non-hypophosphatemic group (13.6% versus 36.9%, p=0.026). DM was more frequent among hyperkalemic subjects in comparison to non-hyperkalemia (61.3% versus 34.0%, p=0.002).

There was a reverse association between HT and hypophosphatemia. Half of these patients had HT while 69.6% of patients without hypophosphatemia had HT (p=0.048).

Associations with Drug Exposures

Detailed descriptions of drug exposures were available in 449 subjects. A quarter of patients with hypophosphatemia had hyperpolypharmacy versus 3.3% of non-hypophosphatemics had hyperpolypharmacy, and there was trend towards significance (p=0.057). No other association was found with polypharmacy or hyperpolypharmacy and any electrolyte abnormality.

Associations with Malnutrition

The MNA score was available in 212 subjects. Among patients with hypermagnesemia, 36.8% had malnutrition, and a similar percent were at risk of malnutrition, while 9.8% and 43.0% of patients without hypermagnesemia had malnutrition and were at risk of malnutrition, respectively (p=0.002).

Multiple Electrolyte Abnormalities

Forty-four (9.5%) had two, and 7 (1.5%) had more than two concurrent electrolyte abnormalities. The most common disorders seen together were hyponatremia plus hypomagnesemia, and hyponatremia plus hyperkalemia each of which were concurrently seen in 8 (1.7%) patients. CKD was present in 35.2%, 40.7%, and 54.9% of patients with no electrolyte abnormality, single abnormality, and multiple abnormalities, respectively (p=0.026). Age, sex, and the frequency of DM were comparable among patients with no electrolyte abnotmality, single abnormality, and multiple abnormalities. Median BADL score for no abnormality, single abnormality, and multiple abnormalities were 85 (70-95), 85 (65-95), and 80 (50-90), respectively (p=0.014). Median IADL score for same groups were 15 (6-20), 14 (5-20), and 10 (5-17), respectively (p=0.08).

Discussion

Our study is the first to evaluate all electrolyte disorders in a single same cohort. The cohort included elderly subjects, who were more prone to develop such imbalances given the increased sensitivity to drug exposures and effects of comorbidities (3). We showed that magnesium disorders comprised the largest part of all abnormalities, particularly among subjects who were aged 80 years or more. Similarly, phosphate disorders were more common after the age of 80 years. In contrast, potassium disorders were less frequently observed in patients with an age of ≥80 years, in comparison to those aged 65 to 79 years. Others reported dramatical increase in prevalences of hyponatremia and hyperkalemia with increasing age, but no such effect for hypernatremia and hypokalemia (14). Given that CKD was more common in the elderly, it is not unexpected to see an increase in the prevalence of hypermagnesemia with aging. However, it was worth to note that, hypomagnesemia was common after 80 years of age, despite the increased frequency of CKD and decreased frequency of DM. The majority of electrolyte imbalances were mild. However, sodium and calcium disorders were significantly associated with dependency based on BADL and IADL indexes. Furthermore, coexistent electrolyte abnormalities were more likely to be associated with dependency.

We recognized the limitation that at least some part of the association with dependency might come from comorbidities such as DM or CKD. Several abnormalities in our cohort were significantly associated with those comorbidities. Liamis et al. (1) studied the prevalence and risk factors of common electrolyte disorders in subjects with an age of 55 years or more who were recruited from the general population. The study mainly focused on hyponatremia, hypernatremia, hypokalemia, hyperkalemia, and hypomagnesemia. Fifteen percent of their cohort had at least one electrolyte disorder, hyponatremia and hypernatremia being the most common disorders. Similar to our study, they found that DM was associated with hyponatremia and hypomagnesemia, while HT was an independent risk factor for hypokalemia. Authors stated that hyponatremia and hypomagnesemia were independently associated with an increased risk of death. Unlike our results, they observed significant associations between use of diuretics, and benzodiazepines with particular electrolyte abnormalities. High prevalence of electrolyte abnormalities was also shown by Woyesa et al. (15). Forty-two percent of their patients with DM had at least one electrolyte abnormality. Some of the associations between comorbidities and electrolyte disorders may be bi-directional. For instance, patients with DM usually have a lower serum magnesium level, while hypomagnesemia itself is associated with a higher risk of DM (16).

Homeostasis of all electrolytes depends on the balance between gastrointestinal absorption and kidney excretion (17). Kidney functions appear to be the most prevailing factor to increase the frequencies of several electrolyte abnormalities in our study, including hyperkalemia, hypermagnesemia, hyperphosphatemia, and hypocalcemia. All of electrolyte abnormalities were mild in our study. However, sample sizes in each group were low, which questioned the representativeness of the sample hindering concrete conclusions. Malnutrition and drug exposures may be other crucial factors that may lead to several electrolyte imbalances. Deficiency of the majority of the ions, particularly hypophosphatemia and hypomagnesemia may in part occur secondary to poor oral intake. Yet, we could not demonstrate a significant association between malnutrition and various electrolyte disorders. Similarly, we expected to observe several associations between particular drug therapies and electrolyte disorders. Although some disorders were common in the case of usage several drugs, none of these associations reached a statistical significance. This might be explained by the multiple

coexistent factors for each electrolyte disorder. For instance, patients with CKD are more likely to have hyperkalemia. On the other hand, these subjects are more likely to receive loop diuretics which commonly cause hypokalemia. If the cause of CKD is DM, than the risk of hyperkalemia is increased due to hyporeninemic hypoaldosteronism. This is the likely explanation for the lack of observation of a significant association between hyperkalemia and drug exposures in subjects who have received renin-angiotensin-aldosteron system inhibitors, or hypokalemia with thiazides and loop diuretics. It is worth to note that considerable interrelationships may also exist across different electrolyte disorders.

Study Limitations

Our study had several limitations. Given the retrospective design, a cause and effect relationship could not be established. Only single serum measurements was available. Some groups included quite low sample sizes questioning the representativeness of the study findings. There are many confounding factors that may cause electrolyte imbalance, and have different impact on functional dependence. Importantly, some of the electrolytes (potassium, magnesium, and phosphorus) are primarily involved in the intracellular compartment, which makes it hard to reach a solid conclusion. On the other hand, we used the same measurement methods which were routinely used in clinical practice while assessing such disorders. However, our study was the first to evaluate prevalence of various electrolyte abnormalities in the same elderly outpatient population, which was the main aim of this paper. This study had a small sample size for assessing frequency of electrolyte abnormalities, so our results should be confirmed by studies with larger sample sizes.

Conclusion

Electrolyte abnormalities are common in outpatient elderly settings and are associated with dependency. Although hyponatremia is the most frequent electrolyte disorder, in total, magnesium abnormalities comprise the largest part and may require special attention.

Ethics

Ethics Committee Approval: Bezmialem University Non-Interventional Research Ethics Committee (01.09.2020).

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: C.H., R.K., Design: C.H., R.K., L.S., P.S., Data Collection or Processing: S.G.T., P.S., Analysis or Interpretation: C.H., S.G.T., R.K., L.S., P.S., Literature Search: C.H., S.G.T., Writing: C.H., L.S., P.S.

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Original Article

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Mapping and Monitoring During Surgery for Congenital Spinal Malformation

Konjenital Spinal Malformasyon Cerrahisinde Haritalama ve Monitörizasyon

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ABSTRACT

Objective: Surgery of complex congenital spinal malformations has a risk to damage functional neural structures. Intraoperative neurophysiological monitoring for congenital spinal pathologies is suggested to reduce this risk for neural tissues and thus improve the surgical results. Our aim is to evaluate which patients are liable to reveal critical neurophysiological changes during surgery by presenting our intraoperative neurophysiological approach and the early clinical outcome of patients with congenital spinal malformations.

Methods: Nineteen patients (8 males and 11 females) were included in the study. Demographic data, symptoms and signs, radiological investigations, and other diagnostic tests for accompanying pathologies were evaluated together with neurophysiological findings.

Results: The mean age of patients was 13.6 years (range: 16 months-62 years). Neurophysiological changes were seen in 7 patients (36.8%) during surgery. Most of them had mass lesion including dermoid and epidermoid tumor or intradural abscess. Motor evoked potential (MEP) changes were seen in 3 patients without any new postoperative motor deficit. Bulbocavernosus reflex (BCR) changed in 4 patients; stimulation threshold (15-25 mA) increased in 3 of them while the other one had additional morphological changes in BCR response and worsening of preexistent urological dysfunction.

Conclusion: Mapping is the most critical part of surgery in terms of neurophysiology before cutting any structure in the operating

ÖZ

Amaç: Kompleks spinal malformasyonların cerrahisi fonksiyonel nöral yapılara hasar verme riskine sahiptir. Kompleks spinal patolojiler için kullanılan intraoperatif nörofizyolojik monitörizasyon, nöral yapılar için olan bu riski azaltmak ve dolayısıyla cerrahi sonuçları iyileştirmek için önerilmektedir. Amacımız konjenital spinal malformasyonlu hastalarda intraoperatif nörofizyolojik yaklaşımlarımızı ve erken klinik bulguları sunarak, cerrahi boyunca hangi olguların kritik nörofizyolojik değişikliklere yatkın olduğunu değerlendirmektir.

Yöntemler: On dokuz hasta (8 erkek and 11 kadın) çalışmaya dahil edildi. Demografik bilgiler, semptom ve bulgular, radyolojik değerlendirmeler ve eşlik eden patolojiler için diğer testler nörofizyolojik bulgularla birlikte değerlendirildi.

Bulgular: Hastaların ortalama yaşı 13,6 (dağılım: 16 ay-62 yıl) idi. Cerrahi süresince nörofizyolojik değişiklikler hastaların 7'sinde (%36,8) görüldü. Çoğunda dermoid, epidermoid veya intradural abseyi içeren kitle lezyonu vardı. Motor uyarılmış potansiyel (MEP) değişikliği postoperatif yeni motor defisit olmaksızın üç hastada görüldü. Bulbokavernöz refleks (BKR) 4 hastada değişti: Üçünde uyarı eşiği artarken diğerinde BKR yanıtında ek olarak morfolojik değişiklik ve postoperatif mevcut ürolojik disfonksiyonda kötüleşme oldu.

Sonuç: Postoperatif nörolojik defisiti önlemek için cerrahinin en kritik kısmı, cerrahi alandaki herhangi bir yapıyı kesmeden önce nörofizyolojik olarak haritalama yapmaktır. MEP ve BKR değişiklikleri, spinal konjenital malformasyonlar içerisinde izole

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area for preventing neurological deficit postoperatively. Among the spinal congenital malformations, MEP and BCR changes seem to occur during surgery for concomitant space occupying lesions or diastometamyelia and dermal sinus tract rather than isolated filum lipoma or tethered cord.

Keywords: Spinal congenital anomaly, dermal sinus tract, diastomatomyelia, mapping, neuromonitoring

filum lipomu veya gergin omurilikten ziyade eş zamanlı yer işgal eden lezyon, diastematomyeli veya dermal sinus traktının cerrahisinde görünmektedir.

Anahtar Sözcükler: Spinal konjenital anomali, dermal sinus traktı, diastematomyeli, haritalama, nöromonitörizasyon

Introduction

Congenital spinal malformations may present in a wide spectrum; ranging from mere junctional defects in the posterior vertebrae elements in its simplest benign form to severe neural malformations accompanied by neurological, orthopedic and urological disorders. Functional neural structures may be damaged during surgery of these serious malformations. Neurophysiological methods are routinely used for the diagnosis of subclinical findings identifying the severity of pathology or surgical decision making in the state of inconsistent clinical and magnetic resonance findings. Intraoperative neurophysiological monitoring (IONM) for congenital spinal pathologies is usually recommended to improve surgical results and reduce the risk of potential damage to the functional neural tissues (1-4). It helps the surgeon to distinguish between the roots and filum terminale, and conus medullaris in tumors even if the pathological condition has disrupted the normal anatomy of surgical region. In general, mapping and monitoring techniques including electromyography (EMG), motor evoked potential (MEP), somatosensory evoked potential (SEP) and bulbocavernosus reflex (BCR) are used during spinal surgery for congenital pathologies. In this paper, we present our neurophysiological approach and the early clinical outcome of patients who are treated for congenital spinal malformations to predict which patients are liable to reveal critical neurophysiological changes during surgery and neurological deficit postoperatively.

Methods

Patients

Nineteen patients (11 females, 8 male) having congenital spinal malformations were analyzed retrospectively. The symptoms and the physical examinations were assessed before and after surgery. All patients were evaluated with spinal magnetic resonance imaging (MRI), computerized tomography (CT) scans and other diagnostic tests including urodynamic and neurophysiological techniques for coexisting pathologies before surgery. Demographic data of the patients are presented in Table 1. Standard surgical techniques for diastometamyelia, tethered cord, dermal sinus tract (DST) and intradural tumors were applied by a single neurosurgeon (A.K). IONM data and early outcome of the patients were documented. All procedures performed in this study were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standard. Informed consent was taken from all study participants.

Intraoperative Neurophysiology

IONM was performed using the Cadwell elite IONM system for monitoring by the same neurophysiologist (E.T). Mapping and monitoring techniques were used during the surgery. Mapping was used to identify nerve roots and to distinguish filum terminale while monitoring was performed to preserve the functionality of sensory and motor pathways and reflex circuits.

Neurophysiological setup included free run EMG, triggered EMG, MEP, SEP and the BCR techniques.

The MEPs were elicited by transcranial electrical stimulation of the motor cortex from C1-C2 or C3-C4 according to the 10-20 International EEG system and recording from extremities and sphincter muscles for evaluating motor system structures. In a standardized setup, constant voltage stimulation with short train technique including 5 to 8 stimuli, pulse duration of 0.5 ms, ISI of 3-4 ms, and stimulus intensity of maximum 400V were used to elicit MEP responses. At least 30 microvolt was accepted for adequate muscle MEP amplitude. Double stimulation technique was tried if the response could not be elicited by standard short train technique.

Tibial SEPs were constitutively elicited by stimulation of the posterior tibial nerve at the ankle (rectangular pulses with duration 0.3-0.5 ms, repetition rate of 4.3 Hz, intensity up to 45 mA) and recorded from scalp electrodes at Cz′-Fz or Cz'-C3'/Cz'-C4', whereas median SEP eliciting median nerve stimulation and recording from C3'-Fz/C4'-Fz was used as control except in one patient with cervical encephalocele.

The BCR was recorded from external anal sphincter (AS) muscles by electrical stimulation of dorsal nerve of the penis/clitoris with train of 4-5 stimuli, ISI of 2.5 ms, stimulus intensity of 25-80mA for stimulation by surface electrode; 5-50mA for needle electrode, duration of 0.3-0.5 ms.

Muscles to be monitored were selected based on the level of vertebra. Iliopsoas, Quadriceps femoris ve vastus lateralis arasına ,adductor longus vastus lateralis, tibialis anterior, gastrocnemius, abductor hallucis (AH), and AS muscles were monitored for thoracic and lumbar levels using bilateral upper extremity muscles as control.

Mapping was performed by classical monopolar/bipolar or concentric bipolar stimulation probe with constant current stimulation (0.05-8 mA) on the nerve roots or intradural neurological structures and recording compound muscle action potentials from related muscles. A bite block was placed to prevent tongue injuries during MEP monitoring.

Table 1. Demographic and clinical findings of the patients

Patient	Age (yrs)/ gender	Symptom	Diagnosis	Coexisting anomalies	Preoperative sensorimotor deficit	IONM	Postoperative exam
1	5/M	Skin sign	FTL + TC + dermoid tumor	Absent	Absent	Loss of MEP amplitude 70-85% in AH bilaterally	No new deficit
2	11/M	Pain	DST + intradural abscess	Bladder dysfunction	Weakness in the left leg	Loss of MEP amplitude 80-95% in AH and AS bilaterally	No new deficit
3	15/F	Pain	DST + epidermoid tumor	Absent	Absent	Loss of MEP in R AH-MEP	No new deficit
4	62/F	No	dermoid tumor + intradural abscess	Voiding and bowel dysfunction	Absent	ST↑ 20mA in R BCR, 30 mA in L and morphological change	Worsened urological dysfunction
5	5/F	Pain	FTL + TC + epidermoid tumor	Aabsent	Absent	ST↑ 15mA in BCR	No new deficit
6	8/F	Skin sign	diastometamyelia + TC	Pes cavus	Absent	ST↑ 20mA in BCR	No new deficit
7	6/F	Skin sign	diastometamyelia + TC + DST	Absent	Absent	ST↑ 25mA in BCR	No new deficit
8	6/M	Skin sign	FTL + TC+ DST	Absent	Absent	No change according to baseline	No new deficit
9	13/F	Pain	FTL +TC	Ureteral duplication, cloacal extrophy, esophageal atresia	Weakness in the left leg	No change according to baseline	No new deficit
10	4/M	Skin sign	FTL +TC	Absent	Absent	No change according to baseline	No new deficit
11	4/F	Pain	FTL +TC	cloacal extrophy	Absent	No change according to baseline	No new deficit
12	35/F	Pain	FTL +TC	Absent	Absent	No change according to baseline	No new deficit
13	21/F	Pain	FTL +TC	Absent	Absent	No change according to baseline	No new deficit
14	2/F	No	FTL +TC	Anal atresia	Absent	No change according to baseline	No new deficit
15	10/M	Pain	FTL + TC + epidermoid tumor	Absent	Weakness in the legs	No change according to baseline	No new deficit
16	3/M	Skin sign	FTL + DST	Absent	Weakness in the right leg	No change according to baseline	No new deficit
17	13/F	Pain	FTL + TC	Absent	Limited neck movement, no walking ability	No change according to baseline	No new deficit
18	21/M	Pain	Diastometamyelia + TC	Pes cavus	Weakness and hypoesthesia in the left leg	No change according to baseline	No new deficit
19	27/M	No	Cervical encephalocele + DST	Absent	Absent	No change according to baseline	No new deficit

FTL: Filum terminale lipoma, TC: Tethered cord, DST: Dermal sinus tract, MEP: Motor evoked potential, ST: Stimulus threshold, BCR: Bulbocavernous reflex, R: Right, L: Left, F: Female, M: Male

Amplitude decrease more than 50% and threshold increase more than 100V for MEP, amplitude decrease more than 50% for SEP were accepted as warning criteria. Regarding BCR, all changes (threshold increase, amplitude decrease, wave form abnormalities) were considered as a warning criterion because of our limited knowledge on its effect on surgical results.

Anesthesia

Total intravenous anesthesia consisting of propofol (1.5-2 mg/kg for anesthesia induction and 6-10 mg/kg/h for maintenance) plus remifentanil (0.15 μg/kg/min) was used in all patients except those below 5 years of age to avoid propofol infusion syndrome. Inhalation anesthesia (sevoflurane, MAC 0.5, BIS 40-60) was used for younger patients. A short-acting muscle relaxant (rocuronium, 0.5 mg/kg) was used only before endotracheal intubation.

Statistical Analysis

The statistical package for the social sciences (SPSS) 22.0 was used for data analysis. Data were presented as percentage distributions for categorical variables and median with ranges for continuous variables. Comparisons between groups were made using Mann-Whitney U test for numerical data. Statistical significance was defined as $p<0.05$.

Results

The mean age of 19 patients (8 males and 11 females) was 13.6 years (median: 11 years, range: 16 months-62 years).

Eleven patients had filum terminale lipoma (FTL) and tethered cord (TC); four of whom had additional pathologies (epidermoid tumor in 2, dermoid tumor in one and DST in one). Other patients had FTL + DST, diastometamyelia + TC, diastometamyelia + TC + DST, dermoid tumor/DST + intradural abscess, DST + epidermoid tumor/cervical encephalocele (Table 1).

The most common complaint was pain in 12 patients, followed by voiding or bowel difficulties in 2. Dermal findings were detected in 6 patients, motor deficit in 5, sensory deficit in 1, and orthopedic deformity in 2 (Table 1).

The MRI revealed TC in 14 of all patients, diastometamyelia in 3, mass lesion in 15 (3 epidermoid, 2 dermoid, 12 lipomas, 2 abscess), DST in 6, and encephalocele in 1 patient. On spinal CT scans, 11 patients showed fusion defect on the posterior elements, 2 had scoliosis and 2 had fusion of adjacent vertebral bodies.

The MEP was recordable in all patients including those with preoperative motor deficit. Threshold values were not different significantly between age the group below 17 years and adult age group. When the patients <5 years old were evaluated as a separate group, there was a difference for threshold values between groups (Mann-Whitney U test $p<0.05$). SEPs were recordable and stabil for all patients including children except one adult. This patient had SEP recordings with severe artefacts during surgery. But it was the same according to baseline at the end of the surgery.

Regarding IONM, MEP and/or BCR changes were noted while SEP did not change during the surgery. Neurophysiological changes were seen in 7 out of 19 patients (36.8%) during surgery. Five of them had mass lesion including dermoid tumor, epidermoid tumor or intradural abscess, 2 had diastometamyelia with DST/TC.

The surgeon and anesthesiologist were immediately informed when significant changes were seen in monitoring during surgery. Changes related to anesthesia were checked. If there were any changes such as end tidal carbondioxide, minimum alveolar concentration of the inhalation anesthetic or mean arterial blood pressure, they were managed by the anesthesiologist. But if the changes were still the same, the surgeon checked his maneuvers and the placement of surgical instruments. Steroid was administered if there was no improvement in potentials with these corrections.

The MEP changes which met the warning criteria were seen in 3 patients: amplitude decreasing in 2 and loss of MEP in 1. All had free run EMG abnormalities in advance of MEP changes. No new motor weakness or worsened clinical findings were observed in the postoperative period of these patients (Table 1).

Patient 1 with FTL + TC + dermoid tumor had no motor deficit preoperatively. TC was released by cutting filum terminale concurrent with mapping and MEP check after the procedure. The left side of the cord was invaded by dermoid tumor. Gross total resection was performed. The last recording of MEP showed a decrease of 70-85% in MEP amplitude of AH muscles bilaterally.

Patient 2 had DST with intradural abscess and proximal 4/5, distal 2/5 motor deficit in the left leg and also bladder dysfunction preoperatively. At the baseline recordings of this patient, monophasic response was elicited on the right side for BCR while the left side had more turn counts. Loss of BCR response was seen immediately after a 95% decrease of MEP amplitude in left AH and loss of MEP in AS muscles bilaterally while abscess formation was evacuated during the surgery. Afterwards, left AH response was lost with a decrease of MEP amplitude in right AH muscle. MEP response of left AS improved partially during dural closure.

Patient 3 had DST with sacral epidermoid tumor without motor deficit preoperatively. During surgery, DST was followed and resected until the dura. Some of the sacral nerve roots and rootlets were seen inside the tumor. Gross total resection was performed and the tumor capsule attached to nerve fibers was left due to loss of MEP in the right AH muscle during resection.

The BCR was recordable in all patients except 2 (pt 11 and 16). Pt 11 who was 4 years old female had FTL and TC with coexisting cloacal extrophy. This patient was one of our first patients. We could not put recording electrodes into the bulbocavernosus muscle instead of external AS due to cloacal extrophy. Pt 16 was 3 years old male having FTL and DST without preexisting voiding and bowel dysfunction. BCR could not be recorded. It was probably because of the inhalation

anesthetics. We could even stimulate his motor cortex with electrical stimulation in high voltage (450 Voltage, 8 pulses with a pulse width 75ms). BCR changes were seen in 4 patients (Table 1). Stimulation threshold (ST) increased 15-25 mA in 3 of them while the rest had additional morphological changes in BCR response. Postoperatively, urinary function worsened in only one patient having ST increase and morphological change as turn count decreased. The patient was 62 -year-old female having constipation and also urinary incontinence before surgery. She had dermoid tumor with intradural abscess formation. Bladder and voiding complaints worsened slightly immediately after surgery. She needed intermittent catheterization for 10 days postoperatively. However, she was discharged without catheterization as her antibiotherapy was completed.

Discussion

Congenital spinal malformation surgery demands nerve root mapping and spinal cord monitoring for the protection of motor pathway and segmental reflexes like bulbocavenosus. There is still no established warning criterion for nerve root monitoring in terms of MEP monitoring according to guideline (5). Some researchers used 50-80% amplitude reduction criteria for nerve root monitoring in the spinal surgery (6,7) and they noticed false positive responses in their studies (6,7). Because of limited number, we took all MEP changes into consideration for this study. MEP changes were seen in only 3 patients; amplitude decrease of more than 50% in 2 and loss of amplitude in 1 who had severe preoperative motor deficit in the related muscle. No new motor weakness was observed in the postoperative period of these patients. Regarding the risk of postoperative motor weakness, MacDonald et al. (8) stated that it was difficult to predict motor deficit after surgery in patients with amplitude reduction due to overlapping of radicular innervation, limited sampling and variabilities in MEP responses. MEP loss may be reliable criterion for patients without preoperative motor deficit. However, we cannot clearly express this opinion about warning criteria when considering our results.

The MEP was recordable in all patients including those with preoperative motor deficit in this study. The difficulty of MEP recording for especially lower extremities was shown for children under 7 years of age and those with preoperative severe motor deficits (9). In fact, we have difficulty to elicit MEP for patients with severe paralysis according to our experiences. Therefore, we examine the patients preoperatively and add the best recordable muscle to the IONM set up according to level of surgery. However, we had no patients with muscle strength lower than 3/5 according to the Medical Research Council system in this study.

It is known that threshold value varies with age because of the myelinization and maturation of corticospinal tract, and interneuronal synaptic connections either at the cortex or spinal cord (10,11). Motor thresholds are reduced during the early development toward mid to late adolescence, and MEP amplitude is increased with age (10). Our threshold values were not different significantly between age groups. When the patients <5 years old were evaluated as a separate group, there was a difference for threshold values between groups. The reduction in thresholds with age could be related to the phasic and synchronous activation of spinal motor circuits because of completed myelination (12). One more reason of this difference might be probably related to usage of inhalation anesthetics as we showed in our previous work (13). In addition, we had also recordable MEP in children under 2 age in this study. But, we could record MEP with more pulses and higher voltage stimulation and if necessary double stimulation technique in this group, as another study carried out in infants (14). On the other way, SEPs were recordable and stabil for all patients including children except one adult. It may be due to the fact that we record from different montages such as Cz'-C3' and Cz'-C4' for the best result.

There are different practical methods reported for recording and stimulation parameters of BCR in the literature. Rodi and Vodusec stimulated pudendal nerve by cup electrodes with rectangular electrical stimuli of 0.5 ms duration and 40 mA intensity for eliciting BCR in adults (15). Skinner et al. (16) suggested double train technique for improving intraoperative BCR acquisition using needle electrodes to stimulate and recommended it as an effective practical method (17). A new study which used surface electrodes for stimulation recommended a biphasic 8-pulse stimulation with 2-msec intervals as the optimal stimulation paradigm (18). Same authors reported that this method had technical failure for eliciting BCR in some patients, because 8 pulses stimulation made it impossible to discriminate between BCR response and stimulation artifact in another study (19). We used surface electrodes in men and needle electrodes in women for stimulating dorsal penile/clitoral nerves using stimulus criteria recommended by Skinner and Vodusec (17). Our response elicited by needle electrodes with bilateral stimulation was more sensitive for recording and correlated with outcome as well.

With respect to interpretation of BCR, no widely accepted BCR warning criteria are ascertained for clinical outcome. Skinner and Vodusec (17) advocate the warning criterion as disappearance of the response under unchanged anesthetic conditions and preserved perfusion. Recently, Morota published an article about BCR warning criteria according to results of 164 operations (20). He notified using the cutoff value of BCR amplitude reduction at 75% for conus spinal lipoma. There is no information yet about threshold increase criterion for eliciting BCR. We observed threshold increase (15-30 mA) for BCR in 4 patients in our center while only one patient showed worsened voiding dysfunction and new fecal incontinence in the postoperative period. The patient showed stimulus threshold increase of 20 mA on the right side, 30 mA on the left with decreasing turn accounts. Congruently, Skinner and Vodusec (17) presented a patient having an obvious reduction of waveform complexity and amplitude (more than 50%) during surgery and who required intermittent catheterization after surgery. The take home message of this patient was that

threshold increase with waveform abnormality in BCR response might be a potential risk for new deficits with this sensitive method.

Mapping technique and tracking free run EMG are used technically to prevent an injury of functional roots and rootlets. We performed mapping using different stimulator probes and stimulus intensities depending on the aim of surgery. Basically, stimulus parameters used in different centers show a discrepancy even if the modalities are the same (21,22). These differences are generally relevant to stimulation type (constant current or constant voltage), stimulus duration and stimulation probes (classical or concentric, monopolar or bipolar). In fact, the most important thing is the experience of each center. Regarding other stimulation probes, Sala et al. used bipolar concentric probe, 0.05-0.2 mA stimulus intensity, a single stimulus of approximately 0.2 to 0.5 ms duration for mapping the functionality of root and rootlets and 2.5 mA for hunting up functional rootlets in the filum or pathological tissue (21). Hoving et al. (22) used classic bipolar and monopolar probe with voltage current, duration of 0.2 ms for TC surgery. They resected the structure if the voltage threshold was three times over the voltage threshold of a previously stimulated nerve root in the operating field. Although we currently started to use bipolar concentric probe in our center, we used to benefit either classical bipolar or monopolar stimulating probe with single stimulus 0.2 ms duration, 0.05-8 mA stimulation in order to distinguish filum terminale and evaluate the functionality of the nerve roots. In our experience, we considered to increase the stimulus duration and intensity up to 8 mA with 0.2 ms to excite degenerated fibers. In this setting, the surgeon was able to cut the structure after mapping as planned without a new motor deficit in any of the patients.

Study Limitations

This study had some limitations. Major limitation of this study was small number of patients. Advanced statistical analysis could not be measured because of limited patients. The last limitation was that this study was a retrospective study.

Conclusion

This study showed that free run EMG, MEP and BCR changes seemed to occur during surgery for concomitant space occupying lesions or diastometamyelia and DST rather than isolated filum lipoma or TC among the spinal congenital malformations. Mapping before cutting any structure in the operating field is the most critical part of surgery to protect neural structures and thus improve postoperative neurological functions.

Ethics

Ethics Committee Approval: All procedures performed in this study were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standard.

Informed Consent: Informed consent was taken from all study participants.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: E.T., R.K., B.K., B.T., A.M.K., Concept: E.T., R.K., Design: E.T., A.M.K., Data Collection or Processing: B.K., B.T., Analysis or Interpretation: E.T., R.K., B.K., A.M.K., Literature Search: E.T., B.K., B.T., Writing: E.T., R.K., B.T.

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Original Article

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Craniomandibular Asymmetry Evaluation of Patients with Eruption Disturbances of Second Molar Teeth

Sürme Bozukluğu Gösteren İkinci Molar Dişlere Sahip Hastalarda Kraniyomandibular Asimetri Değerlendirmesi

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ABSTRACT

Objective: The aim of this study was to evaluate craniomandibular asymmetry in patients with unilateral eruption disturbances of permanent second molar teeth.

Methods: Fifty-two patients showing unilateral eruption disturbances (delayed eruption and impaction) of permanent second molar teeth were included in the study group. Thirty patients with normally erupted second molar teeth were included in the control group. The gonial angle, length of condyle head, length of condyle neck, ramus height, corpus length, and angles between facial skeletal midline and transversal lines formed by connection of some important anatomical points on both sides were measured on orthopantomograms. Asymmetry indices were calculated for each parameter. Paired t-test was used in each group separately when comparing both sides of the face. Unpaired t-test was used when comparing study group and control group with regard to asymmetry index parameters.

Results: In study group; increases in gonial angle, length of condyle head, and ramus height were observed on the eruption disturbance side compared to the normally erupted side ($p<0.05$). Angles between facial skeletal midline and three separate lines formed by connection of articular eminence points, sigmoid notches, and gonion points were significantly higher on the normally erupted side. In control group, there was no statistically significant difference between both sides of the face. All asymmetry index parameters were showing statistically significant differences between study and control groups.

ÖZ

Amaç: Bu çalışmanın amacı daimi ikinci molar dişlerinde tek taraflı sürme bozukluğu gösteren hastalarda kraniyomandibular asimetri değerlendirmesi yapmaktı.

Yöntemler: Daimi ikinci molar dişlerinde tek taraflı sürme bozukluğu (gecikmiş sürme ve gömülü kalma) gösteren 52 hasta çalışma grubuna dahil edildi. Normal süren ikinci molar dişlere sahip 30 hasta kontrol grubuna dahil edildi. Gonial açı, kondil başı uzunluğu, kondil boynu uzunluğu, ramus uzunluğu, korpus uzunluğu ve yüzün her iki tarafındaki bazı önemli anatomik noktaların birleşmesiyle oluşan transvers çizgilerin yüz iskeletsel orta hattıyla yaptığı açılar panoramik film üzerinde ölçüldü. Her parametre için asimetri indeksi hesaplandı. Yüzün her iki tarafının birbirleriyle karşılaştırılmasında her bir grupta ayrı ayrı bağımlı örneklem t-testi kullanıldı. Asimetri indeksi parametreleri açısından çalışma grubu ve kontrol grubu karşılaştırılırken bağımsız örneklem t-testi kullanıldı.

Bulgular: Çalışma grubunda sürme bozukluğu olan tarafta normal sürme tarafına göre gonial açıda, kondil başı uzunluğunda ve ramus uzunluğunda artmış değerler gözlemlendi ($p<0,05$). Yüz iskeletsel orta hattı ile artiküler eminens noktalarının, sigmoid notch noktalarının ve gonion noktalarının oluşturduğu 3 ayrı doğru arasında kalan açılar normal sürme tarafında anlamlı derecede daha yüksekti. Kontrol grubunda, yüzün her iki tarafı arasında istatistiksel olarak anlamlı bir fark yoktu. Çalışma ve kontrol grupları arasında tüm asimetri indeks parametreleri anlamlı fark göstermekteydi.

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Conclusion: Through this retrospective study, eruption disturbances of permanent second molars could be associated with craniomandibular asymmetry.

Keywords: Facial asymmetry, molar, tooth eruption

Sonuç: Bu retrospektif çalışma doğrultusunda, daimi ikinci molarların sürme bozuklukları kraniyomandibular asimetri ile ilişkili olabilir.

Anahtar Sözcükler: Yüz asimetrisi, molar, diş sürmesi

Introduction

The goals of orthodontic treatment are not only to provide dental esthetics, functional occlusion, periodontal health, and stability but also to provide facial esthetics (1). Facial symmetry plays an important role in facial esthetics, which creates the perception of attractiveness. Craniofacial asymmetry is the non-matching of the right and left sides of the face based on the facial midline. Congenital problems such as a cleft lip and palate or hemifacial microsomia as well as environmental factors such as infection or trauma are only a few etiologic factors causing asymmetry of the face (2,3). Parafunctional habits and functional problems as well as dento-occlusal problems also lead to facial asymmetry (4,5). Recent studies have investigated the effect of dental factors such as unilateral tooth absence, early extraction of molar teeth, and a unilateral crossbite on craniofacial asymmetry (6-9). But more dental factors should be investigated for the early detection of craniofacial asymmetry and for an appropriate intervention time. In this way, treatment modalities can be developed, and preventive measures can be taken before severe asymmetry occurs.

On the other hand, dental clinicians confront various kinds of eruption disturbances in daily practice. These challenging problems include ankylosis, premature eruption, ectopic eruption, delayed eruption, over eruption, and impaction. Among these, delayed eruption is defined as the non-eruption of a tooth, even when the tooth has developed more than the root length expected for eruption (10), and impaction is described as non-eruption of a tooth due to a physical obstacle in the eruption path or the abnormal position of that tooth even when root completion has finished (11). Although third molars are the most common teeth showing eruption disturbances, increasing rates of second molar teeth with eruption disturbances are also remarkable (12-14). Since craniofacial asymmetry leads to an unaesthetic appearance, to disharmony of the maxillomandibular complex during dynamic movements, and to malocclusions, underlying dental factors should be investigated to prevent craniofacial asymmetry.

The purpose of this retrospective study was to evaluate the hypothesis that unilateral eruption disturbances such as impaction and the delayed eruption of permanent second molar teeth were associated with craniomandibular asymmetry.

Method

Necmettin Erbakan University, Faculty of Dentistry Ethics Committee approval was obtained for this retrospective study (decision no: 2019.07). Initial diagnostic records of 6,010 patients referred to the Department of Orthodontics, Faculty of Dentistry, Necmettin Erbakan University, between June 2015 and March 2019 were consecutively recruited.

Inclusion criteria for the study group were as follows: 1) patients showing delayed eruption or impaction of at least one second molar tooth on one side and normally erupted second molar teeth on the other side; and 2) patients older than twelve years of age. Inclusion criteria for control group were as follows: 1) patients showing full eruption of 28 teeth except for third molar teeth; and 2) patients older than nine years of age. For both the study and control groups, patients were excluded who had craniofacial anomalies, systemic disease, a trauma history to the head and face region, temporomandibular joint fractures or ankylosis, orthodontic treatment history, missing teeth except for third molars, tumors, or infection in the posterior region.

In total, 82 patients were included in this retrospective archive study. Fifty two patients and 30 patients were in the study group and the control group, respectively.

This study was comprised of two parts. The first part was to use a split-mouth design to compare craniomandibular structures between the eruption disturbance side of the second molar and the normally erupted side of the second molar. The second part was a comparison of craniomandibular structures between the study and control groups.

Measurement Method

All measurements were performed on initial panoramic radiographic images. Panoramic radiographic records were obtained using the same machine (Morita Veraviewepocs 3D R100-P, J Morita MFG Corp., Kyoto, Japan) at 70 kVp, 10mA, and 10 s, with a method standardized by the light beam sensor and the parallelism between the orbital plane and horizontal plane. Reliability and reproducibility were enabled by the autofocus feature of the machine. Measurements were performed using the same software to calibrate each image (Turcasoft Software Co., Ltd., Samsun, Turkey).

All measurements were performed by one examiner. For interexaminer reliability, 104 randomly selected measurements were repeated by another examiner.

On each panoramic radiograph, the orbital plane was determined as the line connecting the orbital points on both sides. A midline perpendicular to the orbital plane and passing through the anterior nasal spine was determined. The line connecting the articular eminence points was the articular eminence plane, the line connecting the sigmoid notches was the sigmoid notch plane, and the line connecting the gonion points was the gonion

plane. The angles of these three planes, with the midline on both the right and left sides, were measured. The angular parameters were as follows: Gonial angle (Gonial A°), articular eminence plane angle (AE-P°), sigmoid notch plane angle (Sg-P°), and gonion plane angle (Go-P°) (Figure 1).

The linear parameters were as follows: condyle head length (Co-CC), condyle neck length (CC-Sg), ramus height, and corpus length (Figure 2).

For comparisons of each parameter between the study and control groups, an asymmetry index was calculated for each parameter. The control group asymmetry index was calculated according to Habets' formula (15). For the study group, the formula was modified according to the values of the normally erupted side of the second molar and the eruption disturbance side of the second molar [(normally erupted side - eruption disturbance side)/(normally erupted side + eruption disturbance side) x100].

Statistical Analysis

The IBM SPSS Statistics Version 22.0 (Chicago, IL, USA) was used in all statistical analyses. Interexaminer reliability was determined with the Pearson correlation analysis. The data distribution of normality was decided by the Shapiro-Wilk test and the Kolmogorov-Smirnov test. In the study group, the comparison of craniomandibular structural parameters between the eruption disturbance side of the second molar and the normally erupted side of the second molar was analyzed with a paired samples t-test. In the control group, the comparison of the craniomandibular structural parameters between the right and left sides was determined by a paired samples t-test. The comparison of all asymmetry indices for each parameter between the study and control groups was evaluated with an unpaired t-test. The p-value was set at 0.05 for statistical significance.

Results

In total, 82 patients (51 female, 31 male, mean age: 14y-5m) were included in this retrospective archive study. The study group consisted of 52 patients (31 female, 21 male, mean age: 14y-7m), while the control group consisted of 30 patients (20 female, 10 male, mean age: 14y-1m).

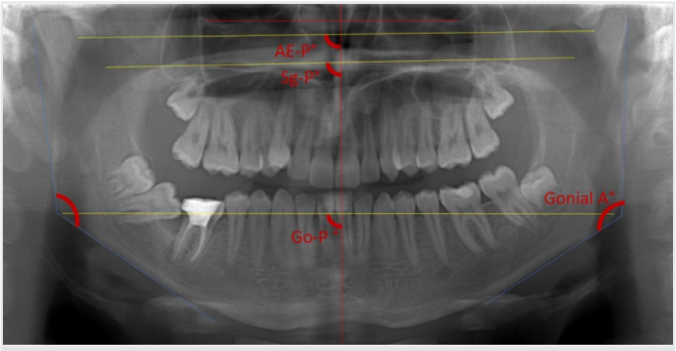

Figure 1. Angular measurements
Gonial Angle (Gonial A°), Articular Eminence Plane Angle (AE-P°), Sigmoid Notch Plane Angle (Sg-P°), Gonion Plane Angle (Go-P°)

According to the Shapiro-Wilk test and the Kolmogorov-Smirnov test, the data were normally distributed (p>0.05). Pearson correlation analysis showed 92% correlation between the measurements of the first and second examiners.

In the study group, AE-P°, Sg-P°, and Go-P° were statistically higher at the normally erupted side of the second molar. The ramus height, Co-CC, and Gonial A° were statistically higher at the eruption disturbance side of the second molar. CC-Sg and corpus length showed no statistical difference between the two sides (Table 1). In the control group, none of the measurements showed statistically significant differences between the right and left sides (Table 2).

The unpaired t-test showed that the index values of all parameters were statistically significantly higher for the study group when compared to the control group (p>0.05) (Table 3).

Discussion

Etiologic factors of the mandibulofacial asymmetries were reviewed in a previous study (16). That review highlighted the following as factors associated with mandibular and facial asymmetries: hemifacial microsomia, congenital hemifacial hypertrophy, hemifacial atrophy, Romberg syndrome, postural deformities such as torticollis and scoliosis, unilateral cranial synostosis, intrauterine pressure, endocrinal disorders, infectious disorders such as rheumatoid arthritis and arthritis associated with psoriasis, temporomandibular joint damage and injuries resulting in fractures and ankylosis, unilateral growth of the condyle, and dentofacial factors such as crossbite, and mandibular deviation. The current study only aimed to investigate the effect of the eruption process of molar teeth on facial asymmetry as a dental factor. Therefore, all above-mentioned factors were eliminated from the study sample with detailed anamnesis and radiologic examination.

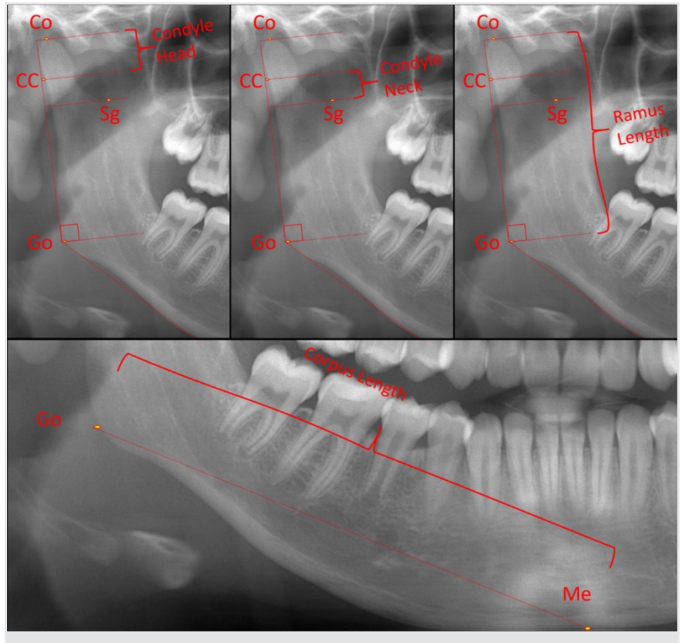

Figure 2. Linear measurements
Condyle Head Length (Co-CC), Condyle Neck Length (CC-Sg), Ramus height (Co-Go), Corpus Length (Go-Me)

Table 1. Comparison between erupted-side and eruption disturbance-side in study group

	Paired differences				
	Mean	SD	t	df	p
Erupted Side Gonial A◦ - Eruption Disturbance Side Gonial A◦	-2.03	3.81	-3.847	51	0.001*
Erupted Side AE-P◦ - Eruption Disturbance Side AE-P◦	0.94	2.40	2.826	51	0.007*
Erupted Side Sg-P◦ - Eruption Disturbance Side Sg-P◦	1.25	2.16	4.149	51	0.001*
Erupted Side Go-P◦ - Eruption Disturbance Side Go-P◦	1.03	2.47	3.021	51	0.004*
Erupted Side Co-CC - Eruption Disturbance Side Co-CC (mm)	-0.17	0.17	-7.288	51	0.001*
Erupted Side CC-Sg - Eruption Disturbance Side CC-Sg (mm)	-0.01	0.31	-.175	51	0.862
Erupted Side Ramus - Eruption Disturbance Side Ramus (mm)	-0.12	0.36	-2.334	51	0.024*
Erupted Side Corpus - Eruption Disturbance Side Corpus (mm)	0.05	0.76	0.430	51	0.669

*p<0.05
95% confidence interval.
SD: Standard deviation

Table 2. Comparison between right side and left side in control group

	Paired differences				
	Mean	SD	t	df	p
Erupted Side Gonial A◦ - Eruption Disturbance Side Gonial A◦	-0.05	0.54	-0.512	29	0.612
Erupted Side AE-P◦ - Eruption Disturbance Side AE-P◦	0.01	0.49	0.126	29	0.901
Erupted Side Sg-P◦ - Eruption Disturbance Side Sg-P◦	0.01	0.43	0.110	29	0.913
Erupted Side Go-P◦ - Eruption Disturbance Side Go-P◦	0.11	0.64	0.907	29	0.372
Erupted Side Co-CC - Eruption Disturbance Side Co-CC (mm)	0.02	0.07	1.668	29	0.106
Erupted Side CC-Sg - Eruption Disturbance Side CC-Sg (mm)	0.01	0.06	0.909	29	0.371
Erupted Side Ramus - Eruption Disturbance Side Ramus (mm)	0.00	0.10	0.037	29	0.971
Erupted Side Corpus - Eruption Disturbance Side Corpus (mm)	-0.01	0.21	-0.312	29	0.757

SD: Standard deviation

Table 3. Comparison of asymmetry indices between study group and control group

	Study group (n=52)		Control group (n=30)			
	Mean	SD	Mean	SD	t	p
Gonial index	1.32	1.116	0.16	.132	5.620	0.001*
AE-P index	1.01	1.001	0.15	.230	4.660	0.001*
Sg- P index	1.08	0.869	0.15	.182	5.736	0.001*
Go- P index	1.09	1.003	0.18	.310	4.835	0.001*
Co-CC index	7.04	5.644	2.65	2.183	4.071	0.001*
CC-Sg index	9.52	8.533	1.82	1.965	4.855	0.001*
Ramus index	1.93	1.761	0.51	.464	4.329	0.001*
Corpus index	2.56	2.106	0.74	.496	4.647	0.001*

*p<0.05
95% confidence interval.
SD: Standard deviation

Root formation stage was the main criteria on decision of tooth eruption status. However, chronological age was also considered in inclusion criteria. Although eruption age of second molar teeth is widely known as age 12, permanent molars' eruption age can show variations (17). Not only the authors' clinical experience but also the initial screening for sample collection referred to the existence of cases who completed the normal eruption process of second molar teeth even at age 9. Therefore, the subjects more than 9 years of age were included in the control group while the age more than 12 was determined for study group.

According to the present study, patients in the control group showed symmetry of craniomandibular structures on the left and right sides of the face. However, in the study group, only the corpus length and condyle neck were symmetric for both sides of the face. Patients in the study group showed a downward tilt of AE-P°, Sg-P°, and Go-P° from the normally erupted side to the eruption disturbance side. The condyle head and ramus were also longer at the eruption disturbance side, with an increased Gonial A°. Patients in the study group showed more asymmetric craniomandibular structures when compared with patients in the control group.

The authors believe that this study is the first to evaluate craniomandibular asymmetry in patients with unilateral eruption disturbances of the posterior teeth. In a previous study (7), condylar asymmetry in patients with unilateral second premolar teeth agenesis was investigated. Unlike the current study's findings, in the study group, the condylar, ramal, and total ramus heights showed no statistically significant difference on either side of the face. According to that study's findings, there was no statistical difference for the asymmetry index of the ramal height and total ramus height. However, a more asymmetric condyle in the study group, when compared with the control group, was consistent with the results of the current study. Another study (18) investigated the effects of early unilateral mandibular first molar extraction on condylar and ramal vertical asymmetry. There was no statistically significant difference in terms of the condylar, ramal and total ramus height between the sides of the face. But asymmetry indices showed asymmetry in only the total ramus height in the study group when compared with the control group. This finding correlated with the results of the present study.

The above-mentioned two studies showed no difference between the study groups with respect to both sides of the face. But in the current study, the length of the condyle head and the ramus height showed statistically significant differences in the study group for both sides of the face. This can be evaluated from different points of view. First, the current study included not only one tooth but also both the upper and lower teeth of the same side during the selection of unilateral eruption disturbances. These subjects could increase the severity of the asymmetry. Second, the above-mentioned studies were investigating agenesis or extraction, while in the current study sample, teeth were totally or partly present in the bone. This could directly affect the bone volume. On the other hand, the common point of these studies was that the nonfunction of a related tooth might lead to chewing on the ipsilateral side. In the current study, this chewing side preference was due to eruption problems, while in the above-mentioned studies, the absence of teeth was the main reason for the preference.

In a previous study, mandibular vertical measurements were performed by using the panoramic radiographs of patients with Class II subdivision and Class I occlusion (19). According to their results, Gonial A° and asymmetry indices for condyle height, ramus height, and condyle + ramus height showed no statistical difference between the study group (Class II subdivision) and the control group (Class I). Therefore, in the present study sample, the authors did not consider the malocclusion type even if it was diagnosed as Class II subdivision or Class III subdivision.

However, in another study, similar parameters were investigated in patients with a posterior crossbite, using a similar method (9). Since the authors concluded statistically higher indices for the group with a posterior crossbite than for the control group, crossbite was excluded from the current study sample to avoid the effect of dental crossbite on asymmetry.

According to the current study, Gonial A° was greater on the affected side. The epigenetic effects of second molar teeth's eruption on craniofacial growth and remodeling could be considered to explain these observations.

Slight degrees of asymmetry are acceptable in daily practice. However, to the authors' knowledge, there wasn't any research in the literature about asymmetry index values within normal ranges. Therefore, a comparison of asymmetry indices between the study group and the control group was performed to a more reliable method.

Study Limitations

A limitation of the present study was the nonexistence of specific exclusion criteria for the third molar teeth. Agenesis of third molars can be considered for further studies, to eliminate the effect of these teeth on the measurements, since they can affect the bone volume in the posterior region. Although all other teeth except for second molars and third molars were in a normal eruption state, it was impossible to check any previous delay at the eruption of these teeth in all patients. This can also affect the measurements.

Cone beam computed tomography images are effective in detecting craniofacial asymmetry. However, the sample was consisting of the patients who were admitted for initial examination. Therefore, panoramic radiographs that were obtained according to the ALARA principle were used in this retrospective study. There was an autofocus feature of the panoramic machine used in this study. The distance to the patient's teeth is measured by the light beam sensor and the arm moves into the optimal position automatically. This feature enables to have panoramic radiographs with a high degree of reproducibility and reliability. On the other hand, some authors have suggested excellent reliability for the total ramal height when panoramic radiographs are used (20). However, panoramic

radiography does not show as good a diagnostic value as for the total ramal height when compared with the asymmetry index of the condylar region. From an ethical perspective, although panoramic radiographs have commonly been used, due to their affordability and low doses of radiation, three-dimensional imaging techniques with a larger sample size may be useful to obtain more precise measurements in further studies.

Conclusion

In support of the authors' hypothesis, eruption disturbances of permanent second molar teeth could be associated with craniomandibular asymmetry. Regular examination of second molar eruption should be considered to prevent possible facial asymmetry of the patient.

Ethics

Ethics Committee Approval: Necmettin Erbakan University, Faculty of Dentistry Ethics Committee approval was obtained for this retrospective study (decision no: 2019.07).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: A.S.A., Design: A.S.A., Data Collection or Processing: A.S.A., A.E.S., Analysis or Interpretation: A.S.A., A.E.S., Literature Search: A.S.A., Writing: A.S.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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Original Article

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The Hand Surgery Subspecialty Education Program in Turkey and its Impact on Productivity in The Hand Surgery Literature

El Cerrahisi Yan-Dal Eğitim Programının Türkiye'nin El Cerrahisi Konusundaki Bilimsel Üretkenliğine Etkisi

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ABSTRACT

Objective: The aim of study of this study is to evaluate the hand surgery fellowship education program in terms of Turkey's productivity in the hand and wrist literature

Methods: Original articles published in five highly cited hand surgery journals between 2009 and 2019 were investigated. In order to examine the increase in quantity and quality of the published articles over time, the publications were divided into two groups according to two equal time periods (A=01.01.2009-30.06.2014 and B=01.07.2014-31.12.2019 period). Period A represented the period before the hand surgery subspecialty training program, and period B represented the period after it.

Results: A total of 5,179 articles on hand and wrist research from five journals were identified in the database of Web of Science from 2009 to 2019. It was found that 51.5% (n=2,665) of the studies were published in period A and 48.5% (n=2514) were published in period B. Turkey had 34 publication in period A (ranked 15th) and 55 publication in period B (ranked 11th). Contribution of Turkey to the total hand and wrist research increased by 69.2% (1.3% versus 2.2%) between the two periods, and a significant increase was observed in articles from 2009 to 2019 in Turkey (R2=0.67, p=0.003)

Conclusion: We observed a significant increase in the number of articles about hand and wrist research from Turkey after hand

ÖZ

Amaç: Bu çalışmanın amacı el cerrahisi yan dal eğitim programının Türkiye'nin el cerrahisindeki bilimsel üretkenliğine etkisini değerlendirmektir.

Yöntemler: 2009-2019 yılları arasından en yüksek etki faktörüne sahip 5 el cerrahisi dergisinde yayınlanan orijinal bilimsel çalışmalar incelenmiştir. Yayınlanan çalışmalar basıldıkları zamana göre iki ayrı gruba ayrılmış ve iki eşit zaman periyodu (periyot A= 01.01.2009-30.06.2014 ve periyot B= 01.07.2014-31.12.2019) oluşturulmuştur. Periyot A el cerrahisi yan dal eğitim programının öncesini temsil ederken, periyot B sonrasını temsil etmektedir.

Bulgular: Web of Science veri tabanı kullanılarak, 5 el cerrahisi dergisinde 2009-2019 tarihleri arasında yayınlanan, el-el bileği konusunda toplam 5.179 orijinal bilimsel makale tanımlanmıştır. Makalelerin %51,5'i (n=2.665) periyot A'da, %48,5'i de (n=2.514) Periyot B'de yayınlanmıştı. Periyot A'da Türkiye'den 34 makale yayınlanmışken (makale sayısına göre 15. sırada), periyot B'de Türkiye kökenli 55 makale (makale sayısına göre 11. sırada) basılmıştır. Türkiye'nin toplam el cerrahisi bilimsel literatürüne katkısı el cerrahisi yan dal eğitim programından sonraki dönemde %69,2 (%1,3 vs %2,2) oranında artmıştır ve bu artış istatistiksel olarak anlamlı (R2=0,67, p=0,003) bulunmuştur.

Sonuç: El cerrahisi yan dal eğitim programı sonrası Türkiye'nin bu konudaki literatüre bilimsel katkısı artmıştır. Yan dal eğitim

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surgery fellowship education program. Hand surgery fellowship training program positively affected scientific productivity of Turkey.

Keywords: Education program, hand surgery, scientific productivity, sub-speciality

programı Türkiye'nin el cerrahisindeki bilimsel üretkenliğini pozitif olarak etkilemiştir.

Anahtar Sözcükler: Eğitim programı, el cerrahisi, bilimsel üretkenlik, yan-dal

Introduction

The total number of scientific publications in a country is an important indicator of the scientific research volume and productivity of that country (1). There are many factors that affect the quantity and quality of scientific publications, and many bibliometric studies have been conducted investigating these issues. Bibliometric studies on many medical sciences such as rheumatology, oncology, neurosurgery, general surgery orthopedics and its subspecialties have been published before (2-9). It has been shown that the most important factors that increase the quality and quantity of a country's scientific publications are the country's per capita gross domestic product, the amount of funds allocated to scientific research, and national English proficiency (10).

Developments in the diagnosis and treatment of surgical diseases have made subgroup branching a necessity, especially in surgical fields. While all surgical procedures were performed by general surgeons at the beginning of the 20th century, today even the main surgical branches were divided into many sub-disciplines. USA is also a pioneer in this regard. According to a study, 91% of doctors who receive basic orthopedic training receive training in subspecialties (11). It has been reported that the main reason why doctors want to receive minor education is the opportunity to work more in the field of interest and the desire to obtain better financial conditions (12-14). Another effect of minor education programs is their positive contribution to scientific productivity (15).

Hand surgery fellowship training program has started in Turkey since 2014. Fellowship assistants determined by the Medical Minor Specialization Education Entrance Examination have been accepted to more than one training center. The aim of this study is to investigate the effect of hand surgery fellowship training program on Turkey's scientific productivity in this subject.

Method

Web of Science (WoS) database was used for literature review. WoS is one of the world's leading databases for academic impact information and has been used in many studies on scientific productivity (5-8). According to the 2018 Journal Citation Reports (2018 Journal Citation Reports, Thomson Reuters, New York, USA) the top 5 hand surgery journals with the highest impact factor in the "Orthopedics" category, Journal of Hand Surgery-European Volume, Journal of Hand Surgery-American Volume, Journal of Hand Therapy, Hand Surgery & Rehabilitation, and Hand Clinics, were the subjects of this study (16). All publications published in these journals between 2009 and 2019 were examined. Only original scientific articles were included in the study. Reviews, letters to the editor, bibliographic articles, corrections and editorial articles were excluded from the study. The flowchart of the study is given in Figure 1. If the authors of the study were from more than one country, that study was registered in the name of the corresponding author's country. Literature review and information gathering were carried out by two independent authors, and any disagreements about publication selection were resolved through discussion.

The total number of scientific publications was used for the quantitative evaluation of the amount of scientific research. In addition, the number of publications per million population [publication per million population (PmP)], which was the regulation of the number of scientific publications according to the population, was also used. For the preparation of the PmP coefficient, the population data of the countries from the United Nations records were used (17). Apart from these, the total number of citations, the average number of citations per article, the H-index, the normalized citation impact (NCI) and the citation impact relative to the world (CIRW) were used for qualitative evaluation. The H-index is the number of articles from a country that attracts at least n citations (n). It quantifies the scientific productivity and scientific impact of the country (2). The amount of citations increases with time. For this reason, NCI and CIRW coefficients were used in the qualitative analysis of scientific publications in two time periods, one of which was older. These data and coefficients were calculated automatically by the software of the WoS database.

The scientific publications that were the subject of the study were divided into two groups according to the time of publication. The median was 2014, the year the hand surgery fellowship training program started in Turkey, and the years 2009 and 2019 were divided into two equal time intervals. Period A represented the pre-fellowship education program (01/01/2009-06/30/2014), while Period B represented the post-fellowship education program (07/01/2014-12/31/2019).

Descriptive statistics were used primarily. The chi-square test was used to compare Turkey's contribution rate to the total publications between the two time periods and the change in the total number of publications in Turkey and around the world. Regression analysis was used to determine the significant changes in the number of publications during the examined period. A p value of 0.05 or less was considered statistically significant for all analyses.

Results

A total of 5,179 articles on hand surgery research from 5 journals were identified in the WoS database between 01/01/2009-31/12/2019 (Table 1). A total of 60 countries contributed to the hand surgery literature during the time period studied. The USA (n=2.414, 46.7%) had the most articles, followed by France (n=347, 6.7%) and the United Kingdom (n=290, 5.6%). According to the PmP coefficient, Switzerland (10.48) was the first, followed by Singapore (9.41) and Sweden (9.08).

In terms of the total number of citations, the USA (25,484) was in the first place, followed by the United Kingdom (2,875) and Japan (2,250). The first three countries were also the same in the H-index ranking of the countries that were directly related to the total amount of citations and the number of publications.

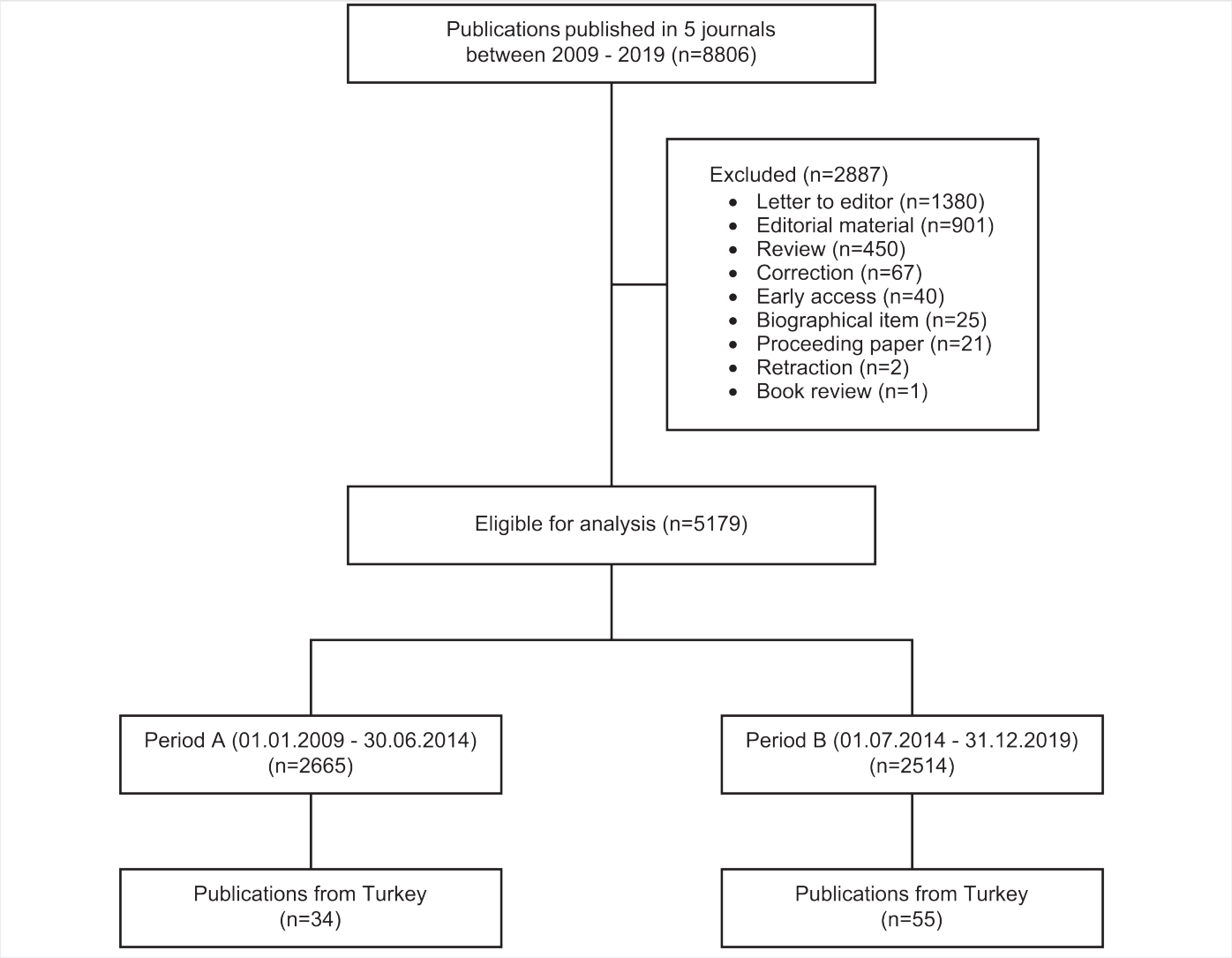

Figure 1. Flowchart of the study

Table 1. The most cited journals on hand surgery indexed in the Science Citation Index Expanded and their impact measurements

	2018 impact factor	5-year impact factor	Number of publications between 2009-2019
Journal of Hand Surgery, American Volume	2.090	2.114	2.663
Journal of Hand Surgery, European Volume	2.225	1.922	1.079
Hand Clinics	1.236	1.477	589
Journal of Hand Therapy	1.532	1.983	433
Hand Surgery & Rehabilitation	0.571	0.571	415

According to the average number of citations per article, Sweden (15.85) came first, followed by Norway (15.27) and Brazil (12.77) (Table 2).

While 51.5% (n=2.665) of the total publications between 2009-2019 were published in Period A, 48.5% (n=2.514) were published in period B. The top three countries according to the total number of publications in both time periods were the USA, France and the United Kingdom. Comparing both time periods showed a 5.7% reduction in the number of hand surgery research publications worldwide. Despite the decrease in the number of publications worldwide, hand surgery publications originating from Turkey increased by 61.8% after the hand surgery fellowship training program was initiated. The number of publications was 34 in period A and 55 in period B in Turkey. According to the total number of publications in 2009-2019, Turkey was in the 12th place (n=89). It was observed that while it was in the 15th rank in the period before the hand surgery fellowship training program (period A), it rose to the 11th rank according to the total number of publications in the period after it (period B). It was observed that Turkey's contribution to total hand surgery publications increased by 69.2% (1.3% vs. 2.2%) between the two time periods (Table 3). As seen in Figures 2a and 2b, while the number of publications in the field of hand surgery in Turkey increased statistically from 2009 to 2019 (R2=0.67, p=0.003), there was no significant increase in the number of publications worldwide (R2=0.41, p=0.53).

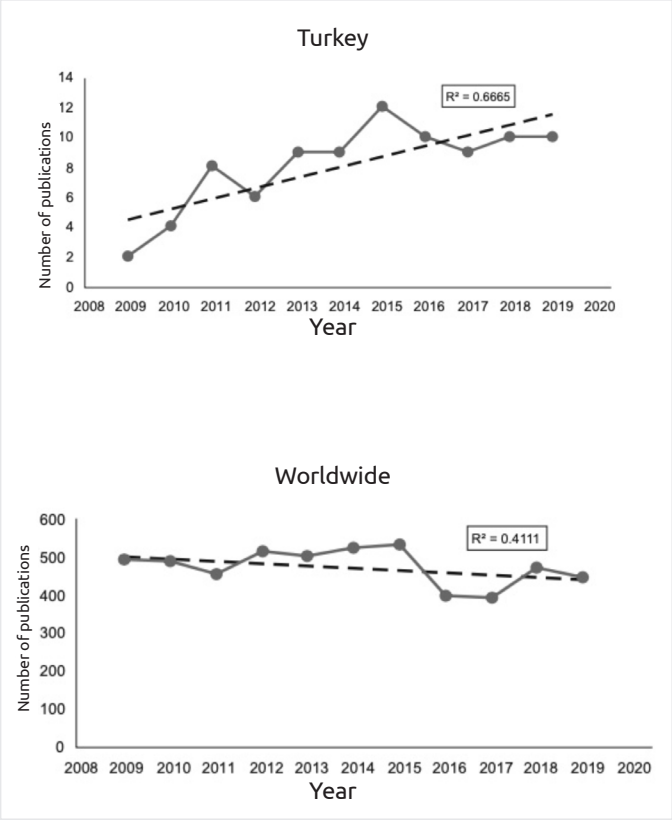

Figure 2. Comparison of the hand surgery publication of Turkey and the World

Discussion

With the present study, we aimed to reveal the quantitative and qualitative impact of the hand surgery fellowship training program on Turkey's scientific productivity in hand surgery. Our study showed that the hand surgery fellowship training program made a significant contribution to Turkey's scientific productivity in the field of hand surgery.

According to the PmP coefficient, which showed the total number of publications according to the population, the top three countries were Switzerland, Sweden and Singapore, respectively. We have seen that industrialized rich countries with low populations lead the way in the number of publications per million population. We observed that countries with similar characteristics rank first in the qualitative ranking of publications. According to the average number of citations per publication, Sweden, Norway and Brazil were in the top three places. According NCI, the first three countries were Norway, Sweden and Denmark, while the first three countries according to CIRW were Sweden, Norway and Brazil. Our study has shown that high quality publications in the field of hand surgery originate from less populated northern European countries. The fact that Northern European countries produce high quality scientific publications is a situation defined in other literature studies on general orthopedics and its subspecialties (6-9,18). Brazil is an exception here, and it's ranking high because of the few studies that have received very high citations (19-21). This situation showed that even a few high-quality scientific articles made by a few researchers can rank countries higher in scientific qualitative rankings.

The increase or decrease in scientific publications indicates the speed of progress in science and technology according to bibliometric theory (2,22). The rapid change in the number of publications marks an important turning point for scientific development (23). Our study showed that the start of the hand surgery fellowship training program was a turning point for the scientific productivity of hand surgery in Turkey. When we looked at the previous publications in the literature, it was stated that doctors who received fellowship training in many medical branches such as general surgery, ophthalmology, plastic surgery and dermatology showed much higher academic productivity (24-28). The same is true for orthopedics. In a study originating from the USA, it was shown that institutions providing arthroplasty fellowship training produced approximately 2/3 of all scientific articles published in the country on this subject (15).

The development of knowledge and techniques on surgical diseases requires surgeons to acquire new skills to provide optimal patient care. This trend has led to the division of the main specialties of surgery into subspecialties (29). Under the orthopedics main specialty, subspecialties started in the USA in the 1970s and spread to the whole world (30). Currently, 90% of the doctors who have completed the orthopedics general education program in the USA continue to subspecialty education programs (31). Perhaps, this may be one of the reasons why the USA is always in the first place in the literature on orthopedics

and its subspecialties (6-9). Hand surgery is the first subspecialty established under the orthopedics main specialty in Turkey, and training activities have started since 2014. We are of the opinion that the opening of other fellowship training programs in both orthopedics and other surgical specialties will contribute to the scientific productivity of the country.

Study Limitations

The present study had several limitations. The 5 hand surgery journals with the highest impact were included in the study. For this reason, publications on hand surgery in general orthopedic journals and basic research journals were excluded from the

Table 2. Data from the top 25 countries with the highest number of publications on hand surgery between 2009 and 2019

Rank	Country	Number of publications	Contribution to the total amount of publications (%)	Number of publications per million population	Total number of citations	Average number of citations per publication	H-index	Normalized citation impact	Citation impact relative to the world
1	USA	2419	46.7	7.59	25,484	10.53	53	0.73	1.11
2	France	347	6.7	5.41	1,804	5.20	19	0.42	0.55
3	United Kingdom	290	5.6	4.43	2,875	9.91	24	0.75	1.04
4	Japan	249	4.8	1.94	2,250	9.04	24	0.61	0.95
5	Canada	205	4.0	5.75	1,825	8.90	22	0.69	0.94
6	Chinese	162	3.1	0.12	1,450	8.95	20	0.88	0.94
7	South Korea	155	3.0	3.06	873	5.63	14	0.48	0.59
8	Holland	130	2.5	7.70	1,063	8.18	17	0.69	0.86
9	Germany	108	2.1	1.33	1,222	11.31	20	0.73	1.19
10	Spain	103	2.0	2.20	1,039	10.09	18	0.78	1.06
11	australia	100	1.9	4.24	1,135	11.35	18	0.87	1.19
12	Turkey	89	1.7	1.15	514	5.78	13	0.59	0.61
13	Sweden	88	1.7	9.08	1,395	15.85	23	1.05	1.67
14	Switzerland	86	1.7	10.48	807	9.38	15	0.85	0.99
15	Belgium	59	1.1	5.26	346	5.86	12	0.64	0.62
16	Italy	53	1.0	0.88	603	11.38	14	0.65	1.20
17	Saudi Arabia	53	1.0	1.71	392	7.40	11	0.42	0.78
18	Singapore	52	1.0	9.41	348	6.69	11	0.53	0.70
19	Brazil	43	0.8	0.21	549	12.77	13	0.72	1.34
20	India	40	0.8	0.03	239	5.98	10	0.52	0.63
21	Denmark	35	0.7	6.18	404	11.54	13	0.9	1.22
22	Finland	31	0.6	5.68	242	7.81	9	0.57	0.82
23	Taiwan	30	0.6	1.28	343	11.43	12	0.79	1.20
24	Austria	25	0.5	2.90	239	9.56	9	0.75	1.01
25	Norway	22	0.4	4.28	336	15.27	11	1.11	1.61

Table 3. Comparison of Turkish hand surgery publications between two different periods

	Period A (01.01.2009-30.06.2014)	Period B (01.07.2014-31.12.2019)
Number of publications	34	55
Rank in the world by number of publications	15	11
Contribution to total publication (%)	1.3	2.2
Total citation	327	187
Average citation per publication	9.62	3.4
H-index	10	7
Normalized citation impact	0.53	0.59
Citation impact relative to the world	0.7	0.78

study. However, we think that the journals included in the study show a general trend since they publish a large part of the total publications on hand surgery. In addition, the WoS database was used for the study; therefore, using another database might cause changes in the results. Citation analysis was used to assess the quality of articles, and the number of citations was considered a proxy measure of influence, reflecting peer recognition and quality of published research (32). However, reasons such as excessive quoting, biased citation and ignorance of the literature reduce the reliability of citation analyzes and become a general problem of literature studies (33).

Conclusion

In conclusion, after the start of the hand surgery fellowship training program, there has been a rapid increase in scientific articles on hand surgery from Turkey. The fellowship training program has positively affected Turkey's scientific productivity in the field of hand surgery.

Ethics

Ethics Committee Approval: İstanbul Medipol University Non-Invasive Clinical Research Ethics Committee (decision no: 369/date: 18/03/2021).

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: B.Ç., U.A., Design: B.Ç., U.A., Data Collection or Processing: B.Ç., U.A., Analysis or Interpretation: B.Ç., U.A.,Literature Search: B.Ç., U.A., Writing: B.Ç., U.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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Original Article

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Maintenance ECT in Recurrent Depression and Treatment Resistant Schizophrenia

Yineleyici Depresif Bozukluk ve Tedaviye Dirençli Şizofrenide İdame EKT

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ABSTRACT

Objective: Electroconvulsive therapy (ECT) has been used for treatment of depression and psychosis for a long time. A less known way of use is as a maintenance treatment for keeping patients stable during remission. Recently ECT has been increasingly used for schizophrenia and depression after remission of the acute exacerbation.

Methods: In this study, we examined files of 24 patients diagnosed as having treatment-resistant schizophrenia (14) or recurrent depression (10) who were treated with ECT on an outpatient basis.

Results: Patients with depression and schizophrenia were followed up for minimum 2 months and maximum 54 months with ECT. The remission rate in both groups were 70%. None of the patients quitted treatment due to adverse effects.

Conclusion: Biases and stigmatization cause a decreased rate of use of ECT in outpatient settings. However, the literature indicates that the morbidity and morbidity due to ECT are negligible. Although our data were collected retrospectively, they showed that ECT might be an option for a maintenance or continuation treatment of recurrent depression and treatment-resistant schizophrenia. Our findings should be supported by randomized studies.

Keywords: ECT, maintenance, recurrent depressive disorder, treatment resistant schizophrenia

ÖZ

Amaç: Elektrokonvülzif terapi (EKT) depresyon ve psikozun akut tedavisinde uzun süredir kullanılan bir nöromodülasyon tedavisidir. Bununla birlikte, hastaların iyilik hallerinin devam etmesi için farmakoterapiye oranla uygulaması daha az bilinen ve tercih edilen bir sürdürüm tedavi şeklidir. Son yıllarda, akut alevlenme tedavisi sonrası sürdürüm tedavisinde de yineleyici depresif bozuklukta ve tedaviye dirençli şizofrenide kullanılmaya başlanmıştır.

Yöntem: Bu çalışmada 2015-2018 yılları arasında yineleyici depresif bozukluk (10) ve tedaviye dirençli şizofreni (14) tanısı ile idame EKT tedavisi alan 24 hastanın verileri retrospektif olarak incelenmiştir.

Bulgular: Remisyon oranları her iki grupta %70 olarak tespit edilmiştir. Hiçbir hasta EKT'ye bağlı yan etkiler nedeniyle tedaviyi bırakmamıştır.

Sonuç: EKT tedavisi hakkındaki ön yargılar ve hastaların damgalanma yaşaması özellikle ayaktan hastalar için az tercih edilen bir tedavi olmasına neden olmaktadır. Ancak literatür verileri incelendiğinde EKT'nin morbidite ve mortalitesinin oldukça düşük olduğu görülmektedir. Bizim bulgularımız retrospektif bir analiz sonucu elde edilmiş olsa da idame EKT'nin yineleyici depresif bozukluk ve tedaviye dirençli şizofreninin sürdürüm tedavisi için bir seçenek olabileceğini göstermektedir. Ancak bulguların gelecek randomize kontrollü çalışmalarla da desteklenmesi gerekmektedir.

Anahtar Sözcükler: EKT, idame, yineleyici depresif bozukluk, tedaviye dirençli şizofreni

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Introduction

Electroconvulsive therapy (ECT) continues to be used as the most effective somatic, non-invasive treatment in psychiatry for nearly a century. This process of experience has proven the reliability and effectiveness of ECT in many psychiatric disorders, especially depression, bipolar disorder, and schizophrenia, which no other somatic treatment can reach (1). Although it is an elective treatment option in many patients that do not respond to pharmacotherapy and psychotherapy, it is the first choice when it is necessary to achieve rapid treatment in patients in whom there are affective, psychotic and catatonic symptoms, who have a risk of suicide, in whom there is worsening in general health, or in whom the use of drugs is not found safe (for example, pregnancy) or cannot be tolerated (1,2).

Contrary to common negative opinions, ECT is a safe and comfortable treatment method. The most common indication for ECT, known to all psychiatrists, is treatment-resistant and severe depression. Major depression is a recurrent disease with a lifetime prevalence of 7-12% for men and 20-25% for women. If left untreated, the possibility of becoming chronic, and the mortality and morbidity are high (3).

ECT can also be seen as the first choice especially in patients with psychotic symptoms, accompanied by suicidal tendencies, and emergency situations such as catatonia and neuroleptic malignant syndrome (4). Although the most well-known indication of ECT is depression, its effectiveness is also known in clinical practice in many non-depressive conditions. In controlled studies, the effectiveness of ECT has also been reported in conditions such as schizophrenia, mania, and catatonia (2). The use of ECT in manic episodes has been established in the literature and treatment guidelines (4). Today, it is applied in patients who have not responded to anti-manic drug therapy or who are in life-threatening manic excitations or catatonic conditions. There are supportive findings in the literature with the administration of maintenance ECT in patients whose acute period of manic episode has been treated with ECT, but whose well-being cannot be maintained with medication (4). In addition to these, there are publications showing that it can also be used in obsessive compulsive disorder (5). Although its effectiveness is known in severe, suicidal and psychotic depression, its use is limited due to widespread stigmatization and misinformation about side effects. In recent years, especially anesthetized ECT has significantly reduced the risk of complications. For example, in large case series, morbidity and mortality associated with ECT have been found to be much lower than previously thought (6,7).

Conservation therapy is generally accepted after a successful ECT response. The most important reason for this is the high rate of relapse in psychiatric disorders. It is still unclear whether the high relapse rate after ECT is related to abrupt termination of ECT, maintenance therapy, or the course of the disease itself. Sackeim et al. treated one group with placebo, one group with nortriptyline, and another group with nortriptyline and lithium following index ECT in their study performed with 84 patients with unipolar depression. They reported that relapse rate was 60% in the group using only nortriptyline, 39% in the group using nortriptyline and lithium, and 84% in the placebo group within 6 months (8). In the nortriptyline and lithium group, all but one relapse occurred in the first 5 weeks after ECT.

Maintenance ECT is an important option to prevent recurrence in the maintenance treatment of patients who have benefited from ECT in acute treatment. Despite the use of ECT for more than eighty years, studies and applications related to maintenance ECT are limited. It is still not known to whom, how often and when maintenance ECT should be administered. More descriptive studies are needed (9,10). Prudic et al. conducted a study to understand the effect of adding drugs at the start of ECT in preventing relapse. Placebo, nortriptyline or venlafaxine were added to the patients at the beginning of ECT. After ECT, lithium was added to all three groups. Even when aggressive pharmacotherapy was applied, relapse rate was reported 50%, and it was thought that adding medication at the beginning of ECT had no effect on relapse. At the end of this study, it was recommended to examine not abrupt but gradual discontinuation of ECT (11). In the CORE (Consortium for research in ECT) studies that started in 1997, patients with depression were randomly divided into groups. The efficacy of maintenance ECT, lithium and nortriptyline in maintenance therapy was compared. While no difference was found between the relapse rates of the two groups, it was reported that relapse was delayed in patients receiving maintenance ECT (12).

In the first phase of the PRIDE studies of the 2010s, 61.7% remission was achieved with the combination of unilateral ECT and venlafaxine in patients with geriatric depression (13). In the second phase, the effectiveness of pharmacotherapy (lithium and venlafaxine) group and both ECT and pharmacotherapy group in the maintenance treatment was compared, and the decrease in the Hamilton Depression Rating scale (HAM-D) scores of the ECT and pharmacotherapy group was found to be statistically higher (14). In these studies, the STABLE algorithm, which was used to determine the frequency of maintenance ECT, was used to determine the individual frequency. In this algorithm, the frequency is determined by applying HAM-D and the Mini Mental State Exam (MMSE) (15).

Nordenskjöld et al. (16), on the other hand, compared only pharmacotherapy with ECT and pharmacotherapy, and found the relapse rates to be significantly lower in the second group. It was also reported that 4 patients who attempted suicide were in the pharmacotherapy group. Cognitive side effects were also evaluated in this study, and they were not found to be statistically significant.

Contrary to maintenance ECT applications in recurrent depression, studies related to maintenance ECT application in treatment-resistant schizophrenia are limited in the literature. Maintenance ECT can also be combined with antipsychotics for maintenance therapy in patients with schizophrenia who have achieved remission with ECT (17). Due to limited literature, there is no consensus on maintenance ECT applications. Patients

with treatment-resistant schizophrenia in whom clozapine and ECT are frequently used together are also reported. These two are the most used combination and most beneficial (18,19). The combination of clozapine and maintenance ECT was found to be effective in patients with catatonic schizophrenia, aggression, suicidal ideation, unresponsiveness to pharmacotherapy, or a previously known ECT response (20). In another study, cognitive side effects did not differ in acute or maintenance ECT (21,22).

In their retrospective study, Krepela et al. found that maintenance ECT was not effective in hallucinations and delusions in 19 patients with chronic pharmacotherapy-resistant schizophrenia; however, they found that maintenance ECT affected behavioral symptoms such as suicidal thoughts/behaviors, aggression, refusal to eat, and catatonia, and that increased social functionality (23).

In our study, we tried to examine the effectiveness of maintenance ECT in these 2 diseases by including patients with recurrent depressive disorder and patients with treatment-resistant schizophrenia who were admitted to a reference psychiatric hospital in Istanbul between 2015-2018 and received maintenance ECT. Considering that there are few studies on maintenance ECT in the literature, it is anticipated that the findings will contribute to the literature on the effectiveness of the method.

Method

In this retrospective study, the data of patients who received maintenance ECT between 2015 and 2018 in a reference center hospital (NP İstanbul Brain Hospital, İstanbul) were retrospectively analyzed. All of the patients received ECT during hospitalization and were followed up with maintenance ECT to prevent recurrence after discharge. Diagnostic groups were recurrent depressive disorder and schizophrenia groups, and both diagnoses were made by a psychiatrist through clinical evaluation according to DSM-4 TR and 5 criteria. The study was designed retrospectively. With the archive scanning method, patients who were given maintenance ECT in the hospital records in 2015-2018 were determined. It was required that the patient was followed up with maintenance ECT for at least 2 months and received at least 2 ECTs. The patients were observed to remain in remission or to relapse during maintenance ECT, and the remission/relapse assessment was made by psychiatrist in the follow up.

Outpatient ECT Method: Findings

The mean age of the group was 35 and the standard deviation was 10.7. Seven of the patients were women. The patients received an average of 5.2 sessions of maintenance ECT (minimum 2, maximum 18). Fourteen of the patients were diagnosed as having schizophrenia and 10 patients were diagnosed as having recurrent depressive disorder, and they received maintenance ECT. Although there were 2 women in the schizophrenia group and 2 women in the depression group, the gender distribution did not reach significance in the chi-square test (p=0.14). The characteristics of the patients can be seen in Table 1 in detail.

According to the results, 10 of 14 patients with schizophrenia were followed up with remission, while 4 of them relapsed. Recurrence was detected in 3 out of 10 patients with depression. When the recurrence risk in the groups was compared with the chi-square test, there was no significant difference (p=0.25). When the two groups were compared in terms of the number of maintenance ECT, no significant difference was found (p=0.22). When the ECT number of the patients who remained in remission and who did not remain in remission during the follow-up was compared, no significant difference was found (p=0.48). When the number of ECT received during hospitalization by patients in remission and patients without remission was compared, no significant difference was found (p=0.48). When the number of ECT received during hospitalization by patients in remission and patients without remission was compared, no significant difference was found (p=0.08).

Discussion

In this study, the effectiveness of maintenance ECT was investigated retrospectively in patients with treatment-resistant schizophrenia and recurrent depressive disorder. In the study, the efficacy criterion was remission/relapse, and a similarly low number of relapses was observed in both groups (remission rate approximately 70%). These findings show that maintenance ECT can be used as an alternative to medication in treatment-resistant schizophrenia and recurrent depressive disorder. Publications on maintenance ECT in the literature mostly consist of case reports, case series and retrospective analyzes (24). Except for the few studies mentioned in the introduction, the number of randomized controlled studies, specifically examining cognitive side effects, is limited. However, psychiatrists frequently apply this treatment only to their patients who are resistant to treatment or who have relapsed. Studies in the literature mostly focus on depression and schizophrenia. The lack of statistically significant difference in relapse rates between the two groups in our study suggests that maintenance ECT can be used more frequently in treatment-resistant schizophrenia, like its widespread use in depression.

An important uncertainty relates to determining the frequency and number of maintenance ECT. Although the general practice in clinical practice is application of ECT as often as the physician deems necessary, there is no standardized decision-making algorithm. The STABLE algorithm is a practical algorithm that proposes to determine the frequency by evaluating the cognitive side effects and change in depressive symptoms (25). In the follow-up workshop held by the participants of the CORE study in 2017, it was suggested that maintenance ECT could be preferred when there were episodic recurrent severe depressive episodes, presence of psychotic features, resistance to previous maintenance drug therapy, bipolar depression, the usefulness of index ECT applied for the second time, cognitive side effects of previous ECTs tolerated by the patient, response to maintenance ECT in the past, the patient's preference, the patient's ability to continue regular psychiatric follow-up, and the patient's medical and cognitive well-being (especially for the elderly) (13,14).

Table 1. Clinical and demographic characteristics of the patients

Patient ID	Diagnosis	Number of index ECT	Number of maintenance ECT	Remission	Age	Gender
1	RDD	11	14	2	31	M
2	RDD	7	6	2	38	F
3	RDD	14	18	1	45	F
4	RDD	12	7	1	45	F
5	RDD	8	3	1	54	F
6	RDD	10	2	1	28	M
7	RDD	7	2	1	69	F
8	RDD	10	5	2	40	M
9	RDD	7	7	1	33	M
10	RDD	10	2	1	33	M
11	SCH	10	13	2	37	M
12	SCH	12	2	2	26	F
13	SCH	10	2	2	27	M
14	SCH	7	2	2	27	M
15	SCH	12	7	1	25	M
16	SCH	11	7	1	33	M
17	SCH	10	6	1	23	M
18	SCH	10	4	1	38	M
19	SCH	10	3	1	23	M
20	SCH	8	2	1	44	M
21	SCH	10	2	1	35	M
22	SCH	10	2	1	27	M
23	SCH	7	2	1	41	M
24	SCH	10	4	1	30	F

RDD: Recurrent depressive disorder, SCH: Schizophrenia, Remission, 1 yes, 2 no index, ECT: ECT applied sequentially at the start of treatment

An important limitation of our study was that it was a retrospective study. In this study, patient files were scanned retrospectively, and evaluation of remission was also done retrospectively. Therefore, structured diagnostic tools such as SCID-I could not be used, and diagnostic reliability was limited to clinician evaluation. Likewise, the inability to include clinical scales to objectively evaluate remission and relapse to the design of our study reduced its power. However, the number of prospective maintenance ECT studies is very few in the literature, and to our knowledge, the number of controlled studies is also limited. Limited objective study data on a clinically known treatment also prevent prejudices from being demolished. The most important reason for this is perhaps the difficulty of maintenance ECT and the difficulties encountered in finding patients for studies.

Study Limitations

Another limitation of our study was that cognitive problems, one of the most important known side effects of ECT, were not measured. Since the confusion and amnesia seen in the acute exacerbation period of the disease can also be seen during maintenance ECT, it will be useful to measure the memory performance of patients during maintenance ECT in future studies.

Conclusion

As a result, although ECT is generally accepted by all physicians, it is a less preferred treatment method due to prejudices about stigmatization and side effects. In this study, we did not observe that any patient discontinued the study due to side effects related to ECT. Therefore, the findings suggest that maintenance ECT can be safely applied in outpatients as well.

Ethics

Ethics Committee Approval: Üsküdar University Non-Interventional Research Ethics Committee Presidency (date: 27.05.2020/no: 61351342/2020-257).

Peer-review: Externally and internally peer reviewed.

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Original Article

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Increasing the Awareness of the Parents Regarding the Oral Health Status of Their 0-3 Years-Old Children

0-3 Yaş Grubu Çocuğu Olan Ebeveynlerin, Çocuklarının Ağız ve Diş Sağlığı Hakkında Farkındalıklarının Artırılması

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ABSTRACT

Objective: This study aimed to: (a) compare nursing students' knowledge about the oral and dental health of children before and after oral health education; (b) evaluate the effectiveness of oral health education of parents with children aged 0-3-year-old by these trained students during home visits.

Methods: In this quasiexperimental study, firstly, 60 senior students in the nursing department were trained on infants' and young children's oral and dental health through standartized training modules. Secondly, 180 parents with children aged 0-3 from low socioeconomic status were trained by the nursing students during home visits with face to face interviews. Both nursing students' and parents' pre and post-training knowledge levels and the changes in their awareness after training were measured using standard questions which were administered as pre-test (preT) and post-test (postT) with 1 week intervals. Wilcoxon test was used to assess the differences of correct answers between pre- and post-tests. The significant value was considered as $p<0.05$.

Results: The mean age of the children of the parents was 18.92±9.96 months. The median values of preT and postT were found to be 28 and 37.5, respectively for the total number of correct answers given to 50 questions related to the education consisting of seven modules. It was determined that the total number of correct answers increased statistically significantly in postT ($p<0.001$). The median

ÖZ

Amaç: Bu çalışmanın amacı, 0-3 yaş grubu çocuğu olan ebeveynlerin, çocuklarının ağız ve diş sağlığı hakkında bilgi düzeylerinin ölçülmesi ve farkındalıklarının hemşirelik son sınıf öğrencileri aracılığı ile ev ziyaretleri kapsamında artırılmasını sağlamaktır.

Yöntemler: İki basamaktan oluşan araştırmanın, ilk basamağında 60 son sınıf hemşirelik öğrencisine çocuk ve yenidoğanlarda ağız ve diş sağlığı hakkında eğitim verildi. İkinci basamakta, 60 son sınıf hemşirelik öğrencisi ev ziyaretleri kapsamında 0-3 yaş çocuğu olan 180 ebeveyni çocuklarda ağız ve diş sağlığı hakkında yüz yüze görüşmeler ve broşürler aracılığı ile bilgilendirdi. Hem 60 son sınıf hemşirelik öğrencisi hem de 180 ebeveynin farkındalık ve bilgi düzeylerindeki değişim, derslerin anlatımından önce ve sonra, eğitimin etkinliğini ölçmeye yarayan standart sorular ön-test (ÖT) ve son-test (ST) olacak şekilde 1 hafta ara ile uygulanarak tespit edildi. ÖT-ST arasındaki değişimler Wilcoxon testi ile $p<0,05$ anlamlılık düzeyinde analiz edildi.

Bulgular: Ebeveynlere ait çocukların yaş ortalaması 18,92±9,96 ay olarak bulgulandı. Yedi modülden oluşan eğitime ait 50 adet soruya verilen toplam doğru cevap sayısının ÖT ve ST medyan değerleri 28 ve 37,5 olarak saptandı. Toplam doğru cevap sayısının ST'de istatistiksel olarak anlamlı düzeyde arttığı belirlendi ($p<0,001$). Ebeveynlere broşürler aracılığı ile uygulanan eğitimdeki 14 adet sorunun ÖT ve ST doğru cevap sayısı medyan değerleri

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values of preT and postT correct answers to 14 questions in the education given to parents through brochures were found to be 6 and 10, respectively. It was determined that the total number of correct answers increased statistically significantly in postT after the training (p<0.001).

Conclusion: The knowledge level of nursing students about the oral and dental health of children can be increased through standardized training programs. Home visits and face-to-face interviews are applicable to increase awareness in parents by non-dental healthcare professionals.

Keywords: Oral health, awareness, health education, home visits, nursing students

6 ve 10 olarak tespit edildi. Toplam doğru cevap sayısının eğitim sonrası ST'de istatistiksel olarak anlamlı düzeyde arttığı belirlendi (p<0,001).

Sonuç: Diş hekimi olmayan sağlık çalışanlarının koruyucu dental programlarda yer alabileceği, yaşamın ilk yıllarında ebeveynlerin ve özellikle annelerin toplum sağlığı için çalışan hemşireler aracılığı ile ev ziyaretleri kapsamında bilgilendirilmesinin ve çocuklarının ağız ve diş sağlığı hakkında farkındalıklarının artırılmasının yararlı olabileceği düşünülebilir.

Anahtar Sözcükler: Ağız sağlığı, farkındalık, sağlık eğitimi, ev ziyaretleri, hemşirelik öğrencisi

Introduction

The oral and dental health of children is essential for general body health and healthy adulthood (1). Considered as a whole, oral health in childhood includes topics related to nutritional and cleaning behaviors, first dentist appointment, tooth cavities, preventive treatments, non-nutritive sucking habits, changes in the jaws and teeth during growth and development, mouth injuries, and other oral diseases (2,3). Early childhood caries (ECC) is defined as the presence of one or more decayed tooth (cavitated or non-cavitated lesions), missing tooth due to caries, or filled surfaces in the primary teeth of children younger than 6 years of age, and any sign of smooth surface caries in children younger than three years is an indicator of severe ECC (S-ECC) (4). According to a study carried out in 2015 (5); caries observed in primary teeth affected 560 million children worldwide and became the 12th most common disease when examined together at all ages. The high prevalence of ECC in children aged 1, 2, and 3, which is 17%, 36%, and 43%, respectively, indicates that this disease is left untreated in children under 3 years of age (6,7). The treatment process of ECC requires sedation/general anesthesia methods with high costs and potential health risks due to the cooperation difficulties of the age group it affects, and the recurrence of lesions is frequently observed after the procedures, thus creating a social and economic burden (8-10). Dental injuries are the most common ones of oral injuries, and luxation injuries are the most common injuries in children aged 1-3 years and usually caused by falls (11,12). Oral injuries are often perceived as a neglected public health problem due to the inability to access appropriate healthcare at the right time (13). The untreated early oral and dental diseases observed in children cause eating difficulties, pain complaints, increase in the risk of infection, growth and development problems, sleeping difficulty, restricted social life, increase in absenteeism at school, behavioral problems, and decrease in the quality of life of the child and family (14-16).

The biological, behavioral, psychosocial characteristics and awareness and knowledge levels of those responsible for the primary care of the child (mostly the mother) are the main factors that have a role in the maintenance of oral and dental health of children (17). In developing countries, social and economic inequalities, insufficient dental care centers and staff, non-dental health professionals who do not have enough equipment in the oral and dental health of children, and inability to integrate oral health into the primary health care system cause preventable oral and dental health problems in children to continue to be relevant and to increase (18,19).

The 0-3 age period is an important time period for parents to have awareness of oral and dental health in children and receive guidance for the development of correct attitudes and behaviors (20). Nurses are among the first healthcare professionals that the family and child encounter in the healthcare system for reasons such as home visits, routine controls, information, vaccination, and childhood diseases. This situation provides an important advantage to this occupational group in terms of informing parents about oral and dental health in children (21,22).

This study aims to educate senior nursing students about oral and dental health in neonatal and childhood periods and to raise awareness of parents with children aged 0-3 about the oral and dental health of children by means of face-to-face interviews and brochures through these nursing students during home visits. Our hypotheses are;

1. After the education to be given to nursing students, awareness and knowledge levels can be increased,

2. With the nursing students and the brochures prepared, the awareness and knowledge level of the parents can be increased after the education.

Methods

Ethical Consideration

The study was approved by the Karadeniz Technical University Committee on Human Research (approval number: 2015/42). Before ethical approval, permission was obtained through correspondence with Georgetown University for use of their courses via online access and the tests prepared in international standards to measure the effectiveness of the education that were available back in 2016 under the title "A Health Professional's Guide to Pediatric Oral Health Management". Although the educational content at the website was no longer available, the training modules were provided as a child oral health resource for healthcare providers previously (23). All the documents

regarding permission, original and/or Turkish versions of training modules, tests and previous presentations are available at the web address of http://tamertuzuner.com/0_3_yas_cocugu_bulunan_ebeveyn_egitimi.zip.

Necessary legal permissions were also obtained from the Republic of Turkey Ministry of Health and Public Health Institution for home visits and field activities involving parental education. Informed written consent was obtained from both nursing students and parents that participated in the study.

Subjects and Sample Size

The study was conducted in Trabzon, Turkey with 180 parents with children aged 0-3 years old who lived in City Center, and 60 senior nursing students studying in Karadeniz Technical University, Faculty of Health Sciences, Class of 2017. Parents selection were made from low socioeconomic status (monthly income below TRY 1770) (24).

Since the number of possible nursing students that could be included to the study population were obtained as 60, we included the whole students into the study design who signed the consent form. Thus, we decided to achieve the final calculation by considering the total number of parents. After considering alpha error =0.05, beta error =0.20 and the effect size as 0.20, the required parent numbers were determined as 164. However, by considering the possible dropouts, missing data, and failures for the study design, we determined to use 180 (averaged 10% increased) parents. Thus, one nurse was matched with 3 parents to complete study design.

Study Design

In this study, pretest-posttest model, one of the quasi-experimental research designs, was used (Table 1). The translation process for educational content and questions asked to both nurses and parents was carried out in two stages. In the first part, the original English version was translated into Turkish separately by a professional interpreter and a pediatric dentist with a good command of English who was not a participant in the study, and a draft was created by combining the Turkish versions. In the second part, the Turkish draft version was answered by 10 nursing students and parents who were not included in the study, and points in the drafts that could not be understood were evaluated and edited. The test-retest (internal consistency) of the answers were also tested between 1 week intervals by nursing students and parents who were not included in the study with final Turkish version. The final Turkish version was translated into English by a professional interpreter and compared with the original one (Table 2). As a result of compliance and internal consistency, all questions were used in the study.

The research was carried out in two stages. In the first stage, 60 senior nursing students were given theoretical and practical education with a training guide which included such topics as; an introduction to infants and young children's oral health, oral conditions and abnormalities, prevention of oral diseases, non-nutritive sucking habits, oral injury, infants and young children with special health care needs and the relationship between general health and oral health, by faculty members from the department of pediatric dentistry, department of pediatric nursing and department of public health nursing. The training content was documented to facilitate the follow-up of the courses by nursing students and to ensure their use later. A survey with 50 questions (Table 3) was applied to nursing students as a pretest before the training to measure the level of knowledge, awareness, and demographic variables. The questionnaire to measure the level of knowledge of the modules at the beginning of the study were re-administered as a posttest one week later and recorded.

In the second stage, some of the survey questions (relatively important topics) applied to nursing students were designed for parents as a survey of 14 questions (Table 4) by faculty members from the department of pediatric dentistry, and applied to parents as a pre-test. Previously trained senior nursing students visited selected families for oral health education with brochures, dental toothbrushes, and models. Home-visits were conducted under supervision of faculty members of Faculty of Health Sciences. The families were visited again one week after training and the same questionnaire to measure level of knowledge and awareness was repeated as a post-test. The results were analyzed to evaluate the success of training.

Statistical Analysis

The data were analyzed with SPSS for Windows 17.0. Descriptive statistics of demographic data were recorded for both nursing students and parents. The distributions of the correct answers to the questionnaires were also calculated with descriptive statistics. The Cronbach alpha level was calculated for test-retest activity. Compliance with normal distribution was evaluated by Shapiro-Wilk test. The Wilcoxon test was used to assess the differences of the correct answers given by students and the parents between one-week intervals. The confidence interval was determined as 95% in all methods.

Table 1. Quasiexperimental research design

First stage	Second stage
50-question baseline survey 60 senior nursing students	14-question baseline survey 180 parents
Nursing students' training about children's oral health	Parents' oral health education by nursing students in home visits with face-to-face interviews
One week after training 50-question survey 60 senior nursing students	One week after educational visit 14-question survey 180 parents

Results

Demographic information of nursing students and parents who participated in the questionnaire was given in Table 5. It was found that nursing students were mostly female, and the majority of the parents were mothers. The educational level of the parents in the research group was found to be generally primary and secondary education levels. The mean age of the children in the study was 18.92±9.96 months. The Cronbach alpha levels were found higher than >0.70 both for nursing students and parents.

Considering the findings of oral health education for nursing students; who were educated through standardizes training modules and whose knowledge/awareness levels were evaluated with pretest/posttest methods (50 questions), it was determined that the number of correct answers were higher than the pretest in the posttest ($p<0.001$) except for the module 5, and even an increase was found in all subheadings ($p>0.05$) (Table 6).

As a result of 14-question pretest/posttest of brochure-based information given to parents about the oral and dental health of their 0-3 year-old children within the scope of home visits, it was found that awareness levels increased significantly ($p<0.001$) (Table 7).

Discussion

In this study with quasi-experimental design, the increase in knowledge and awareness of 60 senior nursing students through standardized training programs and 180 parents with children aged 0-3 years, who were educated by these nurses through home visits, about oral and dental health in children was investigated and all hypotheses were proven to be right.

As far as we know, there was no study through which non-dental health professionals performed a practice in the field in order to raise awareness of parents with children at such young ages in our country. Social and behavioral factors such as the parents' level of education and income, family's level of knowledge of the oral health including the feeding and cleaning habits, the number of children in the family, and the environmental conditions the child lives in are observed among the risk factors for early childhood oral and dental health (26,27). Preventive oral and dental health services in children primarily aim to reach the parent responsible for the primary care of the child and to increase knowledge and awareness on this issue

Table 2. Translation algorithm of educational content

Original English version	
Professional interpreter	Pediatric dentist with good command of English
Combined Turkish versions as a draft	
A pilot study of the Turkish version was performed with 10 nursing students and 10 parents	
Editing	
Test-retest (internal consistency)	
The final Turkish version translated into English by a professional interpreter and compared with the original version	

Table 3. Topics in training modules and questions in nursing students'survey

Module 1 (N=5): An introduction to infants' and young children's oral health
How can health professionals promote the oral health of infants and children?
Which group of children is especially vulnerable to oral disease?
What is the most common chronic childhood disease among children?
What types of medications are most likely to cause intrinsic staining of the teeth if taken
during tooth formation?
Which of the following is a potential outcome of oral health problems in young children?
Module 2 (N=9): Managing infants' and young children's oral health
Dental caries is?
What should health professionals do if they encounter a young child whose teeth
have not erupted within 6 months of the schedule?
When does primary tooth eruption typically begin?
Which of the following is NOT recommended to reduce teething discomfort?
Why is the oral screening important?
How should an infant or child under age 30 months be positioned during the oral
screening?
When should the first oral health examination performed by a dentist?
How often should children receive oral examinations performed by a dentist?
What is anticipatory guidance?
Module 3 (N=9): Oral conditions and abnormalities
How should a child's primary teeth appear?
How should an infant's or young child's healthy lips and tongue appear?
How should a child's healthy facial bones usually appear?
Which of the following is NOT a risk factor associated with early childhood caries?
What typically happens when tooth decay is not treated?
What is dental hypoplasia?
What causes fluorosis?
What can cause extrinsic coloration?
How does candidiasis appear?
Module 4 (N=7): Prevention of oral diseases
What is dental plaque composed of?
What happens if dental plaque is left undisturbed?
When should parents begin cleaning their infant's teeth?
When are children able to clean their teeth effectively without help?
How does drinking fluoridated water affect children?
At what age should fluoridated toothpaste be introduced?
What kinds of snacks should young children be encouraged to eat?

Table 3. Continued

Module 5 (N=6): Non-nutritive sucking habits
Which of the following benefits can non-nutritive sucking provide for infants and young children?
What proportion of children who suck fingers or a thumb discontinue the habit by age 4?
Which of the following factors have NOT been associated with prolonged non-nutritive
sucking habits?
What are the effects of non-nutritive sucking habits on developing teeth in infants and
children under age 3?
Which of the following does NOT determine the ways in which teeth change as a result
of non-nutritive sucking habits?
Which of the following is NOT necessary for an intervention to help a child stop a
non-nutritive sucking habit?
Module 6 (N=10): Oral Injury
What percentage of young children may experience injuries to the primary teeth?
In what age group does injury to the primary teeth occur most often?
Which of the following is NOT appropriate anticipatory guidance for health professionals
to provide parents?
What should a health professional do if he or she suspects child abuse or neglect?
In infants and young children, which teeth are most often affected by oral injury?
What causes discoloration of primary teeth?
What dictates the intervention strategy for injured primary teeth?
How long after oral injuries occur should they be assessed?
Which of the following statements are true in the case of an avulsed primary tooth?
Which of the following should a health professional NOT advise a parent to do in the
case of an avulsed permanent tooth?
Module 7 (N=4): Infants and young children with special health care needs
Which of the following may affect oral health?
What can bruxism lead to?
What can cause gingival overgrowth?
How can health professionals help parents ensure that their child with special health care needs experiences optimal oral health?

(28). This study was initiated by foreseeing that it would be beneficial that nurses took an active role in preventive oral and dental health guidance services for parents following the experiences they would gain by expanding their curriculum.

The necessity of integration of oral and dental health as a part of general health with primary healthcare services is an issue that has been studied in many studies globally (29-31). In the prevention of ECC, as well as general practitioners and pediatricians, with whom family and child meet before the dentist in the health system, nurses, too, have an advantageous position in terms of information, early diagnosis, and anticipatory guidance (32). This kind of integration concept requires a complex structure and should be approached from different perspectives. Common barriers to integration are observed as the absence of appropriate health policies and the lack of education of non-dental health professionals in oral health (33). In a study conducted in Turkey, (25) it was presented that pediatric nurses had insufficient knowledge of oral and dental health in newborns and children.

Table 4. Questionnaire of parents

Which of the following is one of the results of oral health problems in children?
Dental decay is…
When do baby teeth usually start eruption?
Which of the following is not recommended for comforting the child during teething?
When should a child first visit the dentist?
How often should child visit the dentist?
How a child's baby teeth should look like?
Which of the following is not a risk factor for early childhood caries?
When should parents begin to clean the baby's teeth
When children can clean their teeth effectively without help?
When should children start to use fluoride-containing toothpaste?
Which kind of snacks should children be encouraged to eat?
When should oral injuries be examined after they occur?
Which of the following may affect oral health?

In 1986, the American Academy of Pediatric Dentistry recommended that children's first dentist visit should be performed before the age of 1 (34). In our country, the first encounter of a child with the dentist occurs if the oral and dental problems catch the attention of the parents or when these problems progress enough to affect the daily life of the child. The insufficient number of pediatric dentists, the unwillingness of general dental practitioners to care for pediatric patients, and the difficulty experienced by families in accessing an institution providing service for the dental health of their children due to geographical and socioeconomic barriers are among the factors that require the scope of general health services to be changed in preventing ECC. In the report published by the Organization for Economic Cooperation and Development and the European Union (EU), it is stated that due to the income levels, geographical conditions, and the limitations of the health system of 28 member countries of the EU, the unmet oral health needs are disadvantageous to the low-income group, according to the data of 2014 (35). There are studies presenting the prevalence of S-ECC as 51% (36), %78.57 (37), and %61 (38) in Turkey. Considering that these studies were performed on patients presented to dental

Table 5. Demographic variables of the study

	Age (mean ± SD)	Gender (N/%)		Education level (N/%)	
		Female	Male	Female	Male
Children	18.92±9.96 months	93/51.7	87/48.3		
Nursing students	21±1.2 year	46/76.7	14/ 23.3	Senior class in nursing graduate programme	
Parents	32.25±7.32 year	173/96.1	7/3.9	Primary education 100/55.6	Primary education 81/45
				High school 60/33.3	High school 70/38.9
				University graduate 19/10.6	University graduate 27/15
				Postgraduate 1/0.5	Postgraduate 2/1.1

SD: Standard deviation

Table 6. Results of surveys of nursing students (median values of correct answers)

A health professional's guide to pediatric oral health management	Baseline pre-test median (min-max)	1 week later post-test **median (min-max)**
Module 1 (N=5): An introduction to infants' and young children's oral health	**3 (0-5)^{A}**	**5 (2-5)^{B}**
Module 2 (N=9): Managing infants' and young children's oral health	**6 (3-8)^{A}**	**8 (1-9)^{B}**
Module 3 (N=9): Oral conditions and abnormalities	**5 (2-8)^{A}**	**8 (3-9)^{B}**
Module 4 (N=7): Prevention of oral diseases	**5 (2-7)^{A}**	**7 (3-8)^{B}**
Module 5 (N=6): Non-nutritive sucking habits	**2 (0-5)^{A}**	**2 (0-5)^{A}**
Module 6 (N=10): Oral injury	**4 (1-7)^{A}**	**7 (1-10)^{B}**
Module 7 (N=4): Infants and young children with special health care needs	**2 (0-4)^{A}**	**3 (0-4)^{B}**
TOTAL (N=50)	**28 (15-33)^{A}**	**37.5 (20-47)^{B}**

*A-B: p<0.001, **A-A: p=0.169; p>0.05 p values by Wilcoxon Signed Rank test, min: Minimum, max: Maximum

Table 7. Results of the survey of parents (median values of correct answers)

	Baseline pre-test median (min-max)	One week after home visit post-test median (min-max)
14 questions prepared for parents	**6 (1-12)^{a}**	**10 (4-14)^{b}**

*a-b: p<0.001
p values by Wilcoxon Signed Rank test

clinics of universities in developed cities in Turkey, it could be projected that the number of children without access to dental health services across the country was much more. According to Petersen and Kwan (39), the population living in cities has higher rates of access to oral and dental health services compared to those living in rural areas in all income brackets.

Parents who participated in the study were of low socioeconomic status and their educational levels were mostly primary and secondary according to the data of the local Family Health Center. Considering the effect of social inequality on access to dental services, the selection of the sample group was both a strong feature of the study and a risk of bias. For the same reason, the fact that the method chosen to raise awareness in parents was through home visits and face-to-face interviews was among the factors that increased the effectiveness of the study in overcoming cultural and geographical barriers, but partially carried the risk of bias. Home visits are comprehended as a promising approach to the implementation of preventive health services for psychosocially and economically disadvantaged families (40,41). Accordingly, in our study, awareness was decided to be created through home visits.

The training modules used in the study were not only related to ECC, but also included the issues such as anomalies that could be observed in the oral cavity, prevention of oral diseases,

non-nutritive sucking habits, oral injuries, and the relationship between oral health and general health. English-Turkish and Turkish-English translations of these training modules were performed and standardized by different people who were competent in their fields. Quasi-experimental research designs test causal hypotheses and analyse changes in outcomes before and after an intervention (42). The effectiveness of these standardized training modules was evaluated by pre/post-testing on both nursing students and parents. The increase in the levels of knowledge and awareness of nursing students and parents educated by these students about the oral and dental health of children at the end of the tests indicated that these standard training modules were effective. Consequently, we foresee that applying the comprehensive education model in the study to larger populations in the future may be beneficial.

Study Limitations

There were some limitations in the study. Quasi-experimental methods are most often used when it is not possible to randomize individuals or groups to treatment and control groups (42). The lack of randomization in the nursing students and parent groups and the limited number of samples, the fact that there was no long-term test results and motivation follow-up of these groups, and the inability to determine the long-term effect of parent education on the oral health of the child due to the lack of registration and oral examination of the children of the parents who were educated were the limitations of the study. We think that these issues should be taken into consideration in future studies to be conducted on this subject. Home care practices are not a new concept for health legislation in Turkey (43). However, there is a need for more studies by considering the multidisciplinary approach in the process of creating appropriate health policies and their integration into primary health care services.

Conclusion

As a result of this study, which could be considered as a pilot study, it was foreseen that; The knowledge level of nurses about the oral and dental health of children could be increased through standardized training programs. Home visits and face-to-face interviews performed in order to raise awareness in parents were applicable within the scope of preventive dentistry in children. The non-dental primary care providers could be used in increasing the knowledge and awareness of parents about the oral and dental health of children.

Ethics

Ethics Committee Approval: The study was approved by the Karadeniz Technical University Committee on Human Research (approval number: 2015/42).

Informed Consent: Informed written consent was obtained from both nursing students and parents that participated in the study.

Peer-review: Externally peer reviewd.

Authorship Contributions

Concept: T.T., H.K.M., İ.K., Design: T.T., Ö.B., Data Collection or Processing: T.T., H.K.M., İ.K., A.K., Analysis or Interpretation: T.T., H.K.M., Ö.B., E.B., A.K., Literature Search: T.T., H.K.M., Ö.B., E.B., A.K., Writing: T.T., E.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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Original Article

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Physiotherapy Program Applied After Liver Transplantation: Its Effect on Physical Fitness and Mobility

Karaciğer Transplantasyonu Sonrası Uygulanan Fizyoterapi Programı: Fiziksel Uygunluk ve Hareketlilik Üzerine Etkisi

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ABSTRACT

Objective: To investigate the effects of therapeutic exercises added to the comprehensive chest physiotherapy program after liver transplantation on physical fitness, movement level and kinesophobia.

Methods: Forty individuals with liver transplantation were included in the study. Individuals were divided into two groups by using simple randomization method. The first group was included in the comprehensive chest physiotherapy program. In addition to the comprehensive chest physiotherapy, combined therapeutic exercises with respiration were added to the program of the second group. The patients were included in the treatment program for 4 weeks, 1 session a day, and 5 days a week. Physical and demographic characteristics of the individuals were recorded. "Senior Fitness Test", "Patient Mobility Scale and Observer Mobility Scale", "Tampa Kinesophobia scale" were used to evaluate physical fitness, movement level and kinesophobia, respectively.

Results: Physical and demographic characteristics of the individuals were recorded. "Senior Fitness Test", "Patient Mobility Scale and Observer Mobility Scale", "Tampa Kinesophobia scale" were used to evaluate physical fitness, movement level and kinesophobia, respectively. According to the results of "Senior Fitness Test" aerobic endurance, lower extremity muscle endurance, dynamic The improvement in balance and agility parameters was significantly higher in group 2 ($p<0.05$). Results of the "Patient Mobility Scale" showed significant improvements in post-treatment measurements in both groups ($p<0.001$). The development in the 2nd group showed a significant difference compared to the 1st group ($p<0.05$). While a significant improvement was observed in both groups in

ÖZ

Amaç: Çalışmanın amacı; karaciğer transplantasyonu sonrası kapsamlı göğüs fizyoterapi programına eklenen terapötik egzersizlerin fiziksel uygunluk, hareket düzeyi ve kinezyofobi üzerine olan etkilerini araştırmaktır.

Yöntemler: Çalışmaya karaciğer nakli olan 40 birey dahil edildi. Bireyler basit randomizasyon yöntemi ile iki gruba ayrıldı. Birinci grup kapsamlı göğüs fizyoterapi programına alındı, 2. grubun programına kapsamlı göğüs fizyoterapisine ek olarak solunumla kombine terapötik egzersizler ilave edildi. Hastalar tedavi programına 4 hafta boyunca, günde 1 seans, haftada 5 gün alındı. Bireylerin fiziksel ve demografik özellikleri kaydedildi. Fiziksel uygunluk, hareket düzeyi ve kinezyofobiyi değerlendirmek için sırasıyla "Senior Fitnes Test", "Hasta Hareketlilik Ölçeği ve Gözlemci Hareketlilik Ölçeği", "Tampa Kinezyofobi Ölçeği" kullanıldı

Bulgular: Fiziksel uygunluk, hareket düzeyi ve kinezyofobiyi değerlendirmek için sırasıyla "Senior Fitnes Test", "Hasta Hareketlilik Ölçeği ve Gözlemci Hareketlilik Ölçeği", "Tampa Kinezyofobi Ölçeği" kullanıldı. "Senior Fitness Test" sonuçlarına göre, aerobik endurans, alt ekstremite kas enduransı ve dinamik denge ve çeviklik parametrelerinde gelişme 2. grupta anlamlı şekilde yüksekti ($p<0,05$). "Hasta Hareketlilik Ölçeği" sonuçlarında her iki grupta da tedavi sonrası ölçümlerde anlamlılık gösteren gelişmeler kaydedilmiştir ($p<0,001$). İkinci gruptaki gelişim 1. gruba göre anlamlı farklılık göstermiştir ($p<0,05$). "Gözlemci Hareketlilik Ölçeği" ve "Tampa Kinezyofobi Ölçeği" skorlarında tedavi sonrası her iki grupta da grup içi anlamlı bir gelişme görülürken ($p<0,001$), gruplar arasında anlamlı bir farklılık bulunmamıştır ($p>0,05$).

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the "Observer Mobility Scale" and "Tampa Kinesophobia Scale" scores after treatment (p<0.001), no significant difference was found between the groups (p>0.05).

Conclusion: The therapeutic exercise program added to breathing exercises after liver transplantation increased physical fitness, and also had positive effects on movement level and kinesophobia.

Keywords: Exercise therapy, liver transplantation, movement, physical fitness, respiratory therapy

Sonuç: Karaciğer transplantasyonu sonrası solunum egzersizlerine eklenen terapötik egzersiz programı fiziksel uygunluğu artırmıştır, ayrıca hareket düzeyi ve kinezyofobi üzerinde olumlu etkilere neden olmuştur.

Anahtar Sözcükler: Egzersiz tedavisi, fiziksel uygunluk, hareket düzeyi, karaciğer transplantasyonu, solunum terapisi

Introduction

Liver transplantation is a treatment method that is widely used in patients with acute or chronic liver failure, significantly increasing the life span (1). Decrease in skeletal muscle mass and muscle function is quite common in patients awaiting liver transplantation. This situation significantly reduces the quality of life of patients before and after transplantation and negatively affects the prognosis (2). Acid accumulation and edema accompanying the disease negatively affect ambulation, reducing physical activity and performance levels (3). Fatigue associated with low daily physical activity can lead to decreased exercise capacity, avoidance of activities and increased complaints (4).

Physiotherapy has an important role in increasing the activity level of the patient in the postoperative period and preventing complications due to inactivity. Activity planning based on the general condition of the patient, surgical intervention, hemodynamic-metabolic and functional status increases the success of surgical intervention and the quality of postoperative care (2). In the literature, the importance of an exercise program, which is started in the preoperative period and continued in the postoperative period, in terms of improving the health of the individual, has been emphasized in addition to the surgical success (1,4-6). However, the number of studies investigating the effectiveness of exercise program, especially in the early period, is limited.

In this study, we investigated the effects of an exercise program including active joint movements, posture exercises, sitting and walking training in addition to comprehensive chest physiotherapy on physical fitness, movement level and kinesophobia in patients who underwent liver transplantation. Movement level was examined in two ways, both for the patient and the physiotherapist.

Methods

Study Design

This clinical trial was designed as a prospective, randomized controlled trial. This study was conducted in Acıbadem Mehmet Ali Aydınlar University Atakent Hospital. Acıbadem Mehmet Ali Aydınlar University Medical Research Evaluation Board (ATADEK) approved this study with the decision number 2019-05/20. Participants were informed about the purpose of the study and the evaluations to be made, and the "volunteer informed consent form" was received.

Participants

Sixty seven patients who underwent liver transplantation in Atakent Acıbadem Liver Transplantation Center between March 2019 and November 2019 were included in the study. Patients over 18 years of age, spontaneously breathing, hemodynamically stable, conscious, cooperative and oriented were included. Patients with uncontrolled arrhythmia problems, progressive lung disease, multiorgan transplantation, neurological or neuropsychiatric problems, musculoskeletal problems that prevent exercise, and patients undergoing hemodialysis were excluded from the study. Individuals were randomly divided into two groups with the help of the Random Allocation Software program (Figure 1).

Outcome Measures

"Senior Fitness Test" (SFT), "Patient Mobility Scale (PMS) and Observer Mobility Scale" and "Tampa Scale of Kinesiophobia"

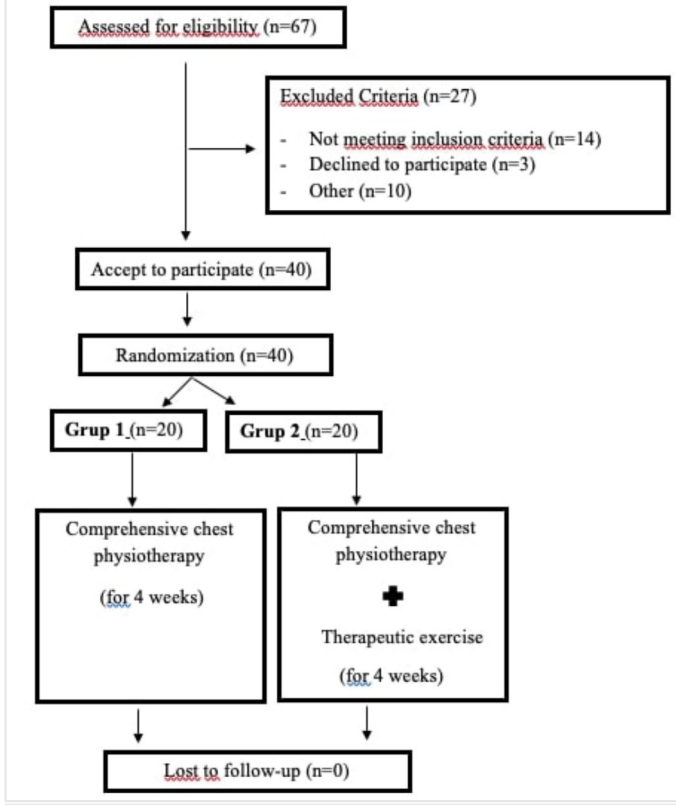

Figure 1. Flow diagram of the study

were used to evaluate physical fitness, movement level, and kinesiophobia, respectively.

The SFT, consisting of six test batteries, was used to assess physical fitness. 1: "Chair Stand Test" to evaluate lower limb muscle strength, 2: "Arm Curl Test" to evaluate upper-limb muscle strength, 3: "Chair Sit and Reach Test" to assess lower limb flexibility, 4: "Two Minutes Step Test" to evaluate aerobic endurance and lower limb muscle endurance, 5: "Eight Foot Up and Go Test" to assess dynamic balance and agility, 6: "Back Scratch Test" to evaluate upper limb flexibility (7).

The PMS evaluates pain and difficulty level caused by four activities performed after surgical intervention through the patient's perception; 1- Turning from one side to the other side of the bed, 2- Sitting at the bedside, 3- Standing up at the bedside, 4- Walking in the patient room. The numerical value of the degree of pain and difficulty was determined by measuring the distance between the sign the patient placed on the scale and 0 with a calibrated ruler. The scale score increase for the answers to the questions in the study indicated that pain and difficulty increased concerning the activity (8).

The Observer Mobility Scale (OMS) evaluates the patient's addiction-independence status by the observer during the four activities after surgery; 1- rotation, 2- sitting, 3- standing, 4-walking. The increase in the score indicates that the patients 'mobility skills are insufficient, and the decrease in the score indicates that the patients' mobility skills are good/sufficient (8).

The Tampa Scale of Kinesiophobia (TSK) is a questionnaire consisting of seventeen questions evaluating pain-related fear. High scores are indicative of the presence of high kinesiophobia. The fear assessment was based on fear of movement and avoidance behavior toward physical activity or fear of re-injury (9).

Follow-up

Hemodynamic and respiratory values were measured before and after treatment: Heart rate (pulse/min), respiratory rate (breath/min), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), peripheral oxygen saturation (%).

Interventions

The patients were randomly divided into two groups: Group 1 received comprehensive chest physiotherapy, Group 2 received comprehensive chest physiotherapy plus a combined breathing exercise program. Exercises were performed for 4 weeks, 5 days a week, 1 session a day. All exercises were done under the supervision of a physiotherapist.

Comprehensive Chest Physiotherapy Program: A comprehensive chest physiotherapy program was applied to both groups. The program included standard breathing exercises, diaphragmatic breathing exercises, thoracic dilation exercises, stimulating spirometry training, cough training, postural drainage and percussion practices. Breathing exercises were taught in a sitting position on the bed and performed under supervision. During the exercises, the patients were asked not to be in a relaxed position and not to shrug their shoulders. The exercises were performed in a single set, 8-10 repetitions (Figure 2).

Therapeutic Exercise Program: In addition to comprehensive chest physiotherapy, a standardized therapeutic exercise program compatible with the clinical characteristics of the patients in the second group was applied. The program was combined with

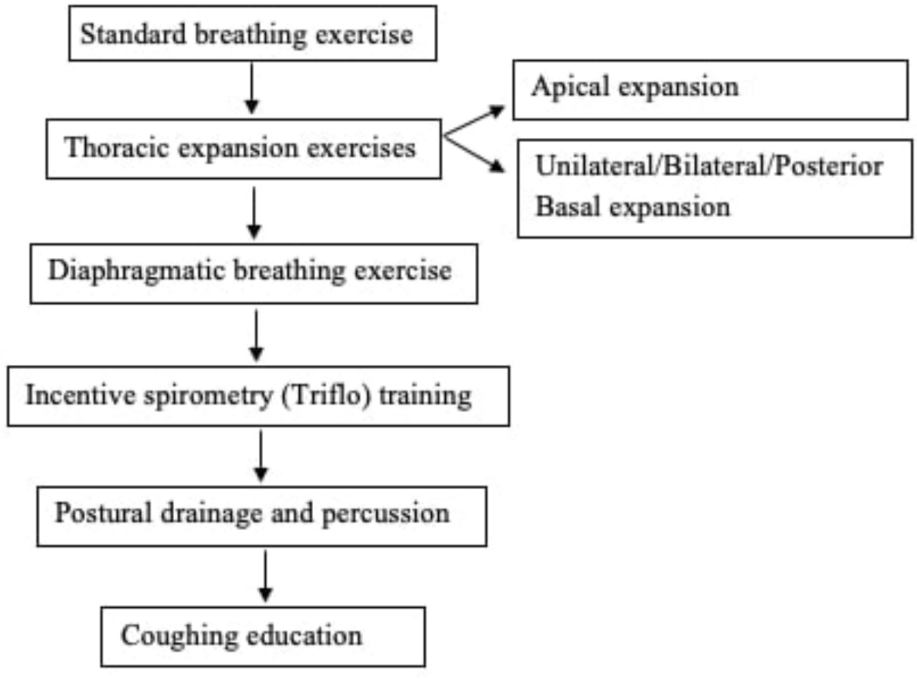

Figure 2. The comprehensive chest physiotheraphy program

breathing. Exercises including active joint movements, posture exercises, sitting and walking training were performed with a set of 8-12 repetitions (Figure 3).

Statistical Analysis

Statistical analyses were performed using SPSS 20.0 statistical program (SPSS Inc., USA). The data were analyzed with the Kolmogorov-Smirnov test to determine the distribution characteristics. In group comparisons: Paired Sample T-test was used for numerical data with normal distribution, and the Wilcoxon test was used for non-normal or ordinal data. In comparisons between groups: Independent Samples T-test was used for numerical data with normal distribution, and the Mann-Whitney U test was used for non-normal or ordinal data. The relationship between the data was evaluated by Pearson or Spearman correlation analysis according to the distribution characteristics. The chi-square test was used for categorical variables. A repeated measures analysis of variance test (ANOVA) was performed to compare the changes in physical fitness, mobility, kinesiophobia. The significance level was accepted as $p<0.05$ for all analyzes.

Sample size calculation was based on post-operative mean values Patient Mobility Scale score (8). We estimated that a sample size of 20 patients in each group would have a power of 95% with α value of 0.001.

Results

The demographic characteristics of the groups were similar ($p>0.05$). Considering the clinical features, the presence of diseases affecting systems such as diabetes mellitus and hypertension did not differ significantly in both groups ($p>0.05$). There was no surgical history in most patients (Table 1). Description of donors is shown in Table 1.

When looking at the SFT sub-items, there was a difference between the baseline scores of the groups in terms of the "Two minutes step test" and "Eight foot up and go test" ($p=0.029$, $p=0.025$), there was no significant difference between the two groups in terms of the initial evaluations of other sub-items ($p>0.05$). Intragroup comparisons of both groups were found to be highly significant between pre- and post-treatment values ($p<0.001$). Considering the evaluation between the groups, a significant difference was found in the improvement in the "Two minutes step test" and "Eight foot up and go test" values ($p=0.026$; $p=0.001$) (Table 2).

There was no significant difference between the groups in terms of the PMS and OMS test scores ($p>0.05$). In PMS, when the development in Group 2 was compared with Group 1, there was a significant difference in pain total score, experiencing difficulty level total score, and overall total score. ($p<0.05$). There was no difference between the baseline values of the

Table 1. Demographic and clinic characteristics of training and control groups*

	Grup 1 (n=20)	Grup 2 (n=20)	p
Demographic features			
Age (year)	53.25 (8.08)	54.05 (11.39)	0.79[a]
Female/male (n)	8/12	4/16	0.17[b]
BMI (kg/m²)	28.13 (4.04)	28.31 (4.79)	0.89[a]
Risk factors			
Duration of symptoms (months)	50.55 (66.34)	39.30 (34.30)	0.73[a]
Hypertension (n)	3 (15%)	2 (10%)	0.97[a]
Diabetes (n)	6 (30%)	8 (40%)	0.97[a]
Other surgical history			
None (n)	16 (80%)	15 (75%)	0.85[a]
Gall bladder (n)	2 (10%)	5 (25%)	0.85[a]
Inguinal hernia (n)	2 (10%)	- (0%)	0.85[a]
Donor selection			
Cadaveric organ	- (0%)	2 (10%)	0.15[a]
Living donor	20 (100%)	18 (90%)	
Relation to recipient			
Child	10 (50%)	12 (60%)	
Sibling	4 (20%)	3 (15%)	
Far relative	3 (15%)	2 (10%)	
External donor	3 (15%)	1 (5%)	0.85[a]
Cadaveric organ	- (0%)	2 (10%)	

BMI: Body mass index, ANOVA: Analysis of variance.
*Data are reported as mean (standard deviation) or n (%).
[a]One-way ANOVA.
[b]Chi-square test.

Exercise	Time	Activity
Warming	5-10 min	Active range of motion exercises
		(1 set of 8-12 reps)
Posture exercises	10-15 min	Thoracic mobility, Stretching exercises to the pectoral muscles
		(1 set of 8-12 reps)
Sit to stand exercise	5-10 min	Sit to stand on the bedside and in the chair
Walking exercise	15-20 min	Walking in the room and corridor

Figure 3. Standardized therapeutic exercise program suitable for the clinical features of the patients

OMS and post-treatment values between the groups (p>0.05) (Table 2).

When the initial and posttreatment values of TSK scores were compared, a significant decrease was observed within the groups (p<0.001), but there was no significant difference between the groups (p>0.05) (Table 2).

A negative correlation was found between TSK and lower extremity muscle strength, aerobic endurance, and lower extremity muscle endurance values which evaluated by Physical fitness test. (r_p=.560, p<0.001; r_p=.409, p<0.05). There was a positive significant correlation between TSK and dynamic balance and agility (r_p=.499, p=0.001, Table 3).

There was a highly significant correlation between TSK and PMS and OMS (r_p=.474, p=0.002; r_p=.574, p<0.001). Also a significant correlation was found between PMS and OMS (r_p=.815, p<0.001) (Table 4).

Discussion

In our study, we aimed to investigate the effects of a physiotherapy program, which included active joint movements along with breathing, posture exercises, sitting, standing and walking training, on physical fitness, movement level and kinesophobia, in addition to comprehensive chest physiotherapy in patients with post-operative liver transplantation. Considering physical fitness parameters, improvement in both groups was one of the main results of our study. However, the second group had better improvements in aerobic endurance, lower limb muscular endurance, dynamic balance, and agility. Neither treatment program was superior to each other in terms of improving patient mobility and fear of movement. The motion perception of the patients improved in both treatment programs, but the patient mobility perception was better in Group 2. OMS scores of the patients were similar after both trainings. Although kinesiophobia decreased in both groups, there was no difference

Table 2. Comparison of scales within the groups and between groups

Assessment	Group	Baseline	After treatment			
		Mean	Mean	Within-group score change	p[a]	p[b]
Senior fitness test						
Chair stand test (repetition)	Group 1	4.75±2.67	11.05±3.64	6.30±3.13	**0.001**	0.32
	Group 2	3.55±1.93	10.75±3.49	7.20±2.58	**0.001**	
Arm curl test (repetition)	Group 1	5±4.40	10.25±5.93	5.25±3.16	**0.001**	0.91
	Group 2	5.10±4.64	10.45±3.41	5.35±2.60	**0.001**	
Two minutes step test (repetition)	Group 1	25.95±25.25	56.50±28.68	30.55±25.95	**0.001**	0.02
	Group 2	8.95±11.39	59.85±31.47	50.90±29.48	**0.001**	
Eight (8) foot up and go test (sec)	Group 1	16.92±4.42	11.35±3.11	-5.56±2.92	**0.001**	0.001
	Group 2	20.25±4.63	11.04±2.02	-9.21±3.15	**0.001**	
Chair sit and reach test (cm)	Group 1	-15.65±14.97	-7±9.66	8.65±6.59	**0.001**	0.27
	Group 2	-16.85±11.25	-6±7	10.85±5.79	**0.001**	
Back scratch test (cm)	Group 1	-17.45±10.14	-8.55±6.77	8.90±4.88	**0.001**	0.91
	Group 2	-15.35±8.94	-6.3±6	9.05±4.32	**0.001**	
Patient Mobility scale						
Pain total score	Group 1	11±3.64	5.8±2.28	-5.20±2.41	**0.001**	0.042
	Group 2	12.4±3.15	5.5±1.5	-6.90±2.69	**0.001**	
Difficulty Total score	Group 1	13.3±3.29	6.55±2.81	-6.75±2.04	**0.001**	0.030
	Group 2	15.1±2.73	6.8±1.73	-8.30±2.29	**0.001**	
Total score	Group 1	24.3±6.48	12.35±4.74	-11.95±4.03	**0.001**	0.022
	Group 2	27.5±5.41	12.3±2.92	-15.20±4.53	**0.001**	
Observer Mobility scale						
Total score	Group 1	14.1±3.24	5.8±2.56	-8.30±2.92	**0.001**	0.107
	Group 2	15.2±2.82	5.45±1.7	-9.75±2.63	**0.001**	
Tampa scale of kinesiophobia						
Total score	Group 1	45.30±3.62	36.55±4.40	-8.75±3.98	**0.001**	0.06
	Group 2	48.50±4.85	37.25±3.90	-11.25±4.37	**0.001**	

Values are expressed as mean ± SD for within-and between-group score changes.
[a]Indicates a statistical significance of within the groups from the baseline to the after-treatment (paired-sample t-test)
[b]Indicates a statistical significance of between-group differences from the baseline to the after-treatment (repeated measures analysis of variance: ANOVA)

Table 3. Relationship between the Tampa Scale of Kinesiophobia and Senior Fitness Test scores

		Tampa scale of kinesiophobia	
		p	r_p
Senior Fitness Test	**Chair stand test (repetition)**	<0.001	-0.560**
	Arm curl test (repetition)	0.341	-0.154
	Two minutes step test (repetition)	0.009	-0.409**
	Eight (8) foot up and go test (sec)	0.001	0.499**
	Chair sit and reach test (cm)	0.106	-0.260
	Back scratch test (cm)	0.309	-0.165

r_p: Pearson correlation coefficient, **Significance of the relationship at 0.01 degrees

Table 4. Relationship between Observer Mobility Scale, Patient Mobility Scale and Tampa Scale of inesiophobia

	TSK		OMS		PMS	
	p	r_p	p	r_p	P	r_p
TSK	-	1	0.002	0.474**	<0.001	0.574**
OMS	0.002	0.474**	-	1	<0.001	0.815**
PMS	<0.001	0.574**	<0.001	0.815**	-	1

TSK: Tampa scale of kinesiophobia, OMS: The Observer Mobility scale, PMS: Patient Mobility scale
r_p: Pearson correlation coefficient, **Significance of the relationship at 0.01 degrees

between the groups. There was also a significant relationship between the motion perception of the patients and kinesophobia.

Physical fitness decreases in liver transplant patients (10). It is emphasized that rehabilitation programs should be planned to increase physical fitness after transplantation (11). In our study, when the sub-items of SFT, which evaluated physical fitness, were examined, a significant improvement was observed between the first and last values in both groups. The improvement in aerobic endurance, lower extremity muscular endurance, dynamic balance and agility in Group 2 was significantly higher than in Group 1. There was no statistically significant difference between the groups in terms of lower extremity muscle strength, upper extremity muscle strength, lower extremity flexibility and upper extremity flexibility. In the study by Ginneken et al. (11) evaluating the physical fitness of liver transplant recipients, it was reported that sedentary individuals showed a 16-34% deficiency in $VO2_{max}$ compared to those who exercised more than 1-2 hours a week. In another study, lower and upper extremity muscle strength, dynamic balance and agility values were found to be lower in patients who underwent liver transplantation compared to healthy sedentary individuals (12). Beyer et al. (13) reported that the exercise program applied after liver transplantation improved physical fitness, muscle strength and functional performance.

Promoting early postoperative ambulation plays an important role in achieving early independence and preventing complications. The patient is moved as much as he/she can tolerate and encouraged in his/her movements (14). In a study evaluating the movement levels of patients in the post-operative period, it was reported that patients had difficulty turning from one side to the other during their in-bed mobilization and needed help (15). In our study, we found that patients had more difficulty in turning from side to side in the bed compared to sitting by the bedside, standing by the bedside and walking in the patient's room during the pre-treatment period. OMS scores were similar to PMS scores. After the treatments we applied, we reduced the difficulties experienced by the patients.

Kinesiophobia leads to the disuse of muscle. This situation affects patients' quality of life negatively, resulting in various degrees of disablement and participation problems (16). In a study in which liver transplant patients were evaluated, the presence of kinesiophobia was reported in 68.8% of the patients (12). In our study, there was a significant decrease in TSK in both groups after exercise training, but no superiority was found between the groups. The most common situation in liver transplant patients before and after transplantation is the decrease in functional capacity. Also, we anticipate that the decrease in physical fitness and movement level has an impact on kinesiophobia. In our study it was found that in both groups, the levels of movement before treatment decreased and their perception of kinesiophobia increased. Significant improvements were noted in both groups after treatment. Stephenson et al. (10) reported that $VO2_{max}$ was 40-60% lower than estimated in liver transplant recipients. Since our patients were in the post-op period, we could not perform a pulmonary function test. However, we think that the main reason for the improvement of movement levels in both groups is primarily due to the increase in oxygen intake.

A negative correlation was found between post-transplantation kinesiophobia scores and the "Chair stand test", which evaluated the lower extremity muscle strength, one of the physical fitness score sub-parameters, and the "Two-minutes step test", which evaluated aerobic endurance and lower limb muscle endurance. Also a positive correlation was found between "Sit in a chair test"

and "Eight foot up and go" which assess agility and dynamic balance. The increase in physical fitness levels of the individuals participating in the study reduced the fear of movement. In the literature, there are no studies evaluating the effect and relationship of the physiotherapy program applied after liver transplantation on physical fitness and kinesiophobia. In this sense, our study carries the importance of being the first study to evaluate the effect and relationship of the physiotherapy program applied to patients after liver transplantation, on physical fitness and kinesiophobia.

Study Limitations

Our study also had some limitations. The patients could not be evaluated before transplantation. The condition of patients before transplantation could change the effectiveness of treatment. Short-term effects after rehabilitation were evaluated in the study. More studies are needed with long-term follow-up.

Conclusion

Physiotherapy program applied in patients whose clinical condition stabilizes after liver transplantation has been deemed important in terms of maintaining the physical fitness of the patients. Early mobilization plays a role in preventing complications that may occur. Breathing exercises and therapeutic exercises applied to patients in the early postoperative period improve the movement level of the patients.

In our study, only breathing exercises were given to the first group, while the second group was given a therapeutic exercise program in addition to these exercises. As a result, all patients showed significant improvements in mobility and fear of moving. There was no significant difference between the two groups in terms of the observer rating scale. There was a better improvement in the scores of the patient's self-assessment scale in the group to which therapeutic exercise was added. We think that this difference is due to the fact that patients feel better after exercise, and these findings will shed light on the rehabilitation programs to be developed for liver transplant recipients.

Ethics

Ethics Committee Approval: Acıbadem Mehmet Ali Aydınlar University Medical Research Evaluation Board (ATADEK) approved this study with the decision number 2019-05/20. **Informed Consent:** Participants were informed about the purpose of the study and the evaluations to be made, and the "volunteer informed consent form" was received.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Concept: S.B., E.A., Design: S.B., E.A., E.E.S., Data Collection or Processing: S.B., Analysis or Interpretation: S.B., E.A., E.E.S., E.S., Literature Search: S.B., E.A., E.E.S., E.S., Writing: S.B., E.A., E.E.S., E.S.

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Original Article

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What is the Awareness Level of the Hypertensive Elderly People on the Blood Pressure Measurement Follow-up and Device Calibration?

Hipertansif Yaşlıların Kan Basıncı Ölçüm ve Takipleri ile Cihaz Kalibrasyonu Farkındalıkları Ne Düzeyde?

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ABSTRACT

Objective: Patient awareness about blood pressure (BP) measurement is important for the management of hypertension. This study was conducted to determine the level of awareness among hypertensive elderly patients regarding how to measure their blood pressure, following up and calibrating the device they use.

Methods: This descriptive and cross-sectional study was conducted between January and May 2018. The population examined in the study consisted of the elderly people who lived in the centre of a province in the Eastern Black Sea Region in Turkey. The study included 363 elderly people.

Results: This study revealed that despite using antihypertensive medicines, some of the elderly patients had out-of-range systolic (79.1%) and diastolic BP values (38.6%). The majority of the elderly people (83.6%) in this study did not have a properly calibrated device for home use. On average, the participants had their sphygmomanometers calibrated every 1.6±1.23 years.

Conclusion: It was concluded that hypertensive elderly patients were not fully aware of the importance of measuring BP, taking follow-up measurements and knowing how to properly calibrate their devices. Therefore, health personnel should train hypertensive elderly patients regarding follow-up on their blood pressure measurements.

Keywords: Elderly individual, hypertension, blood pressure measurement

ÖZ

Giriş: Kan basıncı (KB) ölçümü hakkındaki hasta farkındalığı, hipertansiyon yönetimi için önemlidir. Araştırma, yaşlı hipertansiyonlu hastalarının BP ölçüm ve takipleri ile kullandıkları cihazın kalibrasyonu hakkındaki farkındalıklarını tespit etmek amacıyla yapıldı.

Yöntemler: Tanımlayıcı ve kesitsel türde yapılan çalışma Ocak-Mayıs 2018 tarihleri arasında yürütüldü. Araştırma evrenini Türkiye'nin Doğu Karadeniz Bölgesi'ndeki bir il merkezinde yaşayan yaşlı bireyler oluşturdu. Çalışmaya 363 yaşlı birey dahil edildi.

Bulgular: Bu çalışmada antihipertansif ilaç kullandığı halde yaşlıların bir kısmının Sistolik KB (%79,1) ve Diastolik KB değerlerinin (%38,6) normal sınırlar içerisinde olmadığı tespit edildi. Araştırma, yaşlı hipertansiyonlu hastalarının KB ölçüm ve takipleri ile kullandıkları cihazın kalibrasyonu hakkındaki farkındalıklarını tespit etmek amacıyla yapıldı Katılımcıların %83,6'sının evinde kullandığı cihazın kalibrasyonunu yaptırmadığı, kalibrasyon yaptıranların kalibrasyon yaptırma sıklığı ortalamasının ise 1,6±1,23 yıl olduğu belirlendi.

Sonuç: Hipertansif yaşlı hastaların, KB ölçüm ve takipleri ile cihazlarını uygun şekilde kalibre ettirmenin öneminin farkında olmadığı sonucuna varılmıştır. Bu nedenle sağlık personeli, hipertansif yaşlı hastalara, BP ölçümlerini takip etme konusunda eğitim vermelidir.

Anahtar Sözcükler: Yaşlı birey, hipertansiyon, kan basıncı ölçümü

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Introduction

Hypertension (HT) is a major risk factor for cardiovascular disease and was named the number one factor for overall mortality risk by the World Health Organisation. HT is a common medical condition that has a higher prevalence among elderly people. HT can lead to a number of cardiovascular complications in the elderly such as stroke, coronary heart disease, peripheral artery disease and cognitive impairment (1,2).

The global population is aging; by 2030, an estimated 20% of the global population will be 65 years of age or older. Therefore, the impact of high blood pressure (BP) on mortality rates among older adults is expected to grow over the coming decades (2). Each year, 7.5 million people die from complications due to high BP in the world, making HT responsible for 12.8% of all deaths globally (3). According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High BP (JNC-7), over two-thirds of individuals over the age of 65 years suffer from HT (4). In a representative population of adults in Turkey, the prevalence of HT was reported as 30.3% (5).

The accurate measurement of one's BP is essential to plan therapeutic strategy. The accurate measurement of BP requires the use of a properly calibrated sphygmomanometer (6,7). In a 2011 study, only 30% of the devices were acceptable for use, while 24% of the devices were inaccurate (8). Currently, it is accepted that home BP monitoring (HBPM), office measurement, and ambulatory BP monitoring play important roles in the management of BP (6). HBPM is gaining recognition as a vital tool for effectively managing HT, allowing patients to actively participate in their own treatment (9).

The HBPM offers extensive information about one's BP information that is obtained under fixed timeframes and conditions over a long period of time. It is also a simple procedure to repeat and track. HBPM can provide healthcare providers with timely and relevant clinical data and allows them to provide patients with direct and immediate feedback concerning the diagnosis and treatment of HT. HBPM allows patients to better understand how to manage their HT (10,11).

There are two groups of sphygmomanometers that are currently used for measuring BP: oscillometric and manometric devices. Oscillometric devices provide measurements in the fingers, wrist and above the elbow. There are three types of manometric devices in use: mercury, aneroid and electronic auscultation devices. Preferably, measurements should be carried out using the mercury sphygmomanometer. In addition to mercury manometers, it is also possible to use a calibrated aneroid manometer or electronic BP monitor. However, these devices need to be recalibrated every six months (12,13).

Inadequate sphygmomanometer maintenance and calibration results in systematic error in BP measurements. Furthermore, inadequate sphygmomanometer calibration may lead to untreated HT in some patients and unnecessary treatment in patients receiving antihypertensive treatment (7,14).

Patients' knowledge and attitudes have an impact on how well they manage their illnesses. Studying the level of awareness among patients is the first step when preparing a preventive program for any health problem (15). The present study focuses on hypertensive patients over the age of 65 years who seek healthcare at outpatient clinics within public hospitals in the centre of a province in Turkey. These patients were studied to determine their awareness of how to manage their BP, when to follow-up and how to calibrate their sphygmomanometers.

Methods

Study Design and Study Population

This descriptive and cross-sectional study was conducted in the centre of a province in Turkey between January and May 2018. The population examined in the study consisted of the elderly people over the age of 65 who lived in the centre of a province that was randomly selected in the Eastern Black Sea Region in Turkey (13.216 people- according to Turkish Statistical Institute data). The sample size to be included in the sample was calculated to be 282 with a 5% deviation in the reliability range of 95%. In order to increase the representation power of the sample, 846 elderly people were screened until 30% more than the sample size was reached. This study covered hypertensive patients who were diagnosed by a doctor and who used antihypertensive medicine according to the declarations (363 people - 30% more than the sample calculation). The data were collected from all outpatient clinics of the three hospitals in the city center. These hospitals were physical therapy, chest diseases and education research hospitals. Since hospitals were busier in the first and last days of the week, the data were collected especially on these days. BP of all patients reached in study were measured. In addition, all patients were informed about both BP measurement and device calibration.

Patients to be included in the study group;

- Aged 65 and above
- Diagnosed as having HT by a doctor
- Using antihypertensive medicine
- Having their BP monitored (by himself/herself or someone else's measurement)
- Voluntarily participating in the survey

Patients to be excluded in the study group;

Having a physical, mental or social disease that would impair cooperation

Having an auditory, visual or cognitive function disorder that would impair cooperation

Refusing to participate in an interview

Blood Pressure Evaluation

Within the scope of the project, BP was measured at the outpatient clinics by the researchers using the BP Monitor

with Stroke Risk Detection (BP A6 PC). This device has been reported to detect Atrial Fibrillation (AFIB) and HT with an accuracy of 97-100% (16,17). The device used contains coloured bars, which are referred to as "traffic light indicators", to indicate whether the patient's BP is within an acceptable range. A green-coloured bar within the display panel of the device indicates an optimum BP, yellow indicates a high BP, orange indicates a very high BP and red indicates that the patient's BP is dangerously high. BP measurements were performed according to recommended guidelines (18).

Independent variables of the study: Sociodemographic properties and medical histories are the independent variables of the study.

Dependent variables of the study: Awareness regarding how to measure BP, follow-up measurements and whether the device is properly calibrated are the dependent variables of the study.

Data Collection

The researchers collected data through face-to-face interview methods from elderly people meeting the inclusion criteria. The survey form questions were drafted based on relevant literature. The survey form consists of a total of 26 questions. The form consists of sociodemographic characteristics of the patients, awareness of HT, BP follow-up (type of the device used in BP follow-up, knowing the normal ranges of BP, frequency of BP follow-up, place/person of BP follow-up, points of attention in the BP measurement) and questions about the calibration of the BP device (how often and where the calibration is performed).

The BP measurements of the participants within the survey (846 people) were performed using the BP Monitor (BP A6 PC). The survey was collected from 363 people who met the inclusion criteria, over a period of 30 minutes. After data collection, participants were informed about BP follow-up and control as well as the importance of the calibrating their sphygmomanometers. They were also informed regarding which matters to pay attention to concerning BP. The participating elderly people were informed both verbally and in writing that they could take their personal BP measurement devices to a pre-contracted company for calibration.

Statistical Analysis

The data were evaluated using SPSS 22.0. Normality of the data was analyzed using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were expressed as mean (± standard deviation) values and were compared using the independent t-test/ One-Way ANOVA. Continuous data without normal distribution were compared using the Mann-Whitney U test/ Kruskal-Wallis and logistical regression analysis. The $\chi 2$-test test was used for the categorical data. Tukey's HSD (honestly significant difference) test/Mann-Whitney U test was performed for post hoc analysis to determine individual differences between the groups. Pearson's correlation analyses were used to determine the direction and level of the relationship between the continuous variables. Statistical significance was determined to be p value <0.05.

Ethical Considerations

"Clinical Research Ethics Committee Approval" (KAEK 2017/03) and "institution approval" were obtained for conducting the study and "informed consent form" (in accordance with the Helsinki Declaration Criteria) was verbally declared to the voluntary participants. Written consent was not requested from the voluntary participants since it could reduce participation in the study.

Results

The average age of the elderly people in this research study was 73.96±7.55 years [minimum (min): 65; maximum (max): 103]. Of the participants 61.4% were woman and 38.6% were man. The percentage of the people living in rural areas was 77.4%, 46.1% of the participants were illiterate, 53.2% of participants lived with spouses and 37.5% stated that they found their income sufficient to support their lifestyle.

A total of 52.9% of the participants had a chronic disease other than HT and 48.0% of the participants reported that they were hypertensive for at least 11 years, while 85.1% of them considered HT to be a dangerous condition. The percentage of participants who reported that they didn't know the consequences of not following their treatment protocol for HT was 65.5%.

In this study, 8.5% of the individuals who claimed to be familiar with the normal ranges of BP (44.9%) could not determine the correct systolic BP (SBP) and 6.1% could not determine the correct diastolic BP (DBP). Patients stated that their average SBP value was 123.19±11.74 mm Hg (min: 80, max: 200) and their average DBP value was 77.66±8.99 mmHg average (min: 60, max: 150). According to the results of BP measurements, the percentage of patients within the normal range of SBP was 20.9%, with the percentage with pre-hypertensive values was 38.3%, the percentage in the first stage of HT was 27%, and the percentage of participants in the second stage of HT was 13.8%. The percentages of participants in each range for DBP values were 61.4%, 23.4%, 12.4%, and 2.8%, respectively. A total of 41.6% of the participants stated that they measured their BP themselves, while 22.3% stated that their BP was measured by healthcare personnel. Out of participants who stated that their devices were calibrated, 41.3% preferred having their measurements taken at the pharmacy, 30.5% preferred having the measurements taken at a private institution, 24% preferred a company, and 4.3% preferred to have their BP measured at a health organisation. On average, the participants had their sphygmomanometers calibrated every 1.6±1.23 years (min: 1; max: 6) (Table 1). In this study, the results from the A6 PC measurement results did not provide AFIB warnings to any of the persons.

The following variables were found to be independently effective with respect to having a follow-up BP screening: time since diagnosis of HT, marital status, perception of HT, use of antihypertensive medication and feeling symptoms of high BP ($p<0.05$) (Table 2).

Table 1. Distributions of the Elderly People Related to their Qualities on BP follow-up (n=363)

Variables	Number	%
Knowing the normal ranges of BP		
Knows	163	44.9
Doesn't know	200	55.1
Having BP follow-up		
Yes	201	55.4
Sometimes	63	17.4
Rarely	99	27.2
Place of BP follow-up		
Home	275	75.8
Pharmacy	16	4.4
Community clinic	17	4.7
Hospitals	55	15.2
Person doing the BP follow-up		
Himself/herself	151	41.6
Spouse	37	10.2
Child	72	19.8
Relative	22	6.1
Health personnel	81	22.3
Type of the device used in BP follow-up		
Digital wrist	208	57.3
Digital elbow	90	24.8
Aneroid	65	17.9
Having the device calibrated (n=281)		
Yes	46	16.4
No	233	83.6
Training on blood pressure measurement (n=347)		
Yes	58	16.7
No	289	83.3
Person providing training on blood pressure measurement (n=51)		
Doctor	6	29.4
Nurse	15	11.8
Pharmacy	24	47.1
Company official	6	11.8
Attention paid to in blood pressure measurement*		
Holding the arm aligned with heart	104	28.7
Keeping silent	146	40.2
Being rested	42	11.6
Nothing eaten or drunken	2	0.6
Keeping still	50	13.8
Recording the BP value		
Yes	29	8.0
No	265	73.0
Recording only when high	69	19.0
SBP classification according to BP A6 PC		
Normal	76	20.9
Pre HT	139	38.3
Stage 1 HT	98	27.0
Stage 2 HT	50	13.8
DBP classification according to BP A6 PC		
Normal	223	61.4
Pre HT	85	23.4
Stage 1 HT	45	12.4
Stage 2 HT	10	2.8

*Multiple replies, BP: Blood pressure, PC: Preventive cardiovascular, HT: Hypertension

The statistically significant variables of the study with regards to having the BP measurement device calibrated were the education level of the participants in the study, an awareness of the consequences of not following up their treatment and feeling the symptoms of high BP ($p<0.05$) (Table 3).

Discussion

Compliance with HT treatment protocols will increase the quality of life among elderly patients. Therefore, controlling HT and following up BP screenings are important for determining HT-related risks early on and providing early intervention for these risks. According to the Data of Turkish Adult Cardiovascular Disease Risk Factor, the prevalence of HT among people between the ages of 60 and 69 years is 67.3% among men, and 78.2% among women. For people aged 70 years or above, this value increases to 73.5% among men and 85.6% among women. In Turkey, three out of four people over the age of 60 are reported to be hypertensive (19).

The mortality risk increases significantly when the SBP value is ≥160 mmHg or the DBP value is ≥100 mmHg. The Cardiovascular Disease and Expanded-Cardiovascular Disease mortality risk was lowest when the SBP values were between 120 to 129 mmHg, compared with SBP value <120 mm Hg. This mortality risk also increases when DBP value is ≥90 mm Hg, compared with DBP value <80 mmHg (2). In a study by Framingham, patients with SBP readings between 130-139 and DBP readings between 85-89 mmHg were twice as likely to experience mortality compared to patients with BP readings below 120/80 mmHg with regards to cardiovascular death risk (20).

Table 2. Factors affecting the BP follow-up of the elderly people (n=363)

Variable	β	p	OR	95% CI
Age (in number)	0.09	0.097	1.10	1.10-0.98
SBP (in number)	-0.09	0.825	0.91	0.40-2.03
DBP (in number)	-0.33	0.516	0.71	0.25-1.97
HT time (in number)	-0.07	**0.049**	0.92	0.86-1.00
Sex				
Male			1.00	
Female	0.14	0.865	1.15	0.21-6.15
Place where the most of life is spent				
Rural			1.00	
Urban	0.29	0.696	1.34	0.30-6.02
Marital status				
Married			1.00	
Single, widow, divorced	-1.83	**0.026**	0.16	0.03-0.79
Education level				
Illiterate			1.00	
Literate, no school completed	-1.28	0.116	0.27	0.05-1.37
Primary school	-0.14	0.868	0.86	0.15-4.86
Secondary school	-0.65	0.674	0.51	0.02-11.16
High school	0.19	0.906	1.22	0.04-32.71
University	17.66	0.999	4.7	
Income level perception				
Sufficient			1.00	
Insufficient	-0.48	0.553	0.61	0.12-2.86
Equal	-0.43	0.569	0.64	0.14-2.86
Presence of another chronic disease				
No			1.00	
Yes	1.21	0.097	3.36	0.80-14.11
HT perception				
Dangerous			1.00	
Not dangerous	0.30	0.835	1.35	0.07-24.01
I do not know	-2.27	**0.019**	0.10	0.01-0.68
Awareness on the result of not following HT treatment				
Aware			1.00	
Unaware	0.36	0.606	1.44	0.35-5.85
Use of antihypertensive medicine				
Regular			1.00	
Not regular	-3.54	0.058	0.02	0.00-1.13
Taking when BP is high	-2.47	**0.007**	0.08	0.01-0.50
Feeling high BP				
Yes			1.00	
No	-2.79	**0.001**	0.06	0.01-0.34
Sometimes	0.62	0.55	1.87	0.23-15.05
Presence of HT patient in the family				
Yes			1.00	
No	1.27	0.08	3.48	0.83-14.59

OR: Odds ratio, CI: Confidence interval, HT: Hypertension, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BP: Blood pressure

In the present study, the average BP value of the elderly people receiving HT treatment was found to be 136.06±21.44 mmHg for SBP (min: 84, max: 207) and 76.51±11.07 mmHg (min: 42; max: 112) for DBP. According to the results of the A6 PC measurements, 79.1% of the elderly people had out-of-range SBP values and 38.6% of them had out-of-range DBP values. In another study, Oliveria et al. (21) demonstrated that many patients did not know their BP levels, nor could they accurately determine whether they had elevated or normal BP. Furthermore, 41% of patients reported that were not in the normal range, but in fact they were hypertensive (21). Dastan et al. (22) showed that 59% of individuals were on HT treatment. The percentage of hypertensive individuals whose BP levels were under control was 30% (22).

In this study, the following variables were found to be independently effective with respect to having BP follow-up readings: time since diagnosis, marital status, perception of one's HT, use of antihypertensive medication and feeling symptoms of high BP ($p<0.05$).

The low level of awareness regarding hypertensive status may also be due to the insufficient measurement of BP. With regards to BP follow-up, the percentage of people who do not follow-up with their initial measurements in Turkey is reported be higher in those living in rural areas and in women (23).

In a study conducted by Tokem et al. (24), it was found that hypertensive individuals had a low level of compliance regarding their BP follow-up and only one-fifth of the individuals who claimed to know their BP values and measurement techniques had regular BP measurements. Furthermore, the majority of these hypertensive individuals only had their BP measured when they felt symptoms of HT (24).

The study by Dereli and Baybek (25) stated that the frequency of measuring BP varied with regards to SBP and DBP; it also showed that 18.5% of the patients with high SBP ,and 6.5% of the patients with high DBP didn't have regular BP checks.

In a study where the average participant age was 61.5 years and all patients had been diagnosed as having HT for at least a year, it was found that sex, marital status and education didn't cause any

Table 3. Distribution of having the BP measurement device used by the elderly people calibrated according to some variables

Variables	n	BP device calibration (n=281) Calibrated Number (%)*	Not calibrated Number (%)*	Test and p values
Education level				
Illiterate	131	111 (84.7)	20 (15.3)	
Literate, no school completed	38	33 (86.8)	5 (13.2)	
Primary school	80	71 (88.8)	9 (11.3)	
Secondary school	12	8 (66.7)	4 (33.3)	x^2=12.614
High school	10	6 (60.0)	4 (40.0)	**p=0.027**
University	10	6 (60.0)	4 (40.0)	
Awareness of the outcome of not following HT treatment				
Aware	107	82 (76.6)	25 (23.4)	x^2=6.175
Unaware	174	153 (87.9)	21 (12.1)	**p=0.013**
Ability to feel high BP				
Yes	229	185 (80.89	44 (19.2)	
No	28	28 (100.0)	0 (0.0)	x^2=7.966
Sometimes	24	22 (91.7)	2 (8.3)	**p=0.019**

*Line percentage is taken.
BP: Blood pressure, HT: Hypertension

statistical difference with respect to having BP under control (i.e. having follow-up). In this same study, the SBP and DBP values were found to be statistically different with regards to keeping BP under control; those participants who kept the BP under control had lower readings (26).

In a study conducted by Sozmen (27), 33% of the participants stated that they had a follow-up BP reading. This study showed that the variables associated with high levels of BP control were; being female, having a chronic disease and having a family member with cardiac disease. The reason for the differences in these studies could be due to the fact that participants came from different sociodemographic backgrounds.

A total of 57.3% of the elderly people in this study used a wrist digital sphygmomanometer, 24.8% used an elbow digital sphygmomanometer, and 17.9% used an aneroid sphygmomanometer to measure their BP. In addition, 83.6% of participants did not have their home devices calibrated. Of those who did get their devices calibrated, the average calibration frequency was every 1.6±1.23 years.

Within Turkey, approximately 46.6% of the hypertensive patients have BP measuring devices within their homes (28). In the study conducted by Erdem (29) focusing on individuals between 21 and 93 years of age, 46% stated that they used an automatic wrist sphygmomanometer, 19% used an automatic arm sphygmomanometer, 25% used an aneroid sphygmomanometer and 7% used a mercury sphygmomanometer. This study demonstrated that having a sphygmomanometer at home was associated with an increased level of education among the participants.

According to the study by Zahid et al. (9), 51.3% of participants owned a digital sphygmomanometer and 48.8% owned a manual sphygmomanometer. For those who owned a digital device, 70.0% preferred wearing it on their arm, 25.6% preferred wearing it on their wrist and 4.4% preferred wearing it in of another area. Although 61.7% the participants used a home sphygmomanometer, less than 25% performed HBPM regularly and more than half of the participants recalibrated their devices. These figures might be due to a lack of instruction for recalibrating a device and lack of knowledge regarding the importance of repeat measurements by healthcare professionals.

In recent guidelines from the European Society of HT (ESH) and European Society of Cardiology (ESC) regarding the management of arterial HT, it was stated that BP should be measured using sphygmomanometers that complied with standardised conditions and protocols (18). Although performing BP measurement directly through an arterial catheter is the most accurate method of measurement; it is often not possible to choose this method in routine applications as it is an invasive procedure (30). Therefore, three types of sphygmomanometers are currently used for routine BP measurement: mercury, aneroid and electronic. The literature emphasises the necessity of conducting the BP measurement with mercury sphygmomanometers, which are accepted to be the golden standard for measuring BP (12,30-32). However, they are less preferred due to the toxic consequences of mercury exposure and difficulties in their use and transportation. Today, hypertensive patients more commonly use aneroid sphygmomanometers or electronic sphygmomanometers for BP monitoring. If the aneroid sphygmomanometers are calibrated every six months, their results should be comparable to readings achieved by a mercury sphygmomanometer (12,29,30). On the other hand, the measurements with frequently preferred electronic devices were reported to be higher than the measurements with the mercury

devices. It was reported that the aneroid sphygmomanometers needed to be calibrated for correct measurement (32). The calibration of sphygmomanometers should be performed every 12 months and rechecked every 6 months for optimum readings (7). Uncalibrated sphygmomanometer error is responsible for between 20-28% of all undetected adult systolic and diastolic HT cases, as well as 15-31% of all falsely detected adult systolic and diastolic HT cases (33). In the study, the BP monitoring of most of the hypertensive elderly people with their home BP device highlights the importance of device calibration. The majority of the elderly participants did not have their devices calibrated, and those who did have them calibrated did not perform the recalibration as frequently as they should. A common excuse for this situation was that patients didn't have sufficient and correct information on the importance of BP measurement, follow-up and control.

Today, BP measurement and follow-up are carried out frequently in locations other than clinics, since many patients prefer to measure their BP at home or at the pharmacy. Performing follow-up BP readings at home is practical since it prevents the occupation of health organisations, helps patients maintain the highest level of compliance to their treatment regimen, avoids the white coat effect and meets the criteria of being a part of clinical practice (16,29,34).

Study Limitations

According to the study by Godwin et.al, home measurement did not make any difference with respect to BP control (35). In another study conducted in China, the follow-up BP measurements taken at home better reflected the real BP value. Therefore, home measurement was encouraged among patients (36). According to the 2008 Guide of the American Heart Association, the American Society of HT and the Preventive Cardiovascular Nurses Association (AHA/ASH/PCNA), 38% of the patients carried out BP follow-up at home during the year 2000. However, this value increased to 55% of patients in 2005. The percentage of patients who had a BP monitor increased from 49% to 64% between the years of 2000 and 2005 (29). In the study by Herpin et al. (37), 19% of the individuals over 35 years of age in France performed BP measurement at home, and this rate increased to 36% among those who received treatment.

Conclusion

Almost half of the elderly people were familiar with the normal ranges of BP and carried out the BP follow-up readings themselves. Four out of five participants did not have any training regarding the importance of BP measurements and follow-up. The majority of the elderly people in this study did not have a properly calibrated device for home measurement of BP.

Ethics

Ethics Committee Approval: "Clinical Research Ethics Committee Approval" (KAEK 2017/03) and "institution approval" were obtained for conducting the study and "informed consent form" (in accordance with the Helsinki Declaration Criteria) was verbally declared to the voluntary participants.

Informed Consent: Written consent was not requested from the voluntary participants since it could reduce participation in the study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: F.G., Ç.Y., Design: F.G., Ç.Y., Data Collection or Processing: F.G., Analysis or Interpretation: Ç.Y., Literature Search: F.G., Ç.Y., Writing: F.G., Ç.Y.,

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The Professional Quality of Life for Healthcare Workers During the COVID-19 Pandemic in Turkey and the Influencing Factors

Türkiye'de COVID-19 Salgını Döneminde Sağlık Çalışanlarında İş Yaşam Kalitesi ve Bunu Etkileyen Faktörler

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ABSTRACT

Objective: It is very important to ensure the professional quality of life of healthcare workers in combating the coronavirus disease-19 (COVID-19) outbreak. It is therefore necessary to determine what factors may lead to compassion satisfaction (CS), burnout (BO) and compassion fatigue (CF) in order to ensure the professional quality of life in healthcare workers, and to develop institutional and national strategies and policies to eliminate these factors. Therefore in this study, we aimed to determine the levels of CS, BO and CF among healthcare workers during the COVID-19 pandemic, as well as the influencing factors.

Methods: A descriptive, descriptive-relational and cross-sectional study was conducted, using the Professional Quality of Life scale, with 796 Turkish healthcare workers after the emergence of the COVID-19 pandemic. In the study, the Professional Life Quality of healthcare workers was examined in three dimensions including CS, BO and CF.

Results: The results indicated that while 77.8% of healthcare workers were above the mean CS level, 62.8% of them were below the mean BO level and 87.3% of them were below the mean CF level. Their title, department, professional working year and workmates' diagnosis with COVID-19 were found to affect the CS, BO and CF of healthcare workers.

ÖZ

Amaç: Koronavirüs hastalığı-19 (COVID-19) salgını ile mücadelede sağlık çalışanlarının iş yaşam kalitesinin sağlanması oldukça önemlidir. Bu nedenle sağlık çalışanlarında iş yaşam kalitesini sağlamak için merhamet tatminine, tükenmişliğe ve merhamet yorgunluğuna hangi faktörlerin yol açabileceğini belirlemek gerekir. Bu nedenle bu çalışmada, COVID-19 salgını döneminde sağlık çalışanlarının mesleki tatmin, tükenmişlik ve eş duyum yorgunluğu düzeylerinin ve bunları etkileyen faktörlerin belirlenmesi amaçlanmıştır.

Yöntemler: Bu çalışma, COVID-19 pandemisinin ortaya çıkmasının ardından 796 Türk sağlık çalışanı ile Profesyonel Yaşam Kalitesi Ölçeği kullanılarak tanımlayıcı-ilişkisel ve kesitsel olarak yapılmıştır. Çalışmada, sağlık çalışanlarının Profesyonel Yaşam Kalitesi mesleki tatmin, tükenmişlik ve eş duyum yorgunluğu olarak üç boyutta incelenmiştir.

Bulgular: Sonuçlar, sağlık çalışanlarının %77,8'inin ortalama mesleki tatmin düzeyinin üzerinde olduğunu, %62,8'inin ortalama tükenmişlik düzeyinin altında ve %87,3'ünün ise ortalama eş duyum yorgunluğu düzeyinin altında olduğunu göstermiştir. Sağlık çalışanlarının mesleki tatmin, tükenmişlik ve eş duyum yorgunluğu üzerinde unvan, çalışılan birim, mesleki çalışma yılı ve

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Conclusion: We found that workers had good levels of CS and low levels of BO and CF during the study period. Therefore, we can say that the quality of work life is good. However, due to the increase in the number of cases, we recommend that the study be repeated in future, to continuously evaluate the psychological state of healthcare workers and, using the resulting comparisons, to implement the necessary arrangements timeously.

Keywords: COVID-19 pandemic, healthcare workers, professional quality of life, influencing factors

mesai arkadaşının COVID-19 tanısı alma durumunun etkili olduğu bulunmuştur.

Sonuç: Sonuç olarak, çalışmanın yapıldığı zaman diliminde sağlık çalışanlarının mesleki tatmin düzeylerinin iyi olduğunu, tükenmişliğin ve eş duyum yorgunluğunun düşük olduğunu, dolayısıyla iş yaşam kalitesinin iyi olduğunu söyleyebiliriz. Ancak olgu sayılarının artması nedeniyle çalışmanın ilerleyen zamanlarda tekrarlanması, sağlık çalışanlarının psikolojik durumunun sürekli değerlendirilmesi ve karşılaştırmaların yapılarak gerekli düzenlemelerin bir an önce hayata geçirilmesi önerilmektedir.

Anahtar Sözcükler: COVID-19 salgını, sağlık çalışanları, iş yaşam kalitesi, etkileyen faktörler

Introduction

The Coronavirus disease-19 (COVID-19) emerged in Wuhan, China in December 2019 and led to a global pandemic. The World Health Organization (WHO) declared the COVID-19 outbreak a public health emergency of international concern on 30 January 2020 (1). The first case of COVID-19 in Turkey was observed on 11 March 2020, and it quickly became a pandemic in the country.

Although the WHO and public health officials all over the world have tried to control the COVID-19 pandemic, the rapid spread and severe clinical course of the virus have made the fight against the pandemic difficult and protracted (2). The most important tasks in this struggle undoubtedly fall to healthcare workers.

Healthcare workers have been adversely affected by long working hours and difficult working conditions during the pandemic, the disease's rapid transmission and the high mortality rate, fears of contracting COVID-19 and passing it on to their families and prolonged separation from loved ones (3-7). These reasons cause healthcare workers to have burnout (BO) and compassion fatigue (CF), which lead healthcare workers to develop severe mental problems such as depression and anxiety (1,8-11). These problems cause the compassion satisfaction (CS) of healthcare workers to decrease, and ultimately, the quality of their working life also decreases.

Research has indicated that CS decreases in healthcare workers who constantly experience BO and CF (12,13), and this causes a decreased health service performance and quality of patient care, and negative job attitudes, while also increasing service delivery costs and the number of staff who think of quitting their jobs (14). Therefore BO, CF and CS are important factors that affect the fight against the pandemic and need to be addressed immediately.

The WHO, highlighting the excessive burden on healthcare workers during the pandemic, called for action to address urgent needs and measures to save lives and prevent serious adverse effects on the physical and mental health of healthcare workers (2). Therefore, in this study, we investigated the CS, BO and CF levels of healthcare workers during the COVID-19 pandemic and examined influencing factors.

Methods

Study Design and Setting

A descriptive cross-sectional online survey design and a quantitative research method were used. With permission obtained, a copy of the survey was converted into an online survey using one of the free survey websites, and a link to it was shared on social media platforms (Facebook, Instagram and Twitter) and WhatsApp groups that included healthcare workers. The data were collected between 25 and 30 June 2020. The participants responded to the survey after agreeing to participate in the study. Surveys were completed after data entry were deleted from the website. The researcher protected against multiple uses by exporting the data.

Sample Size and Sampling

Healthcare workers working in healthcare services constituted the population of our study. According to the latest data announced by the Turkish Statistical Institute (15), there were 160,810 doctors, 198,103 nurses, 55,972 midwives and 182,456 other medical staff in 2019 in Turkey. The other medical staff group includes healthcare personnel employed in fields including surgery, anaesthesia, environmental health, dental prosthetics, dentistry, physiotherapy, first and emergency aid, biology, child development, dietetics, laboratory work and audiometry.

With the population known, it was sufficient to reach at least 384 healthcare workers with a confidence interval of 95% by using the sample calculation formula. This study reached 796 healthcare workers using the online survey method. Since there was no existing data on the prevalence of quality of life, p and q-values were taken as 0.5.

Data Collection Tool

The online survey form consisted of 12 questions investigating the sociodemographic and working style of the study participants, and 30 questions from the Professional Quality of Life scale.

Demographic and Work-Related Information Form

The researchers prepared the survey in accordance with the literature (16,17). It consisted of questions related to respondents' age; gender; marital status; title; department; professional, weekly

and daily working hours and the pandemic. It also included questions about providing care for COVID-positive patients during the COVID-19 pandemic and being diagnosed as having COVID-19.

Professional Quality of Life Scale

The Professional Quality of Life scale was developed by Stamm in 2005 (18), and its validity and reliability in Turkish studies were confirmed by Yeşil et al. (16) in 2010. This scale is a self-report evaluation tool consisting of 30 items and three subscales. The items are evaluated on a six-step chart ranging from "never" (0) to "very often" (5). Three subscales consist of CS (10 items), BO (10 items) and CF (10 items) parts. Higher scores obtained from each dimension indicate higher levels of CS, BO and CF, respectively. The minimum and maximum scores obtained from the scale are zero and 50 points, respectively. The Turkish version of the scale has CS.87, BO.72 and CF.80 Cronbach's alpha values, respectively (16). In this study, the Cronbach's alpha coefficient was found to be 0.88 for CS, 0.70 for BO and 0.84 for CF,.

Statistical Analysis

The SPSS 24.0 statistical package programme was used for statistical analysis of the data. Descriptive statistics were used while investigating the prevalence of CS, burnout and CF within the data on demographic and working styles. The independent samples t-test and one-way analysis of variance (ANOVA) were used as parametric tests; the Kruskal-Wallis and Mann-Whitney U tests were used as nonparametric tests. Skewness and kurtosis values were required to be between +1.5 and -1.5 to evaluate the homogeneity of variance (19). Pearson's correlation analysis was used for the prediction results. The results were evaluated at a confidence interval of 95% and a significance level of $p<0.05$.

Ethical Considerations

Permission was obtained for the study from the Ministry of Health (2020-05-21T15_40_06) and KTO Karatay University Medicine and Non-Medical Device Research Ethics Committee (2020/023).

Results

The demographic characteristics of the participants and the descriptive statistics of their working conditions are presented in Table 1. Most of the healthcare workers were female, married and between the ages of 36 and 45. While 39.57% of the study participants were nurses, 45.73% of them worked in departments unrelated to COVID-19. Of the participants 38.57% had been working in their fields for between six and ten years. Furthermore, while 28.26% of the healthcare workers participating in the study worked for more than 45 hours a week, participants working eight hours a day were in the majority (60.05%), while day and shift workers were almost equal in number. While 50.13% of the participants were providing service (care) for COVID-19 positive patients, 98.49% of them were not diagnosed as having COVID-19. Of the study participants, 56.28% reported that their workmates were not diagnosed as having COVID-19 either (Table 1).

The mean scores of the dimensions of CS, BO and CF were found to be 32.93±8.83 (minimum (min)-maximum (max): 5-50 points, median: 33.00), 18.39±6.91 (min-max: 2-42 points, median: 18.00), and 16.09±8.27 (min-max: 0-49 points, median: 15.00), respectively. Furthermore, it was determined that while 77.8% of the participants were above the mean CS level, 62.8% of them were below the mean BO level and 87.3% of them were below the mean CF level. In the paired correlation analysis, CS was found to be moderately but negatively correlated with burnout ($r=-0.572$, $p=0.000$) and weakly and negatively ($r=-0.157$, $p=0.000$) correlated with CF. Burnout was correlated with CF above moderate and in the same direction ($r=0.622$, $p=0.000$).(Table 2).

The statistical analysis of the CS, BO and CF levels of the healthcare workers who participated in the study according to demographic data and working conditions was presented in Table 3.

In terms of CS, differences in age, marital status, title, field, professional working year, weekly working time, daily working hours and workmate's diagnosis with COVID-19 were found to be statistically significant ($p<0.05$ for each). The highest CS was found in those younger than 25 years (35.29±8.71), single (33.84±8.85), working as radiology technicians (35.71±8.54) or in the radiology unit (35.54±8.69), those with less than five years of professional experience (37.35±8.04), those working over 45 hours a week (34.50±8.89), those working 12-hour shifts (36.41±8.55) and those with no COVID-positive workmates (33.71±8.71).

Concerning BO, doctors had the highest average (19.81±7.88), and we found the difference between professions to be statistically significant. Healthcare workers in the COVID-19 intensive care (20.87±7.12), those with six to ten years of professional experience (19.15±.13), those working 24 hours a day (19.70±7.42), those working in shifts (19.63±7.37) and those with COVID-positive workmates (19.76±7.15) had the highest mean BO score, and the difference between the groups was statistically significant ($p<0.05$ for each) (Table 3).

The difference between the groups of gender, title, department, professional working year, and workmates' diagnosis with COVID-19 was statistically significant ($p<0.05$ for each) when it came to CF. The highest CF was seen in women (16.17±8.09), Emergency Medical Technician (EMT)-paramedics (17.85±8.88), those working in family medicine and community health (18.31±7.68), those with six to ten years of professional experience (16.82±8.72), and healthcare workers with COVID-positive workmates (17.11±8.49) (Table 3).

Discussion

This study showed that during the COVID-19 pandemic to date, while 77.8% of healthcare workers were above the mean CS level, 62.8% of them were below the mean BO level and 87.3% of them were below the mean CF level. No research was found on healthcare workers' CS during the COVID-19 period throughout Turkey, and similar results were found in a study

Table 1. Demographic data of the participants and descriptive statistics of working conditions

Characteristics	Variable	n	%
Age	≤25	147	18.47
	26-35	245	30.78
	36-45	313	39.32
	>45	91	11.43
Gender	Female	537	67.46
	Male	259	32.54
Marital status	Married	543	68.22
	Single	253	31.78
Title	Doctor	52	6.53
	Nurse	315	39.57
	Midwife	60	7.54
	EMT-paramedic	104	13.07
	Health officer	74	9.30
	Laboratory technician	31	3.89
	Radiology technician	58	7.29
	Pharmacist	25	3.14
	Anaesthesia technician	77	9.67
Department	Policlinic	23	2.90
	Emergency department	44	5.53
	112 emergency healthcare services	87	10.93
	Laboratory	41	5.15
	Radiology unit	61	7.66
	Family medicine-community health	51	6.40
	COVID-19 service	71	8.92
	COVID-19 intensive care	54	6.78
	Other departments	364	45.73
Professional working time	<5 years	43	5.40
	6-10 years	307	38.57
	11-15 years	146	18.34
	16-20 years	148	18.59
	>20 years	152	19.10
Weekly working time for the last month	<40 hours	195	24.50
	40 hours	195	24.50
	40–45 hours	181	22.74
	> 45 hours	225	28.26
Daily working hours for the last month	8 hours	478	60.05
	12 hours	73	9.17
	16 hours	60	7.54
	24 hours	185	23.24
Weekly working style for the last month	Daytime	238	29.90
	Shift	191	23.99
	Both daytime/shift	251	31.54
	Flexible work	116	14.57
Providing service (care) for COVID-19 positive patients	Yes	399	50.13
	No	397	49.87
Diagnosis with COVID-19 during the pandemic	Yes	12	1.51
	No	784	98.49
Workmate's diagnosis with COVID-19 during the pandemic	Yes	348	43.72
	No	448	56.28
Total		796	100

COVID-19: Coronavirus disease-19

Table 2. Sub-dimensions of the Quality of Life scale for employees and the correlation of the sub-dimensions with one another

The Professional Quality of Life scale	$\bar{X}$ ± SD	Min-max	Median	Quartiles (25-75%)	Pearson's correlation		
					1.	2.	3.
Compassion satisfaction	32.93±8.83	5-50	33.00	27.00-39.00	1		
Burnout	18.39±6.91	2-42	18.00	13.00-23.00	**r=-0.572 p=0.000**	1	
Compassion fatigue	16.09±8.27	0-49	15.00	10.00-21.00	**r=-0.157 p=0.000**	**r=0.622 p=0.000**	1

r: Correlation coefficient, p<0.05: Statistically significant, SD: Standard deviation, Max: Maximum, min: Minimum

conducted using the same scale during the Chinese COVID-19 pandemic (20). However, in an Iranian study, healthcare workers' CS was found to be low (21). Similar studies on BO in Turkey demonstrated that healthcare workers had a moderate BO desensitisation score (22) and that healthcare workers were very optimistic during the COVID-19 period, despite experiencing stress and emotional exhaustion (8). Arpacioglu et al. (10) revealed that frontline healthcare workers in Turkey had high CF during the COVID-19 pandemic to date.

Our findings showed that most healthcare professionals were satisfied with their job and did not experience BO and CF during the period examined. The fact that Turkey experienced low case numbers, low mortality rates and low numbers of critically ill patients relative to other countries (23) might affectthis outcome. Other studies indicated that the severity of disease complications and high mortality rates in COVID-19 had adverse psychological effects on healthcare workers (24,25). Healthcare workers might be positively affected by the increased employment of healthcare workers in Turkey during the pandemic, their perception of adequate working conditions (26), and the provision of adequate protective equipment, drugs and test materials (8). Mobilization was declared in the country at the time of the study, and with media announcements praising healthcare professions, healthcare workers felt supported, praised and motivated. This strengthened healthcare workers emotionally and psychologically and protected them from BO and CF. This, in turn, ensured that CS was at a good level.

According to the results of this study, CS was higher in those younger than 25, single individuals, radiology technicians and other radiology workers, those with less than five years of professional experience and those working for 12-hour shifts. A similar study reported that age, gender, educational status and access to protective equipment affected CS during the COVID-19 process (21). Healthcare workers aged below 25 years of age might have higher CS because they were protected from exhaustion, they had fewer than five years of experience, accordingly worked in low-risk units, were generally single, and had less childcare or other responsibility. The fact that radiology technicians worked "n the background", with relatively little direct contact with patients, might also have a positive effect on CS.

In our study, the BO level of doctors and healthcare workers in COVID-19 intensive care were found to be higher. A similar study found that doctors experienced higher BO, compared to nurses, during the pandemic (13). Matsuo et al. (11) reported that nurses and laboratory workers had higher levels of BO when compared to other workers. Doctors and nurses are at direct risk and therefore experience intense stress, while caring for COVID-19 patients. Due to the problems they experience in the working environment, these medical staff are negatively affected by physical, mental and social issues and face BO (27).

Intensive care units (ICUs) with critically ill COVID-19 patients are locations where healthcare workers face a high risk of infection, and therefore, they are required to wear advanced protective equipment. They are environments with high mortality rates, and in the case of this pandemic, the course and symptoms of the disease have sometimes been unknown (28). Therefore, healthcare workers in the COVID-19 ICUs are severely physically and psychologically affected and experience BO (29,30). A similar study reported that those working in intensive care, emergency and COVID-19-related departments experienced higher levels of BO compared to some others (22). In this study, BO was higher in those with six to ten years of professional experience and those working 24-hour shifts. Contrary to these results, another study reported that healthcare workers with fewer working years had higher levels of BO (11). The Psychiatric Association Mental Trauma and Disaster Study Unit's Guide for the Protection of Healthcare Workers from Burnout during the COVID-19 Pandemic indicates that the working hours of healthcare workers, especially in the COVID-19 intensive care and services, should not be unusually long (31). Factors such as longer working hours, the number of COVID-19 patients being treated, and limited logistical support were associated with mental problems among staff (25). Furthermore, the International Nurses Association's guide states that senior nurses should be employed, especially in places such as COVID-19 ICU (32). Therefore, working in COVID-19 ICU might contribute to BO among senior healthcare workers with ten years of working experience.

According to this study, CF levels were higher in women, and those working in EMT-Paramedic, Family Medicine and Community Health departments. These results are consistent with the existing literature (10). CF is the mood of a person

Table 3. Statistical analysis of compassion satisfaction (CS), burnout (BO) and compassion fatigue (CF) according to demographic data and working conditions (n=96)

Characteristics	Compassion satisfaction $\bar{X}$ ± SD	Test, p	Burnout $\bar{X}$ ± SD	Test, p	Compassion fatigue $\bar{X}$ ± SD	Test, p
Age						
≤25	35.29±8.71		18.47±7.69		15.50±9.11	
26-35	32.88±33.00	**F=4,858**	18.47±7.69	F=0.459	16.56±8.45	F=0.846
36-45	31.96±8.71	**P=0.002**	18.19±6.53	P=0.711	16.24±7.89	p=0.469
>45	32.56±9.00		17.93±6.74		15.26±7.68	
Gender						
Female	33.10±8.61	t=0.803	18.62±6.96	t=1.361	16.17±8.09	**t=3.759**
Male	32.57±9.28	p=0.422	17.91±6.80	p=0.174	14.52±8.45	**p=0.000**
Marital status						
Married	32.50±8.80	**t=-1.993**	18.19±6.77	t=-1.192	16.30±8.26	t=1.041
Single	33.84±8.85	**p=0.047**	18.82±7.19	p=0.234	15.64±8.30	p=0.298
Title						
Doctor	29.92±8.94		19.81±7.88		16.54±9.70	
Nurse	32.92±8.54		18.69±6.89		16.33±8.19	
Midwife	33.42±8.66		18.13±6.50		17.17±6.68	
EMT-paramedic	34.23±9.20		19.26±7.28		17.85±8.88	
Health officer	32.38±8.29	**X^2=16.596**	16.66±6.30	**X^2=20.660**	15.38±7.98	**X^2=19.371**
Laboratory technician	30.77±9.44	**P=0.035**	18.58±5.61	**p=0.008**	15.36±8.19	**p=0.013**
Radiology technician	35.71±8.54		15.69±5.67		13.10±8.25	
Pharmacist	32.64±10.00		16.20±6.74		15.88±5.55	
Anaesthesia technician	32.26±9.11		19.56±7.32		14.90±8.45	
Department						
Policlinic	33.61±9.50		15.57±6.59		14.65±5.57	
Emergency department	34.60±8.73		19.02±6.72		16.07±8.74	
112 emergency healthcare services	33.81±9.06		19.13±7.46		17.72±9.00	
Laboratory	30.95±9.22		18.17±6.27		15.49±8.91	
Radiology unit	35.54±8.69	**X^2=15.926**	15.48±5.86	**X^2=26.552**	13.97±8.17	**X^2=19.074**
Family medicine-community health	31.00±8.62	**p=0.043**	18.80±5.52	**p=0.001**	18.31±7.68	**p=0.014**
COVID-19 service	31.80±9.62		19.80±7.20		17.09±8.25	
COVID-19 intensive care	31.13±7.92		20.87±7.12		18.26±8.80	
Other departments	33.02±8.63		18.13±6.94		15.39±7.99	
Professional working time						
<5 years	37.35±8.04		15.51±5.27		12.26±7.28	
6-10 years	33.15±8.92		19.15±7.13		16.82±8.72	
11-15 years	33.27±8.23	**F=3.863**	17.84±6.48	**F=3.305**	16.38±8.54	**F=3.321**
16-20 years	31.88±8.64	**p=0.004**	18.69±7.18	**p=0.011**	15.32±7.35	**p=0.010**
>20 years	31.93±9.26		17.92±6.78		16.18±7.94	
Weekly working time for the last month						
<40 hours	32.80±8.62		17.60±6.20		15.48±7.64	
40 hours	31.22±8.45	**F=4.885**	18.65±6.90	F=1.266	16.21±7.66	F=0.500
40-45 hours	32.96±9.10	**p=0.002**	17.89±7.02	p=0.285	16.43±8.54	p=0.682
>45 hours	34.50±8.89		18.45±7.37		16.25±9.09	

Table 3. Continued

Characteristics	Compassion satisfaction X̄ ± SD	Test, p	Burnout X̄ ± SD	Test, p	Compassion fatigue X̄ ± SD	Test, p
Daily working hours for the last month						
8 hours	32.59±8.86		17.87±6.49		15.96±8.04	
12 hours	36.41±8.55	**F=4.227**	18.99±7.62	**F=3.477**	17.07±9.63	F=2.284
16 hours	32.73±6.84	**p=0.006**	17.82±7.16	**p=0.016**	13.85±7.68	p=0.078
24 hours	32.49±9.19		19.70±7.42		16.78±8.40	
Weekly working style for the last month						
Daytime	32.07±8.76		18.19±6.39		16.10±8.13	
Shift	32.58±9.27	F=2.210	19.63±7.37	**F=3.992**	17.41±9.03	F=2.481
Both daytime/shift	34.05±8.49	p=0.086	18.33±7.09	**p=0.008**	15.42±8.08	p=0.060
Flexible work	32.85±8.83		16.90±6.46		15.36±7.51	
Providing service (care) for COVID-19 positive patients						
Yes	32.73±9.29	t=-0.650	18.82±7.24	t=1.758	16.57±8.54	t=1.624
No	33.13±8.36	p=0.516	17.96±6.54	p=0.079	15.62±7.98	p=0.105
Diagnosis with COVID-19 during the pandemic						
Yes	30.00±9.38	Z=-1.016	17.00±6.59	Z=-0.398	15.25±6.66	Z=-0.036
No	32.98±8.82	p=0.309	18.41±6.91	p=0.691	16.11±8.30	p=0.971
Workmate's diagnosis with COVID-19 during the pandemic						
Yes	31.92±8.90	**t=-2.857**	19.76±7.15	**t=5.020**	17.11±8.49	**t=3.074**
No	33.71±8.71	**p=0.004**	17.32±6.52	**p=0.000**	15.30±8.03	**p=0.002**

X̄: Arithmetic mean, SD: Standard deviation, F: ANOVA, t: Independent Samples T-Test, X2: Kruskal-Wallis test, Z= Mann-Whitney U Test, p<0.05: Statistically significant

arising from experiencing stressful events in their line of work. The COVID-19 pandemic constantly exposes healthcare workers to stress. Some studies reported that female healthcare workers experienced more psychological problems and were more emotionally affected than their male counterparts during the difficult pandemic process (1,8). EMT-paramedics work in conditions requiring rapid intervention in complex and stressful settings. Primary care workers and emergency service providers are healthcare workers who admit COVID-19 patients for the first time. Moreover, they provide services to society as a whole, without knowing who has COVID-19. Therefore, these workers may develop CF by working under constant stress.

According to our results, BO and CF were high and CS was low in healthcare workers who had workmates diagnosed as having COVID-19. The fact that healthcare workers' workmates were diagnosed as having COVID-19 might negatively affect them and caused them feel stress by highlighting the possibility that their workload would increase, or that they too might be infected and infect their families. Therefore, we found that workmates' diagnosis with COVID-19 reduced the CS of healthcare workers by causing BO and CF.

Study Limitations

The study results and the reliability of the scale used were limited to the responses and sample size of the healthcare workers who participated in the study. The sample of this study consisted of health professionals working in Turkey. Although our sample size was sufficient, we could not reach to an equal number of health professionals working in all regions of Turkey. This was our most important limitation in this study. Also, it was a limitation that the evaluations were not supported by clinical examinations. In subsequent studies, clinical psychiatric examinations of the participants can be performed. There is a need for larger and more universal sample groups to obtain more detailed results.

Conclusion

This study evaluated healthcare workers' CS, BO and CF levels and their influencing factors during the four months of the COVID-19 pandemic in Turkey. We also determined that the title, professional working time, department and workmates' diagnosis with COVID-19 affected the CS, BO and CF levels of healthcare workers. We saw that the number of cases was low and the number of inpatients in health institutions was less in the fourth month of the pandemic throughout the country compared to the present day. This situation potentially led to good CS, BO and CF levels among healthcare workers. However, the psychological state of healthcare workers may change depending on the uncertainty of the pandemic process, the number of cases and the density of hospitals. Therefore, we recommend that CS, BO and CF levels of healthcare workers be continuously evaluated and compared to previous ones, so that the necessary arrangements can be made and implemented as soon as possible.

Ethics

Ethics Committee Approval: Permission was obtained for the study from the Ministry of Health (2020-05-21T15_40_06) and KTO Karatay University Medicine and Non-Medical Device Research Ethics Committee (2020/023).

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Authorship Contributions

Concept: A.Y., Design: A.Y., B.Ö., Data Collection or Processing: A.Y., F.B., Ö.E., Analysis or Interpretation: F.B., A.Y., Ö.E., Literature Search: A.Y., F.B., B.Ö., Writing: A.Y., Ö.E.

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Original Article

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A Preliminary Investigation on the Chromosome Aberrations in Acute Lymphoblastic Leukaemia Using Multiprobe Fluorescence In Situ Hybridization Panel

Multiprob Floresan In Situ Hibridizasyon Paneli Kullanılarak Akut Lenfoblastik Lösemide Kromozom Aberasyonları Üzerine Bir Ön Çalışma

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ABSTRACT

Objective: Acute lymphoblastic leukemia (ALL) is a disease related to the overproduction of immature lymphocytes. For diagnosis and classification of ALL, recognizing chromosome aberrations using conventional cytogenetic analysis (CCA) is essential. However, limited ability of CCA to capture cryptical chromosomal aberrations is a major drawback. The aim of this study was to investigate recurrent aberrations in patients with ALL with normal karyotype or unsuccessful karyotyping using the fluorescence in situ hybridization (FISH) method.

Methods: Ten patients with ALL were included in this study. CCA was done according to the standart protocols, and then, multiprobe FISH panel was used for analyzing different chromosomal regions located on 12p13.2/21q22.12, 9q34.11-q34.12/22q11.22-q11.23, 9p21.3, 19p13.3, 11q23.3, 8q24.21, 14q32.33, 10p11.1-q11.1, 17p11.1-q11.1 and 4q12.

Results: Analyses of the specific chromosomal regions with FISH assay revealed undetected chromosome rearrangements. Among all the cases, four of them harbored chromosomal abnormalities. *MYC, TCF3, IGH* rearrangements, *CDKN2A* deletion and hyperdiploidy were detected in the study.

ÖZ

Amaç: Akut lenfoblastik lösemi (ALL), olgunlaşmamış lenfositlerin aşırı üretimi ile ilişkilendirilen bir hastalıktır. ALL'nin teşhisi ve sınıflandırılmasında klasik sitogenetik analizi (KSA) ile kromozom anomalilerinin tanımlanması önem teşkil etmektedir. Fakat KSA'nın kriptik kromozom değişimlerini saptamadaki sınırlılığı, bu yöntemin büyük bir dezavantajıdır. Yapılan çalışmanın amacı; floresan in situ hibridizasyon (FISH) yöntemi kullanılarak normal karyotipli veya değerlendirilecek metafazı olmayan ALL hastalarında mevcut kromozom anomalilerini araştırmaktır.

Yöntemler: Çalışmaya 10 ALL hastası dahil edildi. KSA, standart protokollere göre uygulandı, ardından 2p13.2/21q22.12, 9q34.11-q34.12/22q11.22-q11.23, 9p21.3, 19p13.3, 11q23.3, 8q24.21, 14q32.33, 10p11.1-q11.1, 17p11.1-q11.1 ve 4q12'de yer alan kromozom bölgelerinin analizi için multiprob FISH paneli kullanıldı.

Bulgular: Spesifik kromozom bölgelerinin FISH metodu ile analizi, önceden saptanmamış kromozom düzenlemelerinin bulunduğunu ortaya çıkardı. İncelenen tüm olguların dördünde kromozom anomalileri tespit edildi. Çalışmada *MYC, TCF3, IGH* genlerinin yeniden düzenlemeleri, *CDKN2A* delesyonu ve hiperdiploidi tespit edildi.

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Conclusion: Diagnostic sensitivity of FISH probes in comparison with CCA is effective in the detection of multiple chromosomal rearrangements with prognostic significance. For the improvement of the cytogenetic examination and achieving optimum results for patients with ALL , FISH panels are needed to be used combining with conventional cytogenetics routinely.

Keywords: Acute lymphoblastic leukemia, cytogenetics, fluorescence in situ hybridization, chromosome aberrations

Sonuç: Klasik sitogenetik analiz ile karşılaştırıldığında, FISH problarının tanıdaki duyarlılığı prognostik önemi olan çoklu kromozom anomalilerinin saptanmasında yararlıdır. Sitogenetik incelemelerin geliştirilmesi ve ALL olgularında en iyi test sonuçlarının elde edilmesi için, rutinde FISH panellerinin klasik sitogenetik yöntemler ile birleştirilerek kullanılması gerekmektedir.

Anahtar Sözcükler: Akut lenfoblastik lösemi, sitogenetik, floresan in situ hibridizasyonu, kromozom aberasyonları

Introduction

Acute lymphoblastic leukemia (ALL) is a type of disease characterized by overproduction of malignant and immature lymphocytes. As a consequence of failure to produce mature blood cells and uncontrolled proliferation of lymphoblasts, it spreads to the blood and metastasizes other areas (1). Although the cause of ALL remains unknown, it is thought that various complex mechanisms such as chromosomal damage due to physical or chemical exposure are required for the development of the disease (2).

Conventional cytogenetic analysis (CCA) plays an essential role in the identification of structural and numerical chromosome aberrations that are useful prognostic indicators in patients with ALL. Chromosome aberrations are observed in 60-85% of patients with ALL (3). Hyperdiploidy, hypodiploidy, t(9;22)(q34;q11.2) [BCR-ABL1], t(v;11q23.3) MLL rearrangements, t(12;21)(p13;q22) [ETV6-RUNX1], t(1;19)(q23;p13.3) [TCF3-PBX1], t(5;14)(q31;q32) [IL3-IGH] and intrachromosomal amplification in chromosome 21 (iAMP21) are commonly observed and play significant role in the classification and prognosis of ALL (4). Inadequate specimens, low mitotic index and difficulty of obtaining high-quality metaphases in bone marrow (BM) are impeded or rendered the CCA impossible. Furthermore, some of the structural abnormalities, such as t(12;21) [ETV6-RUNX1] may exist cryptically and be undetectable by CCA. Since fluorescence in situ hybridization (FISH) allows determination of chromosomal changes at interphases besides metaphases with high specificity and sensitivity, it is advantageous for the examination of ALL related abnormalities in the patients with low mitotic activity or normal karyotype (5, 6). FISH panels using different probe combinations are available to detect common rearrangements for ALL simultaneously (7).

In our study, we aimed to investigate recurrent aberrations in patients with ALL with normal karyotype or unsuccessful karyotyping using the FISH method. We used a multiprobe panel carrying probes for t(12;21) [ETV6-RUNX1], t(9;22) [BCR-ABL1], deletion of 9p21.3 (CDKN2A), rearrangements of TCF3 located on 19p13.3, MLL located on 11q23.3, MYC located on 8q24.21, and IGH located on 14q32.33, also enumeration probes for chromosomes 4, 10 and 17.

Methods

Patients

Ten patients with normal karyotype (n=7) or karyotyping failure (n=3) were selected for this study from our patients with ALL whose BM samples were referred by hematology section for CCA. Equal patients of males and females were included in the study and three of them were patients with childhood ALL. Peripheral blood (PB) samples of healthy individuals (n=5) were used for establishing cutoff values. The median ages of patient and control groups were 24 and 23, respectively. The characteristics of the patients are given in Table 1. The informed consent forms were obtained in accordance with the Declaration of Helsinki and the study had the permission of our University's Research Ethics Committee (approval number: 135385).

Conventional Cytogenetics Analysis

Twenty-four-hour and 48 h unstimulated BM cultures and 72 h unstimulated PB cultures were performed according to the standard protocols and banding was applied to slides using Giemsa-Trypsin-Leishman (GTL) method (8). To perform conventional karyotyping, at least 15 metaphases were analyzed per patient and karyotypes were defined according to the International System for Human Cytogenetic Nomenclature (ISCN 2016) (9).

Fluorescence In Situ Hybridization

For FISH assay, Chromoprobe multiprobe ALL panel (Cytocell Ltd, Cambridge, UK) consisted of 12p13.2 (*ETV6*)/21q22.12 (*RUNX1*), 22q11.22 (*BCR*)/9q34.11-q34.12 (*ABL1*), 9p21.3 (*CDKN2A)*, 19p13.3 *(TCF3)*, 11q23.3 (*MLL*), 8q24.21 *(MYC),* 14q32.33 (*IGH*), 10p11.1-q11.1 (centromere of chromosome 10), 17p11.1-q11.1 (centromere of chromosome 17) and 4q12 (*CHIC2,* chromosome 4) chromosomal regions were used. The experimental protocols were performed according to the previous study and manufacturer's instructions (10). Slides were analyzed under the fluorescence microscope (Olympus BX51, Tokyo, Japan) with filter sets (TxRed, FITC, Aqua, DAPI). FISH scoring was performed independently by two investigators. The cutoff values were determined by examination of control subjects and calculated using inverse beta distribution (betainv) (11).

Results

The FISH assay revealed cytogenetically undetected chromosome rearrangements in target regions of the multiprobe panel in our patient group (Figure 1). The results are summarized in Table 1.

MYC

The *MYC* rearrangements were detected higher than cutoff values (13%) in two patients; Case No. P3 (25%), and Case No.P5 (25%).

CDKN2A

Deletions of *the CDKN2A* region were found in only Case No. P2 (28%) (Cutoff value: 10%).

TCF3

The rearrangements of *TCF3* were detected in two patients; Case No. P2 (18%) and Case No. P8 (28%) (Cutoff value: 16%)

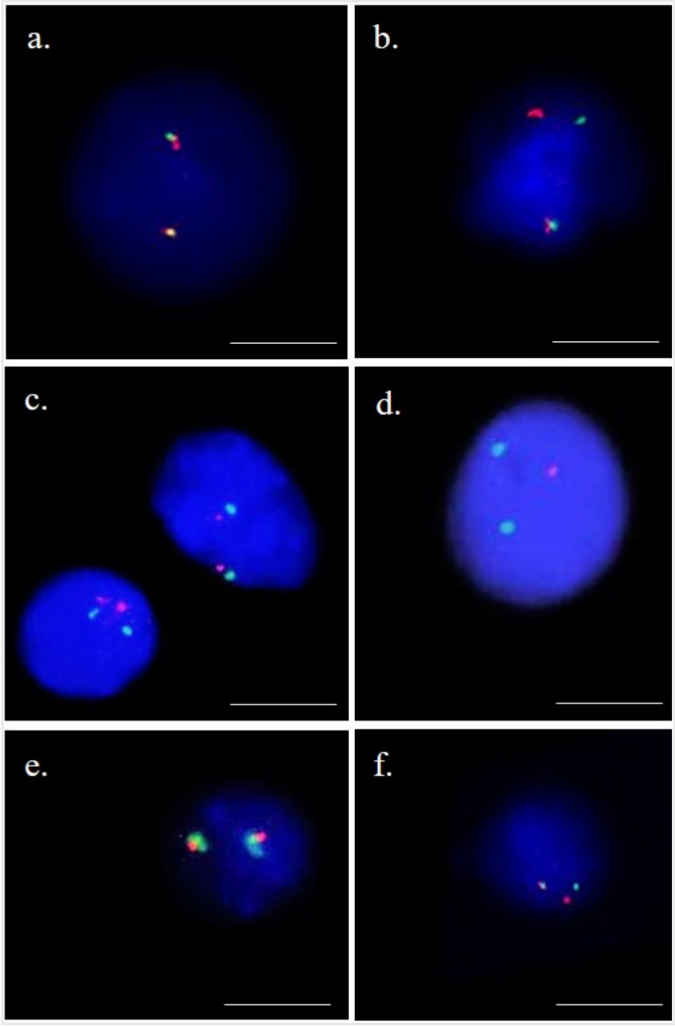

Figure 1. Examples of interphase nuclei with *MYC, CDKN2A* and *IGH* probe signals, signifying normal cells (a, c and e, respectively), a *MYC* rearrangement (b), a *CDKN2* deletion (d) and an *IGH* rearrangement (f) (objective, x100). Rearrangements have led to the separation of green and red signals, whereas deletion is seen with only one red signal on a chromosome and absent signal on the other chromosome (scale bar: 10 µm)

Table 1. Clinical, cytogenetic and FISH results of the patient (P) and control (C) groups

Case no	Age/sex	Diagnosis	Karyotype	*MYC* rearrangements	*TCF3* rearrangements	*MLL* rearrangements	*IGH* rearrangements	*CDKN2A* deletion	Hyperdiploidy	*ETV6/RUNX1* translocation	*BCR/ABL* translocation
P1	9/F	B-ALL	46,XX	-	-	-	-	-	-	-	-
P2	33/M	B-ALL	46,XY	-	+	-	-	+	+	-	-
P3	23/M	B-ALL	46,XY	+	-	-	+	-	-	-	-
P4	41/M	B-ALL	-	-	-	-	-	-	-	-	-
P5	60/F	B-ALL	46,XX	+	-	-	-	-	-	-	-
P6	23/F	B-ALL	46,XX	-	-	-	-	-	-	-	-
P7	7/F	ALL	-	-	-	-	-	-	-	-	-
P8	4/F	ALL	-	-	+	-	+	-	-	-	-
P9	24/M	B-ALL	46,XY	-	-	-	-	-	-	-	-
P10	18/M	B-ALL	46,XY	-	-	-	-	-	-	-	-
C1	28/F	-	46,XX	-	-	-	-	-	-	-	-
C2	22/F	-	46,XX	-	-	-	-	-	-	-	-
C3	24/M	-	46,XY	-	-	-	-	-	-	-	-
C4	21/F	-	46,XX	-	-	-	-	-	-	-	-
C5	21/M	-	46,XY	-	-	-	-	-	-	-	-

* The positivity and negativity ratings were determined by cutoff values.
F: Female, M: Male, ALL: Acute lymphoblastic leukemia, B-ALL: B-cell ALL

Chromosome 4

The cutoff values for gains and losses of the *CHIC2* region of chromosome 4 were determined separately as 6% for gains and 5% for losses. All of the patients were negative for both losses and gains of the *CHIC2* region.

Centromere 10

The cutoff values for gains of centromere 10 were 10% and 6% for the losses. Only case P2 was positive for the gain of chromosome 10 (32%).

Centromere 17

The cutoff values for gains of centromere 17 were 6% and 13% for the losses. While there was no patient with the gain of chromosome 17, two patients were positive for loss; case no. P5 (15%) and case no. P8 (14%).

ETV6/RUNX1

The cutoff value was 3% and none of the patients had *ETV6/RUNX1* translocation.

MLL

The cutoff value was 9% and none of the patients had *MLL* rearrangements.

BCR/ABL1

The cutoff value was 3% and none of the patients had *BCR/ABL1* translocation.

IGH

The rearrangements of *IGH* were detected in two patients; case no. P3 (19%) and case no. P8 (19%) (cutoff value 17%).

While Case P2 (*TCF3*, *CDKN2A* and gain of chromosome 10) and Case P8 (*TCF3, IGH* and loss of chromosome 17) had three abnormalities, Case P3 (*MYC* and *IGH*) and Case P5 (*MYC* and loss of chromosome 17) had two abnormalities. The other six patients had no abnormalities for the multiprobe panel. *TCF3, MYC, IGH* rearrangements, and loss of chromosome 17 were detected twice in the study while *CDKN2A* deletion was observed once. *MLL* rearrangements, translocations of *ETV6/RUNX1* and *BCR/ABL1*, gains of chromosomes 4 and 17, losses of chromosomes 4 and 10 were not detected in this study.

Discussion

Multiprobe FISH panels provide an advantage to detect disease-specific genetic abnormalities that do not only have prognostic significance but also play roles in classification, follow-ups, and treatment of hematological malignancies (7). Previous studies showed that using FISH panels was effective to detect additional chromosomal abnormalities not detected by CCA in nearly 50% of patients with ALL (12,13). In this study, a FISH panel including probes for common abnormalities for ALL was applied to the 10 patients with ALL with normal karyotype or karyotyping failure. The reason for failure in conventional karyotyping in our 3 patients could either be culture failure, insufficient metaphase quality, or technical problems in trypsin digestion and staining stages, besides the known difficulty of obtaining chromosomes in ALL. However, in these patients, the FISH assay showed efficiency for identifying the chromosome aberrations. Chromosomal abnormalities were observed in 4 (40%) of the patients using FISH method. All of these patients had two or three abnormalities. Although adult and childhood patients with ALL were evaluated as separate groups generally, we discussed our adult and childhood patients altogether because of the smallness of our study group. Case P8 was our only childhood patient with positive FISH findings and had three abnormalities (TCF3 rearrangements, CDKN2A deletion, and hyperdiploidy).

The *ETV6/RUNX1* translocation is the most frequent abnormality in childhood B-cell ALL (B-ALL) and associated with favorable outcome (4,14,15). It is difficult to detect this cryptic translocation by CCA (16, 17). Previous studies with FISH panels reported frequent occurrences of *ETV6/RUNX1* translocation (10-44.3%) (6,12,18-21). However, there were no findings of *ETV6/RUNX1* translocation in our patients. This was probably due to small number of patients, 3 of whom were in childhood.

The *BCR/ABL1* fusion caused by t(9;22)(q34;q11) is present in 15-50% of adults and 3-5% of patients with childhood ALL and it is associated with poor outcome (4,16,22). CCA has relatively high (80%) sensitivity for detection of t(9;22)(q34;q11) (4,13,18). Similar to karyotypic results, we did not detect *BCR/ABL1* translocation in any of the patients by FISH either.

The *MYC* rearrangements are usually found as translocations between *MYC* locus (8q24) and *IGH* heavy and light chain gene loci located on 14q32, 2p12, and 22q11, respectively. Rearrangements of *MYC* are characteristic in Burkitt lymphoma cytogenetics, also present in subtypes of mature B-cell neoplasms (less than 5% in both adults and children) (16,23,24). Kim BR et al. found gains of *MYC* in two (20%) patients with ALL using FISH panel including *MYC* rearrangement probe (18). In our study, *MYC* rearrangements were found in two patients (Cases P3 and P5) too. In Case P3, both *MYC* and *IGH* rearrangements were observed. The coexistence of these two rearrangements points out to the existence of t(8;14). The closeness of the ratios of *MYC* (25%) and *IGH* (19%) rearrangements also support this conclusion. The other patient (Case P5) with *MYC* rearrangement had no *IGH* rearrangement, but she had monosomy 17 meaning hypodiploidy. It was commonly assumed in previous studies that isolated *MYC* rearrangements were rare in B-ALL and we did not observe *MYC* rearrangement as sole abnormality either (23,24).

Study Limitations

Although *IGH* rearrangements are frequent in lymphomas and mature leukemias, several studies have revealed that these rearrangements account for 5% of patients with ALL with both B-cell and T-cell, mostly in adolescents and young adults. Multiple partner genes are involved in *IGH* translocations (4,25,26). We found that *IGH* rearrangements coexisted with *TCF3* rearrangements and monosomy 17 in Case P8, and *MYC* rearrangements in Case P3. In previous studies, *TCF3* has not

been reported among partner genes of *IGH* translocations (25,26).

The *TCF3* gene locus are involved in t(1;19)(q23;p13) and t(17;19)(q21;p13). While t(1;19)(q23;p13) has been reported in 2% of patients with childhood ALL and 6% of patients with adult ALL and associated with intermediate-risk, t(17;19)(q21;p13) is seen more rarely, in <0.1% of patients with B-cell precursor ALL (BCP-ALL) (4,27). We observed rearrangements of *TCF3* in combination with *CDKN2A* deletion and hyperdiploidy in one further patient (Case P2) apart from Case P8 discussed above. *CDKN2A/2B* deletions are frequent (30-50%) abnormalities in both patients with childhood ALL and patients with adult ALL and are associated with poor prognosis (28). Hyperdiplody is another frequent abnormality in childhood ALL, and high hyperdiploidy is considered a good prognostic factor (4,16,22). Case P8 was our childhood patient, and had *CDKN2A* deletions and hyperdiploidy.

Conclusion

In our study, despite the small number of patients, chromosomal abnormalities related to ALL were found in a significant amount of patients with normal karyotype or unsuccessful karyotyping. Using multiprobe FISH panels was effective in the detection of multiple chromosomal rearrangements with prognostic significance simultaneously. Of all the patients with ALL we analyzed, multiprobe FISH was able to detect *MYC, TCF3* and *IGH* rearrangements, deletion of the *CDKN2A,* gains of centromere 10, losses of the centromere 17. Identification of these chromosome abnormalities in hematological malignancies, especially in ALL, may provide prognostic value for treatment planning, response or follow-up. Therefore, we suggest that FISH panels are needed to be used combining with conventional cytogenetics routinely to achieve optimum results for patients with ALL.

Ethics

Ethics Committee Approval: The informed consent forms were obtained in accordance with the Declaration of Helsinki and the study had the permission of our University's Research Ethics Committee (approval number: 135385).

Informed Consent: Obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: B.G., S.A., A.Ç., Y.T.A., R.D.K., Ş.Y., Ş.Ö., A.D., Design: B.G., S.A., A.Ç., Y.T.A., R.D.K., Ş.Y., Ş.Ö., A.D., Data Collection or Processing: B.G., S.A., A.Ç., Y.T.A., R.D.K., Ş.Y., Ş.Ö., A.D., Analysis or Interpretation: B.G., S.A., A.Ç., Y.T.A., R.D.K., Ş.Y., Ş.Ö., A.D., Literature Search: B.G., S.A., A.Ç., Y.T.A., A.D., Writing: B.G., S.A., A.Ç., Y.T.A., R.D.K., Ş.Y., A.D.

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Original Article

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Knowledge and Attitude of New Coronavirus Epidemic (COVID-19) Among Health Care Workers

Sağlıkçılar Arasında Yeni Koronavirüs Hastalığı (COVID-19) Salgınıyla Mücadele Bilgi Düzeyi, Korunma ve Tedavi Hakkındaki Görüşlerinin Değerlendirilmesi

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ABSTRACT

Objective: The recent spread of new coronavirus disease-19 (COVID-19) pandemic causing worldwide concern is a public health emergency situation. The risk of getting infected due to close contact with the infected patients as well as the concern levels of the health professionals on this issue are very high. The aim of this study is to evaluate the concern level of being infected of the health professionals, as well as their view and perception of different applications used during the treatment of the COVID-19 cases together with their whole approach during this pandemic situation.

Methods: The study was conducted through an online survey that was sent to all the health professionals of a pandemic hospital in a city in Turkey between 8-15 May 2020. This online survey was sent to all the professionals through social media platforms. The survey included both multiple-choice and true-false questions regarding COVID-19 diagnosis, clinical staging, treatment approach, concerns, knowledge, and awareness of the situation together with some social demographic characteristics of the health professionals. SPSS v20 program was used to evaluate the statistical analysis of the data collected. Data are shown through mean ± standard deviation and percentage.

Results: The study population consisted of 250 (59.9%) doctors and 169 (41.1%) assistant healthcare professionals and the average age of the participants was 33.21±6.88 years. Of 128 participants who smoked during the pandemic 76 (18.1%) wanted to quit smoking. Three hundred and ninety (93.1%) participants thought that they were in a group with high risk of being infected and that they concerned about this matter. Of the participants 109

ÖZ

Amaç: Yeni coronavirüs hastalığı (COVID-19) salgını, uluslararası endişe duyulan bir halk sağlığı acil durumudur. Bu çalışma, mevcut salgın sırasında sağlık çalışanları arasında enfekte olma endişesini, tutumlarını, tedavi ve COVID-19 ile mücadeledeki çeşitli uygulama modifikasyonları konusundaki görüş ve davranış tarzlarını değerlendirmek amacıyla yapılmıştır.

Yöntemler: Türkiye'de bir ilin pandemi hastanesindeki sağlık personeline 8-15 Mayıs 2020 tarihleri arasında bir çevrimiçi anket uygulayarak gerçekleştirilmiştir. Ankette sosyodemografik özelliklere dair sorular ile beraber COVID-19 tanı, klinik, tedavi tutumu, kaygı, bilgi ve farkındalık ile ilgili çoktan seçmeli sorular ve doğru yanlış soruları soruldu.

Bulgular: Katılımcıların 250'si (%59,9) doktor, 169'u (%41,1) yardımcı sağlık personelinden oluşuyordu, yaş ortalamaları 33,21±6,88 yıl idi. Sağlık sektöründe çalıştığı için COVİD-19 bulaşma riskinin yüksek olduğunu düşünenlerin ve kaygı duyanların sayısı ise 390 (%93,1) kişidir. Yüz dokuz (%26,01) kişinin yakınlarında COVID-19 testi pozitif çıktığı beyan edilmiştir. Altmış dört (%15,3) sağlık çalışanı polimeraz zincir reaksiyonu (PCR) testi yaptırdığını bildirmiştir ve 3 (%0,7) sağlık çalışanı da COVID-19 PCR testin pozitif çıktığını bildirilmiştir.

Sonuç: Salgın sırasında pandemi hastanesinde çalışan sağlıkçılar COVİD-19 hakkında genel olarak yeterli bilgiye sahip olduklarını ve ülkemizin salgınla mücadelede başarılı olacağına inandıklarını ortaya koymuştur.

Anahtar Sözcükler: Sağlık çalışanları COVID-19 bilgi düzeyi, hidroksiklorakin profilaksisi, COVID-19

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(26.01%) had COVID-19 positive relatives or friends. Sixty four (15.3%) participants claimed to have a polymerase chain reaction (PCR) test, and 3 (0.7%) of them reported that their COVID-19 PCR tests were positive. Eighty-four (20.04%) stated that they used hydroxychloroquine for prophylaxis.

Conclusion: The healthcare professionals working in the pandemic hospital during the pandemic stated that they generally had sufficient knowledge about COVID-19 and believed that our country would be successful with its fight against this pandemic. Moreover, our study proved the importance of knowledge levels in fighting communicable diseases.

Keywords: COVID-19 health care professionals, knowledge levels of COVID-19, hydroxychloroquine prophylaxis

Introduction

New type of coronavirus disease-19 (COVID-19) which emerged in China had negative effects on all parts of daily life (1). First patients of the epidemic presented with pneumonia without any etiology and associated with the seafood exposure epidemiologically at the end of December 2019 in the city of Wuhan which was located in the Hubei province of China. (2). The World Health Organization (WHO) declared the disease as public health epidemic and international state of emergency on 30 January 2020 when it already spread to 34 different districts of China up to that date (3).

Structurally, new type of coronavirus is an ss-RNA enveloped virus with positive polarity which is approximately 350 kbp in size (4). The droplet feature was identified as the primary cause of the spread of the virus (5).

Incubation period which was the time until the symptoms development after exposed to the virus was between 2 to 14 days with an average of 5 days (6). Upper respiratory tract infections, high fever, dry cough, difficulty in breathing, myalgia, pain in throat, nausea, vomiting and diarrhoea are some of the common symptoms of the infection (7). When the vital role of the immune system of the body is considered, the risk of elderly people and people with chronic diseases which weaken the immune system is much higher when they are infected with the virus compared with young and health people with stronger immune systems (8). COVID-19 might result in acute coronary syndrome, acute respiratory failure and mortality in severe patients (9). Even though the mortality rate associated with COVID-19 is quite low, it has the potential of spreading very quickly (10). It is strongly recommended to place the possibly infected individuals into quarantine and observe them after real time real time reverse transcriptase polymerase chain reaction (RT-PCR) samples are taken until further investigations are carried out (11). Unfortunately there is no antiviral vaccine developed at the moment. Therefore patients have to rely on supportive treatments such as vitamin A, C and D (12). Due to COVID-19's fast spreading and devastating attitude, a lot of countries have shut down education institutions, social gatherings, sports events, airports and even banks or brought flexible working hours for them to be able to control the spread of the virus. Besides, most of the individuals play their parts in the society quarantining themselves by staying inside their homes to minimize the spread of the virus. At the same time having all the hospitals functioning actively during these difficult times is vitally important and they are rarely shut down during epidemic conditions. The health care professionals are at high risk of contamination due to their close contact with the infected patients. Therefore, there is a high risk of health care professionals getting infected from their patients and potentially they can spread the virus to their friends, relatives and even to other patients. Under these circumstances, development of anxiety of getting infected from the patients in health care professionals might be considered as a natural behaviour (13).

Even though Ministry of Health has issued guidance on prevention, most of the health care professionals are scared of conducting detailed examination and treatment for the patients with COVID-19 risk. Actually, health care professionals might not be updated with the latest guidelines. Because of this, we conducted a survey based study to evaluate the current status and the perception of the health care professionals locally in our city. This study aimed to evaluate and understand the knowledge levels of the health care professionals working actively during the COVID-19 epidemic on the infection, as well as their behavior and attitude, their knowledge level on treatment process, their own methods for prophylaxis, and their overall concerns.

Methods

The study was conducted through an online survey which was sent to all the Health professionals (mostly doctors and the nurses in the COVID-19 units) of a pandemic hospital in a city in Turkey between 8-15 May 2020. For this purpose a very well designed survey was developed on https://docs.google.com/forms website. The professionals were contacted through social media and called personally to inform them about the details of the survey and their responses were recorded. The survey was completed manually by the professionals that could not be contacted through social media. The health professional involved in the diagnosis, treatment and the follow-up process of COVID-19 were included in the study. The survey included multiple choice

questions regarding COVID-19 diagnosis, clinical staging, treatment approach, knowledge and awareness of the situation together with some social demographic characteristics of the health professionals. Also, there were questions to evaluate the attitude and the concern levels of them with true-false or unsure choices.

Statistical Analysis

The SPSS v20 program was used for the statistical analysis of the data which were transferred to Microsoft Excel from the Google form format by adhering to the original states of them. Data were shown through mean ± standard deviation, number of samples and percentages.

Survey Question Form

Demographic characteristics of the participants including age, sex, marital status and occupation were recorded. The occupation and the designation of the participants were categorized. Participants were asked to answer the questions on following subjects: The symptoms of COVID-19, diagnosis and treatment, blood parameters, risk groups, routes of contamination, precaution and prevention methods, level of their knowledge on the infection, treatment and prophylaxis, as well as their concerns during this epidemic. Answers for the questions were as follows: Present- not present, yes-no, true-false- do not know, multiple choices with multiple answers, open ended answers, and agree-disagree- unsure.

Results

When looking at the demographic characteristics of the participants following findings were recorded. Two hundred and thirty two (55.4%) males and 187 (44.6%) females were included in the study (a total of 419 participants) with a mean age of 33.21±6.88 (20-57). Of them 276 had minimum one child or more. Of them 250 (59.9%) were doctors and the other 169 (41.1%) were assistant health care professionals such as nurses. When the participants were classified according to their designation; 169 (40.1%) were assistant health care professionals, 124 (29.6%) were doctors, 106 (25.3%) were academic member doctors, 10 (2.4%) were associate professor doctors and 10 (2.4%) were professor doctors.

Of the participants 67 (16%) had chronic diseases including 17 (4.05%) with asthma, 13 (3.1%) with functional thyroid disorder, 8 (1.9%) with diabetes mellitus and 8 (1.9%) with high blood pressure.

Of the participants 128 (30.5%) were smokers and they smoked an average of 23.2 packets of cigarettes per year. Of the 128 smoking participants 76 (18.1%) wanted to quit or made an attempt to quit during the COVID-19 epidemic.

Of the participants 151(36%) claimed sensitivity towards cold and flu-like sicknesses, therefore they were scared of being infected with the COVID-19 virus. Moreover 390 (93.1%) of the participants considered themselves as high risk group for the contamination of the virus because they worked in the healthcare sector.

Of the participants 282 (67.3%) selected the correct choice of "a virus with positive polarity enveloped onto RNA" for the question to evaluate the understanding of the health care professionals' knowledge of SARS-CoV-2 and the COVID-19 virus family. Almost all the participants, 418 (99.8%), selected "China" as the emerging country of the virus. Of the participants 397 (94.7%) selected the "droplet infection" choice as the primary route of transmission of COVID-19 .

Of them 227 (54.2%) selected "polymerase chain reaction" as a means of final diagnosis of the virus and 105 (25%) of them selected "Thorax computed tomography (CT) together with polymerase chain reaction" choice to the question on final diagnosis of COVID-19.

Of them 194 (46.3%) selected the "oropharyngeal sampling" and 183 (%43.7) of them selected "bronchoscopy sampling" as an answer to the question on sampling method which had the highest value for the diagnosis of the COVID-19.

Of them 241 (57.5%) gave the answer of "lymphopenia" to the question regarding the hemogram parameter of the COVID-19. The answers of the participants to the question on procalcitonin levels when there was no accompanying bacterial infection were as follows; 168 (%40.1) answered "does not change', 114 (27. 2%) "will increase", 109 (26%) "will decrease" and 28 (6.7%) did not answer at all.

Of them 149 (35.6%) gave the answer of "fever, dry cough and fatigue", whereas 62 (14.8%) of them gave the answer of "fever, dry cough and loss of sense of taste and smell" to the question on the most common clinical signs and symptoms of COVID-19.

Of them 152 (36.3%) gave the answer of "75 mL/min", whereas 141 (33.7%) gave the answer of "80 mL/min" to the question on the threshold saturation value of the patients with respiratory difficulties for the intubation procedure.

Of the doctors 208 (82.5%) answered "yes", when they were asked if they changed their approach on usage of non-steroid anti-inflammatory medicines towards paracetemol like medicines during COVID-19 epidemic.

Nineteen questions with the answers of true-false on means of transmission of the coronavirus and the anxiety towards the virus were answered with the "true" choice by almost all the participants (Table 2).

Of the participants 122 (29.1%) stated that they did not have any contact with anyone with the COVID-19 and 96 (22.9%) with contact stated that those patients were in their units where they were working.

When asked if any of the relatives and friends were diagnosed as having COVID-19, 109 (26.01%) of them stated that they had friends and relatives with COVID-19 positivity.

Of them 64 (15.3%) answered "yes" when they were asked if they either had COVID-19 PCR or fast antigen- antibody tests. Of the participants who had the tests 3 (0.7%) stated that their own COVID-19 PCR test results were positive.

Table 1. Socio-demographic characteristics of the participants

		n	%
Mean age	33.21±6.88		
Gender	Male	232	55.4
	Female	187	44.6
Occupation	Research assistant doctor	124	29.6
	Assistant profesör	106	25.3
	Associate professor	10	2.4
	Professör	10	2.4
	Assistant health personnel	167	39.9
	Pharmacist	2	0.4
Marital status	Married	280	66.8
	Single	128	30.5
	Divorced	11	2.6
Smoking	Yes	128	30.5
	No	291	69.5

Table 3 shows the answers to the most common precautions and the preventions health care professionals take against the COVID-19.

Of them 158 (37.7%) believed that using hydroxychloroquine (plequanil) might be beneficial for prophylaxis, however 151 (36%) of them believed that there was not enough evidence to support the usage of it. Of them 90 (21.5%) stated that their doctor friends recommended, 85 (20.3%)stated that they used the literature as reference, 66 (15.8%) referred to the panels conducted by the specialists and 36 (8.6%) referred to media when they were asked about the source of information on the effect of hydroxychloroquine for prophylaxis.

Of them 84 (20.04%) stated that they used hydroxychloroquine for prophylaxis to protect themselves from the COVID-19. Three of these 84 participants stated that they used hydroxychloroquine for prophylaxis in line with the Ministry of Health's high risk contact criteria due to their contact with the COVID-19 infected patients. The dosage and the frequency of hydroxychloroquine for prophylaxis are shown at Table 4.

Discussion

Our study showed that most of the health care professionals of a pandemic hospital in one of the cities of Turkey had comprehensive knowledge about the COVID-19 and that they followed the relevant algorithms with necessary literature references. Of them 94.7% were confident with their knowledge on means of transmission of the virus whereas 98.1% of them with their knowledge on the general symptoms as well as how to protect themselves from the virus. Of the participants 93.1% believed that they were in high risk group for the infection and 82.3% of them believed that our country would be successful with its fight against the infection.

Our study used a survey mainly focused on closed end questions to collect information on health care professionals' knowledge level of COVID-19 epidemic, their behaviours and attitude towards the treatment process, their concerns together with precaution measures taken during the COVID-19 epidemic. It is proven that studies based on surveys collect the information about preferences, attitude, perceptions and the experiences of the participants. However, careful data collection and interpretation are required (14).

The common symptoms of COVID-19 include fever, dry cough and difficulty in breathing. Myalgia, developing phlegm and sore throat are the other symptoms which are less common (7). Virus is transmitted among the humans through droplets as a result of coughing. Touching at own face after touching to a contaminated area is believed to be another means of transmission of the virus (15,16). Incubation period which is the time until the symptoms develop after exposing to the virus is between 2 to 14 days with an average of 5 days (6). Standard diagnostic method is to conduct rRT-PCR tests with nasopharyngeal swab taken from the individual (17). Diagnosis of the infection can be made by evaluating the symptoms, risk factors and computerized chest tomography scans pointing to pneumonia all together (18). The answers which were similar to literature regarding most of the basic knowledge about the COVID-19 were obtained in our study and nearly all the participants gave correct answers to the questions.

Due to long incubation (up to 14 days) period of SARS-CoV-2, it is nearly impossible to determine the individual's exposure to the virus during different stages like isolation, quarantine and till the mortality stage. Because of this, very fast pace transmission of COVID-19 which impacted millions of people around the world was causing severe physiological stress and fear among the people (19). Additionally, non-availability of an approved treatment or a prophylaxis vaccine treatment increases the anxiety of being infected. Therefore, health care professionals are at high risk of being exposed to the virus during this COVID-19 epidemic and this leads to a great level of anxiety among them (20).

Primary transmission means of the COVID-19 happens through droplets (5). That is why the likelihood of heath care professionals being infected and spreading the virus further increase. Current study showed that health care professionals anxiety of getting infected through their colleagues was similar to the anxiety they had by getting infected in the society which had very fast pace of spread of the virus among the people (21). The other concern the health professionals had was transmitting the virus to their family members after they completed their work. Coronavirus may be alive on some surfaces from few hours to few days and due to long incubation period of the virus, people will not show any symptoms and health care professionals are scared of being infected from these people who are admitted to the hospital for other reasons than COVID-19 (22). During the outbreak of COVID-19 the importance of hand hygiene is emphasized repeatedly and this issue is even more important for the health care professionals. The studies show that washing the hands with soap and water or cleaning them with alcohol based disinfectants is an important precaution to control the spread of respiratory diseases including SARS (23,24). Because

Table 2. Knowledge about COVID-19 among health care workers

Questions	True	False	Unknow
Headache, fever, cough, myalgia are symptoms of COVID-19	411 (98.1%)	4 (1%)	4 (1%)
Unlike the common cold, stuffy nose, runny nose, and sneezing are less common in persons infected with the COVID-19 virus.	333 (79.5%)	54 (12.9%)	32 (7.6%)
There currently is no effective cure for COVID-2019, but early symptomatic and supportive treatment can help most patients recover from the infection	380 (90.7%)	24 (5.7%)	15 (3.5%)
COVID-19 patients can't infect the virus when they don't have a fever	6 (1.4%)	386 (92%)	27 (6.4%)
COVID-19 is transmitted through air, contact, fecal-oral routes	403 (96.2%)	8 (1.9%)	8 (1.9%)
Ordinary residents can wear general medical masks to prevent the infection by the COVID-19 virus	385 (91.9%)	24 (5.7%)	10 (2.4%)
It is not necessary for children and young adults to take measures to prevent the infection by the COVID-19 virus	24 (5.7%)	379 (90%)	16 (3.8%)
To prevent the infection by COVID-19, individuals should avoid going to crowded places such as train stations and avoid taking public transportations	409 (97.6%)	2 (0.5%)	8 (1.9%)
Isolation of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus	408 (97.4%)	2 (0.5%)	9 (2.1%)
People who have contact with someone infected with the COVID-19 virus should be immediately isolated in a proper place.	407 (97.1%)	2 (0.5%)	40 (2.4%)
COVID-19: Coronavirus disease-19			

Table 3. Precautions against virus transmission

Questions	Answers n %
I don't leave the house unless it is necessary	379 (89.8%)
I wash my hands with soap for at least 20 seconds during the day	387 (91.7%)
I wear a mask if I have to go out	%
I pay attention to social distance	385 (91.2%)
I don't stand too close to people 1 meter away from crowded environments.	383 (90.8%)

Table 4. The use of hydroxychloracine in prophylaxis

How to use hydroxychloroquine	n	%
Twice a week, one	31	7.2
One in twenty one days	25	6.0
One every day	10	2.4
Once every two weeks	6	1.4
Two days three times during my contact with patients	6	1.4
Once a week	2	0.5
I used a total of three doses	2	0.5
Once a week, two doses	1	0.2
I use it because of rheumatism	1	0.2
Total	84	20.04

of this, WHO suggests washing the hands or using alcohol based disinfectants very frequently during the health care procedures. Use of a particulate respiratory device like N-95 mask is recommended for the treatment of patients with the suspicion of COVID-19. Otherwise when the distance is less than 1 meter between the professional and the patient, at least a surgical mask should be used to treat all the patients (5). Most of the participants (93.6%) of our study believed that they had higher risk of getting infected than other people and that they were worried about this. Besides, 385 (%91.5) of the participants were observed adhering to the preventive measures. Participants were observed following the literature for the updates, adhering to social distance rules as well as paying attention to the usage of masks. The also stated that they adhered to the social distancing and hygiene rules among each other and at their homes.

The study of Ling Hu et al. (25) showed increase of COVID-19 risk with the presence of chronic diseases and smoking. In parallel to that study, 76 (18.13%) of 128 smoking participants in our study stated that they tried to quit smoking because they were worried of getting infected with COVID-19. Also 88.5% of the participants stated that elderly people, obese people and people with chronic diseases had higher possibility of having severe COVID-19.

How to provide the most effective ventilator support to the patients with COVID-19 with respiratory insufficiency is still being investigated. Apart from intubation, high flow nasal cannula and positive airway pressure methods can be used (31). These two methods provide similar benefits with intubation to the patients at critical stages of the disease, therefore there is nothing certain about in which situation intubation should be done (26). Most of the participants of our study believed that intubation should be performed if the saturation measured from the finger fell below 75 mL/min and the clinical situation of the patient permitted as well as providing non-invasive mechanical ventilation through a helmet mask with two hoses before the intubation might provide better results.

Because of the high fever symptom of COVID-19, fever-reducing therapies should be conducted and non-steroid anti-inflammatory medicines and paracetemol like medicines are considered to be the primary resources. Sridharan Gt et al. showed that the usage of ibuprofen and other non-steroid anti-inflammatory medicines increased the risk of deterioration of COVID-19 (27). Of the doctors who read this study and similar studies in the literature 82.5% stated that they chose paracetemol like medicines.

Schuetz et al. (28) determined that there was a correlation between the procalcitonin level elevation and the severity of the bacterial infections and that it was blunted during the viral infections. Most of the participants in our study gave the answer of "does not change" to the question on the procalcitonin level due to the fact that COVID-19 was a viral infection.

Although there is no definite treatment for COVID-19, hydroxychloroquine and chloroquine which are antimalarial agents with imminomodulator and antienflamatuar activities are recommended for their possible role in the treatment of COVID-19 (29). Even though there is no evidence or data to support the use of these medicines as preventive treatment, there is a lot of interest among the people who are not infected but with high risk of being infected to use these medicines as prophylaxis (30). Our study also showed that some of the health care professionals considered usage of hydroxychloroquine beneficial as prophylaxis and started taking at different doses based on their individual choices. Our study also showed that participants were aware of most of the current studies conducted as well as the experimental treatments.

Study Limitations

Some of the limitations of the study were as follows: Considering the fast impact of the health care professional on the diagnosis, treatment and the preventive measure of COVID-19, data were collected in a very short time period. The knowledge on COVID-19 treatment of the health care professionals shows differences due different studies emerging everyday on the subject. Moreover, the study was conducted only in a pandemic hospital in a city. Even though the survey was applied to almost all the doctors and to nurses working inside the COVID-19 units or having interaction with the patients, there were the presence of lack of response and small sample size. Further studies should be done with larger sample sizes and the data of the studies should be interpreted carefully. Even though survey was sent out to all the health care professionals, it was planned to be applied to the doctor based health care professionals.

Conclusion

There was not any study conducted in our country before which evaluated the knowledge level, concerns, attitude to treatment and the approach to prophylaxis to COVID-19 of the health care professionals. Even though health care professionals have high level of knowledge and application standards, they have the responsibility to keep themselves up to date with all the new information and treatment procedures of COVID-19 emerging due to it is epidemic status. Only a small number of doctors prefer to use hydroxychloroquine for prophylaxis as it only has hypothetical recommendations for its usage on COVID-19 which does not have an approved treatment method yet.

Health care professionals have a special role in the management of this crisis situation as a part of the COVID-19 epidemic. It shows that they care about the epidemic and they keep up with all the current literature information related to the epidemic. They state their sensitivity to preventive measures as they consider themselves in a high risk group to get infected with the virus. It shows that health care professionals in the pandemic hospital have sufficient level of knowledge on COVID-19 and they believe that as a country we will be successful against the fight with the COVID-19 epidemic. This study also proves the importance of knowledge level as a key factor on the management of the communicable diseases. This positive attitude and strong level of faith on the success could be related to their level of knowledge and training even though they know that they are in a high risk group for the infection and more than half of them have either direct or indirect contact with the infected patients.

Ethics

Ethics Committee Approval: 2020/199 numbered Afyonkarahisar Health Sciences University Ethical Committee approval was obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: A.B., Ş.Ç., İ.G.C., Design: A.B., Ş.Ç., İ.G.C., Data Collection or Processing: A.B., Ş.Ç., İ.G.C., Analysis or Interpretation: A.B., Ş.Ç., İ.G.C., Literature Search: A.B., Ş.Ç., İ.G.C., Writing: A.B., Ş.Ç., İ.G.C.

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Original Article

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Comparison of Knowledge Levels of Nursing Students and Clinical Nurses Related to Hemovigilance: Preliminary Work to Develop a Measurement Tool

Hemşirelik Öğrencileri ve Klinik Hemşirelerin Hemovijilans ile İlgili Bilgi Düzeylerinin Karşılaştırılması: Ölçüm Aracı Geliştirme Ön Çalışması

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ABSTRACT

Objective: In this study, it was aimed to evaluate the knowledge level of the nursing students and clinical nurses who completed the clinical practice related to hemogivigilance.

Methods: This research was designed to be comparative and cross-sectional. The measurement tool consists of two parts in the collection of research data. The first part included the demographic variables, and the second part included the "hemovigilance information index" (HII) created by the researcher. The sample included 146 nursing students and 137 clinical nurses working in the hospital for clinical practice, who volunteered to participate in the research. Ethical permissions were obtained from ethics committee to conduct the research.

Results: It was concluded that there was a significant relationship between the knowledge about hemovigilance or hemovigilance nursing, thinking that he/she was competent about hemovigilance, the necessity of education related to the subject, the meaning of the term "near miss" related to hemovigilance, knowledge of the transfusion follow-up form, and having knowledge about the reactions that might occur as a result of blood transfusion, and the number of correct answers ($p<0.05$).

Conclusion: It was concluded that the knowledge level increased as the clinical experience increased in nursing students. It was determined that clinical nurses had a high level of knowledge of hemovigilance and students were not at the desired level. In-service trainings were found to be sufficient in this regard.

ÖZ

Amaç: Bu araştırmada, klinik ders uygulamasını yapmış hemşirelik öğrencilerinin ve klinik hemşirelerinin hemovijilans ile ilgili bilgi düzeylerinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Bu araştırma karşılaştırmalı ve kesitsel olarak tasarlanmıştır. Araştırma verilerinin toplanmasında kullanılan ölçüm aracı iki bölümden oluşmaktadır. Birinci bölüm demografik değişkenleri içermektedir. İkinci bölümü ise araştırmacı tarafından oluşturulmuş "hemovijilans bilgi indeksi" (HBİ) oluşturmaktadır. Klinik uygulama için hastanede çalışan, araştırmaya katılımı gönüllü olan 146 hemşirelik öğrencisi ve 137 klinik hemşiresi ile örneklem tamamlanmıştır. Araştırmanın yapılabilmesi için etik izinler Ankara Yıldırım Beyazıt Üniversitesi Beşeri ve Sosyal bilimler Etik Kurulu'ndan alınmıştır.

Bulgular: Hemovijilans ya da hemovijilans hemşireliği hakkında bilgi durumu, hemovijilans konusu hakkında yeterli olduğunu düşünme, konu ile ilgili eğitim gerekliliği, hemovijilans ile ilgili "ramak kala" teriminin anlamı, transfüzyon izlem formu hakkında bilgi durumu ve kan transfüzyonu sonucunda oluşabilecek reaksiyonlar hakkında bilgi sahibi olma durumu ile doğru sayısı arasında anlamlı ilişki olduğu sonucuna ulaşılmıştır ($p<0,05$).

Sonuç: Hemşirelik öğrencilerinde klinik deneyim arttıkça bilgi düzeyinin arttığı sonucuna varılmıştır. Klinik hemşirelerin hemovijilans ile ilgili bilgi düzeylerinin yüksek olduğu, öğrencilerde ise istenen düzeyde olmadığı belirlenmiştir. Hizmetiçi eğitimlerin bu konuda yeterli olduğu görülmüştür.

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Anahtar Sözcükler: Hemovijilans, hemşire, kan ve kan ürünleri, transfüzyon, hemovijilans hemşireliği

Introduction

Since taking, storing, transporting and transfusing blood and blood products for therapeutic purposes within the scope of health care services is an important service and it should be carried out in accordance with the standards (1). In our country, the current regulations regarding the blood supply system have been made within the scope of the main directive numbered 2002/98/EC, which is also included in the closing criteria of the 28th chapter titled "Protection of the Consumer and the Health of the Consumer" (2). Establishing standardized definitions for adverse events is crucial to achieving the goal of all surveillance systems (3). In this direction, in the main directive, hemovigilance is defined as "a series of surveillance that covers the entire transfusion chain, including the follow-up after blood collection and delivery to the recipient, collecting and evaluating all kinds of undesirable and unexpected effects arising from the use of blood products, preventing these events from occurring and preventing their reoccurrence" (4) .

The first official studies on hemovigilance started with the establishment of the blood monitoring system by the "Blood Transfusion Committees" in France in 1991. It was implemented in Canada in 1997 after the Krever report. With the establishment of SHOT (serious hazards of transfusion) in 1997 in England, notifications of hemovigilance began. With the establishment of EHN (European Haemovigilance Network) in 1998, an international analysis platform was formed. The European Blood Directive 2002/98/EC was published on 8 February 2003 (4). In this directive, on October 1, 2005, regulations regarding traceability, serious side effects, and blood institutions quality and standards were made. In 2005, many countries outside of Europe developed their national hemovigilance systems and became involved in this communication network. In 2006, a hemovigilance program was established in the USA with the AABB (American Association of Blood Banks). Since 2009, hemovigilance information exchange has been carried out at the international level with INH (International Hemovigilance Network) (5). Studies were initiated in our country in line with the "EU legislation to adapt", and the National Hemovigilance Guide was created in 2013 and published in 2016 (2).

The aim of hemovigilance is to determine the cause of unexpected situations in blood transfusion and to prevent their reoccurrence, and as a result, to ensure safe blood transfusion (6). For this purpose, issues such as inadequate blood supply structure, insufficient blood supply, increased need, unequal distribution, weak quality systems, risks of infection transmitted by transfusion, and inappropriate use of blood products are priorities in ensuring blood transfusion safety, especially in healthcare services in developing countries (7). Hemovigilance is an important part of the quality system for blood transfusion. It includes methods for identifying errors, adverse events, and reactions, such as alert systems, complaint investigation, traceability systems, notification systems, and application controls (6).

"Conditions related to the collection, testing, processing, storage, distribution of blood and blood products that may cause death, permanent and significant disability, hospitalization or lengthening of hospital stay in individuals as a result of transfusion of affected products". describes serious adverse event (SAE). SAEs that occur in the patient during and after blood and blood product transfusion form the basis of the hemovigilance system and must be reported (8). These are;

- Early SAEs; Hemolysis during transfusion, non-hemolytic fever reaction, rash, erythema, urticaria, anaphylactic shock, bacterial contamination, transfusion-induced acute lung injury.
- Past SAEs; hemolysis, transfusion-associated graft versus host disease, post-transfusion purpura, ALT elevation.
- Virus, parasite or prion contamination.
- Development of alloimmunization against erythrocyte, human leukocyte antigen or platelet antigens. At the same time, undesirable events may occur in the donor (9).
- Hemovigilance is a control system that every healthcare worker responsible for transfusion of blood and blood products should know. Nurses are active members of this system. In the "National Guide to Hemovigilance" published in 2016, the roles of nurses in hemovigilance are clearly stated. These roles are;
- Every personnel with duties and responsibilities related to transfusion can make notifications about hemovigilance. The hemovigilance officers of the relevant clinics and the hospital hemovigilance nurse are responsible for making these notifications appropriately.
- He/she checks whether the forms submitted to him are filled in appropriately and completely, and reports the situation to the hemovigilance committee.
- In case of a problem with transfusion, if he/she receives information from the responsible doctor that the problem is due to non-transfusion reasons, he/she notifies the hemovigilance committee.
- The nurse or doctor working in the relevant clinic is responsible for the hemovigilance clinic. He/she is responsible for transmitting the Transfusion Monitoring Form of the patients and other data requested for the sustainability of the hemovigilance system to the Hemovigilance Nurse.
- Organizes trainings.
- Informs the hemovigilance committee about the activities (2).

Problem Definition

Definitions are available for a better understanding of hemovigilance. These are adverse event, serious adverse event, serious uneventful transfusion error, incorrect transfusion, near miss, adverse reaction, serious adverse reaction, trace-back, donor-to-patient tracking (Look-back), recall, return, and attribution (2). Clear definitions of the concept of hemovigilance are important for both reporters and those who will analyze reports. Reporting adverse events as soon as possible is essential for quality assurance. SAEs should be reported promptly. Hemovigilance systems enable rapid assessment of serious reports by the hemovigilance task group and additional information requested shortly after reporting. The reporter sometimes needs advice on root cause analyzes and corrective and preventive measures. Health professionals in the hemovigilance committee can provide advice and assistance (10).

It is clear that hemovigilance systems and their staff can help collect and analyze the necessary data. Training of hospital transfusion committees, transfusion workers, clinicians and laboratory personnel plays an important role in controlling the hemovigilance systems of transfusion units. In summary, optimal use of the hemovigilance system, consensus, common criteria, analysis and regulatory measures are required for the periodic evaluation of hemovigilance studies. At the same time, these studies can support developments (11).

Due to the recent history of hemovigilance, there is a lack of information among healthcare professionals (12). In the healthcare field, the term hemovigilance focuses on transfusion. However, the transfusion part constitutes a part of the hemovigilance (4). Studies in the literature focused on transfusion. Studies involving all components of hemovigilance are insufficient. For this reason, it is seen that the level of knowledge of healthcare workers in studies on hemovigilance is compared with studies on transfusion (13). Studies emphasize that the knowledge levels of both nurses and nursing students about hemovigilance are insufficient (13-15). Similar results are observed in studies conducted with physician groups (16). For this reason, effective training of healthcare professionals on hemovigilance during the clinical or school period is necessary for quality systems, patient safety, and reduction of malpractices. A structured measurement tool is needed to monitor the process, to return when necessary, and to measure the success of the trainings. In this study, it was aimed to determine the knowledge levels of nursing students and clinical nurses practicing clinical courses for knowledge, skills and experience, and to create an applicable semi-structured scale. Hemovigilance is accepted as a new term in the world and in our country. For this reason, it has been seen that the literature on this subject is not sufficient. In this direction, our study question was determined as follows: "How is the knowledge level of nursing students and clinical nurses about hemovigilance and related concepts?".

Method

Research Type

In this study, a comparative, cross-sectional study was conducted in order to evaluate the knowledge levels of nursing students and clinical nurses about hemovigilance who practiced clinical courses.

Universe Sample Selection

The population of the research consisted of all nursing students studying at a state university in Ankara and all clinical nurses working in a public hospital. In the study, 146 nursing students and 137 clinical nurses who agreed to participate in the study on a voluntary basis were included in the study without choosing a sample.

Data collection Tool

Demographic Data Form: The data form created by the researchers was used. In this form; age, gender, presence of smart device, duration of daily use of smart device, monthly internet usage quota, channels related to occupation, information status about hemovigilance, where this information was obtained, and the importance of having sufficient level of knowledge about hemovigilance and getting training on this subject were recorded. In the form, nursing students were asked what grade they were in, and nurses were asked in which clinic they worked.

Hemovigilance Information Index (HBI): It was created by the researchers in line with the literature. Seven of the questions (1, 2, 12, 13, 15, 17, 20) were asked to measure attitude. The remaining questions were directed to the students in order to measure the level of knowledge. The answers to these questions, which we directed to determine the level of knowledge, were evaluated.

Obtaining expert opinion/content validity index (CVI): Items created for the HBI were examined by a total of 10 experts in the field of nursing. CVI values of the expressions for the created knowledge index were found to be between 0.80 and 1.00, and the average CVI value was found to be 0.92. In line with expert opinions; some of the items that were not understood, had similar meanings, contained more than one judgment and were stated not to measure attitude were corrected, and some items were removed completely. The form took its final form after the expert opinions.

Application

Data collection tools were applied at the end of a suitable course determined according to the students' curriculum and it took approximately 20 minutes to collect the data for each form. It was applied to the nurses in a face-to-face manner during working hours after obtaining the institutional permissions. It took about 10 minutes to fill out the questionnaire.

Ethical Aspects of Research

In order to conduct the research, permission was obtained from the institution where the study was conducted and the research

was approved by the Ankara Yıldırım Beyazıt University Ethics Committee (29.05.2019/decision no: 51). Data were collected in accordance with the Declaration of Helsinki. Participants were informed about the purpose of the research, its content and the way the data were collected. Participants were given confidence that their participation in the study was voluntary, their information would be kept confidential, and that they could withdraw from the study at any time.

Evaluation of Data

The IBM SPSS Statistics 22.0 (IBM Corp. Released 2014. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was used to evaluate the data. Non-parametric tests were used in statistical analysis since the data did not fit the normal distribution. Percentage, frequency, mean, Kruskal-Wallis H, Mann-Whitney U, t-test and chi-square statistical analyzes were used to evaluate the data. The results were evaluated within the 95% confidence interval. Statistical significance level was accepted as $p<0.05$.

Results

The ages of the nurses participating in the study ranged from 20-54, with an average of 32.17±8.43. The demographic data of the individuals belonging to the study are given in Table 1. Women in both groups constituted the majority of the participants in the study. Of the students 32.19% were first year students, and 43.06% of the nurses worked in internal medicine units. Most of the participants in both groups used smart devices for 2-4 hours, and the database they used mostly for professional research was Google scholar. While the monthly internet usage quota of the students was 4-6 gb (Giga bytes), the nurses used 10 gb and above. Nurses had more knowledge about hemovigilance or hemovigilance nursing, while students accessed this information from the internet, nurses obtained from in-service training. Both groups stated that the students did not have sufficient knowledge about hemovigilance and that education on this subject was important. The correct numbers of clinical nurses and student nurses regarding hemovigilance are given in Table 2.

Looking at the nursing students, it was determined that there was a significant difference between the class variable and the number of correct answers. It was determined as a result of statistical tests that this difference was due to the fact that the correct numbers of 1st year students were lower than those of 3rd and 4th grade students. It was concluded that there was a significant relationship between the knowledge of hemovigilance or hemovigilance nursing, thinking that he/she had sufficient knowledge about hemovigilance, the need for education on the subject, the meaning of the term "near miss" about hemovigilance, the state of knowledge about the transfusion follow-up form, and the late and early reactions that might occur as a result of blood transfusion, and the number of correct answers ($p<0.05$).

When the clinical nurses were examined, it was determined that there was a significant difference between the units they worked in and the number of correct answers. It was determined as a result of statistical tests that this difference was due to the fact that the correct number of emergency service workers was higher than surgical units and intensive care clinics. It was concluded that there was a significant relationship between the state of having information about hemovigilance or hemovigilance nursing, thinking that he/she was competent about hemovigilance, self-sufficiency about blood transfusion, the meaning of the term "near miss" about hemovigilance, knowledge about the transfusion follow-up form, and late and early reactions that might occur as a result of blood transfusion, and the number of correct answers ($p<0.05$).

Discussion

Individuals who agreed to participate in our study were examined in two groups as nursing students and clinical nurses. Nursing students made up 51.59% of the sample, while clinical nurses made up 48.41% of the sample. Students participating in the study covered all classes, while nurses included internal medicine units (43.06%), surgical units (30.66%), intensive care units (13.87%) and emergency services (12.41%). In the study conducted by Jimenez-Marco et al. on hemovigilance with nurses, they reported that they worked in surgery (27.27%), internal medicine (22.04%), emergency service (16.8%), blood bank (11.85%) and intensive care (11.29%) clinics (17). In another study on hemovigilance nursing by Gün et al., the nurses were reported to work in intensive care unit (35.0%), emergency room (6.9%), internal medicine clinic (6.9%), pediatrics clinic (7.6%), gynecology clinic (6.3%), general surgery clinic (5.8%) and laboratory (7.9%) (13).

Nursing students' knowledge levels were evaluated on the basis of the number of correct numbers and it was found that there were minimum 0 and maximum 13 correct answers and the mean knowledge level was 4.00±3.72. It was found that the number of correct answers regarding the knowledge level of the clinical nurses was at least 2 and the maximum was 13, and the average of correct answers was 10.36±2.00. It was determined that there was a high difference in the averages of the correct answers of nurses compared to nursing students. This difference led us to conclude that in-service training in the hospital was effective, while nursing students were lacking in training on this subject. It was determined that 64.23% of the nurses within the scope of the study received hemovigilance training in in-service training.

In a study on hemovigilance, the knowledge level of 135 health personnel was evaluated out of 24 points, and it was reported that all participants got 16.30±3.16 points. They concluded that the highest score among the groups belonged to nurses and the lowest score belonged to nursing students (14). In another study, they reported that the scores of the group they worked with (nurse, doctor, other health worker) varied between 1 and 19 (out of 20) and their average was 9.7±4.2. In the same study, they found that the mean knowledge of nurses was 10.0±4.2 (13). In another study on blood transfusion with midwives in a maternity hospital, the rate of correct answers was found to be between 5% and 98%, depending on the questions (18). In the study conducted by Shamshirian et al. (15) with nursing students, the results of the study indicated that only 25.9% of nursing

Table 1. Comparison of demographic data distributions of nursing students and clinical nurses

		Nursing student		Clinical nurse	
Variables	Groups	Sample (n=146)	Percentage (%)	Sample (n=137)	Percentage (%)
Gender	Female	131	89.73	119	86.86
	Male	15	10.27	18	13.14
Grade	1st grade	47	32.19	-	-
	2nd grade	40	27.40		
	3rd grade	35	23.97		
	4th grade	24	16.44		
Working unit	Surgery unit	-	-	42	30.66
	Internal medicine unit			59	43.06
	Intensive care unit			19	13.87
	Emergency room			17	12.41
Daily smart device usage	0-2 hours	9	6.16	31	22.63
	2-4 hours	46	31.51	41	29.92
	4-6 hours	41	28.08	29	21.17
	6-8 hours	34	23.29	25	18.25
	8-10 hours	11	7.53	11	8.03
	10 hours or above	5	3.42	0	0
Monthly internet usage quota	0-2 gb	6	4.11	12	8.76
	2-4 gb	30	20.55	12	8.76
	4-6 gb	33	22.60	30	21.90
	6-8 gb	29	19.86	17	12.41
	8-10 gb	18	12.33	30	21.90
	10 gb or above	30	20.55	36	26.27
Occupational research database	Google Scholar	72	49.32	82	59.85
	Youtube Videos	15	10.27	37	27.00
	Pubmed-Medline	8	5.48	20	14.60
	Any Website	51	34.93	46	33.58
	Other	0	0	17	12.41
Do you know about hemovigilance or hemovigilance nursing?	Yes	28	19.18	131	95.62
	No	118	80.82	6	4.38
Where did you get this information?	Internet	19	13.01	30	21.90
	Undergraduate courses	8	5.48	50	36.50
	TV	0	0	2	1.46
	Friend shares	0	0	12	8.76
	In-service training	0	0	88	64.23
	Other	6	4.11	4	2.92
Do you think you have enough knowledge about hemovigilance?	Yes	3	2.05	75	54.74
	No	143	97.95	62	45.26
Do you think it is necessary and important to receive training on hemovigilance?	Yes	127	86.99	132	96.35
	No	19	13.01	5	3.65

Table 2. Evaluation of knowledge attitudes of nursing students and clinical nurses

	The average of correct answers	The number of correct answers min-max
Nursing student	4.00±3.72	0-13
Clinical nurse	10.36±2.00	2-13

Min: Minimum, max: Maximum

students had knowledge and awareness about blood transfusion. In another study, care standards for hemovigilance were evaluated instead of knowledge level, and as a result, neonatal clinics reported that the compliance rate of nurses working in neonatal intensive care units was 56% (19).

It was determined that there was a statistically significant difference between the classes and knowledge levels of nursing students (p=0.049). As a result of the statistics, it was determined that the difference was due to the fact that the knowledge levels of the 3rd and 4th grade students were higher than the other grades. In our study, it was found that there was a statistically significant difference between the unit where the clinical nurses worked and their level of knowledge (p=0.030). As a result of the statistics, it was determined that the knowledge levels of the nurses working in the intensive care unit were higher than the other units. In the study of Gün et al. (13), it was found that there was no significant difference between the clinics where the nurses worked and the level of knowledge of hemovigilance. In a study conducted with a group of physicians, they reported that those working in the anesthesia department received high scores following those working in internal medicine clinic (16). In a study by Rudrappan, it was found that there was no relationship between the clinical experience of the nurses and their knowledge and practices (20). We think that the fact that students take more active roles in the clinic with the following years has a positive effect on their level of knowledge. In the findings, the distribution of in-service training according to the units was examined. As a result, it was determined that only 36.84% (n=7) of the nurses working in the intensive care unit participated in in-service training. It was determined that more than half of the nurses working in other clinics participated in hemovigilance training. It was thought that the result was due to the low rate of participation in in-service training on hemovigilance.

In our study, it was concluded that there was a significant difference in both groups between those who answered "yes" to the question and those who answered "no" to the question "Do you have information about hemovigilance or hemovigilance nursing?". The percentage of those who answered this question was 19.18% among nursing students and 95.62% among clinical nurses. According to research sources, it was determined that nursing students obtained the most information about hemovigilance from the internet environment, and clinical nurses obtained the most from in-service training. In a study, 55.55% of the doctors and 9.09% of the nurses who participated in the study reported that they knew the term hemovigilance (21). In a study by Aneke et al., they reported that the majority of the participants were not aware of the transplant units or committees for hemovigilance (22). In the literature, when the nurses were questioned whether they participated in training programs such as in-service training and seminars related to hemovigilance, they stated that they answered "yes" at low rates such as 9.24% and 10% (23, 24). In the study of Jimenez-Marco et al. (17), 76.03% of the nurses stated that they did not receive any formal training on transfusion before starting to work at the workplace, and 83.75% of the nurses did not receive in-service training during their work in their hospitals. Unlike the literature, the clinical nurses participating in our study received in-service training on the subject as 64.23%. In our study, the insufficient knowledge of nursing students on this subject makes us think that it is not included in the core curriculum followed in undergraduate nursing programs in our country. Considering that student nurses use the most internet resources for hemovigilance information, it is thought that they can obtain insufficient, incomplete and incorrect information from the internet.

The question "Do you think you have enough knowledge about the subject?" was directed to the participants of the study. It was found that the knowledge levels of the group who answered "yes" to the questions "I know what "near miss" means from hemovigilance terms" and "I have information about the transfusion monitoring form" were statistically significantly different in both groups (p<0.05). It was determined that the knowledge level of the group who answered "yes" was higher. In line with this result, it is thought that the group who thinks that they are inadequate on the subject can increase their awareness on this issue. At the same time, with this result, it has been determined that individuals can correctly identify their deficiencies in terms of knowledge and are aware of these deficiencies. In a study where nurses were asked a different question, "Do you think the reactions are dangerous?" 70% of the nurses answered "yes" to the question (25). In the study of Jimenez-Marco et al., it was found that nurses who received transfusion training felt that they had a better level of knowledge than those who did not receive training (17). It was found that the level of knowledge of the nurses who answered "yes" to the statement "I don't see myself enough about blood transfusion." was lower than the others. In line with the literature, this result suggests that the knowledge level of nurses affects their self-confidence in practice.

In our study, it was questioned whether education about hemovigilance was necessary. Of the students 86.99% and 96.35% of the nurses thought that education was necessary and important. At the same time, it was found that there was a significant difference between the knowledge levels of nursing students who answered "yes" to this question and those who answered "no" (p= 0.004). There was no significant difference in the nurses. In a study conducted with midwives, their knowledge of blood transfusion was questioned, and 99.2% of midwives reported that education was necessary (18). In another study, 63% of nurses reported that they had participated in a blood bank training program before (20). In the studies in the literature, the activities of the education on the level of knowledge were evaluated by making a pre- and post-education evaluation, and they found that the trainings were positively effective (13, 26). Raising awareness about hemovigilance through in-service training will lead to improved reporting of transfusion reactions (23). Most of the graduates have a positive attitude towards transfusion reaction reporting, but their knowledge of the hemovigilance program is low and the reporting procedure is less in recent graduates (24). Reporting and data collection should not be the sole purpose of the hemovigilance system, and the use of hemovigilance data sources in practice may be beneficial to increase transfusion safety (17).

Table 3. Statistics of nursing students and clinical nurses' mean of various variables and correct answers

Variables	Groups	Nursing student The average of correct answers	Clinical nurse The average of correct answers
Gender	Female Male	3.58±3.22 4.47±4.10 Z: -0.738; p= 0.460	10.38±1.81 10.22±3.04 t: 0.307; p=0.759
Grade	1st grade 2nd grade 3rd grade 4th grade	2.68±2.87 3.88±3.24 4.51±3.74 4.04±3.31 **x^2: 7.818; p= 0.049**	-
Working unit	Surgery unit Internal medicine unit Intensive care unit Emergency room	**-**	9.95±1.82 10.73±1.78 9.53±2.97 11.00±1.37 **F: 3.068; p=0.030**
Daily smart device usage	0-2 hours 2-4 hours 4-6 hours 6-8 hours 8-10 hours 10 hours or above	2.89±3.86 3.28±2.86 4.10±3.82 3.94±3.22 3.54±3.30 3.60±3.44 x^2: 1.506; p= 0.912	10.94±1.61 10.34±2.25 10.00±2.17 10.16±1.67 10.18±2.18 - x2: 4.456; p= 0.348
Monthly internet usage quota	0-2 gb 2-4 gb 4-6 gb 6-8 gb 8-10 gb 10 gb or above	3.17±3.60 3.80±3.20 4.10±3.28 4.72±3.57 2.11±2.30 3.10±3.45 x^2: 9.222; p= 0.101	10.17±1.80 10.67±1.15 9.93±2.35 10.58±1.62 10.50±2.11 10.44±2.09 x2: 1.917; p= 0.860
Do you know about hemovigilance or hemovigilance nursing?	Yes No	7.82±2.60 2.69±2.64 **Z: -6.594; p= 0.000**	10.67±1.56 6.82±2.99 **Z: -4.154; p= 0.000**
Do you think you have enough knowledge about the subject?	Yes No	9.00±1.73 3.56±3.25 **Z: -2.433; p= 0.015**	10.89±1.48 9.71±2.34 **t: 3.598; p= 0.000**
Is training required on the subject?	Yes No	3.95±3.35 1.79±2.39 **Z: -2.904; p= 0.004**	10.38±1.90 9.80±4.15 Z: -0.310; p=0.756
I do not consider myself sufficient about blood transfusion.	Yes No Not sure	3.87±3.27 3.90±3.52 3.13±3.28 x^2: 2.152; p= 0.341	9.70±2.36 10.75±1.73 10.21±1.97 **F: 3.575; p= 0.031**
I know what it means to miss the hemovigilance terms.	Yes No Not sure	6.71±3.69 4.87±3.66 2.35±2.81 **x^2: 17.892; p= 0.000**	10.86±1.65 9.79±2.46 9.68±1.94 **F: 5.676; p= 0.004**

Table 3. Continued

Variables	Groups	Nursing student The average of correct answers	Clinical nurse The average of correct answers
I have information about the transfusion follow-up form.	Yes	4.88±3.27	10.48±1.84
	No	3.77±3.46	-
	Not sure	1.83±2.37	8.38±3.29
		x^2: 30.743; p= 0.000	**Z: -1.970; p= 0.049**
I know what are the early and delayed reactions that may occur as a result of blood transfusion.	Yes	4.73±3.41	10.41±1.97
	No	3.23±3.14	8.00±5.20
	Not sure	2.40±2.75	10.41±1.44
		x^2: 17.753; p= 0.000	x^2: 0.985; p=0.611

Z: Mann-Whitney U, F: One-way ANOVA, t: Independent groups t-test, x2: Kruskal-Wallis H

Study Limitations

The groups compared in our study were studied as a single center in their own universe. The universe was accepted as a sample and all individuals who voluntarily agreed to participate in the habituation were included in the study. Therefore, power analysis was not performed. The results could be generalized to the sample group.

Conclusion

It was determined that clinical nurses had a high level of knowledge about hemovigilance, while students were not at the desired level. It was concluded that as the clinical experience of nursing students increased, the level of knowledge increased. The database in which both groups made researches was determined as any website after Google Scholar. Due to the low level of hemovigilance knowledge of nursing students, necessary studies can be done to include this subject in the nursing education curriculum. It is recommended to support nurses with continuous training after graduation in terms of the directly proportional development of behavior, attitude and clinical skills. It is thought that in-service trainings are functional in this regard, and that their awareness and knowledge about hemovigilance will increase by working integrated with the clinic and including nursing students in in-service training. The applicability of the HII is found to be effective, but it is recommended to update it in terms of measurement and evaluation and develop a fully structured scale in similar groups.

Ethics

Ethics Committee Approval: In order to conduct the research, permission was obtained from the institution where the study was conducted and the research was approved by the Ankara Yıldırım Beyazıt University Ethics Committee (29.05.2019/ decision no: 51).

Informed Consent: Data were collected in accordance with the Declaration of Helsinki. Participants were informed about the purpose of the research, its content and the way the data were collected.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: A.K., E.T., Design: A.K., E.T., Data Collection or Processing: A.K., E.T., Analysis or Interpretation: A.K., E.T., Literature Search: A.K., E.T., Writing: A.K., E.T.

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Review

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Medical Management and Nursing Care of a Patient with Acute Respiratory Distress Syndrome

Akut Respiratuvar Distres Sendromlu Hastanın Tıbbi Yönetimi ve Hemşirelik Bakımı

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ABSTRACT

Acute respiratory distress syndrome (ARDS) is a critical, life-threatening condition involving both lungs, characterized by capillary endothelial damage, diffuse pulmonary infiltration, and oxygen-resistant hypoxemia. The incidence in intensive care units is between 7.1-12.5% and its mortality can be up to 40% in severe cases. Pathological processes with exudative, proliferative and fibrotic stages in the lungs in response to different etiological factors in ARDS result in hypoxemia, hypercapnia and decreased lung compliance. There is no drug with proven efficacy in treatment. The most crucial parameter of ARDS management is protective mechanical ventilation, including low tidal volume, high positive end-expiratory pressure regulations, prone position, and recruitment maneuvering. In addition, supportive approaches such as fluid management, nutritional support, reduction of oxygen consumption, prevention of ventilator-associated pneumonia, pain management, deep vein thrombosis prophylaxis, peptic ulcer prophylaxis, blood sugar regulation, and maintaining skin/tissue integrity are applied. This review will briefly describe ARDS and related factors, then focus on treatment, care, and patient follow-up from the physician and nurse perspective.

Keywords: Acute respiratory distress syndrome, ARDS, mechanical ventilation

ÖZ

Akut respiratuvar distres sendromu (ARDS) akut gelişen, her iki akciğeri içine alan, kapiller endotelyal hasar, yaygın pulmoner infiltrasyon ve oksijen tedavisine dirençli hipoksemi ile karekterize, yaşamı tehdit eden bir durumdur. Yoğun bakım ünitelerinde insidans 7,1-12,5 arasında olup, ciddi olgularda mortalite %40'lara kadar çıkabilmektedir. ARDS'de farklı etyolojik faktörlere yanıt olarak akciğerlerde oluşan eksüdatif, proliferatif ve fibrotik aşamaları olan patolojik süreçler hipoksemi, hiperkapni ve akciğer kompliyansında azalma ile sonuçlanır. ARDS tedavisinde etkinliği kanıtlanmış herhangi bir ilaç bulunmamaktadır. ARDS yönetiminde en önemli parametre düşük tidal volüm, yüksek PEEP düzenlemeleri, prone pozisyonu ve recruitment manevrasını içeren koruyucu mekanik ventilasyondur. Ek olarak sıvı yönetimi, beslenme desteği, oksijen tüketiminin azaltılması, ventilatör ilişkili pnomoninin önlenmesi, ağrı yönetimi, derin ven trombozu profilaksisi, peptik ülser profilaksisi, kan şekerinin regülasyonu ve deri/doku bütünlüğünün sürdürülmesi gibi destekleyici girişimler uygulanır. Bu derleme makalede ARDS ve ilişkili faktörler kısaca tanımlanacak, takiben hekim ve hemşire perspektifinden tedavi, bakım ve hasta izlemi konuları ele alınacaktır.

Anahtar Sözcükler: Akut solunum sıkıntısı sendromu, ARDS, mekanik ventilasyon

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Introduction

Acute respiratory distress syndrome (ARDS) is a life-threatening condition that involves both lungs, characterized by capillary endothelial damage, diffuse pulmonary infiltration, and oxygen-resistant hypoxemia (1).

From 1967, when it was first described as "ARDS" by Ausbaugh et al. (2), to the end of the 1980s, ARDS was called by various names such as shock lung, congestive atelectasis, post-perfusion lung, and traumatic wet lung (3).

In 1988, Murray et al. (4) developed the Lung Injury score, which was rated between 0 and 4 by using chest radiography, hypoxemia (PaO_2/FiO_2 ratio), positive end-expiratory pressure (PEEP) and ventilation and lung compliance; thereby, ARDS began to be diagnosed as a clinical syndrome (4).

In 1994, ARDS diagnostic criteria were revised at the American European Consensus Conference; finally, in 2012, the Berlin definition of ARDS was adopted in the literature. According to the Berlin definition, any patient with respiratory failure which develops or worsens in the last week, involves diffuse infiltration in both lungs, and cannot be explained by the presence of heart failure or fluid overload with a PaO_2/FiO_2 ratio below 300 is considered as ARDS (5). The severity of the clinical picture is classified as mild ARDS when 300≥ PaO_2/FiO_2 >200 (PEEP ≥5 cmH_20), as moderate ARDS when 200≥ PaO_2/FiO_2 >100 (PEEP ≥5 cmH_20), and as severe ARDS when PaO_2/FiO_2 ≤100 (PEEP ≥5 cmH_20) (6).

Study results on ARDS incidence differ considerably. Diagnosing ARDS requires evaluation of blood gases and chest radiography. The fact that routine accessibility of these examinations varies from country to country, from region to region, or from hospital to hospital is also reflected in the epidemiological study results. The incidence of ARDS in intensive care units (ICU) in Europe is between 7.1% and 12.5%. In a study conducted with 29,144 ICU patients from more than 50 countries, the prevalence of ARDS was 10.4%, and 23.4% of patients who underwent mechanical ventilation (MV) met the Berlin ARDS diagnostic criteria (7). ARDS is a health problem with significant consequences in terms of mortality and morbidity. Mortality can be up to 40% in patients with severe ARDS (7). Polyneuropathy, persistent muscle weakness, joint contractures, cognitive dysfunctions, post-traumatic stress disorder, and depression are common in patients who have survived with treatment, even after five years of discharge. Those problems negatively affect the quality of life of both the patient and the patient's family. In addition, ARDS has high costs to the households and the national economy due to the need for treatment in the ICUs and post-discharge expenses (8).

Many risk factors such as massive blood and plasma transfusion, intoxications, gas/smoke inhalation, sepsis, aspiration, lung infection, fat embolism, acute pancreatitis, major trauma play a role in the etiology of ARDS (9-11). It has been reported that chronic alcohol usage (12), passive smoking (13), and vitamin D deficiency (14) may increase ARDS susceptibility.

More than 40 genes such as angiotensin converter enzyme, pro-inflammatory interleukin (IL-1 B, IL-6, IL-8), anti-inflammatory molecule (IL-10), and tumor necrosis factor have been identified in the pathogenesis of ARDS (15,16). Although there are different etiological factors, the exact pathological response occurs in the lungs in ARDS is not known. The pathological process in ARDS includes exudative, proliferative and fibrotic stages. In the exudative phase, which is seen in the first 72 hours, edema is observed in the interstitium and alveolar area due to extensive alveolar damage (11). Fibrin formation and granulation start in the proliferative phase, which is generally observed between 4-10 days. In the fibrotic phase, fibrosis develops with collagen accumulation (1,11). Recovery takes months after the fibrotic stage (10). Various biological processes, especially inflammation, apoptosis, and thrombosis, play a role in the pathogenesis of ARDS. All these pathological processes result in hypoxemia, hypercapnia, and decreased lung compliance (1,10,11).

Treatment and Nursing Care

An individualized approach is the essential element in its treatment and nursing care. First of all, plans should be made to reduce existing lung damage and prevent further damage to the patient. ARDS management can be examined under three headings: MV, supportive approaches, and pharmacological treatment.

Mechanical Ventilation

The most significant parameter of ARDS management is MV. With the ventilator, both oxygenations are provided safely, and the ventilator undertakes the majority of increased respiratory load due to increased breathing requirement, decreased compliance, and increased alveolar dead space. Moreover, MV plays a role in reducing pulmonary edema as it decreases venous return to the heart (10,17).

However, it should be kept in mind that MV support may lead to lung damage and exacerbate existing lung damage (11). Therefore, volutrauma, barotrauma, and atelectrauma are tried to be prevented by following protective MV strategies (18,19), including low tidal volume (TV), high PEEP arrangements, prone position (PP), and recruitment maneuver (RM) practices (17).

With RM, also known as opening maneuvers for atelectasis, high pressure is applied to patients for a certain period at certain intervals after separating from the ventilator (11). Extracorporeal membrane oxygenation can be used when preventive MV strategies achieve no result in ARDS treatment (11).

Tidal volume should be adjusted to be 4-8 mL/patient's ideal weight (6). The collapse of the alveoli should be prevented by keeping the airway pressure above atmospheric pressure with a high PEEP value (minimum ≥5 cmH_2O) (11). The PEEP level should be explicitly titrated for the patient in a way that does not deteriorate hemodynamics and maintains FiO_2 at 60% or less and arterial oxygen saturation at >0.88, plateau pressure at <30 cmH_2O, and drive pressure [plateau pressure (PEEP) end-expiratory positive pressure)] at <15 cmH_2O, while PaO_2 should

be maintained at 55-85 mmHg or SpO_2 at 88-95%. Ventilation rate can be set up to 35/min and the ratio of inspiration/expiration should be 1:1 or 1:3 (6).

Patients with ARDS should be placed in the PP for at least 12 hours a day. PP acts synergistically with both TV and PEEP (20). Vital signs should be checked before PP is given with monitoring ensured by attaching electrocardiography electrodes. Eye pomade should be applied to prevent corneal abrasions, eyes should be covered with a sterile eye pad, and oxygenation should be provided with 100% FiO_2 for 10 minutes before giving PP. Intubation materials should be kept ready during PP administration against the possibility of extubation (21,22).

PP should be given with a team of at least five people. The patient's neck and spine should be supported during positioning, respiratory indicators (SpO_2, blood gas values, compliance with the ventilator, ventilator alarms, etc.) should be monitored, if negative changes in respiratory functions (<SpO_2: 88-90%, etc.) are detected, support should be called by pressing the emergency call button (22). The locations of the infusion pumps, hence their lengths, should be appropriately adjusted to prevent the tension of the catheters attached to the patient during the application (21).

Before the procedure, the level of pain sedation/agitation should be examined to ensure the patient's tolerance to PP. The need for additional sedation should be evaluated. If the patient develops ventilator incompatibility during the procedure, begins to wake up, and sudden deterioration is observed in the patient's general condition, the emergency response should be performed (21). When placing the patient back in the supine position, hemodynamic data and ventilation/perfusion ratio should be closely monitored (21,22).

Hemodynamic follow-up, including oxygen saturation, blood pressure, cardiac apex beat/nb, respiration, and body temperature, should be done in patients connected to the ventilator. High- and low-pressure alarm limits should be set specially for each patient and monitor alarms should not be silenced. They should be continuously audible even if the patient's condition is stable (22).

Intratracheal aspiration should not be performed in patients with ARDS unless it is needed. Because, every time the patient leaves the ventilation machine for aspiration, the enlarged alveoli collapse, and it takes time to reopen. Inflammation may also develop. The closed suction systems used in the patient do not provide any advantage in this regard. On the other hand, the closed system aspiration technique seems advantageous in preventing droplet and aerosol formation in terms of contamination risk during aspiration (21).

Supportive Approaches

Respiratory failure is the sole cause of mortality in very few patients with ARDS. Mortality is usually associated with the primary cause of ARDS, and the presence and association of secondary complications such as multiple organ failure and sepsis. Therefore, conditions that may affect mortality and morbidity, and lung interventions in patients with ARDS, should be controlled. Supportive approaches in ICU in general and in patients with ARDS, in particular, can be summarized as fluid management (23), nutritional support (22,24), reduction of oxygen consumption (25), prevention of ventilator-associated pneumonia (19,26,27), pain management (28,29,30), prevention of deep vein thrombosis (DVT) (31), peptic ulcer prophylaxis and bleeding control (32), providing glycemic control (33) and protecting and maintaining skin/tissue integrity (21,22,26).

Fluid Management

Fluid restriction in the early stages of ARDS may be beneficial in reducing pulmonary edema. However, it should be kept in mind that fluid restriction may reduce cardiac output and perfusion, thus exacerbating impaired oxygenation, which is already the main problem in ARDS. Therefore, the fluid regimen should be carefully planned according to the ARDS period. The patient's clinic and the fluid intake and removal should be monitored (23).

Nutritional Support

It is significant in patients with ARDS to switch to enteral or parenteral nutrition at an early stage by evaluating the gastrointestinal system. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines should be taken into consideration in assessing the nutritional parameters and determining the amount of energy and content needed (24).

Enteral feeding is started within the first 24 hours in patients who do not have gastrointestinal system (GIS) problems such as vomiting, peritonitis, paralytic ileus, etc. Enteral feeding can be administered by giving formula continuously (with an enteral infusion pump), intermittently (4x1 or 6x1 at intervals/day), or as a bolus (3x1 or 5x1/day with a gavage injector). In patients with enteral feeding, gastric residual volume control should be done every 4-6 hours, feeding bags should be filled to be finished in 6 hours, and no medication should be added to the formula. Parenteral feeding should be started if intolerance symptoms such as nausea, vomiting, gastric distension, high residual volume, and diarrhea develop in patients, if the daily calorie intake is insufficient, or if there are gastrointestinal problems such as peptic ulcer (22). In parenteral nutrition, the infusion should be started with a low amount (20 mL/hour), and the dose should be increased every 6 hours, considering the patient's tolerance (22).

Reduction of Oxygen Consumption

One of the vital supportive strategies in patients with ARDS is to reduce oxygen consumption. Increased oxygen consumption surges the amount of oxygen removed from the arterial blood, thus causing a decrease in the saturation of mixed venous blood returning to the lungs. Fever, pain, anxiety and active use of respiratory muscles significantly increase oxygen consumption. Therefore, it is vital to control the patients' fever and toprovide pain management, deep sedation, and analgesia (25).

Prevention of Ventilator-Associated Pneumonia

The VAP is one of the most common complications seen in patients ventilated. It is essential to apply handwashing protocols meticulously, raising the bed head (30-45°, especially in patients with enteral feeding), and performing oral care with chlorhexidine every 4-6 hours to prevent VAP in patients undergoing MV. When necessary, it is recommended to perform a tracheal aspiration, which will be administered to maintain airway patency in less than 15 seconds and take at least a 1-minute break for the second aspiration (19,26,27).

Pain Management

Pain experience is known to be common in ICU patients. These patients may experience pain for many reasons, such as an endotracheal tube, drain insertion/removal, bladder catheterization, CVC catheter application, positioning and immobility, and existing health problems (28). In addition, physical and psychological factors such as being in an ICU environment, anxiety, and fear of death due to dyspnea, can increase pain perception (29).

Pain may exacerbate ARDS by causing the release of endogenous metabolites, hyper-metabolic activity, increased myocardial oxygen consumption, myocardial ischemia, and pulmonary dysfunction. Hence, it is significant to evaluate and manage pain with appropriate scales in patients with ARDS (29).

Initially, the source of pain should be investigated in the patient. If the patient is conscious, it should be questioned whether the diagnosis and treatment attempts have caused pain. If there is pain, its severity should be determined. If the patient has difficulty in speaking or if data collection is desired without exhausting the patient and with consuming minimum oxygen, as in ARDS, the patient may be asked to answer the questions with short answers as "yes" and "no" or by opening and closing her/his eyes. Using a standard scale for pain assessment is helpful for comparing raters, but the scales should be as short as possible (28,29,30).

Pain can be evaluated with behavioral (clenching teeth, clenching fists, frowning, and crying) and physiological symptoms (increase-decrease in respiratory rate, nausea-vomiting, sweating, and decrease in saturation) in patients who are unconscious due to sedation or MV, or who have changes in consciousness. For this purpose, scales such as "Non-Verbal Pain Scale for Adults," "Pain Observation Scale in Intensive Care," "Ramsay Sedation Scale," "Pain Diagnosis and Intervention Form," and "Motor Movement Rating Scale" can be used. Respiratory distress experienced in ARDS may also be reflected in the physiological symptoms of pain; hence, the evaluation should be done carefully. It is best to assess the pain as soon as the patient comes to the ICU unit, followed by an assessment every 8 hours if there is no pain, 2 hours for mild pain, hourly for moderate pain, and every half hour for severe pain (29,30).

DVT Prophylaxis

Deep vein thrombosis can develop asymptomatically in ICU patients. MV, various catheters, and immobility can increase DVT risk. It is recommended to evaluate patients in terms of venous thrombosis and apply primary DVT prophylaxis (such as unfractionated heparin, low molecular weight heparin, fondaparinux, and warfarin) in risky patients. In addition to anticoagulant therapy, mechanical protective methods such as elastic stockings and intermittent pneumatic compression can be applied (31).

Peptic Ulcer Prophylaxis and Bleeding Control

Peptic ulcers, which are common in ICU patients, are caused by increased corticosteroids released in response to stress, decreased bicarbonate release, and reduced gastric blood flow. Peptic ulcer increases the risk of GIS bleeding. Therefore, peptic ulcer prophylaxis is performed with proton pump inhibitors or H2 receptor blockers in ICU patients. Patients should be monitored regularly in terms of bleeding. Cannula insertion points should be checked routinely in terms of hematoma and urine color should be checked routinely in terms of hematuria. Anticoagulation doses should be adjusted by regularly evaluating blood gas values and bleeding findings (32).

Blood Sugar Regulation

Stress-induced cortisol and cytokines increase hepatic gluconeogenesis, disrupt glucose utilization, and cause insulin insufficiency. If the patient has diabetes, not giving anti-diabetics that the patient have previously taken, using corticosteroids, and enteral/parenteral nutrition contribute to hyperglycemia. Uncontrolled hyperglycemia in ICU patients is directly related to mortality and morbidity, especially infection. For these reasons, it is essential to ensure optimal glucose control. However, glucose control should be adjusted so as not to cause hypoglycemia. The American Diabetes Association recommends checking HbA1C in all hospitalized diabetic patients, in critically ill patients if they have not been examined in the last three months, or patients with hyperglycemia (blood glucose >140 mg/dL), and initiating insulin therapy according to standard protocols. When blood sugar is ≥180 mg/dL, insulin therapy should be adjusted to keep blood sugar within the limits of 140-180 mg/dL to prevent kidney damage. Lower blood glucose levels can be aimed at patients with a low risk of hypoglycemia (110-140 mg/dL) (33).

Protecting and Maintaining Skin/Tissue Integrity

For the dried crusts, residues around the eyes are softened by keeping the gauze soaked with warm water on the eyelid for a while. The eye should be cleaned by wiping from the inner part towards the outer part with a sterile sponge. Eye pomade should be applied before PP to prevent corneal abrasions. Eyes should be covered with a sterile eye pad (22).

During positioning, the patient's spine, especially the neck and waist, should be supported (21). In preventing pressure sores, a position change should be made every 2 hours, pressure zones should be supported, the pressure exerted by the catheters should be checked, and necessary measures should be taken (22). In patients given PP, the facial area should be checked for pressure and edema and routine pressure zones (21). In keeping the skin dry and clean, it should be cleansed and moisturized following

the protocols. Oral care should be done with chlorhexidine to prevent dry mouth and mucositis, and lips should be moistened (22,26).

Pharmacological Treatment

Except for neuromuscular blockers, which facilitate ventilator compliance and reduce the need for ventilation by slowing down metabolism, there is no drug with proven efficacy in ARDS. If there is an infection in the etiology of ARDS, antibiotic treatment is applied (34). Sedation and analgesia are beneficial insofar as they increase MV tolerance and reduce oxygen consumption (18). Although their routine usage is not recommended, inhaled nitric oxide is helpful by selectively decreasing pulmonary vascular resistance, performing pulmonary vasodilation, increasing oxygenation in well-ventilated lung areas, and decreasing pulmonary edema (11). The usage of corticosteroids in patients with ARDS is controversial, and it is recommended that patients using corticosteroids should be followed up for infection (35).

Conclusion

Although many risk factors for ARDS have been identified, there is no clear strategy for prevention so far. It is known that the only treatment method that reduces mortality in the management of the clinical picture is low TV + limited plateau pressure. Therefore, the importance of awareness, early diagnosis, early intervention with an integrated approach, and good clinical follow-up cannot be denied in ARDS prognosis.

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