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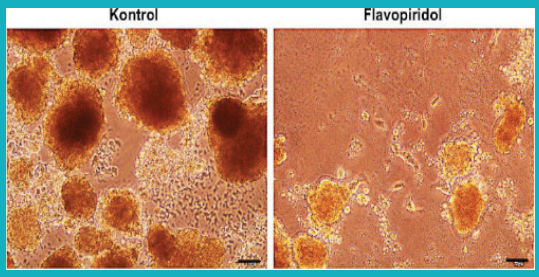

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Original Articles

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EDITORIAL

Dear Readers;

We are happy to be with you in the 3rd issue of 2020. As in the world, efforts to normalize our country are continuing after a very serious pandemic. Everything has changed in this process, which has entered our literature as the new normal. Due to the intensity and demands of COVID publications during this period, the offer to publish a special issue was accepted by our editorial board. We were happy to have around forty articles accepted in this field and to have a keen interest in both our magazine and the subject. I would like to thank both our readers and our academics who share their work with us in this field.

I would like to mention our cover art and selected articles in this issue. Açıkgöz et al. Effect of flavopyridol on cell cycle, apoptosis and biomolecule structure changes in breast cancer stem cells…

Açıkgöz et al. "The effect of flavopyridol on cell cycle, apoptosis, and biomolecule structure changes in breast cancer stem cells", Tonak et al. "Investigation of activity, participation and quality of life in elderly people living in Ankara and Antalya provinces" Kumaş et al. "Investigation of the effects of isotretinoin on spermatogenesis in BALB/c mice "Baki et al. "Effect of Serum bone Sialoprotein levels on Tympanosclerosis" writings are some of our articles that have come to the forefront. We are honoured by the increasing demand for publications and we are pleased to see the coming of articles from new domestic and international institutions.

We'll meet you right after this issue with our Covid special issue. We all look forward to this special issue, where there is intense labor and participation. The pandemic process once again showed us the importance of open access studies. I would like to thank our publishing house, our editorial board and our referees for taking the time to make sure that even during this period when their work load has increased a lot.

I wish you all the best to meet in our next issue.…

Kindest regards

Prof. Dr. Adem AKÇAKAYA
Editor-In-Chief

Original Article

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Bezmialem Science 2020;8(3):215-21

Effects of Reflexology Massage on Hair Regrowth After Chemotherapy-induced Alopecia Among Women with Cancer: A Randomised Clinical Trial

Refleksoloji Masajının Kanser Kadınlarında Kemoterapiye Bağlı Alopesi Sonrası Saçların Uzamasına Etkisi: Randomize Bir Klinik Çalışma

Haleh GHAVAMİ, Leyla ARJOMAND, Moloud RADFAR, Hamid Reza KHALKHALİ

Urmia University of Medical Sciences, Nursing, Urmia, İran

ABSTRACT

Objective: Chemotherapy-induced alopecia (CIA) is a common unwanted effect related to anti-neoplastic agents. Due to potential CIA, some patients with cancer consider refusing treatment. It negatively affects a patient's perception of appearance and sexuality. This study aimed to determine the effectiveness of reflexology massage on hair regrowth after CIA.

Methods: This randomised clinical trial was conducted in 60 women with cancer with full alopecia due to chemotherapy. They were divided randomly into two groups: the experimental and control groups. The patients in the experimental group received reflexology massage for 15 min, 3 times daily (per 8 h), for 3 months. Those in the control group only received treatment as usual and routine health care. Data were obtained from the patient information and hair measurement forms. Couliss Vernier was used for hair regrowth measurement. The minimum and maximum hair lengths were measured thrice monthly after intervention started in both groups.

Results: Considering baseline full alopecia in both groups, hair regrowth in the experimental group significantly improved compared with the control group ($p<0.001$).

Conclusion: In women with CIA, reflexology massage can improve hair regrowth after chemotherapy. This study may be added as evidence to the use of reflexology as a nonpharmacologic symptom management technique.

Keywords: Alopecia, cancer, chemotherapy, hair, reflexology

ÖZ

Amaç: Kemoterapiye bağlı alopesi (KBA) anti-neoplastik ajanların yaygın olan yan etkisidir. Potansiyel KBA'nın etkisi o kadar derin ki, bazı kanserli hastalar tedaviyi reddediyorlar. KBA, hastanın görünüm algısı ve cinselliğini olumsuz etkiler. Bu çalışmanın amacı, refleksoloji masajının KBA sonrası saç uzaması üzerine etkisini belirlemekti.

Yöntemler: Bu randomize klinik çalışma, KBA kanserli 60 kadın üzerinde gerçekleştirildi. Hastalar rastgele yöntemi ile iki gruba ayrıldılar; deney grubu ve kontrol grubu. Deney grubundaki örnekler, 3 ay boyunca her gün 15 dakika, günde 3 kez (8 saatte bir) refleksoloji masajı aldılar. Kontrol grubu, tedavilerini sadece rutin, sağlık hizmetlerini normal şekilde aldılar. Veriler hasta bilgi formundan ve saç ölçüm formundan elde edildi. Saç uzama ölçümü için Couliss Vernier kullanıldı. Müdahalenin başlamasından sonra her ay minimum ve maksimum saç uzunlukları her iki grupta 3 kez ölçüldü.

Bulgular: Çalışmanın iki grubunda başlangıçtaki tam alopesi göz önüne alındığında, çalışmanın sonunda deney grubu kadınlarda saçların yeniden uzaması, kontrol grubuna göre anlamlı olarak artmıştır ($p<0,001$).

Sonuç: KBA'sı olan kadınlar için, refleksoloji masajı kemoterapiden sonra saçlarının yeniden uzamasını artırabilir. Bu çalışma, refleksoloji masaji farmakolojik olmayan bir semptom yönetimi tekniği olarak kullanılmasına ilişkin kanıtlar ekleyebilir.

Anahtar Sözcükler: Alopesi, kanser, kemoterapi, saç, refleksoloji

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Introduction

The roles of hair are protection, sensory functions, thermoregulation and sexual attractiveness (1). Although hair disorders or hair loss is not life-threatening; they negatively affect self-confidence, self-esteem and quality of life (QOL) (2). Due to significant improvement of modern chemotherapies, survival and prognosis also improved in majority of cancer entities; however, the number of related side effects also increases (3). Chemotherapy-induced alopecia (CIA) is a common unwanted effect related to anti-neoplastic agents. It generally starts at 1–3 weeks after the first chemotherapy cycle and is aggravated after subsequent cycles. Fortunately, patients usually recover from CIA spontaneously after 3–6 months. However, several patients experience permanent CIA, and many patients experience changes in hair colour, texture and growth rate even after hair regrowth (4). CIA can result in a negative body image, anxiety, depression, lower self-esteem and reduced sense of well-being and QOL (5,6). In addition, CIA negatively affects a patient's perception of appearance and sexuality. Moreover, patients feel deprived of their privacy because hair loss is interpreted as being associated with cancer (7). The incidence and severity of CIA are variable and associated with particular chemotherapeutic protocols. Approximately 65%–85% of chemotherapy patients experience some degree of alopecia. Overall, 47%–58% of female cancer survivors considered hair loss to be the most traumatic aspect of chemotherapy, and 8% of them fear that the cause of hair loss is decline from cancer treatment (5). No therapy for CIA has been established as a complete protection against all alopecic chemotherapies in human studies. Both scalp cooling and the immune modulating drug AS101 have reduced the severity of CIA in clinical trials (8).

Reflexology, which is defined as a holistic healing technique, is an ancient art involving various techniques and philosophical approaches (9) and considered to be a form of complementary and alternative medicine, which refers to treatments used either as an adjunct to or instead of conventional medical care (10). Reflexology defines reflexive zones both in the hands and feet, which are associated with glands, organs and other parts of the body (11). Reflexology, unlike other body therapies, is gentle and noninvasive. Only the feet and hands are considered. Therefore, it is an ideal modality for children or persons debilitated by cancer and cancer therapies (12).

Numerous studies have indicated that reflexology massage during and after cancer therapy can improve physical function, QOL and cancer-related symptoms, such as nausea and vomiting, fatigue, anxiety and pain, in cancer survivors (11,13-19). Because no study was published regarding the impact of reflexology on CIA, this randomised clinical trial aimed to evaluate the effect of reflexology massage on hair regrowth after CIA in women with cancer. We hypothesised that reflexology massage could enhance hair regrowth in the experimental group.

Method

Ethical Considerations

This study was approved by research ethics committee of the affiliated university. The participants were provided written information and allowed 3 days to consider their decision. All participants were informed that they were entitled to withdraw from the study at any time without any negative consequences. All participants provided their written informed consent to participate in the study. Furthermore, the researcher had received a reflexology massage certification from an international complementary and alternative medicine academy before this study.

Design

This was a randomised clinical trial conducted in women with cancer with full alopecia due to chemotherapy.

Details of Power Calculations and Sample Size

Because no study investigated the effects of reflexology massage on hair regrowth in the cancer population, appropriate information is unavailable for computation. However, considering the study of the effect of reflexology on the QOL in patients with breast cancer during chemotherapy (13), we chose role playing as a dimension of QOL, which seems to have a corresponding change with the subject; thus, the sample size is calculated using the following formula:

$$n = \frac{(s_1^2 + s_2^2)^2 (z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2}{(\bar{x}_1 - \bar{x}_2)^2}$$

$$n = \frac{(1/96+0/84)^2 (15/7 + 13/9)^2}{(70-57/5)^2} = \mathbf{29}$$

We concluded that recruitment of 30 patients for each group could give us 90% power to detect a difference in hair regrowth at an α level of 0.05. Thus, we registered 60 patients (30 for each group).

Patient Inclusion Criteria

Patient inclusion criteria included women with cancer classified as stage I–III; patients who completed cancer primary treatment (surgery, chemotherapy and radiotherapy) 3 months prior; patients on one of these three chemotherapy drugs, namely adriamycin, cyclophosphamide and taxotere, because these more likely cause hair loss or thinning (20); patients with full alopecia; patients without any problem with their hands (especially with their fingers); patients without movement disorders; patients who did not receive any reflexology massage; and patients not using drugs to help hair regrowth or who underwent hair transplantation. Patients must be interested in attending reflexology educational and consultation sessions at least thrice a

month for 3 months; patients must be adults (19–49 years) and able to read and write in Persian.

Patient Exclusion Criteria

Patient exclusion criteria included the use of other medications that could have any effect on hair growth, such as minoxidil, iron complements, oral contraceptive (OCP), anticoagulants, beta-blockers and antiepileptic drugs; patients with thyroid disease or severe infection; patients with history of surgery 3 months prior; or patients with malnutrition and iron deficiency anaemia; patients with metastatic cancer and with inoperable disease; patients with severe nausea, anorexia, or other diseases affecting health (e.g., arthritis and multiple sclerosis); patients who are unable for other reasons to continue participating in this research.

Data Collection and Measures

Data were obtained from the patient information and hair measurement forms. Couliss Vernier (Guanglu Caliper, 111-101 HB, China) was used to measure hair regrowth. All patients in the experimental and control groups were instructed to complete the patient information questionnaire before the intervention. The patient information form was a researcher-made form.

Clinical Interventions

Initially, 86 patients were assessed for eligibility; of these, 60 women (according to the inclusion and exclusion criteria of the study) were randomised to the experimental or control group. An independent researcher randomised the patients by using random allocation cards using computer-generated random numbers. The allocator kept the original random allocation sequences in an inaccessible third place and worked with a copy. Instead, of the letters A and B, codes E and C (experimental and control groups, respectively) were used to avoid further confusion. Subsequently, randomisation was continued until 30 samples were allocated for each group (CONSORT flow diagram).

Clinical Interventions in the Experimental Group

The patients in the experimental group received the following interventions: initially, their hands were washed with water and soap then dried with a towel. Subsequently, they received reflexology massage on points that are known as hair-growing points under the fingernail beds of the hands daily for the first 3 days for 15 min. Because the points under the fingernail beds or Balayam (nail acupressure for hair growth) are strongly associated with scalp health and hair growth, as the nerve endings underneath each fingernail are believed to be connected directly to the hair roots (21).

The following instructions were given to the patients in the experimental group: their hands should be put together in front, with fingernails touching the fingernails of the other hand (elbows at an angle approximately 90°; thumbs straight out, resting on your index fingers). Their fingernails should be rubbed together vigorously (up and down in short, quick motions). This exercise should be performed at least 15 min thrice daily for 3 months.

Moreover, they received a reflexology check list and were instructed to check it when receiving reflexology massage. These check lists were controlled weekly by the researcher. In addition, the minimum and maximum lengths of the hair on the top of the head were measured monthly for 3 months after the beginning of intervention by using Couliss Vernier (Guanglu Caliper, 111-101 HB, China), such that its measuring instinct is between 0.01 mm and 0.001 inch.

Clinical Intervention in the Control Group

The patients in the control group only received their treatment as usual and routine health care, without receiving any massage.

Statistical Analysis

Statistical Package for Social Sciences ver.15 software was used for statistical analysis. Numbers were shown as percentage, mean and standard deviation for identifying characteristics of patients, and chi-squared, independent sample t-test and repeated measurement analysis of variance (ANOVA) test were used to evaluate statistical significance of socio-demographic data, disease characteristics and hair lengths between the experimental and control groups before and after the study. The results were

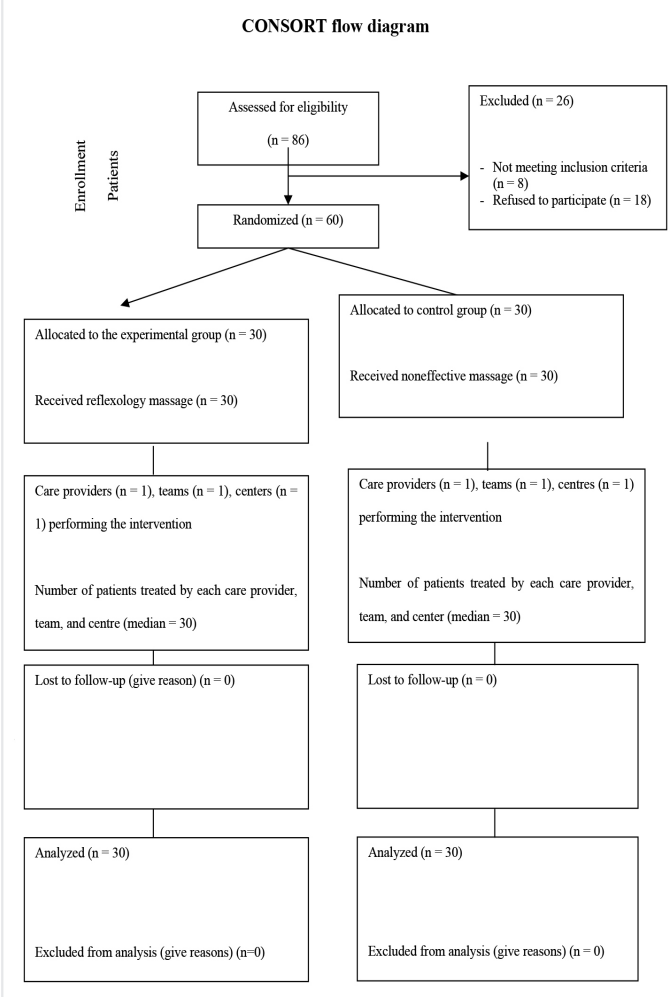

Figure 1. CONSORT flow diagram

accepted at confidence level of 95% and statistical significance level of p<0.05.

Results

Demographic or Medical Characteristics

Variables that might affect the study results, such as marital status; education level; use of adriamycin, cyclophosphamide and taxotere; employment status; income and age, were compared. No baseline differences existed between the two study groups for either demographic or medical characteristics and groups were similar together (Table 1).

Hair Regrowth

The study results showed better hair regrowth in the experimental group compared with the control group after the intervention (Tables 2-5).

All women in the two groups had full alopecia before the study. However, the result of repeated measurement ANOVA showed that the minimum hair regrowth rate between the two groups were statistically significant after the intervention [F (1, 58)=5.72; p<0.001; partial eta squared=0.99] (Table 3).

In addition, the result of repeated measurement ANOVA showed that the maximum hair regrowth rate between the two groups were statistically significant after the intervention [F (1, 58]=8.52; p<0.001; partial eta squared=0.99) (Table 5).

Table 2 shows that the mean and standard deviation of the minimum hair regrowth rate were 1.85±0.52, 12.45±1.72, and 22.28±2.39 in the experimental group and 1.32±0.46, 11.44±1.46, and 21.53±2.14 in the control group in the first, second, and third months, respectively.

Table 3 shows the three effects tested (on the minimum hair regrowth rate):

Table 1. Socio-demographic characteristics by group (n=60)

	Experimental (n=30)		Control (n=30)		
Characteristics	n	%	n	%	
Age (mean ± SD)	39.50±6.57		40.30±7.05		p=0.65
Marital status					
Single	5	16.7	5	16.7	X^2=0.75
Married	23	76.7	21	70	df=2
Divorced	2	6.6	4	13.3	p=0.68
Level of education					
Primary	6	20	7	23.3	X^2=1.34
High school	20	66.7	16	53.3	df=2
University	4	13.3	2	23.3	p=0.51
Working status					
Housewife	23	76.7	20	66.7	X^2=0.73
Employee	7	23.3	10	33.3	df=1
					p=0.39
Income					
<10,000,000 R	12	40	16	53.3	X^2=1.07
>10,000,000 R	18	60	14	46.7	df=1
					p=0.30
Chemotherapy drugs					
Adriamycin	27	50	27	50	X^2=0.35
Cyclophosphamide	27	50	27	50	df=2
Taxotere	28	49.1	29	50.9	p=0.55

df= Degree of freedom, X^2= Chi-squared test, SD: Standard deviation

Table 2. Mean and standard deviation of minimum hair regrowth rate in both groups

Group	Mean and standard deviation of minimum hair regrowth rate		
Month	First month	Second month	Third month
Experimental	1.85±0.52	12.45±1.72	22.28±2.39
Control	1.32±0.46	11.44±1.46	21.53±2.14

A. Interaction Between Time and Intervention: The statistical test indicates that the interaction between time and intervention during the first to third month is not significant on the mean of the minimum hair regrowth rate (p=0.61).

B. Main Effect of Time: A statistically significant difference was found in the minimum hair regrowth rate in the first to third month at different times (p<0.001).

C. Main Effect of Intervention: The main purpose of this study is to investigate this effect, and ANOVA results show that the mean of the minimum hair regrowth rate in the first to third month has a significant difference between the experimental and control groups (p<0.001) (Table 3).

Table 4 shows that the mean and standard deviation of the maximum hair regrowth rate were 4.99±0.78, 17.73±2.19, and 29.93±3.08 in the experimental group and 4.21±0.50, 16.91±1.40, and 28.24±2.22 in the control group in the first, second, and third months, respectively.

Table 5 shows the three effects tested (on the maximum hair regrowth rate):

A. Interaction Between Time and Intervention: The statistical test indicates that the interaction between time and intervention in the first, second, and third months is not significant at the maximum hair regrowth rate (p=0.20).

B. Main Effect of Time: A statistically significant difference was found in the frequency of hair growth during the first to third month at different times (p<0.001).

C. Main Effect of Intervention: The main purpose of this study was to investigate this effect. The ANOVA results showed that the mean of the maximum hair regrowth rate during the first to third month had a significant difference between the experimental and control groups (p<0.001) (Table 5).

Discussion

This randomised controlled trial study aimed to determine the effects of reflexology massage on hair regrowth after CIA among women with cancer. Our study findings support our priori hypothesis that reflexology massage among women with cancer can improve hair regrowth after full alopecia.

Table 3. Analysis of measured minimum hair growth rate

Minimum hair growth	Total squared error	Degree of freedom	Mean squared error	F	p value	Partial eta squared
Main effect of time	12,388.47	2	6194.23	3476.98	<0.001	0.984
Interaction of time with reflexology intervention	1.736	2	0.868	0.487	0.616	0.008
Component of time effect error	206.65	116	1.78	-	-	-
The main effect of intervention	25,139.48	1	25,139.48	5.722	<0.001	0.99
Component of intervention effect error	254.83	58	4.39	-	-	-

F= F test in analysis of variance (ANOVA)

Table 4. Mean and standard deviation of maximum hair regrowth rate in both groups

Group	Mean and standard deviation of maximum hair regrowth rate		
Month	First month	Second month	Third month
Experimental	4.99±0.78	17.73±2.19	29.93±3.08
Control	4.21±0.50	16.91±1.40	28.24±2.22

Table 5. Analysis of measured maximum hair growth rate

Maximum hair growth	Total squared error	Degree of freedom	Average squared error	F	p value	Partial eta squared
Main effect of time	17,996.28	2	8998.14	3621.24	<0.001	0.98
Interaction of time with reflexology intervention	8.01	2	4.00	1.61	0.20	0.02
Component of time effect error	288.23	116	2.48	-	-	-
Main effect of intervention	52,074.41	1	52,074.41	8.522	<0.001	0.99
Component of intervention effect error	354.39	58	6.11	-	-	-

F= F test in analysis of variance (ANOVA)

The findings of this study were consistent with previous studies indicating that reflexology massage during and after cancer therapy can improve physical function, QOL and cancer-related symptoms, such as nausea and vomiting, fatigue, anxiety and pain in cancer survivors (11,13-19). For example, Quattrin et al. in 2006 aimed to examine the effectiveness of reflexology foot massage in hospitalised cancer patients undergoing second or third chemotherapy cycles. They concluded that reflexology foot massage can be considered a support treatment used in combination with traditional medical treatments and executed by an expert, qualified person to help cancer patients receiving chemotherapy feel better and also cope better with their disease (14).

Another study by Razi et al. determined the effect of reflexology on the QOL of patients with breast cancer who were receiving chemotherapy. Their results demonstrated considerable improvement in the different aspects of QOL in the reflexology group compared with the placebo and control groups (13).

In addition, Ben-Horin et al. (22) in 2017 conducted a retrospective study to evaluate the efficacy of acupuncture and reflexology protocol on chemotherapy-induced peripheral neuropathy (CIPN) in patients with breast cancer who were concomitantly treated with chemotherapy. Their study results demonstrated that a joint protocol of acupuncture and reflexology has a potential to improve symptoms of CIPN in patients with breast cancer (22).

In addition, our study is consistent with the study by Kang et al. (23) in 2018 who conducted a 3-year prospective cohort study. They concluded that permanent CIA is a common adverse event of breast cancer adjuvant cytotoxic chemotherapy. Clinicians should be aware of this distressing adverse event and develop supportive care strategies to counsel patients and minimise its impact on the QOL (23).

Although a qualitative study on Korean women with breast cancer reported that CIA never improved and remained visible several years after treatment (23,24), the effects of different biological agents, such as minoxidil, AS101, cyclosporine A, parathyroid hormone (PTH) and PTH-related protein, have been evaluated in the management of CIA. Different results regarding the effectiveness of these approaches on hair regrowth after alopecia were obtained (5,6,25).

Study Limitations

Our study has limitations, such as relatively small sample size, short study duration for hair regrowth, location of the programme, scheduling conflicts and transportation. The limitation of enrolling patients from two institutions also contributed to the small study population because many eligible patients could not participate in the reflexology massage programme due to location, transportation and conflicts in schedule.

Conclusion

The present study showed that the hair regrowth rate in women with cancer with CIA may improve by participating in reflexology massage programmes. Furthermore, this simple, effective, comfortable and low-cost programme for cancer survivors may apply to other types of alopecia. Additional research in reflexology massage along with using natural nutrient solutions on the scalp also may be beneficial. The study results may contribute to the growing body of knowledge supporting the feasibility and effectiveness of reflexology massage as a nonpharmacologic option for enhancing hair regrowth, body image and self-esteem in cancer survivors.

Ethics

Ethics Committee Approval: This study was approved by research ethics committee of the affiliated university.

Informed Consent: All participants were informed that they were entitled to withdraw from the study at any time without any negative consequences.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: L.A., Concept: H.G., M.R., Design: H.G., H.R.K., Data Collection or Processing: L.A., H.R.K., Analysis or Interpretation: H.G., H.R.K., Literature Search: H.G., L.A., M.R., Writing: H.G., M.R.

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Original Article

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Effect of Gender and Physical Activity Level on Sit-to-Stand Test Performance Among Young Adults

Genç Yetişkinlerde Cinsiyet ve Fiziksel Aktivite Seviyesinin Otur-kalk Test Performansı Üzerine Etkisi

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ABSTRACT

Objective: Our study aimed to determine the sit-to-stand (STS) test performance and physical activity levels of young adults and investigate the relationship of STS tests with gender and physical activity levels.

Methods: Sixty volunteers randomly performed the 5×STS, 10sSTS, 30sSTS and 60sSTS tests. Fatigue was rated using the Borg category ratio scale. Physical activity level and weekly energy expenditure of volunteers were calculated using the International Physical Activity Questionnaire.

Results: The 5×STS, 10sSTS, 30sSTS and 60sSTS test scores were statistically different between genders (p=0.004; p=0.002; p=0.000; p=0.000, respectively). Fatigue levels after STS tests did not show any difference between genders (p=0.636; p=0.295; p=0.888; p=0.150, respectively). Weekly energy expenditures were positively correlated with STS tests except 5×STS test (r=–0.458, p=0.000; r=0.427, p=0.001; r=0.606, p=0.000; r=0.545, p=0.000, respectively). All STS tests had significant differences between participants with moderate or high physical activity level (p=0.016; p=0.007; p=0.000; p=0.000, respectively).

Conclusion: Our study shows that STS tests scores correlate to gender and physical activity levels in young adults.

Keywords: Sit-to stand test, functional capacity, weekly energy expenditure, adolescent

ÖZ

Amaç: Genç yetişkinlerde otur-kalk test (OKT) performansını ve fiziksel aktivite seviyesini belirleyerek OKT performansının cinsiyetle ve fiziksel aktivite seviyesi ile ilişkisini belirlemektir.

Yöntemler: Altmış gönüllü rastgele sırayla 5 tekrarlı OKT, 10 sn OKT, 30 sn OKT ve 60 sn OKT'lerini gerçekleştirdi. Test sonu yorgunluk seviyeleri Borg Yorgunluk skalasıyla değerlendirildi. Katılımcıların fiziksel aktivite seviyeleri ve haftalık enerji tüketimi değerleri Uluslararası Fiziksel Aktivite Anketi kullanılarak belirlendi.

Bulgular: Kadın ve erkek katılımcılar arasında 5 tekrarlı OKT, 10 sn OKT, 30 sn OKT ve 60 sn OKT skorlarında istatistiksel olarak anlamlı farklılık tespit edildi (sırasıyla, p=0,004; p=0,002; p=0,000; p=0,000). OKT sonundaki yorgunluk seviyelerinde ise anlamlı bir fark bulunmadı (sırasıyla, p=0,636; p=0,295; p=0,888; p=0,150). Tüm katılımcıların haftalık enerji tüketimi değerleri 5 tekrarlı OKT skoru dışında tüm testlerle pozitif olarak ilişkili bulundu (sırasıyla, r=-0,458, p=0,000; r=0,427, p=0,001; r=0,606, p=0,000; r=0,545, p=0,000). Orta ve yüksek fiziksel aktivite seviyesine sahip katılımcıların OKT skorları karşılaştırıldığında istatistiksel olarak anlamlı farklar saptandı (sırasıyla, p=0,016; p=0,007; p=0,000; p=0,000).

Sonuç: Bizim çalışmamız genç yetişkinlerde OKT performansının cinsiyetle ve fiziksel aktivite seviye ile ilişkili olduğunu göstermektedir.

Anahtar Sözcükler: Otur-kalk testi, fonksiyonel kapasite, haftalık enerji tüketimi, adölesan

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Introduction

The sit-to-stand (STS) manoeuvre is one of the essential activities for mobility according to the International Classification of Functioning, Disability, and Health (1). It is generally used as a measure of knee extensor strength (2). STS tests that include more than a single repetition of STS manoeuvre assess physical fitness and functional capacity in elderly people (3). Several variations of STS test exist; five repetitions (5×STS), 10 s, 30 s and 60 s STS (10sSTS, 30sSTS and 60sSTS) tests are the most frequently used tests in studies and clinical practice (4-7). These are generally used among the older population and some neurological conditions (8,9).

Physical activity is defined as any bodily activities produced by the skeletal muscles and joints that result in energy expenditure, heart rate and respiratory frequency increment and fatigue in different levels (10). Physical activity level is generally classified as high, moderate and low. Functional capacity is known to be associated with physical activity level of healthy men and women (11). In addition, sex-related differences in physical activity show that male adolescents are more physically active than female adolescents (12,13). However, studies comparing STS test performance among different physical activity levels and between genders in the young population are limited (8,9,14). This leads to difficulties in comparing the STS performance of young patients to their age and gender-matched healthy controls.

This study aimed to determine STS test performance and physical activity levels of young adults and investigate the relationship of STS tests with gender and physical activity levels.

Method

Study Design

Sixty healthy volunteers (30 women and 30 men) aged between 18 and 25 years were included in the study. Exclusion criteria were participation in competitive sports, smoking, hospitalisation history in the last 6 months, diagnosed chronic diseases which may affect exercise capacity, diagnosed visual and/or vestibular disorders and pathologies, and pain in the lower extremities that may impede mobilisation (traumas, fractures, etc.).

The demographic data of subjects were recorded. All participants performed the STS tests (5×STS, 10sSTS, 30sSTS and 60sSTS tests), and physical activity levels of participants were assessed using the International Physical Activity Questionnaire-Short Form (IPAQ-SF) on the same day.

The aim of the study and testing methods were explained to the participants in advance, and informed consent was obtained before testing. The research was approved by the research ethics committee of the university hospital (protocol number: 71306642/050-01-04/07).

Outcome Measures

Sit-to-Stand Tests

STS tests were performed according to Bohannon's 2012 guideline (15). A standard height chair (45 cm) without arm rests which was stabilised against the wall, was used for testing. The participants were instructed to move forward until their feet are flat on the floor. They were instructed to stand up all the way and sit down as fast as possible while the upper limbs were folded across the chest for five times and also for 10, 30 and 60 s. The order of the tests was determined by random draw. The time required for completing five STS manoeuvres was measured for 5×STS test, and the number of completed STS manoeuvres in the given period was recorded for the timed tests. 5-min rest intervals were given between each STS test. Fatigue was rated using the modified Borg scale after each test.

Physical Activity

The IPAQ-SF includes seven questions divided into frequency, intensity and duration of participation in physical activities at low (walking), moderate and vigorous levels, and quantifies the total physical activity for the past week. The data collected are reported as continuous data (expressed as metabolic equivalent task [MET-min/week]) and as a categorical score (divided into low [<600 MET-min/week], moderate [600–3000 MET-min/week] and high [>3000 MET-min/week] activity level) (16).

Statistical Analysis

Statistical analysis was performed using SPSS software (Version 16.0; SPSS; Chicago, IL, USA). Normality of all variables was tested using the Shapiro-Wilk test. The differences in functional capacity, fatigue level after STS tests between female and male subjects and difference in STS scores between subjects with moderate and high physical activity levels were analysed using the chi-squared test and Student t-test. The correlation between weekly energy expenditure and STS test scores were analysed using Pearson correlation coefficient (r= at least 0.8, very strong; 0.6–0.8, moderately strong; 0.3–0.5, good; and <0.3, poor). The significance level for tests was determined as 95% ($p<0.05$).

The sample size of the study was determined using G-Power 3.1 software (Universität Dusseldorf, Germany) (17). Literature suggests that the effect size of the difference between functional capacity of men and women is 0.88 (18). Considering this, minimum of 22 subjects were needed for each gender to detect this difference with 95% confidence level and 80% power.

Results

Demographic data (age, sex, height, weight and body mass index [BMI]), weekly energy expenditure and physical activity levels of participants are shown in Table 1. Of the female participants, 22 (73%) and 8 (27%) had moderate and high physical activity levels, respectively; of the male participants, 14 (47%) and 16 (53%) had moderate and high physical activity levels, respectively (between gender difference, $p=0.025$). None of the participants had low physical activity level.

Statistically significant differences were found in all STS tests between women and men (5× STS, $p=0.004$; 10sSTS, $p=0.002$; 30sSTS, $p=0.000$; 60sSTS, $p=0.000$) (Table 2).

Fatigue levels after STS tests did not show any difference between genders (5× STS, p=0.636; 10sSTS, p=0.295; 30sSTS, p=0.888; 60sSTS, p=0.150) (Table 3).

Weekly energy expenditures were correlated to STS tests (5×STS, r=–0.458, p=0.000; 10sSTS, r=0.427, p=0.001; 30sSTS, r=0.606, p=0.000; 60sSTS, r=0.545, p=0.000) (Table 4).

Table 1. Demographic data and MET, level of physical activity

		Female (n=30) X ± SD	Male (n=30) X ± SD	p
Age (year)		22.13±1.16	22.33±1.26	0.111
Height (m)		1.61±0.06	1.76±0.04	0.000*
Weight (kg)		57.27±7.73	73.83±9.70	0.000*
BMI (kg.m^{-2})		21.97±2.34	22.97±2.59	0.064
MET.min.wk^{-1}		1909±1148	3503±2250	0.001*
Physical activity level	**Moderate**	22 (73%)	14 (47%)	0.025**
	High	8 (27)	16 (53%)	

*p<0.05, **x^2=4,444, p<0.05, SD: Standard deviation, MET: Metabolic equivalent task

All STS tests had significant differences between participants with moderate or high physical activity level (5×STS, p=0.016; 10sSTS, p=0.007; 30sSTS, p=0.000; 60sSTS, p=0.000) (Table 5).

Discussion

The present study showed that gender-related differences are present for all STS tests. In addition, STS tests had a moderate correlation with weekly energy expenditure and were affected by the physical activity level of the participants.

Table 2. Effects of gender on functional capacity measured by STS tests

	Female (n=30) X ± SD	Male (n=30) X ± SD	p
5× STS test (s)	6.07±1.13	5.15±1.26	0.004*
10sSTS test (number of repetitions)	7.67±1.18	8.93±1.83	0.002*
30sSTS test (number of repetitions)	21.67±2.74	25.67±4.77	0.000*
60sSTS test (number of repetitions)	41.10±6.33	49.40±10.5	0.000*

*p<0.05, SD: Standard deviation, STS: Sit-to-stand

Table 3. Effects of gender on fatigue level after STS tests

		Female (n=30) X ± SD	Male (n=30) X ± SD	p
Modified Borg Scale (0-10)	After 5× STS test	0.37±0.65	0.45±0.69	0.636
	After 10sSTS test	0.48±0.67	0.73±1.10	0.295
	After 30sSTS test	1.98±1.47	2.03±1.26	0.888
	After 60sSTS test	4.13±2.16	4.90±1.90	0.150

SD: Standard deviation, STS: Sit-to-stand

Table 4. Correlation of weekly energy expenditure to sit-to-stand tests (n=60)

		5× STS test	10sSTS test	30sSTS test	60sSTS test
Weekly energy expenditure (MET min wk^{-1})	r	–0.458	0.427	0.606	0.545
	p	0.000*	0.001*	0.000*	0.000*

*p<0.05, STS: Sit-to-stand, MET: Metabolic equivalent task, min: Minimum

Table 5. Effects of physical activity level on functional capacity measured by STS tests

	Moderate physical activity level (n=36) X ± SD	High physical activity level (n=24) X ± SD	p
5× STS test (s)	5.93±1.29	5.13±1.10	0.016*
10sSTS test (number of repetitions)	7.83±1.27	9.00±1.93	0.007*
30sSTS test (number of repetitions)	22.11±3.12	26.00±4.93	0.000*
60sSTS test (number of repetitions)	41.72±7.26	50.54±10.26	0.000*

*p<0.05, SD: Standard deviation, STS: Sit-to-stand

Most of the previous studies showed that men are more physically active than women (19-22). However, there is no consensus about it. Vašíčková et al. compared the physical activity levels between genders using the IPAQ and pedometer. The study did not show any differences in the average daily steps but reported that fewer women participated in vigorous and moderate physical activity according to IPAQ (23). Our study presented that almost half of the male subjects had high physical activity level (53%), whereas only 27% of females were at the same level.

STS tests are simple and cheap clinical tests that require only a small space, a stopwatch and a chair. However, these tests are generally used in the literature to assess older adults, and only few studies investigated young adults (8,14,24). Studies reported that men had greater scores than women for 5×STS and 60sSTS tests across a wide age span (8,9,25). Bohannon et al. found that the mean 5×STS score was 6 s in the young population (age between 20 and 29 years) (9). Butler et al. reported that the median 5×STS test scores of men and women aged between 20 and 24 years were 50 and 47 repetitions, respectively, in the Swiss population (8). Tveter et al. found that 30sSTS scores were different between men and women aged 18–29 years (27 and 26 repetitions, respectively) (26). In the present study, all STS test scores in men were higher than those in women. However, our STS test results were lower than those of previous studies. We speculated that different physical activity habits of different populations may affect STS scores. In addition, most female subjects in the present study had moderate physical activity level. To the best of our knowledge, no study investigated the effect of gender on 10sSTS test in young adults.

Previous studies indicate that the rating of perceived exertion (RPE) is not influenced by gender (27-29). The study of Faulkner J et al. suggests that the Borg scale reflects exercise intensity independent from gender, age, exercise modality or physical activity level in healthy young adults (28). In our study, RPE was assessed using the Borg scale. The findings showed that Borg scores after STS tests were not different between women and men, which supported the results of the previous studies (25-27). The study of Scherr J et al. indicates that Borg scale reflects exercise intensity independent of gender, age, exercise modality or physical activity level in healthy young adults, as well (30).

Weekly energy expenditure can be calculated from self-reported questionnaires. A study showed that self-reported weekly energy expenditure, which was calculated using the Paffenbarger physical activity and exercise index, was related with 5×STS test score in patients with asthma (age range, between 21 and 77 years) (31). The 5×STS, 10sSTS, 30sSTS and 60sSTS tests have significant correlations with self-reported weekly energy expenditure in the present study. It suggests that self-reported weekly energy expenditure may provide information regarding functional capacity in healthy young adults. This idea is supported by another result of our study that STS scores were not the same between adults with moderate and high physical activity levels.

Study Limitations

As a limitation, the effect of gender on STS test scores in different physical activity levels was not analysed because of the small number of sample size of female subjects having high physical activity level.

Conclusion

In conclusion, our study shows that STS tests scores are different between young men and women. In addition, all STS tests can discriminate between subjects with moderate and high physical activity levels, indicating an interaction between STS performance and physical activity level. Future studies implementing STS tests in various diseases in young adults may benefit from our results for comparing the STS results of patients to healthy subjects.

Ethics

Ethics Committee Approval: The research was approved by the research ethics committee of the university hospital (protocol number: 71306642/050-01-04/07).

Informed Consent: Informed consent was obtained before testing.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: H.N.G., Design: H.N.G., H.D.K., E.D., M.Z., Data Collection or Processing: H.N.G., H.D.K., E.D., M.Z., Analysis or Interpretation: H.N.G., H.D.K., E.D., M.Z., Literature Search: H.N.G., H.D.K., E.D., M.Z., Writing: H.N.G., H.D.K., E.D., M.Z.

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Original Article

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The Effect of Simulation-based Training on the Self-confidence and Self-satisfaction of Nursing Students Dealing with Patients under Isolation

Temas İzolasyonlu Hastada Simülasyona Dayalı Eğitimin Hemşirelik Öğrencilerinin Özgüven ve Memnuniyetine Etkisi

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ABSTRACT

Objective: Simulation is an innovative education model that is highly effective in nursing training. The implementation of innovative training programmes on the importance of infection control increases the awareness of nursing students and ensures less anxiety when providing care to patients under isolation.

Methods: The study was conducted on 30 second-year students at a university nursing school. The students first gave a pretest and their initial performance was evaluated through a low-fidelity simulator. This was followed by a theoretical training. Every student in the study group worked with a standardised patient based on an appropriate scenario regarding the care of the patient under contact isolation. Debriefing sessions were then conducted in groups of five students. Following the application, the students were tested on the satisfaction and self-confidence scales through a post-test.

Results: The post-test scores were significantly higher than the pretest scores ($p<0.05$). A significant relationship was found between the self-confidence and satisfaction scores of the students ($p<0.05$, $r=0.538$).

Conclusion: The training provided through a standardised patient was found to contribute to the knowledge scores of the students regarding the care of a patient under contact isolation.

Keywords: Simulation, contact isolation, nursing training, standardised patient

ÖZ

Amaç: Yenilikçi bir eğitim modeli olan simülasyon hemşirelik eğitiminde oldukça etkilidir. Enfeksiyon kontrolünün önemi ile ilgili yenilikçi eğitim programlarının uygulanması, hemşirelik öğrencilerin konuyla ilgili farkındalığını artırmakta ve izole hastaların bakımı sırasında öğrencilerin kaygı düzeyinin azalmasını sağlamaktadır.

Yöntemler: Araştırmanın örneklemini, bir üniversitenin hemşirelik bölümünde 2. sınıfta öğrenim gören 30 öğrenci oluşturmuştur. Çalışmada öğrencilere öncelikle ön test uygulanmış ve ilk performansları düşük gerçeklikli simülatör ile değerlendirilmiş daha sonra teorik eğitim verilmiştir. Araştırmaya katılan her öğrenci senaryo eşliğinde standart hastayla çalışmıştır. Çözümleme görüşmeleri 5 öğrenciden oluşan gruplar şeklinde yürütülmüştür. Uygulama sonrasında öğrenciler öğrenmede memnuniyet ve özgüven ölçeğini uygulamış ve son test yapmışlardır.

Bulgular: Araştırmadan elde edilen sonuçlara göre öğrencilerin bilgi puanları incelendiğinde son test puanlarının ön test puanlarından anlamlı derecede yüksek olduğu bulunmuştur ($p<0,05$). Çalışmaya katılan öğrencilerin özgüven ve memnuniyet puanları arasında anlamlı bir ilişki görülmektedir ($p<0,05$, $r=0,538$).

Sonuç: Araştırma sonuçlarına göre; hemşirelik öğrencilerine temas izolasyonlu hasta bakımına yönelik standart hasta kullanılarak verilen eğitimin öğrencilerin bilgi puanlarının katkı sağladığı görülmüştür.

Anahtar Sözcükler: Simülasyon, temas izolasyonu, hemşirelik eğitimi, standart hasta

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Introduction

Advances in science and technology is growing continuously, changing and influencing all industries, healthcare being one of them. They also affect directly or indirectly the nursing care provided to the patient (1,2). Nursing students new to clinical practice are affected negatively from factors such as the complex technological environment, inexperience, fear of making mistakes, stress and the negative attitudes of the staff (3,4). When performing certain procedures for the first time, the students are extremely intimidated and anxious about making a mistake or harming the patient. They are also concerned about their limitations as to learn or perform adequately due to insufficient practice and supervision (5). In addition, nursing training is currently facing many difficulties such as decreased teaching staff and an increased number of students, requiring trainers to consider innovative strategies (6).

Nursing education and modern healthcare are both changing rapidly. Simulation has become an innovative and effective educational model. It has been used in many countries for the last 20 years, however, in our country, it has been started to be used only recently. Simulation is used to create realistic environments for training. According to the definition of Gaba (7), "Simulation is a technique-not a technology-to replace or amplify real experiences with guided experiences that evoke or replicate substantial aspects of the real world in a fully interactive manner".

Learning in simulation-based training takes place in a risk-free environment, where the student is allowed to make mistakes. This enables training and care to be provided while ensuring patient safety and without violating patient rights. The technique allows students to learn from their mistakes because these mistakes are allowed to reach their natural consequences, unlike in clinical practice where this would not be ethical (8,9).

The use of a standardized patient is one of the most effective simulation approaches in nursing training. It has been shown to be very effective in increasing the knowledge, performance, self-confidence and satisfaction of students in many studies (10-12). A randomised controlled study conducted by the National Council of State Boards of Nursing in USA nursing schools has reported the simulation environment to be as realistic as the hospital environment. It was also found to be risk-free in terms of student and patient safety (13).

Hospital infections or "Healthcare Acquired Infections" constitute a threat to the safety of both the patients and healthcare employees. They are among the most important health problems both in our country and globally (14). Anderson et al. (14) have reported nurses being afraid when providing care to patients infected with Methicillin-Resistant *Staphylococcus aureus* (MRSA). However, these nurses were able to provide care more comfortably to such patients after receiving training on MRSA control and prevention (15). The use of a standardized patient for infection control training enables students to use appropriate infection control methods such as correct hand hygiene practice (9).

Increasing the awareness of students on infection control and decreasing their anxiety requires preparing relevant training programmes on how microorganisms cause infection and how these can be prevented (15).

Students report that isolation procedures create specific physical and psychological patient requirements. They also affect the care provided to the patient and the relationship between the patient and the nurse. Assigning students to departments related to infection or giving them responsibility for the care of patients under isolation accelerates learning. The mechanism is believed to be forcing them to use their theoretical knowledge in clinical practice and reinforcing the trust relationship between the patient and the nurse. Patients under isolation have been found to be visited less often; the nurses also have less contact with the patient (15,16). It is important for infection control purposes for nurses to have good knowledge of infection control and prevention methods, personal protective equipment use and hand hygiene (13,17).

Simulation is an innovative education model that is highly effective in nursing training. The implementation of innovative training programmes on the importance of infection control increases the awareness of nursing students and ensures less anxiety when providing care to patients under isolation.

Methods

The Form of the Study

The aim of this semi-experimental study was to investigate the effect of training using a standardized patient on the self-confidence and satisfaction of the students when caring for a patient under contact isolation.

The Population and Sample of the Study

The study was conducted on the university nursing students taking the "Surgical Diseases Nursing" course during the spring semester of the 2016-2017 academic year. A total of 125 students were taking this course.

The study sample size was determined as 40 students. The number was originally calculated as 28 students according to the study universe (n=125) and the no-response rate was then taken into account. The study was finally conducted on 30 students who volunteered and accepted to participate.

Data Collection Forms

Data collection forms such as the "Pretest/Post-test for Measuring the Level of Knowledge on Contact Isolation", "Student Evaluation Guidelines in the Care of the Patient under Contact Isolation", "Debriefing Form" and "Student Satisfaction and Self-confidence Scale in Learning" based on literature study were prepared by the researchers and used to collect data.

Corrections were made for content validity according to the recommendations of three experts on the subject (two nursing teaching staff and a physician). The data collection tools used for the measurement were evaluated by a measurement and evaluation specialist.

Contact Isolation Knowledge Test: The "Pretest/Post-test for Measuring the Level of Knowledge on Contact Isolation" included 14 multiple-choice questions. The test was based on the literature, and it was used to measure the level of knowledge of the nursing students regarding contact isolation.

Student Evaluation Guidelines in the Care of the Patient under Contact Isolation: These guideless consisted of 21 items, also taken from the literature. The aim was to determine whether the student had performed the steps appropriately. Scoring options were "Observed Correct/Complete", "Observed Incomplete/Incorrect" and "Not Observed" with a score of 2, 1 and 0, respectively.

Student Satisfaction and Self-confidence Scale in Learning: This scale was prepared by the National League for Nursing and the validity and reliability study for Turkey was conducted by Unver et al. (18). The original scale was developed by Jeffries and Rizzolo (19) and included 13 items, which was reduced to 12 during the adaptation to Turkish. The scale used was a 5-item Likert type (1: I definitely do not agree, 2: I do not agree, 3: I am undecided, 4: I agree, 5: I definitely agree). It also included the "Satisfaction with Present Learning" and "Self-confidence in Learning" subtopics, consisting of five and seven items, respectively. There were no negative items. The total of the sub-dimension scores did not give the total score in this scale. The scale scores were obtained by dividing the total sub-dimension scores by the number of items. An increased total scale score indicated increased student satisfaction and self-confidence.

Debriefing Form: This form was created to receive feedback from the students. It was also used to evaluate the student after the practical session with a standardised patient. The form consisted of open-ended queries on issues such as "how the student felt" and "what they could do differently after the practice".

Implementation of the Research

The students included in the study first gave a pretest. The aim was to evaluate their knowledge on the care of a patient under contact isolation. The initial performance of each student was evaluated using a low-fidelity simulator. This evaluation was conducted at the Nursing Department Skill laboratory by the investigator using the student evaluation guidelines. The students were then given a theoretical training on both the verbal methods and the demonstration regarding their approach to the patient under contact isolation.

Each student practiced at the simulation laboratory with the standardised patient. An appropriate scenario regarding the care of the patient under contact isolation was used. The students were observed by the investigator during the practice and their performances were then evaluated according to the student evaluation guidelines. Also, a video recording of this practice session was made.

Debriefing sessions were then conducted in groups of five students. During this session, the students watched their video recordings and their corresponding responses during the session were recorded as audio files. They were given feedbacks on their performance by the investigator and other students. At the end of the study, all students evaluated their satisfaction and self-confidence rate. The Student Satisfaction and Self-confidence Scale on Learning was used for this purpose. Finally, the level of knowledge was determined with the post-test (Figure 1).

Ethical Dimension of the Study

This study was approved by the university Ethics Committee on 22 February 2017 (Decision no: 10). A written permission, dated 9 January 2017 (Number: 78033166/15), was also obtained from the head of the Nursing Department. All participants signed an informed consent form prior to the study.

Study Limitations

The lack of a control group in our study and the small number of students are among our limitations. The inability to observe student performance with an actual hospital patient can also be considered a limitation.

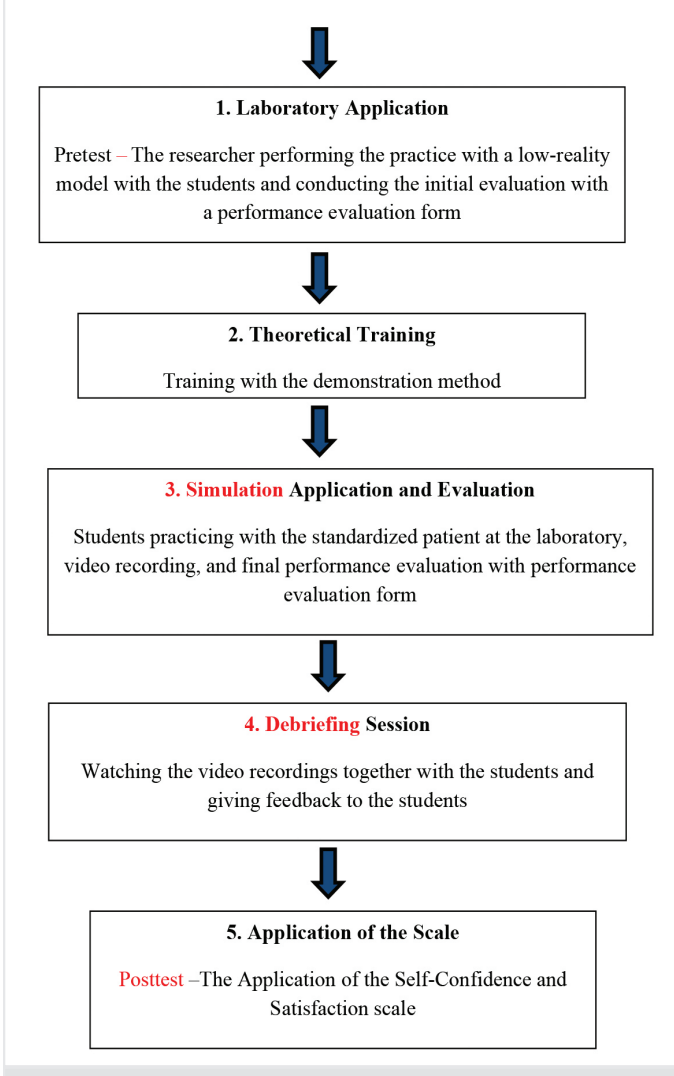

Figure 1. Application flow chart of the study

Evaluation of the Data

Data were analysed using the IBM SPSS Statistics software program, version 22. The Shapiro-Wilk test was used to evaluate whether the variables had a normal distribution. The number and percentage values were presented for frequency distributions. The mean, standard deviation and other descriptive statistics were used for the distribution of the scores. The Pearson's Correlation Coefficient was used to evaluate the correlation between normally distributed variables. The variables were normally distributed, and the paired sample *t*-test was used to evaluate the difference between two dependent variables. A p value of 0.05 was accepted as the significance level when interpreting the results. Values of 95% confidence, 84% theoretical power and 0.5 effect size were used for power analysis. At least 30 subjects were planned to be studied.

The questions used in the analysis were prepared in a semi-structured interview form. The views of the students were presented without performing content analysis.

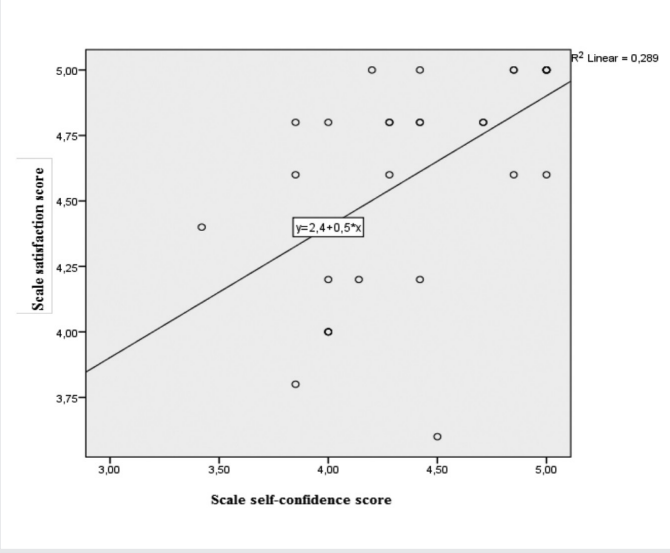

Figure 2. Relationship between self-satisfaction and self-confidence

Results

Females and males made up 86.7% (n=26) and 13.3% (n=4) of our student population, respectively.

The mean contact isolation pretest knowledge score was 65.05±14.13. The mean post-test knowledge score was 87.83±9.41. The post-test scores were significantly higher than the pretest scores (p<0.05) (Table 1).

The mean contact isolation pretest knowledge score was 65.05±14.13. The mean post-test knowledge score was 87.83±9.41. The post-test scores were significantly higher than the pretest scores (p<0.05) (Table 1).

The mean performance score of the students before the training was 59.54±12.06 with the low-reality simulator. The score was 74.69±8.39 during the practice with the standardised patient. The performance scores showed a significant increase after the training (p<0.05) (Table 2).

A significant relationship was found between the Self-confidence and Satisfaction scores (p<0.05, r=0.538) (Figure 2). The satisfaction scores of the students increased with their self-confidence scores. A significant relationship was also present between the increase in the self-confidence scores and the knowledge scores (p<0.05, r=0.373); the self-confidence score increased as the knowledge score increased.

Students' Views

During the debriefing session, the students stated that they had noticed their mistakes while working with the standardised patient. They felt that the practice had raised their awareness and self-confidence and self-satisfaction. They also felt they could now provide care to the patient under contact isolation more comfortably and with increased courage during clinical practice:

"They are not paying attention to these at the hospital. I realized what I needed to do to for approaching patients under contact isolation after this practice".

"Watching myself on the video made me better realize the mistakes I had made".

Table 1. Student Contact Isolation Knowledge Test score distributions

Contact Isolation Knowledge score	n	Mean	Median	Minimum	Maximum	SD	t	p value
Pretest score	30	65.05	64.27	35.70	85.71	14.13	–8.1	0.0001
Post-test score	30	87.83	85.68	64.26	100.00	9.41		

SD: Standard deviaiton

Table 2. Student Performance Score Distribution for the care of the patient under contact isolation

	n	Mean	Median	Minimum	Maximum	SD	t	p value
Low-reality simulator	30	59.54	59.09	31.81	84.09	12.06	–6.01	0.0001
Standardised patient	30	74.69	75.00	56.81	93.18	8.39		

SD: Standard deviation

"I noticed that I needed better knowledge to provide better training for the patient".

"I was afraid to approach this kind of patient but I can now provide care more comfortably".

Discussion

It was found that training using a standardized patient on the care of patients under contact isolation resulted in a significant increase in the knowledge scores of the students ($p<0.05$).

Crowe et al. (20) in their study also reported a significant increase in the knowledge scores of the students after a simulation-based training. The use of standardised patients in training has been reported to provide an ease of learning to the nursing students. It was also found to have a positive effect on their knowledge and performance in the clinical environment, similar to our study (10,21). Shin et al. (22) have reported simulation-based training to be more effective than traditional training in their 2015 article with a meta-debriefing on simulation practices for nursing students. Simulation training enables one-on-one learning in an interactive environment. This kind of environment is student-centred, with the educator merely acting as a guide to the student.

A significant relationship was found between the self-confidence and knowledge scores before and after the training with a standardized patient with respect to providing care to the patient under contact isolation ($p<0.05$, $r=0.373$). The self-confidence scores increased as the satisfaction scores increased.

The students reported being satisfied with the training using a standardized patient and an increased self-confidence while learning the content. Zulkosky (23) has also reported increased student satisfaction in a similar study. Our study revealed that student satisfaction increased as the self-confidence increased.

Moura et al. (24) investigated the effect of simulation on the development of clinical skills for the evaluation of the pressure ulcer risk. They found a significant increase in the critical thinking, self-confidence and skill scores of nurses after the training (24). Simulation training has been reported to increase the self-confidence and self-satisfaction of students in other studies as well (25-27).

In a study conducted by Basak et al. (28) in 2018, with the aim to develop the hygienic care skills of first-grade nursing students, the satisfaction and self-confidence scores of the students in the standardized patient group were found to be significantly higher than the students in the simulator group.

A student is generally a passive listener in the classical training method but participates actively during training with a standardised patient. This gives them a more active role in the training process together with increased performance and self-confidence. Traditional training is usually teacher-centred and learning is only superficial. The simulation method enables students to learn from their mistakes, thus allowing them to observe the natural consequences of their mistakes, contrary to the clinical practice.

An important point of our study was the feedback of the students after the debriefing session. The debriefing session is one of the main building blocks of simulation-based training (29). Using debriefing sessions in simulation training has been reported to help systematic learning with the students experiencing less anxiety afterwards (30,31).

Conclusion

Our results indicate that training nursing students with a standardized patient makes a positive contribution to the knowledge scores, self-confidence and satisfaction of the students on providing care to patients under contact isolation. We recommend enabling nursing students to practice with a standardized patient before clinical training and integrating simulation training to the curriculum in all nursing schools. Similar future studies on larger student groups and using a control group could also help reinforce our conclusions.

Ethics

Ethics Committee Approval: This study was approved by the university Ethics Committee on 22 February 2017 (Decision no: 10).

Informed Consent: All participants signed an informed consent form prior to the study.

Peer-review: Internally peer reviewed.

Authorship Contributions

Concept: Ç.K., H.T., Design: Ç.K., H.T., Data Collection or Processing: Ç.K., Analysis or Interpretation: Ç.K., H.T., Literature Search: Ç.K., Writing: Ç.K.

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

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Original Article

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The Effect of Vitamin D3 on Skeletal Muscle in Rat after Ischemia Reperfusion Injury: Preliminary Report

Sıçan İskelet Kasında İskemi Reperfüzyon Hasarı Sonrası Vitamin D3'ün Etkisi: Ön Çalışma

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ABSTRACT

Objective: Vitamin D is a vitamin that has gained popularity in recent years and has an anti-inflammatory and immunmodular effect. In the literature review we conducted, there was no study investigating the effect of vitamin D to prevent ischemia reperfusion (I/R) injury in skeletal muscle. The aim of this study was to investigate the effect of vitamin D on skeletal muscle in I/R injury.

Methods: Six rats were used in each group including ischemia group (group I) and experimental group (group D given vitamin D). In the histopathological examination, inflammation and apoptosis levels were studied in gastrocnemius muscle. In biochemical analysis, total oxidative stress and total antioxidant and catalase levels were evaluated in anterior tibialis muscle.

Results: The number of apoptotic cells in group D were found significantly lower than group I. In the terms of total antioxidants and catalase levels, there were significant difference between group D and group I.

Conclusion: Our results support the hypothesis that vitamin D is an agent that can be used to prevent I/R injury.

Keywords: Vitamin D, ischemia-reperfusion injury, skeletal muscle

ÖZ

Amaç: Vitamin D, son yıllarda giderek popülarite kazanan ve anti-enflamatuvar ve immünomodülatör etkiye sahip bir vitamindir. Yaptığımız literatür taramasında iskelet kasında iskemi reperfüzyon (İ/R) hasarını önlemeye yönelik vitamin D'nin etkisini inceleyen bir çalışma bulunamamıştır. Çalışmamızda; iskemi reperfüzyon hasarında vitamin D'nin iskelet kası üzerindeki etkisinin araştırılması amaçlanmıştır.

Yöntemler: İskemi grubu ve deney grubu (D vitamin verilen) olmak üzere her grupta 6 adet, toplam 12 adet sıçan kullanılmıştır. Histopatolojik incelemede gastroknemius kasında enflamasyon, apopitozis düzeyi araştırıldı. Biyokimsayal analizde ise anterior tibialis kasında total oksidatif stres, total antioksidan ve katalaz seviyelerine bakıldı.

Bulgular: Apoptotik hücre sayısının, D vitamin uygulanan grupta kontrol grubuna göre anlamlı olarak daha az olduğunu saptandı. Katalaz ve total antioksidan seviyeleri açısından Grup D ve Grup İ arasında anlamlı fark saptanmıştır.

Sonuç: Bu çalışmada iskelet kası İ/R hasarına vitamin D'nin olumlu yönde etki gösterdiği saptanmıştır.

Anahtar Sözcükler: Vitamin D, iskemi-reperfüzyon hasarı, iskelet kası

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Introduction

In reconstructive surgery, flaps are used to repair complex tissue defects due to trauma or tumor ablation. Despite surgical and technical advances, flap losses are still an ongoing clinical problem. One of the most important causes of this loss is ischemia reperfusion (I/R) injury. Therefore, experimental and clinical studies are ongoing to increase flap survival in plastic surgery (1-3). Numerous agents have been used experimentally to reduce the effects of I/R injury (4). Vitamin D, on the other hand, is a vitamin that has role especially bone metabolism and has anti-inflammatory and immunomodulatory effects, and its other effects have been investigated in recent years. In particular, its effect on recovery after muscle damage has been shown. In the literature review we conducted, no study investigating the effect of vitamin D to prevent I/R injury in skeletal muscle was found. The purpose of this study was to investigate the effect of vitamin D on skeletal muscle after I/R injury.

Method

Group Selection

This study was approved by Bezmialem Vakıf University Animal Care and Use Committee with the decision number 2015-126 and all protocols were carried out in accordance with the National Institute of Health Guidelines for the Care and Use of Laboratory Animals. In the study, a total of 12 Sprague-Dawley genus 280-370 g female rats, 6 in each group, were used with a: 95% and b: 80% confidence level. Rats were obtained from Bezmialem Vakıf University Animal Center and randomly divided into two groups. Rats were fed with standard feed and care was provided in accordance with day and night rhythm.

Experiment Protocol

Rats were divided into two groups as n=6. Ketamine hydrochloride (35 mg/kg IM) and xylazine hydrochloride (5 mg/kg IM) were applied as anesthetic to 6 rats in Group I (ischemia group). A 4.6 mm x390 mm plastic clamp tourniquet (Würth®, Gaisbach, Germany) was applied to right back limb of the rat and tightened until distal pulses could not be obtained and pale leg was observed. Blood flow ceased for 4 hours. After the ischemia, the blood flow was restarted and for the next 7 days, intraperitoneal 0.05 mL of saline was injected. The left posterior extremities of the rats in the ischemia group in which ischemia was not created were named as Group C (control group). In Group D (experimental group) tourniquet was applied to right posterior extremity of 6 rats and blood flow was cut for 4 hours. Blood flow after ischemia was started again for the next 7 days and intraperitoneal 0.5 mg/kg/day vitamin D3 (Devita-3®, Deva, İstanbul, Turkey) was injected. The left posterior limbs of the rats in the experimental group without ischemia were named as Group DC. The rats in both groups were given ketamine hydrochloride (35 mg/kg IM) and xylazine hydrochloride (5 mg/kg IM) as anesthetic after 7 days. Both posterior limb gastrocnemius and anterior tibialis muscles to be used in the examination were taken. The animals were then sacrificed using ether anesthesia. In histopathological examination, inflammation in the gastrocnemius muscle and apoptosis level (Tunel method), and total oxidative stress and total antioxidant levels in the anterior tibialis muscle were examined.

Histological Examination

For histological examination, the gastrocnemius muscle was completely taken and fixed in 10% neutral buffered formalin for 72 hours. Tissues were dehydrated by passing through rising alcohol series (70%, 90%, 96%, 100%), made transparent with xylene, kept in 60 °C paraffin overnight and embedded in paraffin. Sections prepared 5 µm thick from paraffin blocks were stained with Hematoxylin-Eosin (H&E) stain for morphological evaluation. Stained sections were examined and viewed with Nikon Eclipse i5 (Tokyo, Japan) light microscope with Nikon DS-Fi1c (Tokyo, Japan) camera attachment and NIS Elements version 4.0 image analysis system (Nikon Instruments Inc, Tokyo, Japan).

TUNEL Method

It is the labelling of apopitotic cells in situ. Five µm thick sections taken on the positive charged slides were deparaffinized with xylene, passed through the descending alcohol series, rehydrated and washed with PBS. The TUNEL method was performed according to the method in the user manual provided by the manufacturer (Apoptag Plus Peroxidase In situ apoptosis Kit, Chemicon International, S7101). The sections taken were kept in Proteinase K (20 µg/mL, Sigma) for 15 minutes. After washing with distilled water, the sections were left in 3% hydrogen peroxide prepared in PBS for 5 minutes, washed with PBS and left for 30 minutes in equilibration buffer. Then all sections were kept in 37 °C oven for 1 hour with terminal deoxynucleotidyl transferase (TdT) enzyme and incubated for 10 minutes at room temperature in wash buffer. After washing 3 times for 1 minute in PBS, it was kept in the anti-digoxigenin conjugate for 30 minutes. It was washed 4 times in PBS with each for 2 minutes. It was washed 4 times in PBS for 2 minutes each. After the sections were kept in peroxidase substrate for 6 minutes for staining, they were washed 3 times for 1 minute each in distilled water, stained with Mayer Hematoxylin and closed with entellan. TUNEL positive cells were counted on images taken at x200 magnification in 5 similar areas randomly selected by shifting the preparation clockwise in each section.

Biochemical Analysis

Measurement of Catalase Activity (CAT)

Catalase is one of the antioxidant enzymes that neutralize free oxygen radicals after I/R injury. Skeletal muscle CAT activity was determined using the colorimetric method described by Goth in which H_2O_2 substrate was incubated, and the enzymatic reaction was stopped by the addition of ammonium molybdate. The density of the yellow complex formed by molybdate and H_2O_2 was measured at 405 nm.

Measurement of Total Antioxidant Status (TAS)

The TAS value of the supernatant fractions was determined using a new automatic measurement method developed by Erel

(5). In this method, hydroxyl radicals, the strongest biological radicals, are produced. In the experiment, the ferrous ion solution contained in Reagent 1 is mixed with the hydrogen peroxide present in Reagent 2. Later produced radicals, like brown dianicidinyl radical cations produced by hydroxyl radicals, are also strong radicals. Using this method, the antioxidative effect of the sample is measured against weak radical reactions initiated by the hydroxyl radicals produced.

The analysis has excellent sensitivity values which are less than 3%. The results are expressed in the "nmol Trolox Equiv./mg protein" unit.

Measurement of Total Oxidant Status

The total oxidant status (TOS) value of the supernatant fractions was determined using a new automated measurement method developed by Erel (6). The oxidants present in the sample oxidize the iron ion-odianidine complex to the ferric ion. The oxidation reaction is enhanced by glycerol molecules that are abundant in the reaction medium. The iron ion makes a colored complex with xylenol orange in an acidic environment. The color density, which can be measured spectrophotometrically, is related to the total amount of oxidant molecules in the sample. The analysis is calibrated with hydrogen peroxide and the results are expressed in "nmol H_2O_2 Equiv./mg protein" unit.

Statistical Analysis

Statistical analysis was done using Graph-Pad Prism 5.0 (GraphPad Software, San Diego, CA, USA) program. One-Way ANOVA method and Tukey test were used for statistical analysis. $p<0.05$ was considered significant. (*): $p<0.05$, (**): $p<0.01$, (***): $p<0.001$ and (****): $p<0.0001$ (Table 1).

Results

TUNEL positive labelled cells were not found in muscle tissue in Group C and Group DC, which were extremities without ischemia (Figure 1 A, B). A large number of TUNEL positive labelled cells were observed to be dark brown in Group I (Figure 1C). It was observed that the number of TUNEL positive labelled cells in Group D was lower compared to Group I (Figure 1D). While the number of apoptotic cells was 1±0.4 in Group C, it was 1±0.3 in Group DC, 159±6 in Group I and 147±5 in Group D. Compared to Group C and DC, the number of apoptotic cells increased significantly in Group I and Group D ($p<0.0001$). Compared to Group I (159±6), a significant decrease was observed in Group D (147±5) (Table 2). When examined in terms of CAT, enzyme level was significantly increased in group D (21.17±10.83) compared to group I (0.18±0.02) ($p<0.0001$).

Table 1. $p<0.05$ was considered significant. (*): $p<0.05$, (**): $p<0.01$, (***): $p<0.001$ and (****): $p<0.0001$

Catalase		
Tukey's multiple comparisons test	Significance	p value
Group C vs. Group I	*	0.0206
Group I vs. Group D	***	0.0004
TAS		
Tukey's multiple comparisons test	Significance	p value
Group C vs. Group D	*	0.0331
Group DC vs. Group D	*	0.0254
Group I vs. Group D	**	0.0092
TOS		
Tukey's multiple comparisons test	Significance	p value
Group C vs. Group I	*	0.0376

TAS: Total antioxidant status, TOS: Total oxidant status, (*): $p<0.05$, (**): $p<0.01$, (***): $p<0.001$ and (****): $p<0.0001$

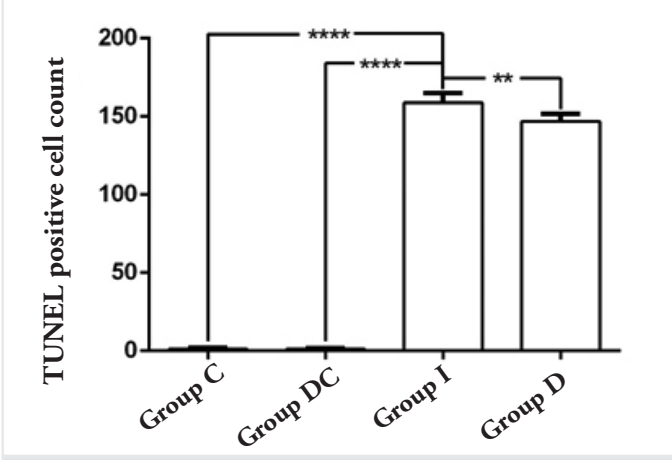

Table 2. Graph of TUNEL positive cells with statistical analysis between groups

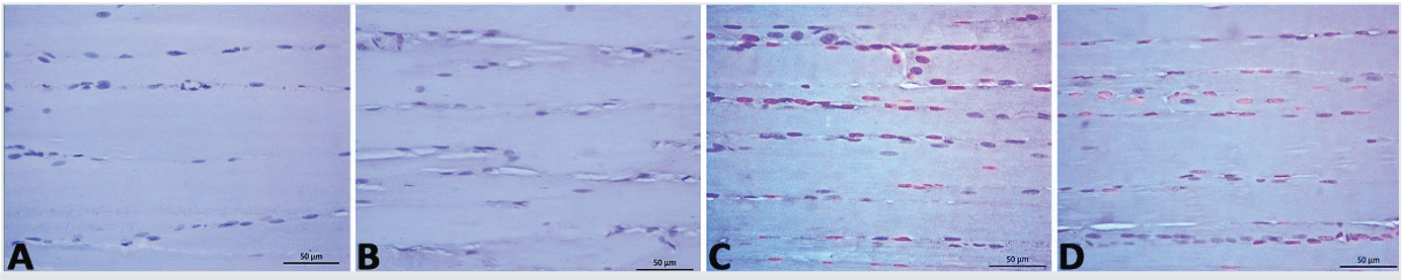

Figure 1. Preparations stained by TUNEL method. There are no TUNEL positive cells in Group C (A) and DC (B). There are many positive stained cells in Group I (C). With the increase in the number of positive stained cells in Group D, fewer stained TUNEL positive cells are seen compared to Group I

When examined in terms of TAS, a significant difference was found between group D (0.33±0.24) and group I (7.2±2.89) ($p<0.01$). When examined in terms of TOS, no significant difference was found between group D (9.94±3.61) and group I (7.29±2.34) ($p>0.05$).

Discussion

Vitamin D is an oil-soluble vitamin that is taken orally and absorbed from the intestines and synthesized by the skin with the effect of the sun. The liver converts circulating vitamin D into 25-hydroxycholecalciferol [25 (OH) D2]. This prehormone is then metabolized by the kidneys into the active form of vitamin D (1 alpha, 25 dihydroxyvitamin D [1.25 (OH) D2]). Although there is evidence that vitamin D has effects on myogenesis, muscle function and muscle strength, its effect on the injured muscle is largely unknown (7).

The I/R injury occurs when tissues restore molecular oxygen after ischemia. It can occur as a result of broad spectrum vascular events such as transplantation, thrombolytic therapy, limb trauma and cardiovascular surgery. If the ischemic tissue is as large as the legs, I/R injury may not only be local, but also may involve distant organs. It may affect organs such as skeletal muscle and cause death (3,8). Reactive oxygen radicals and metabolites are formed as a result of chemotactic stimuli. During reperfusion, inflammatory mediators are produced by ischemic tissues, and this causes leukocyte migration and adhesion. As a result, endothelial damage and impaired microvascular integrity; causes edema, thrombosis and tissue necrosis (1). Numerous studies have been done to reduce I/R injury with small molecules, proteins, cytokines, and drugs (1-4). It has been claimed that antioxidants such as vitamins A, C or E and selenium increase endogenous oxidative defenses to prevent cellular injury mediated by reactive oxygen species (1,2). Use of plasma rich platelet has been found to be beneficial in the skin flap I/R injury model in mice (2).

This level of exposure is also associated with factors such as energy demand of tissue. The tissue with the least tolerance to ischemia in all extremity tissues is skeletal muscle (4 hours). Nerve tissue can withstand ischemia for 8 hours, adipose tissue 13 hours, skin 24 hours, and bone tissue for 4 days (9). Especially in plastic surgery routine, ischemic conditions can be seen in tissues after replantations, free and pedicled flap surgery. Skeletal muscle is the most susceptible tissue to ischemia and I/R injury effects can occur more quickly and severely. As a result of ischemia, injury begins and this injury increases with reperfusion paradoxically, and muscle and other tissues are affected by this injury. Antioxidant enzymes such as CAT (catalase), SOD (superoxide dismutase) and glutathione peroxidase are produced as defense mechanisms against ROS molecules. Oxidant and antioxidant activities balance themselves in all physiological processes. Disruption of this balance towards pro-oxidant activity causes dangerous damage to functional tissues and organs. Free radicals attack polyunsaturated fatty acids in the cell membrane, but antioxidants prevent and stop free radical activity against lipid peroxidation. Free radicals can change the biological structure and property of molecules such as proteins, lipids, carbohydrates, and DNA. Antioxidants can remove oxygen-derived radicals by delaying the peroxidation process of polyunsaturated fatty acids. As a result, the human body can be protected against injury due to free radicals and reactive oxygen species (ROS)by antioxidants (3). The use of antioxidant substances, hesperidin and ellargic acid, has been observed to have positive antioxidant effects on induced skeletal muscle I/R injury in rats (3). It has been shown that colchicine significantly reduces levels of malondialdehyde, tumor necrosis factor-alpha and interleukin-1 beta (IL-1β), and that increases SOD activity in injured muscle tissues, and that reduces peroxidation and inflammatory cytokine levels in skeletal muscle I/R injury created in rats (10).

The efficacy of many antioxidants that reduce or prevent I/R injury has been demonstrated by experimental animal studies. Melatonin (11), vitamin E, superoxide dismutase, catalase, mannitol, allopurinol, iron chelating compounds, angiotensin converting enzyme inhibitors, calcium channel antagonists, N-acetylcysteine are some of them (12). Vitamins, including A, C, D and E, have been found valuable in preventing I/R injury, especially in clinical and animal models. Vitamins reduce the damage caused by superoxide, the most common free radical, by protecting the enzyme superoxide dismutase. Among them, 1,25 dihydroxyvitamin D3 (vitamin D3) has also been investigated. These studies have shown that vitamin D3 inhibits *in vitro* production of IL-6, increases regulator T cells and their immune tolerance (13).

While vitamin D is most often associated with bone growth and healing, new studies have identified a much broader spectrum of activity. Vitamin D deficiency has been associated with metabolic changes, oxidative stress and fibrosis. There are promising studies that vitamin D treatment increases regeneration in injured muscles. It has been shown to promote cardioprotection after myocardial infarction with anti-inflammatory, anti-fibrotic and antiapoptotic mechanisms (14). It has been shown that it is a supportive agent in the treatment of hepatocellular carcinoma and that it improves I/R injury in the lungs, kidneys and muscles (15,16). There is limited knowledge about the effect of vitamin D on local and distant tissue damage and systemic inflammation after I/R injury (13).

Vitamin D affects intracellular regulatory phosphates by clinging to its receptors in skeletal muscle cells and maintaining cellular proliferation and differentiation. In muscle biopsies taken from people with low vitamin values, it was observed that muscle tissues were more atrophic (17). A significant relationship was found between rotator cuff muscle tears and vitamin D level (17). Shih et al. (13) Showed that local muscle edema was decreased with vitamin D3 treatment in the rat model, where they investigated the effect of lung and muscle damage after ischemia created by clamping bilateral femoral vessels; however in that study, the mechanism of inhibition of local tissue damage could not be demonstrated. That study differs from our study due to the administration of vitamin D before I/R injury (13).

In previous studies, vitamin D levels were not measured before administration and were given systemically (13,15-17).

The dose of vitamin D in our study was adjusted in accordance with the method Shih et al. (13) previously used while investigating the effects of I/R injury on skeletal muscle.

Although there is a consensus that vitamin D is beneficial, its effects on muscle regeneration and whether it induces cellular response against ischemia are unknown, and this issue is still controversial. Vitamin D has been found to show anti-apoptotic properties for injured muscle tissue by increasing the level of insulin-like growth factor-1 (7).

The fact that CAT enzyme level and TAS value were higher in the vitamin D group was interpreted as vitamin D increased the protective mechanism of action. We believe that the lower levels of apoptotic cells in the group given vitamin D supports the biochemical result and indicates that fewer cells are affected. We consider the low number of subjects in the groups as one of the weaknesses of this study. Although the difference between the two groups is statistically significant, we think that it should be correlated with the studies with higher number of subjects. It supports our hypothesis that vitamin D is an agent that can be used to limit the effects of I/R injury.

As a result, in this study, it was determined that vitamin D had a positive effect on skeletal muscle I/R injury. We believe that there is a need for new studies with groups that have a higher number of subjects in terms of duration and dose adjustment and have been subjected to ischemia for different periods.

Ethics

Ethics Committee Approval: Bezmialem Vakıf University Animal Care and Use Committee with the decision number 2015- 126.

Informed Consent: No need for experimental work.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: O.K., A.Y., Ç.Y., Design: O.K., O.E.T., Ö.F.Ö., Data Collection or Processing: O.K., O.E.T., Ö.F.Ö., M.E., A.K., Analysis or Interpretation: O.K., A.Y., E.G., O.E.T., Ö.F.Ö., Ç.Y., Literature Search: O.K., A.Y., K.Y., Writing: O.K., A.Y., K.Y.

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

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Original Article

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Investigation of Activity, Participation and Quality of Life in Elderly Living in Ankara and Antalya Provinces

Ankara ve Antalya İllerinde Yaşayan Yaşlılarda Aktivite, Katılım ve Yaşam Kalitesinin İncelenmesi

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ABSTRACT

Objective: This aim of this study was to investigate the relationship between activity, participation and quality of life in the elderly living at home.

Methods: This study was applied to 120 elderly people (60 females, mean age: 71.4±5.3 years; 60 males, mean age: 70.8±4.7 years, ranged between 65-83 years) aged 65 years and older and living at their home in Ankara and Antalya. The community participation levels were assessed with World Health Organisation Disability Assessment Schedule, Second Version (WHO-DAS-II). Canadian Occupational Performance Measure (COPM) was used to evaluate the activity performance of participants. The elderly's quality of life levels were assessed with Health Survey Questionnaire Short Form-36 (SF-36).

Results: The important daily living activities of participants in which they had problems were: Cooking (n=52), shopping (n=48), having a shower (n=38) and praying (salaat) (n=37). According to the results of WHO-DAS-II, COPM and SF-36, there were no statistical differences between gender groups ($p>0.05$). There was a moderate significant negative correlation between the sub-scores of COPM and total score of WHO-DAS-II ($p<0.05$). Also, There was a weak-strong significant negative correlation between all sub-parameters of SF-36 and WHO-DAS-II total score and community participation sub-parameter ($p<0.05$).

Conclusion: Our study showed that the community participation of elderly people living in the home increased with the increase in

ÖZ

Amaç: Çalışmamızın amacı; evde yaşayan yaşlıların aktivite, katılım ve yaşam kalitesi düzeyleri arasındaki ilişkiyi incelemektir.

Yöntemler: Çalışmamız Ankara ve Antalya illerinde, kendi evlerinde yaşayan 65 yaş ve üstündeki 120 yaşlı bireyde (60 kadın, ortalama yaş: 71,4±5,3yıl; 60 erkek, ortalama yaş: 70,8±4,7yıl; yaş aralığı: 65-83 yıl) gerçekleştirildi. Toplumsal katılım düzeyleri, Dünya Sağlık Örgütü tarafından geliştirilen Yetiyitimi Değerlendirme Çizelgesi-II (WHO-DAS-II) ile değerlendirildi. Katılımcıların aktivite performanslarını değerlendirmek için Kanada Aktivite Performans Ölçümü (KAPÖ) kullanıldı. Yaşlıların yaşam kalitesi düzeyleri Kısa Form-36 (KF-36) Sağlık Taraması Anketiyle değerlendirildi.

Bulgular: Katılımcıların günlük yaşamlarında performans problemi yaşadıkları önemli aktiviteler; yemek yapma (n=52), alış-veriş yapma (n=48), duş alma (n=38) ve namaz kılma (n=37) aktiviteleriydi. WHO-DAS-II, KAPÖ ve KF-36 değerlendirme ölçeklerinin sonuçlarında cinsiyetler arasında istatistiksel olarak anlamlı bir fark tespit edilmedi ($p>0,05$). KAPÖ'nün alt puanları ile WHO-DAS-II'nin toplam puanı arasında istatistiksel olarak orta derece negatif yönde anlamlı bir ilişki bulundu ($p<0,05$). KF-36 ile WHO-DAS-II arasındaki ilişkiyi incelediğimiz zaman ise KF-36'nın bütün alt parametreleriyle WHO-DAS-II'nin toplumsal katılım alanı ve toplam puanı arasında istatistiksel olarak zayıf-güçlü derece negatif yönde anlamlı bir ilişki olduğu tespit edildi ($p<0,05$).

Sonuç: Çalışmamızda, evde yaşayan yaşlı bireylerin aktivite performanslarının artmasıyla toplumsal katılımlarının arttığı,

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their activity performance, and their quality of life increased with their increased community participation. Future studies should be designed to investigate the effects of environmental factors and different living conditions on activity, participation and quality of life of elderly individuals.

Keywords: Elderly, participation, activity, quality of life

toplumsal katılımlarının artmasıyla da yaşam kalitelerinin arttığı yönünde sonuçlar elde edilmiştir. Gelecekteki çalışmalar çevresel faktörlerin ve farklı yaşam koşullarının geriatrik bireylerin aktivite, katılım ve yaşam kalitesi üzerine etkilerini araştırmak amacıyla tasarlanmalıdır.

Anahtar Sözcükler: Yaşlı, katılım, aktivite, yaşam kalitesi

Introduction

Aging is an inevitable part of life cycle and it is a normal process which has chronological, psychological and social dimensions, is characterized by progressive physiological changes, and is associated with increased rate of acute and chronic diseases (1,2). Aging is a deficiency condition accompanied by different diseases, in which physiological, morphological and pathological changes occur, and physical, mental and spiritual abilities in the individual change negatively (3). One of the impenetrable results of aging is the decrease in the biological capacity of the person. With aging, some changes occur in all tissues, organs and system functions. Due to the changes in the muscular and skeletal systems, respiratory system, nervous system, cardiovascular system and metabolism in old age, geriatric individuals are restricted from their activities in their daily lives or they have difficulty in performing these activities (4,5).

Old age is the last stage in the development of people. In this period, all features of aging become visible (6). In old age, there is a decrease in participation in activity, a decrease in positive emotions, a decrease in quality of life and a limited community participation (7). Although it is generally accepted that the participation of elderly individuals in community life is decreasing, their needs for community participation are similar to those of middle-aged individuals. In this context, the decrease in community participation, which is one of the consequences of old age, is a result of the decrease in the interaction of other individuals in the society with older individuals (8).

One of the conditions of being healthy is to participate in an activity and be able to do it properly and correctly. It has been concluded that participation in activities supports people to feel healthy and better (6). Very few elderly people who live at home and do not participate in regular activities feel healthy. Participating in daily life activities or entering a social creation process makes individuals feel healthy (9). Activity performance and community participation of older adults are particularly important. Because, with aging, the participation of adults in many activities and tasks decreases with negatively affected health (8). Community participation and activity performance is important for the quality of life in general among elderly individuals (10).

Old age, which is an inevitable phase, can be turned into a quality and fun time. One of the most fundamental rights of people is to take equal advantage of all the opportunities offered by social life (11). Like every person, older individuals should be equal and participatory in all areas of social life. Being in life makes one feel important and develop, socioculturally (10). Participation in meaningful and purposeful activities ensures the continuity of health and quality of life. Participation in social and physical activity reduces the risk of mortality, improves quality of life and increases survival rate (12). When the literature is examined, there are studies examining the activity preferences, community participation levels and life satisfaction of the elderly. It is seen that these studies are generally done in nursing homes. At the same time, it has been observed that these studies have not examined community participation, activity performance and quality of life levels together (6,13,14).

Inadequacy and restrictions may occur in old age. Due to this limitation and inadequacy, there is a general acceptance that the participation of elderly individuals in community life, their activity performance and quality of life have been impaired (13). From this point of view, examining the community participation, quality of life and activity performances of elderly people living at home will be important in terms of learning their roles in social life. For this reason, the purpose of our study was to examine the community participation, activity performance and quality of life levels of the elderly living at home and to reveal the relationship between them.

Methods

This study was approved by the Clinical Research Ethics Committee of Akdeniz University Faculty of Medicine (70904504/85, decision no: 178). All elderly people included in the study were given detailed information about the study and their written consent was obtained before the evaluation. Our study was carried out cross-sectionally in Ankara and Antalya between February 2019 and May 2019, in individuals aged 65 and over who lived in their own homes.

Criteria for inclusion in the study were; (1) being 65 years old or older, (2) living in a home, (3) functionality not affected by a disease or disability diagnosed by the doctor, (4) having 24 points or more points in the Standardized Mini Mental Test. Exclusion criteria were; (1) not agreeing to participate in the study, (2) having undergone surgery in the past 6 months, (3) having a diagnosis of chronic disease such as neurological, rheumatological, psychiatric, orthopedic disorders and cancer, and (4) having an advanced communication problem due to mental and cognitive problems.

Community participation levels of elderly individuals living in the home environment were evaluated using the World Health Organisation Disability Assessment Schedule, Second Version

(WHO-DAS-II). The Turkish validity and reliability study of WHO-DAS-II was done by Uluğ et al. (15). In this evaluation schedule, how much difficulty the individual has had during the last month is determined and it is completed in 20 minutes. In scoring, field scores and total score are evaluated over 100. The low value of each field and the total score indicates that the participation is higher (16).

Canadian Occupational Performance Measure (COPM) was used to evaluate the activity performances of the participants from their own perspective. The Turkish validity and reliability study of COPM was performed by Torpil et al. (17). COPM is an interview that helps identify problems in activity performance. COPM is a measurement that evaluates the activity performance in self-care, productivity and leisure time and how satisfied they are with this perspective from one's own perspective. COPM focuses on the activities that are wanted or needed by the individual and in which the individual has a performance problem. Firstly, the importance of each activity, as perceived by the individual, is evaluated on a 10-point scale. In the next step, the individual is asked to choose the activities that are most important to him/her and score the performance and satisfaction levels separately for these activities. The performance and satisfaction scores obtained are totaled separately and the total performance and satisfaction scores are calculated by dividing the performance and satisfaction scores with the number of activities which are stated important by individual (18).

The quality of life levels of the elderly individuals who participated in the study were evaluated with the Health Survey Questionnaire Short Form-36 (SF-36). SF-36, which was launched in 1992 and could evaluate both positive and negative aspects of health status, could be completed in five minutes. The scale includes 36 items and they provide evaluation of 8 dimensions; physical functionality, social functionality, pain, general health, energy/vitality, physical role weakness, emotional role weakness and mental health. The last 4 weeks are taken into consideration when evaluating with SF-36. The scale does not only give a single total score, it gives different results for each subscale. Results evaluate health between 0 and 100 points, and 0 indicates poor health, while 100 indicates a good health (19,20). The Turkish reliability and validity study of the SF-36 was conducted by Koçyiğit et al. (21).

Statistical Analysis

The data obtained in our study were analyzed statistically using Windows based SPSS (IBM SPSS Statistics, Version 23.0, Armonk, NY, USA) package program. The sample group was calculated using GPower V.3.1.7 (University of Kiel, Kiel, Germany). The number of individuals to be included in the study was determined to be 78 according to 80% power and 95% confidence interval (13). Analytical (Kolmogorov-Smirnov / Shapiro-Wilks test) and visual (Histogram and probability graphs) methods were used to test the normal distribution of the data. Descriptive statistics were given as mean ± standard deviation ($\bar{x}$ ± SD) and %. In order to measure the statistical significance of the difference between male and female elderly people, t-test was used for independent groups in normally distributed data groups. Sperman Correlation Analysis was used to analyze the relationship between community participation, activity performance and quality of life levels. In the evaluation of the relationship, the relationship was accepted as weak if the correlation coefficient was 0-0.24, moderate if it was 0.25-0.49, strong if it was 0.50-0.74, very strong if it was 0.75-1.00 (22). Multiple linear regression analysis was performed between the community participation and the model created with independent variables that were significant. In our study, statistical significance level was accepted as $p<0.05$.

Results

In our study, 60 (50%) females aged between 65 and 83, with a mean age of 71.4±5.3 years, and 60 (50%) males with a mean age of 70.8±4.7 years (a total of 120 elderly individuals) were included. Forty seven (39.17%) of the participants were primary school graduates and 11 (9.17%) were university graduates. Ninety seven (80.83%) of the elderly individuals who participated in the study were retired. The right extremities of 116 (96.7%) participants were dominant. While 101 (84.17%) of the participants stated that they lived with their spouse, only 7 (5.83%) of the participants stated that they lived alone. Other descriptive information of the elderly individuals included in the study is given in Table 1.

When the important activities that the participants experienced performance problems in their daily lives were examined, it was found that taking a shower (n=38) in the self care area, cooking

Table 1. Descriptive features of the elderly

Variables	n=120	%
Gender		
Female	60	50
Male	60	50
Education level		
Illiterate	8	6.67
Literate	19	15.83
Primary school	47	39.17
Secondary school	33	27.5
University	11	9.17
Postgraduate	2	1.67
Place of residence		
Apartment	109	90.83
Separate	11	9.17
Home layout		
Lone	7	5.83
Leaving with partner	101	84.17
Living with relatives (child, brother, sister nephew, etc.)	12	10
Income level		
<2000 TL	78	65
>2000 TL	42	35

(n=52) in the productivity area, and praying (n=37) in the leisure activities area were at the forefront (Table 2).

When all sub-parameters and total score of WHO-DAS-II were compared by gender, no significant difference was found between male and female participants (p>0.05). Total performance, total satisfaction, and total score in COPM were found to be similar in female participants compared to male participants (p>0.05). There was no statistically significant difference between sub-parameters of SF-36 in terms of gender (p>0.05).

Table 2. Activities that participants have performance problems according to the canadian occupational performance measure

COPM	n	%
Self care area		
Having a shower	38	31.67
Praying	37	30.83
Shaving	22	18.33
Walking	21	17.50
Getting dressed	19	15.83
Cutting nail	16	13.33
Performing wudu	14	11.67
Productivity area		
Cooking	52	43.44
Shopping	48	40.00
Cleaning	33	27.50
Washing the clothes	31	25.83
Ironing	30	25.00
Using mobile phones	28	23.33
Using computer	20	16.66
Going to work	13	10.83
Leisure activities area		
Hand making	25	20.83
Visiting relatives	21	17.50
Visiting friends	16	13.33
Driving a car	14	11.67
Reading books	8	6.67
Watching TV	7	5.83
Playing backgammon/ playing cards	3	2.50

When we examined the relationship between community participation and activity performance, a statistically moderately negative correlation was found between total performance, total satisfaction and total scores of the COPM and the total score of WHO-DAS-II (p<0.05) (Table 3). When we examined the relationship between community participation and quality of life, a statistically weak negative correlation was found between SF-36's pain parameter and WHO-DAS-II's community participation area and total score; a statistically moderately negative correlation between SF-36's physical functionality, social functionality, general health and mental health parameters, and WHO-DAS-II's community participation area and total score; and a statistically strong negative correlation was found between SF-36's energy/vitality, physical role weakness and emotional role weakness and WHO-DAS-II's community participation area and total score (p<0.05) (Table 4).

As a result of the multiple linear regression analysis performed with the total score of WHO-DAS-II and with the model created with COPM's total performance, total satisfaction and total score, and SF-36's physical functionality, social functionality, pain, general health, energy/vitality, physical role weakness, emotional role weakness, and mental health sub-parameters, all of which were found significant in univariate analysis; COPM's all scores and SF-36's sub-parameters were found to have an independent effect on community participation (p<0.05). Accordingly, a negative correlation was found between all scores of COPM and all sub-parameters of SF-36 and the total score of WHO-DAS-II (p<0.05) (Table 5).

Discussion

In our study, which was planned to examine the community participation, activity performance and quality of life levels of elderly people living at home and to reveal the relationship between them; it was shown that community participation was increased with the increase in activity performance and

Table 3. Examining the Relationship Between WHO-DAS-II Results and COPM Scores

	COPM					
WHO-DAS-II	Total performance score		Total satisfaction score		Total score	
	rho	p	rho	p	rho	p
Understanding and building relationships	-0.132	0.288	-0.019	0.881	-0.089	0.473
Mobility	0.010	0.935	-0.193	0.118	-0.083	0.503
Self care	-0.149	0.188	-0.047	0.611	-0.079	0.302
Human relationship	-0.159	0.198	-0.069	0.577	-0.129	0.298
Life activities	-0.335	0.017	-0.188	0.127	-0.291	0.017
Community participation	-0.138	0.301	-0.027	0.776	-0.301	0.027
Total	-0.354	0.003*	-0.302	0.013*	-0.355	0.003*

COPM: Canadian Occupational Performance Measure, WHO-DAS-II: World Health Organisation Disability Assessment Schedule, second version; *p<0.05

Table 4. Investigation of the Relationship Between WHO-DAS-II Sub-Parameters and SF-36 Results

WHO-DAS-II	SF-36																	
	Physical functionality		Social functionality		Pain		General health		Energy / vitality		Physical role weakness		Emotional role weakness		Mental health	
	rho	p	rho	p	rho	p	rho	p	rho	p	rho	p	rho	p	rho	p
Understanding and building relationships	-0.138	0.222	-0.218	0.054	0.114	0.315	-0.217	0.053	-0.030	0.793	-0.207	0.065	-0.150	0.183	-0.192	0.088
Mobility	-0.136	0.228	-0.207	0.065	-0.190	0.091	-0.210	0.061	-0.085	0.518	-0.130	0.322	-0.229	0.078	-0.024	0.853
Self care	0.002	0.983	-0.121	0.285	-0.030	0.793	-0.207	0.065	-0.118	0.369	-0.210	0.061	-0.182	0.165	-0.229	0.078
Human relationship	0.002	0.983	-0.121	0.285	-0.136	0.228	-0.080	0.542	-0.216	0.097	-0.229	0.078	-0.136	0.228	-0.182	0.165
Life activities	-0.133	0.311	-0.207	0.113	-0.150	0.183	-0.030	0.793	-0.207	0.065	-0.080	0.542	0.024	0.857	-0.224	0.085
Community participation	**-0.300**	**0.007***	**-0.454**	**0.000***	**-0.236**	**0.035***	**-0.287**	**0.010***	**-0.527**	**0.000***	**-0.633**	**0.000***	**-0.517**	**0.000***	**-0.396**	**0.000***
Total	**-0.494**	**0.000***	**-0.470**	**0.000***	**-0.221**	**0.048***	**-0.374**	**0.001***	**-0.574**	**0.000***	**-0.673**	**0.000***	**-0.544**	**0.000***	**-0.426**	**0.000**

SF-36: Health Survey Questionnaire Short Form-36, WHO-DAS-II: World Health Organisation Disability Assessment Schedule, second version, *p<0.05

that quality of life was increased with increasing community participation. Evaluation of all the community participation, activity performance and quality of life of elderly people living at home and showing the interactions between them were the main differences that distinguished our study from other studies.

The concept of community participation is multidimensional. It is important what individuals do, their personal preferences, interests, how and where they do it, how much they have fun and are satisfied (11). Community participation levels increase by ensuring the participation of elderly individuals in various activity groups in basic and auxiliary daily life activities, ensuring that the elderly are productive and socialized and that the sense of isolation in them decreases (6). Person, activity and environmental factors are related to each other and these factors should be taken into consideration while examining community participation. As for all people, community participation is very important for the elderly who live at home. In studies on community participation, participation has been shown to be effective on quality of life and general well-being (11,23-25). Decrease in community participation does not only adversely affect physical health, it also affects the person emotionally and psychologically (26).

It has been shown that the activity preference and participation in the elderly individuals are generally associated with the socioeconomic status and health level, therefore, regardless of the activity performance area, the quality of life and community participation of the elderly who continue their performance and participation in the activities they choose are higher (24). Göktaş et al. (6) stated that the most affected activity performances

Table 5. Examining the relationship between community participation and variables

	Unstandardized beta	Standardized beta	p
Constant	63.572		**0.00***
COPM Total performance score	-0.956	-0.192	**0.00***
COPM Total satisfaction score	-0.873	-0.186	**0.00***
COPM Total score	-0.673	-0.094	**0.00***
SF-36 Physical functionality	-0.163	-0.332	**0.00***
SF-36 Social functionality	-0.094	-0.333	**0.00***
SF-36 Pain	-2.063	-0.137	**0.02***
SF-36 General health	-0.483	-0.082	**0.00***
SF-36 Energy/vitality	-3.092	-0.135	**0.00***
SF-36 Physical role weakness	-4.652	-0.127	**0.00***
SF-36 Emotional role weakness	-2.193	-0.173	**0.00***
SF-36 Mental health	-1.984	-0.393	**0.00***

COPM: Canadian Occupational Performance Measure, SF-36: Health Survey Questionnaire Short Form-36, *p<0.05

among the geriatric individuals were in activities including cleaning, praying, visiting and shopping, respectively (6). In a study conducted on the elderly in the nursing home, it was found that the activity of taking a bath was expressed as the most common problem and praying as the second most common problem (27). In parallel with these two studies, the most difficult and problematic activities of the elderly were cooking (n=52), cleaning (n=33), shopping (n=48), taking a shower (n=38), and praying (salaat) (n=37) in our study. While performing these activities, it has been shown in the literature that muscle strength and endurance are needed and there is a decrease in lower and upper extremity muscle strength and endurance along with aging (28,29). Göktaş et al. (6) has stated that the reasons for having problem while performing activities such as cooking, shopping, praying and cleansing are; less movement due to the decrease in muscle strength and endurance; not having people living with them and supporting them; and getting not enough support (6). In our current study, we thought that the reason for the presence of activities such as ironing (n=30), washing clothes (n=31), shopping (n=48) and driving (n=14), which we identified as different activities that the participants had problems with, was that geriatric individuals living at home had to fulfill their responsibilities themselves. At the same time, in our study, it was seen that the most important problem of elderly people living in their homes was taking shower (n=38). We think that this is due to the fear and danger of falling because of the difficulty of taking the necessary support during the shower from the family members or their relatives, and due to the wet shower area which is considered not a safe area.

When we examined the relationship between the community participation and activity performances of the elderly individuals included in the study, a statistically significant relationship was found between the total performance, total satisfaction and total score of the COPM and the total score of the WHO-DAS-II. Pino et al. (26) stated in their studies in 2014 that participation in the activity and performance in the activity increased the level of community participation of the person. In studies where it has been shown that appropriate physical activity and social activity in older individuals have increased their community participation, it has also been shown that participation in activity also poses a low risk for dementia by preventing cognitive decline (30,31). Salar et al. (23) determined in their study on 55 elderly individuals living in their homes in 2016 that their participation in activities that were important and meaningful for them and their environment affected the participation levels of elderly individuals. Similar to these studies, it was found that the level of community participation was positively affected by the increase in activity performance in our study. In a study conducted in 2010 that supported our current work with this aspect, Kayıhan et al. (32) found that there was a relationship between activity performance and environmentally compatible behavior, and that the level of participation of individuals increased with the increase in activity performance and that they lived more socially. Likewise, there are also studies showing that as the general well-being of individuals increases, their activity performance increases and thus their community participation levels increase (11,24,26,33).

In our current study where we examined the relationship between community participation and quality of life; there was a statistically significant relationship between community participation field and the total score of WHO-DAS-II and the parameters of SF-36 including physical functionality, social functionality, pain, general health, energy/vitality, physical role weakness, emotional role weakness and mental health. Meaningful activities and participation in the elderly are important for the continuity of quality of life (23). Human beings continue their health and quality of life as long as they continue to participate in activities that have meaning and purpose for themselves. Participation in daily life activities and free time activities has been stated to be the most important parameter of being a part of the society as well as maintaining the personal well-being (26). In this way, it was found that the quality of life of elderly individuals increased (26). In a study where community participation was evaluated with WHO-DAS-II and quality of life with SF-36, it was shown that the level of quality of life was positively affected by the increase in community participation (11). In a study examining the functional status and quality of life levels of a total of 164 elderly individuals; as the Tinetti score increased, an increase in the physical functionality and mental health scores of the SF-36 quality of life scale was detected (25). In a study conducted with 283 participants with an average age of 71.11±7.74 years and examining the factors affecting the quality of life of the elderly living in their homes, it was found that as the functional independence of the elderly was restricted and their participation levels decreased, their quality of life decreased (2). As shown in the other studies, it was shown that the quality of life increased with the increase in community participation of elderly people living at home in our study. With the preparation of person-centered rehabilitation programs for elderly individuals living in their homes, we think that the quality of life levels can be changed positively by increasing the self-care, productivity, leisure activities and community participation levels of elderly individuals.

Study Limitations

One of the limitations of our study was that it was conducted with healthy elderly people living in Ankara, the capital city of our country, in Antalya, one of the leading cities of tourism, and in city centers. Also, the fact that the elderly living in the nursing homes were not included in our study as a separate group could be among the limitations of our study. In addition to these limitations, we think that the data obtained from the participants may yield different results in similar studies that will be performed in other cities, districts or villages.

Conclusion

Our results show that necessary interventions should be made in order to increase the quality of life of elderly people living in the home, to increase community participation which is not enough and to increase their activity performance. Necessary measures must be taken to prevent the isolation of elderly people living at home. In this context, it is very important to make plans that support healthy aging processes of geriatric individuals. However,

we think that the data obtained from our study may contribute to geriatric rehabilitation studies that can be planned to increase the level of community participation, activity performance and quality of life of the elderly living in the home.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of Akdeniz University Faculty of Medicine (70904504/85, decision no: 178).

Informed Consent: Their written consent was obtained before the evaluation.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

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

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

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Original Article

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Investigation of the Effects of Isotretinoin on Spermatogenesis in Balb/c Mice

Balb/c Cinsi Farelerde İzotretinoinin Spermatogenez Üzerine Etkilerinin Araştırılması

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ABSTRACT

Objective: It was aimed to investigate the effect of isotretinoin (ISR), a retinoid derivative of vitamin A, on spermatogenesis via follicle-stimulating hormone (FSH), luteinizing hormone (LH) and testosterone levels.

Methods: Twelve male Balb/c mice were divided into two groups: Control and ISR groups. FSH, LH and testosterone levels were biochemically determined by ELISA assay. All statistical analyses were made with SPSS 20.0 (IBM, New York, USA) and graphics were prepared with Graph Pad Prism Version 6.01 (USA). The parametric Student's t-test was applied for comparison among groups. A p value ≤0.05 was accepted as statistically significant.

Results: Mean FSH, LH and testosterone levels were increased in the ISR group when compared to those of control group. The increases in all hormone levels were found statistically significant between the two groups ($p<0.05$).

Conclusion: The increase in serum levels of FSH, LH and testosterone of the ISR group compared to the control group suggests that a dose of 40 mg/kg of ISR may have stimulant effect on spermatogenesis.

Keywords: Isotretinoin, follicle stimulating hormone, testosterone, luteinizing hormone, Balb/c mice

ÖZ

Amaç: Vitamin A'nın bir retinoid türevi olan izotretinoinin (ISR) spermatogenez üzerindeki etkisinin follikül stimüle edici hormon (FSH), luteinize edici hormon (LH) ve testosteron seviyeleri üzerinden araştırılması amaçlandı.

Yöntemler: Bu çalışma 12 adet Balb/c cinsi 3 aylık erkek fare ile gerçekleştirildi. Deney grupları kontrol (n=6) ve ISR (n=6) olmak üzere ikiye ayrıldı. Serum örneklerinde FSH, LH ve testosteron seviyeleri ELISA yöntemiyle belirlendi. Tüm analizler ve grafikler için SPSS 20,00 (IBM, New York, USA) ve Graph Pad Prism Version 6,01 (USA) programları kullanıldı. İstatistiki karşılaştırılmalarda parametrik student t-testinden yararlanıldı. Anlamlılık seviyesi $p\leq0,05$ olarak kabul edildi.

Bulgular: ISR grubunda ortalama FSH, LH ve testosteron seviyelerinde kontrol grubuna göre artış belirlendi. Bu artış her üç hormon için de iki grup arasında istatistiksel açıdan anlamlı bulundu ($p<0,05$).

Sonuç: ISR grubunda kontrol grubuna kıyasla serum FSH, LH ve testosteron seviyelerindeki artış, ISR'nin 40 mg/kg dozunun spermatogenezi uyarıcı bir etkiye sahip olduğunu düşündürdü.

Anahtar Sözcükler: İzotretinoin, follikül stimüle edici hormon, testosteron, luteinize edici hormon, Balb/c fare

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Introduction

Vitamin A, also known as retinol, is stored in cells called lipocyte or Ito cells localized in the perisinusoidal space of the liver (1). It activates retinol, which is inactive in the liver, in the target tissues. Its active form in tissues is called retinoic acid (2). It is known that vitamin A and retinoic acid have many important functions in the organism such as growth, reproduction, embryogenesis, differentiation and proliferation of cells, and paradoxically high doses have a teratogenic effect (3-5). Gonadotropins, steroid hormones, somatic cells of testis and vitamin A play an important role in the regulation of spermatogenesis (6). Vitamin A is required for fertility and normal spermatogenesis (7). During spermatogenesis, vitamin A is effective in differentiation of type A spermatogonia to type A1 spermatogonia, initiation of meiosis division, release of spermatozoa into the lumen of germinal epithelium of seminiferous tubules and formation of tight connections that participate in the blood testicle barrier (8-14).

Follicle stimulating hormone (FSH), luteinizing hormone (LH) and testosterone play an important role in the hormonal regulation of spermatogenesis (7). While FSH provides development of spermium from spermatogonium, LH affects Leydig cells and provides testosterone release. The high levels of these hormones in serum indicates that spermatogenesis has begun and continues.

There are studies suggesting that isotretinoin, one of the 5 known isomers of retinoic acid, may have an inductive effect on spermatogenesis depending on the dose (15,16). Based on this information, in our study, we aimed to examine FSH, LH and testosterone levels in serum to evaluate the spermatogenesis stimulating or suppressive effect of 40 mg/kg dose of isotretinoin in Balb/c mice.

Methods

Study Groups

In our study, a total of 12 Balb/c 3-month-old male mice were used, 6 in each group. During the 6-week experiment, all mice were fed ad libitum.

A dose of 40 mg/kg ISR (Alfa Aeser, J61666, Massachusetts, USA) dissolved in 0.1 ml of dimethyl sulfoxide (DMSO) + saline solution (SS) was given daily by oral gavage for 6 weeks (5,17). The control groups were administered 0.1 ml DMSO + SS, the ISR solvent, during the experiment. At the end of the experiment, blood samples were taken from the heart for biochemical analysis under anesthesia administered intraperitoneally with 5 mg/kg xylazine and 80 mg/kg ketamine.

Study methods were approved by Bezmialem Vakif University Experimental Animals Local Ethics Committee with decision number 2013-237.

Biochemical Analysis

Blood samples from the study groups were taken into heparinized tubes by cardiac puncture. Material taken into biochemistry tube was centrifuged at 3000 x g for 10 minutes. The obtained serum was taken into the Eppendorf tube and kept at -80 °C until the measurement day.

Biochemical analyzes were performed on the plate reader (Thermo Scientific Multiskan FC, 2011-06, USA) using Enzyme-Linked Immunosorbent Assay (ELISA) method, using kits suitable for studying mouse serum samples. Levels of testosterone (Catalog No ADI-900065, ENZO Life Sciences, Plymouth, PA), FSH (Catalog No MyBioSource Inc., USA, MBS2507988) and LH (Catalog No MyBioSource Inc., USA, MBS041300) in serum samples were measured and all results were evaluated statistically. All biochemical analyzes were carried out through service procurement.

Statistical Analysis

The suitability of the normal distribution was determined by the Shapiro-Wilk test. According to this test, since the data with a p value greater than 0.05 fit the normal distribution, the difference between groups was compared with the student t-test, which was one of the parametric tests. The p value indicating the significance level was 0.05 in the 95% confidence interval. Average data of all analysis results were given with standard deviations. In comparisons with a p value below 0.05, the difference between the groups was considered statistically significant. All statistical analyzes were done with SPSS 20.0 (IBM, New York, USA) program and graphics were prepared with Graph Pad Prism 6 program.

Results

The mean testosterone hormone level in the control group was 18.05±1.01 pg/mL and this value was found to be 30.05±1.33 pg/mL in the ISR group. This increase in testosterone level in the ISR group was also statistically significant (p=0.004; Figure 1).

The FSH level was similarly higher in the ISR group (10.83±0.26 ng/mL) than the control group (6.41±0.48 ng/mL), (p=0.002; Figure 2). A significant increase was observed in the LH level in the ISR group (7.54±0.34 mlU/mL) compared to the control group (4.74±0.45 mlU/mL), (p=0.002; Figure 3).

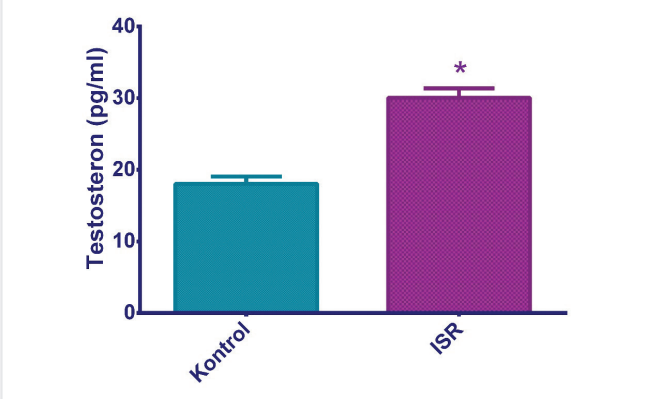

Figure 1. Average testosterone levels of experimental groups are shown (*p<0.05, ISR: isotretinoin)

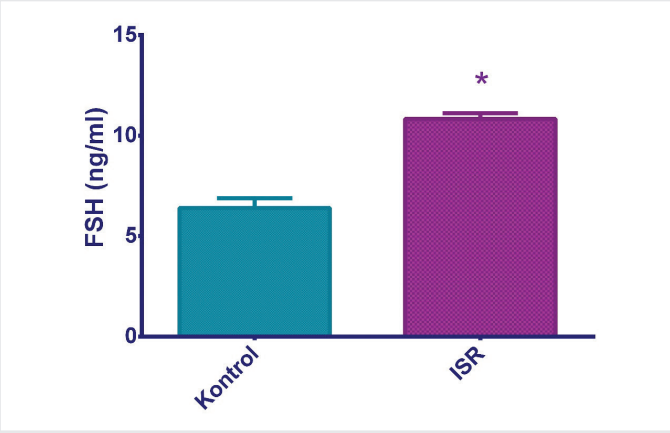

Figure 2. Average FSH levels of experimental groups are shown (*p<0.05, ISR: isotretinoin)

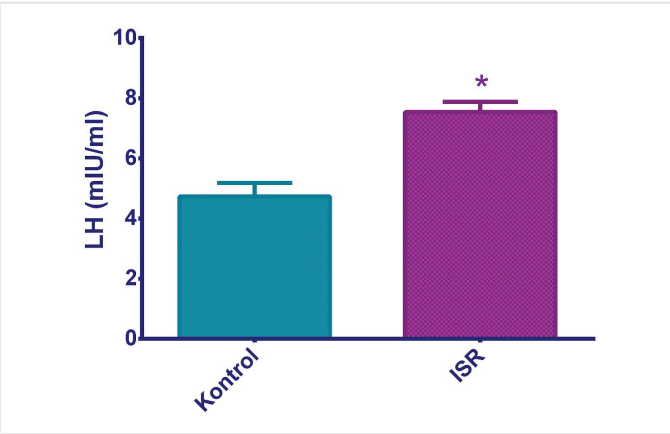

Figure 3. Average LH levels of experimental groups are shown (*p<0.05, ISR: isotretinoin)

Discussion

Spermatogenesis that occurs in testicle tubules together with puberty is the event that spermatogonia divide and differentiate and form spermatids (1,18). Endocrine control of spermatogenesis takes place through hormones synthesized from Sertoli and Leydig cells, which are somatic cells of testis, and gonadotropins and steroids. It has been noted that these cells have retinoic acid receptors and Vitamin A has an agonistic effect in their activation (7,11,12). FSH, LH and testosterone hormones have direct and indirect effects on spermatogenesis that takes place by meiosis (6). While FSH is necessary for stimulating spermatogenesis, testosterone is functional in maintenance (7). In order for testosterone to function, it must be stimulated by LH (1,6). Vitamin A and its metabolite retinoic acid are very critical for spermatogenesis (13,14,18). In the studies investigating the effects of vitamin A and its metabolites on spermatogenesis, highly controversial data have been revealed.

Vitamin A is very important for the production of spermatozoa. In its deficiency, it has been observed that germ cells degenerate, testosterone is under-synthesized and spermatogenesis stops (19-22). On the contrary, high doses have also been shown to be teratogenic, reduce testicular mass, disrupt the usual process of spermatogenesis and adversely affect Leydig cells (5,15,16,23). In addition, it was observed that spermatogenesis was normal and was not different compared with the control groups after an 8-week experiment in rats administered 40 mg/kg dose of isotretinoin (24).

In a study, rats fed a diet devoid of vitamin A were found to have a higher FSH level compared to the control group, as well as a decrease in LH and testosterone levels. In the same study, it was revealed that there was no change in FSH levels in the group given vitamin A at a dose of 1 mg for 60 days, LH increased, but testosterone remained low (25). These findings are also highly controversial. Although there are no different studies showing that vitamin A deficiency or deprivation has an inducing effect on FSH level, there is no clear scientific explanation for those findings. In another study investigating the effects of retinoic acid on rat Leydig cells in cell culture, retinoic acid was shown to increase testosterone and LH synthesis (26). In our study, it was determined that there was a significant increase in the level of all three hormones in the group we applied isotretinoin at a dose of 40 mg/kg without any restriction in the diet of the experimental groups ($p<0.05$). In a clinical study, it was stated that FSH, LH and testosterone levels did not show any change in patients who received isotretinoin treatment at a dose of 0.5-1 mg/kg for 6 months compared to the control groups (27). We think that this difference may be due to the genetic variation between the species, the duration and dose of treatment in patients, and the duration and dose of treatment in experimental animals.

Conclusion

The significant increase in FSH, LH and testosterone levels in the ISR group compared to the control group in our study suggests that isotretinoin induces spermatogenesis. We think that non-toxic doses of isotretinoin may be beneficial for patients who have a low sperm count due to disruptions in the spermatogenesis process and who are at risk of sterility or have sterility.

Ethics

Ethics Committee Approval: Study methods were approved by Bezmialem Vakıf University Experimental Animals Local Ethics Committee with decision number 2013-237.

Peer-review:

Authorship Contributions

Concept: M.K., Design: M.K., Data Collection or Processing: M.K., Analysis or Interpretation: M.K., M.E., Literature Search: M.K., Writing: M.K., M.E.

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

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Original Article

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How The Nurses' Attitude for Dying Patients and Their Knowledge about Palliative Care?

Hemşirelerin Ölmekte Olan Hastaya ilişkin Tutumları ve Palyatif Bakım Hakkındaki Bilgi Durumları Nasıldır?

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ABSTRACT

Objective: To determine nurses' level of knowledge when it comes to palliative care as well as to investigate their attitudes regarding the care of terminally ill patients.

Methods: This descriptive and cross-sectional study was conducted with the voluntary participation of 350 nurses in three major hospitals affiliated to the General Secretariat of the Union of Public Hospitals of Sakarya. Data were gathered via a Self-description Form, the Frommelt Attitudes Toward Care of Dying scale (FATCOD), and Palliative Care Knowledge Test (PCKT), and analysis was conducted using percentages and average scores as well as the Mann-Whitney U, Kruskall-Wallis H and Pearson's correlation tests.

Results: The nurses, whose age average was 35.58±7.63 years, were predominantly female (84.3%). More than half of them were married (60.9%), nearly half of them were university graduates (51.4%), and 62.9% of them work in Internal Diseases units. The nurses' average PCKT score was 6.35±3.31 and their average FATCOD score was 77.98±8.81. Marital status, level of education, and their employment units did not affect the attitudes towards death ($p>0.05$) but they did affect palliative care knowledge levels.

Conclusion: In the study, it was determined that palliative care knowledge levels of nurses were low and their attitudes toward care giving to terminally ill people were at the medium level.

Keywords: Attitude, death, knowledge, nurses, palliative care

ÖZ

Amaç: Çalışma hemşirelerin palyatif bakım hakkındaki bilgi düzeylerini ve ölmekte olan hasta bakımına ilişkin tutumlarını belirlemek amacıyla yapıldı.

Yöntemler: Tanımlayıcı ve kesitsel özellikte planlanan çalışma, kurum izni ve etik kurul onayı alındıktan sonra, Sakarya İli Kamu Hastaneleri Birliği Genel Sekreterliği'ne bağlı üç hastanede çalışan 350 hemşireyle yapıldı. Sosyo-demografik özellikleri içeren tanıtım formu, Frommelt Ölmekte Olan Bireye Bakım Vermeye İlişkin Tutum ölçeği (FATCOD) ve Palyatif Bakım Bilgi Testi (PBBT) ile toplanan verilerin analizi bilgisayar ortamında yüzdelik, ortalama, Mann-Whitney U, Kruskall-Wallis H ve Pearson's korelasyon testleri kullanılarak yapıldı.

Bulgular: Yaş ortalaması 35,58±7,63 olan hemşirelerin %84,3'ü kadın, %60,9'u evli, çoğunluğu lisans mezunu (%51,4) ve %62,9'u dahili birimlerde çalıştığı belirlendi. Hemşirelerin PBBT'den aldıkları ortalama puan 6,35±3,31, FATCOD puan ortalaması ise 77,98±8,81 olduğu saptandı. Medeni durum, öğrenim düzeyi ve çalışılan birim hemşirelerim ölüme ilişkin tutumlarını etkilemezken palyatif bakım bilgi düzeylerini etkilediği görüldü.

Sonuç: Çalışmada hemşirelerin palyatif bakım bilgi düzeylerinin düşük ve ölmekte olan bireye bakım vermeye ilişkin tutumlarının orta düzeyde olduğu saptandı.

Anahtar Sözcükler: Tutum, ölüm, bilgi düzeyi, hemşireler, palyatif bakım

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Introduction

The World Health Organization defines palliative care as "an effort that improves the quality of life of patients and their families facing problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual."(1). Palliative care accepts death as a normal part of life and aims at managing how patients actively spend their lives until death. With palliative care, the patient is provided with counseling and a peaceful death in the last moments of life and the family also receives appropriate counseling services (1-3).

The number of people worldwide who are 60 or older is increasing, especially in developed countries. In the 1950s, 8% of the population were 60 or older population. This is now 12% and it is predicted that this number will reach 21% in 2050 (4). Along with the increase of the elderly population, it is thought that chronic diseases will increase and that in 2020, the most common diseases will remain heart diseases, cerebrovascular diseases, chronic respiratory diseases, respiratory infections, and lung cancers (5). The gradual increase in the population of the elderly and chronic diseases around the world ensures that palliative care will retain an important place among medical practices. The aim of the palliative care is to increase the quality of life of individuals suffering chronic diseases that affect their lives and those of their families (6). Recent developments in medical science have increased life spans and delayed times of death. With scientific and medical developments, many diseases have been prevented or their appearance is delayed, but other methods that patients and relatives use in order to ensure survival affect the patients' quality of life negatively (7). In addition to this, multiple problems can occur as a result of a decrease in treatment options and the progression of diseases, inadequate control of pain and other symptoms, and failure to provide the necessary technical support (8). An increase in the treatment options related to a disease or, alternatively, a lack of action may cause problems in terms of the quality of care given to patient in the last stage of their lives. In order to remove or lessen these issues, palliative care is necessary to increase patients' quality of life and for their relatives to develop coping strategies (1). Caring for a dying patient is one of the responsibilities of health professionals, especially nurses, who tend to spend more time with patients. Nurses can be emotionally affected by the process of giving care to terminally ill patients as death generally affects individuals deeply and painfully. Nurses, who are the primary members of the medical team which provides palliative care, are expected to support the patient's family before death and posthumously during the grieving process as well as support their general well-being in psychosocial terms (9,10). In fulfilling these expectations, both the attitudes of nurses towards death and their level of knowledge of palliative care play a huge role. In this context, this study intended to determine the knowledge level of nurses with regard to palliative care and to investigate their attitudes towards terminally ill patients.

Method

This descriptive and cross-sectional study was conducted between November 2014 and April 2015 after consent had been received from the institution concerned and approval had been given by the Ethics Committee. The study universe was formed of a total of 684 nurses who were working in three major hospitals affiliated to the Public Hospitals Association in the center of Sakarya province: Sakarya Training and Research Hospital (460 nurses), Sakarya Yenikent State Hospital (156 nurses) and Sakarya Toyotasa Emergency Relief Hospital (68 nurses). The research dates and sample formed by these volunteer nurses (350 nurses) were valid in that nurses not on vacation during the research dates the nurses and none of the nurses had any communication problems.

Statistical Analysis

Data in this research were gathered via a Self-description Form, the Palliative Care Knowledge Test (PCKT) (11) and the Frommelt Attitudes Toward Care Of Dying scale (FATCOD) (12). Data input and evaluation was carried out in a computerized environment. The knowledge levels of nurses regarding palliative care and factors that affected their attitude related to care given to dying patients were presented as percentages and average scores. In comparative statistical analysis, the difference between the averages of the two groups was examined with the Mann-Whitney U test, the difference between 3 or more groups was examined with Kruskall-Wallis-H variance analysis, and the relation between the two numerical variables was analyzed with Pearson's correlation test.

Results

As shown in Table 1, 33.4% of nurses were between 35 and 44 years old, most nurses were female (84.3%) and more than half of them were married (60.9%). 51.4% of these nurses were college or university graduates and 62.9% of them worked in inpatient units. The period of employment of the majority of the participants (35.7%) was between 1 and 5 years.

It was found that more than half of the nurses had relatively good knowledge about palliative care (57.7%) gaining this either while getting their Bachelor's degrees (29.7%) or from the internet (17.7%). When the answers related to palliative care were examined, the most wrongly answered question (57.7%) was with regard to the statement, "Palliative care is only given to patients in the terminal stage." It was found that most of the nurses (62.6%) had given care to a terminally ill patient and/or confronted the concept of death (80.6%) (Table 2). It was also noted that 93.4% of the nurses experienced deep sadness while giving care to terminally ill patients and that 32.3% of them accepted death as a natural process when they first faced the fact of the patients' death (not given in the table).

While no significant statistical difference was found between the marital status of nurses and FATCOD on the one hand, and PCKT Psychiatric Problems sub-dimension scores on the other ($p>0.05$), there was a substantial difference between PCKT

General, Philosophy, Dyspnea (p<0.05) and Gastrointestinal Problems sub-dimension scores. It was seen that single nurses had PCKT General (p<0.01), Philosophy (p<0.05), Dyspnea (p<0.05) and Gastrointestinal Problems (p<0.01) sub-dimension average scores that were higher than those of the married ones.

A statistically significant difference was determined between the workplace variable and PCKT general (p<0.001), philosophy (p<0.01), pain (p<0.01) and psychiatric problems (p<0.001) sub-dimension scores. According to this result, it was observed that nurses who worked in inpatient units had a greater knowledge of general, philosophy, pain and psychiatric problems subjects related to palliative care than nurses who worked in surgical units (Table 4).

On the other hand, a statistically significant difference was noted between the ages of nurses and the PCKT general (p<0.01), philosophy (p<0.01) and gastrointestinal problems (p<0.01) sub-dimension scores. In particular, nurses who were in their mid-twenties and younger had higher scores, but no effect of age was found in relation to Pain, Dyspnea and Psychiatric Problems sub-dimensions and FATCOD scores (p>0.05)(Table 4).

There was no substantial difference when regard to the education variable and PCKT Philosophy, Gastrointestinal Problems sub-dimension and FATCOD scores (p>0.05). However, a statistically significant difference was found between PCKT general, pain, dyspnea and psychiatric problems sub-dimension scores (p<0.05). It was seen that the PCKT General scores of nurses who had graduated from an HVH (Health Vocational High School) were higher than the PCKT scores of nurses who had an Associate degree. In the sub-dimensions of Dyspnea and

Table 1. Frequency and percent results of the demographic characteristics of the nurses ınvolved in the survey (n=350)

Characteristics	n (%)
Age	
25 years old and lower	101 (28.9)
Between 26 - 34 years	113 (32.3)
Between 35 - 44 years	117 (33.4)
45 years old and over	19 (5.4)
Gender	
Women	295 (84.3)
Men	55 (15.7)
Marital status	
Married	213 (60.9)
Single	137 (39.1)
Education level	
Vocational health highschool	79 (22.6)
Associate degree	91 (26.0)
Bachelor/master degree	180 (51.4)
Working unit	
Internal units	220 (62.9)
Surgical units	130 (37.1)
Vocational working time	
Between 1-5 years	125 (35.7)
Between 6-10 years	76 (21.7)
Between 11-15 years	55 (15.7)
16 years and over	94 (26.9)

Table 2. Characteristics of palliative care and dying patient care (n=350)

Characteristics of palliative care and dying patient care		n (%)
Knowledge situation related to palliative care	Yes	202 (57.7)
	No	148 (42.39)
Knowledge acquisition type*	Undergraduate education	104 (29.7)
	Inservice training	51 (14.6)
	Book and magazines	27 (7.7)
	Congress/symposium/ seminar	19 (5.4)
	ınternet	62 (17.7)
	Other	20 (5.7)
Statements related to palliative care	Yes	99 (28.3)
PC is only given to cancer patients	No	251 (71.7)
PC is a treatment that applied fort o increase life time	Yes	139 (39.7)
	No	211 (60.3)
PB is only implemented to patients in terminal stage	Yes	202 (57.7)
	No	148 (42.3)
In PC, only paint control is done	Yes	121 (34.6)
	No	229 (65.4)
Encountering death concept at work	Yes	282 (80.6)
	No	68 (19.4)
Care giving status or dying patient	Yes	219 (62.6)
	No	131 (37.4)

Table 3. Distribution of nurses' overall scores of palliative care's general and lower dimensions and attitudes related to the care of the frommelt dying patient (n=350)

Scales and sub dimensions	M ± SD	Min - max point
Palliative care general	6.35±3.31	0-14
Philosopy sub dimension	1.21±0.82	0-2
Pain sub dimension	1.70±1.09	0-5
Dyspnea sub dimension	0.73±0.88	0-4
Psychiatric problems sub dimension	1.49±1.01	0-4
Gastrointestinal problems	1.20±0.98	0-4
Frommelt attitudes toward care of dying scale	77.98±8.81	54-100

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

Psychiatric Problems, it was determined that HVH graduate nurses had higher scores than nurses who had Bachelor's and associate degrees. It was noted that the period of professional employment affected the PCKT general, philosophy, dyspnea and gastrointestinal problems sub-dimension scores in a statistically meaningful way (p<0.01), and that nurses who had worked for 1 to 5 years had higher average scores than those who had worked for 16 years and over. Educational level and period of employment were determined to have no effect on the attitudes of nurses towards the care of terminally ill patients (Table 4).

Nurses who had encountered death in the units where they worked had better knowledge levels in the palliative care general, pain and dyspnea sub-dimensions (p<0.05); those who provided care to terminally ill patients also had better knowledge levels in the PCKT General (p<0.01), Philosophy (p<0.01), Pain (p<0.01), Psychiatric Problems (p<0.001) and Gastrointestinal Problems

Table 4. Attitude and palliative care knowledge level on the dying care according to socio-demographic characteristics (n=350)

Characteristics	FATCOD (Frommelt attitudes toward care of dying)	PCKT (Palliative care scale)	Philosophy	Pain	Dyspnea	Psychiatric problems	Gastrointestinal problems
Marital status							
Married (213)	173.22	162.03	164.44	169.10	165.31	167.90	163.46
Single (137)	179.05	196.45	189.59	185.46	191.34	187.31	194.22
	z=-0.526	**z=-3.12**	**z=-2.25**	z=-1.53	**z=-2.56**	z=-1.82	**z=-2.90**
	p=0.599	**p=0.002****	**p=0.024***	p=0.125	**p=0.010***	p=0.069	**p=0.004****
Working unit							
Internal units (220)	177.93	191.45	186.44	186.86	180.80	197.35	182.60
Surgical units (130)	171.38	148.50	156.98	156.28	166.52	138.52	163.48
	z=-0.585	**z=-3.85**	**z=-2.84**	**z=-2.84**	z=-1.39	**z=-5.46**	z=-1.78
	p=0.558	**p=0.000*****	**p=0.004****	**p=0.004****	p=.163	**p=0.000*****	p=0.074
Age							
a-25 years and under	183.27	198.83	183.67	188.45	195.86	190.31	199.17
b-between 26-34 years	168.15	174.34	181.32	174.41	170.21	172.66	177.27
c-between 35-44 years	169.12	164.96	172.38	172.31	167.06	172.27	158.70
d-45 years and over	217.24	123.29	116.68	132.79	150.74	133.53	142.61
	x^2=4.89	**x^2=11.8**	**x^2=8.81**	x^2= 5.59	x^2= 7.57	x^2= 6.06	**x^2=11.8**
	p=0.179	**p=0.008****	**p=0.032***	p=0.133	p=0.056	p=0.107	**p=0.008****
Significant Difference Status	--	**a-d**	**a-d** **b-d**	--	--	--	**a-c**
Education Level							
a-VHH (79)	187.53	203.79	174.52	197.56	200.62	204.28	190.09
b- Associate degree (91)	178.74	158.36	166.27	153.21	161.57	166.81	164.77
c-Undergraduate/ graduate (180)	168.58	171.75	180.60	177.09	171.52	167.26	174.52
	x^2=2.05	**x^2=9.11**	x^2=1.42	**x^2=8.88**	**x^2=8.20**	**x^2=8.92**	x^2=2.94
	p=0.358	**p=0.010***	p=0.491	**p=0.012***	**p=0.017***	**p=0.012***	p=0.230
Significant difference status	--	**a-b**	--	**a-b**	**a-b** **a-c**	**a-b** **a-c**	--
Vocational working time							
a-1-5 years(125)	174.36	199.70	188.58	188.71	194.90	190.09	197.09
b-6-10 years(76)	167.32	175.71	187.44	181.98	159.83	170.40	183.23
c-11-15 years (55)	194.48	164.85	168.82	165.68	185.36	162.75	163.25
d-16 years (94)	172.53	149.37	152.36	158.44	156.60	167.68	147.71
	x^2=2.53	**x^2=14.1**	**x^2=9.67**	x^2=6.09	**x^2=12.2**	x^2=4.56	**x^2=15.3**
	p=0.469	**p=0.003****	**p=0.022***	p=0.107	**p=0.007****	p=0.207	**p=0.002****
Significant difference status	--	**a-d**	**a-d**	--	**a-d**	--	**a-d**

z: Mann-Whitney U, x^2: Kruskall-Wallis H testi *p<0.05, **p<0.01, ***p<0.001, VHH: Vocational Health Highschool

(p<0.01) Sub-dimensions, and those who had encountered death in their inner circle (family, relative, friend) had better knowledge in the PCKT general (p<0.01), pain, dyspnea and gastrointestinal problems sub-dimensions (p<0.05) (Table 5). It was determined that these variables did not affect their attitudes towards the care of terminally ill patients (p>0.05).

Meanwhile, it was found that nurses who saw palliative care as only applying to patients with cancer had lower knowledge levels in the PCKT general (p<0.01), philosophy (p<0.01), pain (p<0.01) and dyspnea (p<0.05) sub-dimensions, but they had more positive attitudes towards the care of terminally ill patients (p<0.001).

It was determined statistically that the scores of nurses who stated that palliative care is only given to patients who are in the terminal stage were significantly lower in the PCKT general (p<0.05), philosophy (p<0.05) and pain (p<0.01) sub-dimensions than the scores of those who did not think that it only to be given to patients in the terminal stage.

Discussion

Palliative care is a service that provides effective symptom management with the aim of improving the quality of life. The duty of providing effective palliative care basically falls to nurses. In order to carry out these responsibilities, a necessary level of knowledge about palliative care is expected from nurses. In many studies conducted, it has been found that nurses who work in multidisciplinary teams with a caring focus, do not have enough knowledge of palliative care (13-19). In this study, too, it was found that similar nurses did not have enough knowledge of palliative care (Table 3).

One of the most powerful aspects of nursing is encountering death and providing care to near-death patients. Nurses encounter death in settings where, on the one hand, they have to provide continuous professional nursing care, while on the other coping with the fact of death emotionally. Every individual's reaction towards death, as well as in caring for terminally ill patients, differs significantly according to one's personal attitude (7). Attitudes concerning the care of terminally ill patients affect the quality of care which nurses provide (9,20,21). In this study, the FATCOD average score (77.98±8,81) which shows attitudes towards the care of dying patients was found to be lower than in other studies conducted on the basis of FATCOD average scores (22-25). We think that this situation is due to cultural differences as well as educational differences in relation to end-of-life care and palliative care.

Table 5. Attitudes and palliative care knowledge level related to dying care according to features related to the concept of palliative care and dying patient care (n=350)

Features	FATCOD	PCKT	Philosophy	Pain	Dyspnea	Pyschiatric problems	Gastrointestinal problems
Encountering with death fact while working							
Yes	179.26	180.86	177.66	181.24	180.52	177.19	179.41
No	159.89	153.27	166.53	151.71	154.68	168.49	159.30
	z=-1.41	**z=-2.02**	z=-.879	**z=-2.24**	**z=-2.06**	z=-0.662	z=-1.54
	p=0.156	**p=0.043***	p=0.379	**p=0.025***	**p=0.039***	p=0.508	p=0.124
Status of care giving to dying patient							
Yes	169.60	192.42	192.84	187.73	181.10	191.70	185.30
No	185.36	147.21	146.51	155.06	166.15	148.42	159.11
	z=-1.41	**z=-4.06**	**z=-4.47**	**z=-304**	z=-1.46	**z=-4.02**	**z=-2.45**
	p=0.158	**p=0.000*** **	**p=0.000*** **	**p=0.002****	p=0.144	**p=0.000*** **	**p=0.014***
Palliative care is a service that only given for cancer Patients							
Yes	207.39	149.23	139.09	151.20	157.55	162.37	162.72
No	162.92	185.86	189.86	185.09	182.58	180.68	180.54
	z=-3.70	**z=-3.06**	**z=-4.56**	**z=-2.93**	**z=-2.27**	z=-1.58	z=-1.55
	p=0.000* **	**p=0.002****	**p=0.000*** **	**p=0.003****	**p=0.023***	p=0.113	p=0.120
Palliative care only implemented to patients who are in terminal stage							
Yes	179.17	165.23	166.33	163.54	169.97	169.63	171.44
No	170.49	189.51	188.02	191.82	183.05	183.51	181.04
	z=-0.794	**z=-2.22**	**z=-2.13**	**z=-2.68**	z=-1.30	z=-1.31	z=-0.917
	p=0.427	**p=0.026***	**p=0.032***	**p=0.007****	p=0.192	p=0.187	p=.0359

z: Mann-Whitney U, *p<0.05, **p<0.01, ***p<0.001

In the studies conducted, no significant difference was found between knowledge of palliative care, attitudes towards giving care to the dying patient and the variable of gender (13,16,19,22-26). Likewise, in the pertinent literature, no statistically significant difference was found between genders in terms of FATCOD, PCKT general and sub-dimension scores ($p>0.05$). A statistically significant difference was found between the marital status of nurses and PCKT general, philosophy, dyspnea and gastrointestinal problems sub-dimension scores. It was observed that single nurses had significantly higher PCKT general, philosophy, dyspnea and gastrointestinal problems sub-dimensions average scores than married ones (Table 4). We think that the reason for the higher PCKT scores is that most of the single nurses are younger and had less experience after their graduation, and that in recent years training related to palliative care has been included in the education curricula.

A statistically significant difference was detected between the place of employment variable and PCKT general, philosophy, pain and psychiatric problems sub-dimensions. Accordingly, it was observed that the knowledge of nurses who worked in inpatient units related to general, philosophy, pain and psychiatric problems was higher than that of those who worked in surgical units (Table 4). This situation may be due to the fact that those nurses deal with patients who stay longer in the clinics and have diseases that need palliative care. Similarly, in another study conducted, it was observed that nurses who worked in inpatient units had a better knowledge of palliative care (19).

In addition, in this study, a statistically significant difference was found between the variable of age and PCKT general, philosophy, gastrointestinal problems sub-dimension scores. By contrast, there was no statistically significant difference between pain, dyspnea and psychiatric problems sub-dimensions and FATCOD scores ($p>0.05$). According to this result, nurses in the 25 years or younger age group had higher PCKT average scores (Table 4). When the literature was examined, it was determined that this was similar to another study in which nurses under 29 years had higher PCKT average scores (11). In other studies, age did not affect level of knowledge of palliative care (16,17,19). It can be concluded that the reason for this difference is due to the relative novelty of the concept of palliative care and its recent inclusion in training, which results in the younger group having a higher level of awareness. Again, in studies similar to this current study, it was seen that age did not affect FATCOD scores (22,27).

In the study, it was determined that educational level did not affect PCKT philosophy, gastrointestinal problems sub-dimensions and FATCOD scores. However, it affected PCKT general, pain, dyspnea and psychiatric problems. Nurses who graduated from an VHH (Vocational Health Highschool) were found to have higher scores in comparison to nurses with Bachelor's and associate degrees (Table 4). In the study by Nakazawa et al. (11), it was also found that the PCKT scores of nurses who graduated from high schools were similar to those in the current study. In another study, it was observed that the average score of Associate degree graduates was higher than that of undergraduates and high school graduates (26). On the other hand, in many studies a positive relationship was determined between the educational level of nurses and their knowledge of palliative care (28-30). The reason for the higher scores of the HVH graduates in the present study is probably due to the fact that they had worked longer in the clinic, especially in the inpatient clinics, than those graduates with Associate and Bachelor's degrees. It was also determined that in other studies conducted to determine attitudes related to providing care to dying patients, educational status did not affect the attitudes of the nurses, and this shows parallelism with the present study (27,31).

While there was a statistically significant difference ($p <0.01$) between the duration of professional employment and PCKT general, philosophy, dyspnea and gastrointestinal problems sub-dimension scores, no significant difference was found between the other variables and FATCOD scores. Statistically, the nurses who had worked for 1-5 years were found to have higher scores on the PCKT general philosophy, dyspnea and gastrointestinal problems subscales than nurses working in this area for 16 years or more (Table 4). In another study, it was determined that nurses with less than 4 years of working experience had a better knowledge of palliative care (11). Similarly in another study, less experienced nurses (1-10 years) were found to be more knowledgeable about palliative care than those with 10-20 years of experience (15). In a similar study, it was seen that the duration of professional employment (FATCOD) did not affect attitudes related to providing care to terminally ill patients (24).

In the current study, it was determined that the variable of "experiencing death in the work place" affected the scores for the General, Pain and Dyspnea sub-dimensions related to palliative care ($p<0.05$). Those who had provided care to terminally ill patients had higher PCKT general, philosophy, pain, psychiatric problems and gastrointestinal problems sub-dimension scores that were statistically significant, compared to those who had not provided such care (Table 5). In many other studies, a positive relationship was determined between knowledge of palliative care and nurses' having encountered death, and having provided care to terminally ill patients (11,15,26,28,30). It is thought that experiences that gained through providing end-of-life care, which is part and parcel of palliative care, positively affect the nurses' level of knowledge and this tallies with the results of the current study. In a different study, it was seen that nurses who had encountered terminally ill patients and provided care to them had higher FATCOD scores than those who did not have such experience (25). It is thought that this difference is due to the fundamental differences found in the environments in which individuals live, receive education, work and provide this kind of care.

Conclusion

The main findings of this study, conducted to determine nurses' levels of knowledge and their attitudes towards providing care to terminally ill patients, are:

- Nurses were found to have a low level of knowledge of palliative care. However, their attitudes towards providing care to terminally ill patients were found to be positive.
- Taking into consideration the socio-demographic characteristics, marital status, education level, employment period and working unit, it was determined that having encountered death and provided care to terminally ill patients affected nurses' knowledge of palliative care, whereas it did not affect their attitudes when it came to providing care to terminally ill patients.

In light of these findings:

- There should be a constant evaluation of health professionals' levels of knowledge of palliative care and their attitudes towards providing care to terminally ill patients as well as the factors affecting these.
- Effective undergraduate or postgraduate education programs should be implemented in order to eliminate any inadequacies in knowledge of palliative care and develop positive attitudes towards death.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Faculty of Medicine of Sakarya University, Approval no.71522473/050.01.04/113.

Informed Consent: Written informed consent was not received due to the nature of this study.

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Authorship Contributions

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Original Article

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Investigation of Motor Abilities According to Gender in Children with Diplegic Cerebral Palsy

Diplejik Serebral Palsili Çocuklarda Cinsiyete Göre Motor Becerilerin İncelenmesi

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ABSTRACT

Objective: The aim of this study was to compare the fine and gross motor skills of children with diplegic cerebral palsy (CP) according to gender.

Methods: This study included 73 children with diplegic CP (39 males, mean age: 8.76±1.4; 34 females mean age: 8.29±1.31 years) aged between 6 to 12 years. Bruininks-Oseretsky Test 2-Short Form (BOT2-SF), consisting of 8 subtests and 12 items, was used to evaluate the gross and fine motor skills of children. Fine and gross motor skills of children with CP were compared with Student's t-test.

Results: According to gender, the BOT2-SF total score and fine motor precision, bilateral coordination and upper-limb coordination scores of sub-tests were statistically significant higher in girls than in boys ($p<0.05$).

Conclusion: The results of our current study reflect that fine and gross motor skills of girls with diplegic CP are better than boys. Physiotherapists and ergotherapists should first determine the fine and gross motor skill problems with objective measurement methods and especially consider the differences between genders when determining an integrated multi-factor therapeutic approach for children with diplegic CP.

Keywords: Diplegic, child, cerebral palsy, development, gender

ÖZ

Amaç: Bu çalışmanın amacı, diplejik serebral palsili (SP) çocuklarda cinsiyete göre ince ve kaba motor becerileri karşılaştırmaktır.

Yöntemler: Çalışmaya yaşları 6 ile 12 yaşları arasında değişen, 73 diplejik (39 erkek, ortalama yaş: 8,76±1,4; 34 kız ortalama yaş: 8,29±1,31) SP'li çocuk dahil edildi. Çocukların kaba ve ince motor becerilerini değerlendirmek için 8 alt test ve 12 maddeden oluşan Bruininks-Oseretsky Test 2- Kısa Form (BOT2-KF) kullanıldı. Kız ve erkek SP'li çocukların ince ve kaba motor becerileri Student t-testi kullanılarak karşılaştırıldı.

Bulgular: Cinsiyete göre BOT2-KF toplam skoru ve alt testlerinden ince motor doğruluk, bilateral koordinasyon ve üst ekstremite koordinasyon skorları kızlarda erkeklere göre istatistiksel olarak anlamlı derecede yüksekti ($p<0,05$).

Sonuç: Güncel çalışmamızın sonuçları, diplejik SP'li kız çocukların ince ve kaba motor becerilerinin erkeklerden daha iyi olduğunu yansıtmaktadır. Fizyoterapist ve ergoterapistlerin, diplejik SP'li çocuklar için çok faktörlü entegre terapatik bir yaklaşım belirlerken öncelikle çocukların ince ve kaba motor beceri problemlerini objektif ölçüm yöntemleri ile belirlemeleri ve özellikle cinsiyetler arasındaki farkları göz önünde bulundurmaları gerekmektedir.

Anahtar Sözcükler: Diplejik, çocuk, serebral palsi, gelişim, cinsiyet

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Introduction

Cerebral Palsy (CP), the most common cause of childhood physical impairment, is a group of permanent disorders in the development of posture and movement in the developing fetal or infant brain, causing activity limitation (1). In CP, motor disorders are often accompanied by sensorial, perceptional, cognitive, communicational and behavioral disorders, epilepsy and secondary musculoskeletal problems (2). Spastic diplegia is the most common type of CP with a rate of approximately 44% (3-5). In spastic diplegia seen as a result of perinatal hypoxic-ischemic lesion or periventricular leukomalacia, motor failure in the lower extremities is often more severe than in the upper extremities (3-5). Lack of gross and fine motor skills in children with diplegic CP due to non-progressive brain lesions and accompanying secondary pathologies (eg spasticity, muscle weakness, muscle contractures, increased co-contraction, decreased selective motor control) negatively affect daily life activities (6-8).

Motor development is expressed as the individual gaining of the mobility in parallel with the physical growth and the development of the central nervous system, and plays an important role in the recognition and management of the child's environment, gaining independence and ensuring social participation. In order to determine the motor development level of children with diplegic CP in the rehabilitation process and to organize appropriate rehabilitation programs, fine and gross motor skills should be evaluated in detail (9,10). There are different tests, such as the Gross Motor Function Measurement (GMFM), Bruininks-Oseretsky Test of Motor Proficiency Second Edition (BOT-2), Bruininks-Oseretsky Test of Motor Proficiency Second Edition Short Form (BOT2-SF), Ability for Basic Movement Scale, Developmental Sequence of Fundamental Motor Skills Inventory and Test of Gross Motor Development (11-13). The tests to be used in the evaluation of motor ability in children with diplegic CP should be able to detect the lack of fine and gross motor development in the child, to show the child's highest performance, to be easily applicable and accessible (13,14).

When the features of the motor skill tests are examined in general, BOT2-SF differs from other tests in terms of both its speedy application and easy availability of test materials (13). In addition, another feature that distinguishes BOT2-SF from other tests is the philosophy in creation of the test. Dr. Robert H. Bruininks developed this test with the idea of developing a product that evaluates sensory-perception-motor performances rather than a test that evaluated only motor performance (15). The fact that the test has been developed with this perspective, it does not contain too many materials and its easy application makes BOT2-SF stand out in the evaluation process (14).

Few studies in the literature have investigated the difference in gross motor development between boys and girls with spastic diplegic CP. In a study by Romeo et al. (16) the development of CP in children with gross motor function was examined by using GMFM, and it was shown that girls' gross motor skill levels were better than boys. Similarly, it was concluded in the literature that in different studies investigating the difference in motor development between genders, girls had a better level of gross motor skills than boys (17-19). In the light of our up-to-date information, no studies revealing the difference between gross and fine motor skills in boys and girls with diplegic CP with BOT2-SF have been found (4). The purpose of our study planned due to these limitations in the literature was to reveal the difference between the fine and gross motor skills of children with diplegic CP by using BOT2-SF.

Methods

Ethical approval was obtained from the Health Sciences University, Non-Interventional Research Ethics Committee (date: 16.10.2018, number: 18/249). The children and their families included in the study were given detailed information about the study and were informed.

Seventy eight children with diplegic CP aged between 6 and 12 years who were admitted to the hospital between November 2018 and March 2019, were included in the study. Criteria for inclusion in the study were; (1) Being diagnosed as having diplegic CP, (2) being in level I, II or III according to the Gross Motor Function Classification System (GMFCS), (3) having a cognitive level that could understand and apply verbal commands, and (5) not having a systemic problem and epileptic seizures that could not be controlled. Exclusion criteria were; (1) families and children who did not agree to participate in the study, (2) having undergone surgery or Botulinum Toxin application in the last 6 months, (3) taking place in levels IV and V according to the Hand Manual Ability Classification System (MACS). Three of the children with diplegic CP included in the study were excluded from the study because they had Botulinum Toxin-A injections, one was excluded due to undergoing a surgical procedure, and one was excluded due to having upper respiratory tract infection.

The BOT2-SF was used to evaluate the gross and fine motor skill levels of all children included in the study.

The Bruininks-Oseretsky Test of Motor Proficiency, Second Edition, Short Form (BOT2-SF)

The BOT was developed by Robert H. Bruininks in 1972 to measure the motor functions of children in the age group of 4.5-14.5 years, based on the Oseretsky Test of Motor Proficiency (11). The BOT was updated in 2005 and became BOT2. The BOT2 is a test with both short and long forms to evaluate motor skill levels in children aged 4 to 21 years (10). The validity and reliability of the BOT2 long form was made by Mülazimoğlu Ballı in 2012 (10), and the validity and reliability of the short form by Köse in 2018 (14). In our study, BOT2-SF consisting of 8 subtests and 12 items was used. The application period of the test, which evaluates the gross and fine motor skills of children, is on average 15-20 minutes. The subtests, items and scores of BOT2-SF are as follows:

- Fine Motor Precision (0-10 points)
  - ◊Filling in A Star (0-3 points)
  - ◊Drawing A Line Through A Path (0-7 points)

- Fine Motor Integration (0-11 points)
  - ◊Copying Overlapping Circles (0-6 points)
  - ◊Copying Diamond (0-5 points)
- Manual Dexterity (0-9 points)
  - ◊Stringing Blocks (0-9 points)
- Bilateral Coordination (0-9 points)
  - ◊Touching the Tip of the Nose with Forefinger (Eyes Closed) (0-4 points)
  - ◊Creating a Square with the Index Finger and the Thumb (0-5 points)
- Balance (0-4 points)
  - ◊Walking Forward on A line (0-4 points)
- Running Speed and Agility (0-10 points)
  - ◊One Legged Stationary Hop (0-10 points)
- Upper-Limb Coordination (0-12 points)
  - ◊Catching the Throwed Ball (One Hand) (0-5 points)
  - ◊Dribbling A Ball (0-7 points)
- Strength (0-9 points)
  - ◊Knee Push-Ups (For Boys) (0-9 points)
  - ◊Sit Ups (For Girls) (0-9 points).

Statistical Analysis

Windows based SPSS (IBM SPSS Statistics, Version 23.0, Armonk, NY, USA) package program was used in the statistical analysis of the data obtained in our study. In the representation of the descriptive statistics of the data obtained from the subjects participating in the study, the data that fit the normal distribution as a measure of central tendency were given as mean ± standard deviation, and the data that did not fit to the normal distribution were given as median (25-75%). Analytical (Kolmogorov-Smirnov/Shapiro-Wilks test) and visual (Histogram and probability graphs) methods were used to test the compliance of the data to normal distribution. In order to measure the statistical significance of the difference between girls and boys, Student t-test was used in normally distributed data groups. In our study, statistical significance level was accepted as $p<0.05$.

Results

A total of 73 children with diplegic CP (39 boys, 34 girls) with an average age of 8.54±1.37 years were included in our study. Right extremity of 45.2% of the children was dominant and left extremity of 54.8% was dominant. Girls' weight and body mass index were statistically significantly lower than boys. The demographic characteristics of all diplegic CP children included in the study are presented in Table 1.

When the BOT2-SF results were compared by gender, it was found that girls with diplegic CP scored significantly higher than boys with diplegic CP in terms of fine motor precision, bilateral coordination, upper-limb coordination subtests and total score ($p<0.05$) (Table 2).

Discussion

In our study where we examined the fine and gross motor skills of children with diplegic CP using BOT2-SF; it was found that girls with diplegic CP scored significantly higher than boys with diplegic CP in terms of fine motor precision, bilateral coordination, upper-limb coordination subtests and total score. Especially, in our study where only fine and gross motor skills of children with diplegic SP were evaluated, the use of BOT2-SF in evaluation and the difference found between genders according to this evaluation distinguished our study from other studies.

The localization and severity of the lesion in the brain affect fine and gross motor skills of children with CP. These children try to perform daily life activities despite the limitations in their fine and gross motor skills (20). Although there are studies in the literature evaluating the fine and gross motor skills of children in all subgroups of healthy children and CP (4,6,17), there are not many studies evaluating the motor skills of children with diplegic CP only. In these studies, it was observed that the children with diplegic SP were not compared in terms of fine and gross motor skills specifically by gender (9,21,22). In the studies reviewed, it was found that either comparisons were made between all the subgroups of CP or they examined the differences between healthy children. Related studies concluded that children with normal development had better gross and fine motor skills than children with CP (9). However, the evaluation methods they frequently used when evaluating motor skills were GMFM, MACS, Bimanual Fine Motor Function and GMFCS (4,6,9,21,22). In our current study, we used BOT2-

Table 1. Children's demographic features

Variables	Girl (n=34)		Boy (n=39)		p[a,b]
Age (year) (Mean ± SD)	8.29±1.31		8.76±1.4		0.14[a]
Height (cm)	127.05±9.81		130.56±5.36		0.05[a]
Weight (kg)	27.35±6.26		30.33±4.85		0.02[a]
BMI (kg/m²)	16.7±1.74		17.67±1.68		0.01[a]
GMFCS	n	%	n	%	0.78[b]
Level 1	8	23.5	7	17.9	
Level 2	11	32.4	12	30.8	
Level 3	15	44.1	20	51.3	
MACS					0.11[b]
Level 1	21	61.8	30	76.9	
Level 2	12	35.3	6	15.4	
Level 3	1	2.9	3	7.7	

p[a]: Student's t-test, p[b]:Chi-square test, SD: Standard deviation, BMI: Body mass index, GMFCS: Gross Motor Function Classification System, MACS: Hand Manual Ability Classification System

Table 2. Comparison of the Bruininks-Oseretsky Test 2-Short Form results by gender

BOT2-SF	Girls with diplegic CP (n=34)		Boys with diplegic CP (n=39)		t	p[a]
	$\bar{x}$ ± SD	(min - max)	$\bar{x}$ ± SD	(min - max)		
Fine motor precision	1.76±1.04	(0-3)	1.25±0.96	(0-4)	-2.15	0.03*
Fine motor ıntegration	5.32±1.90	(3-9)	4.58±1.44	(2-8)	-1.86	0.06
Manual dexterity	1.64±1.32	(0-4)	1.17±0.94	(0-3)	-1.75	0.08
Bilateral coordination	1.26±1.18	(0-4)	0.74±0.81	(0-3)	-2.20	0.03*
Balance	0.97±0.90	(0-3)	0.79±0.76	(0-3)	-0.89	0.37
Running speed and agility	0.61±0.77	(0-3)	0.35±0.62	(0-2)	-1.57	0.12
Upper-limb coordination	1.20±1.29	(0-5)	0.66±0.62	(0-2)	-2.31	0.02*
Strength	0.41±0.65	(0-2)	0.20±0.40	(0-1)	-1.63	0.10
Total	13.2±8.15	(3-30)	9.76±5.77	(2-25)	-2.09	0.04*

p[a]: Student's t-test, *p<0.05, BOT2-SF: Bruininks-Oseretsky Test 2-Short Form, CP: Cerebral Palsy, SD: Standard deviation, min: Minimum, max: Maximum

SF, which was developed with the idea of producing a product that evaluated sensory-perception-motor performances rather than just a test that evaluated motor performance, apart from these tests frequently used in the literature. It has become more valuable in defining how motor development changes in children with diplegic CP depending on gender, using more specific assessment tools, obtaining more objective results and providing more objective results in creating appropriate physiotherapy interventions (23).

Motor skill disorders faced by children with CP affect individuals in different clinical types of CP, which is a highly heterogeneous group, to different degrees (24). In our current study children with diplegic CP with GMFCS levels I, II and III were included and a homogenous group was formed. Romeo et al. (16) evaluated in their study the gross motor skills of 171 children with CP, including 73 girls with CP with an average age of 4.6±2.4 years, and 98 boys with CP with an average age of 4.3±2.3 years and found that girls' GMFM scores were higher than boys (55% vs. 29%). However, in that study, they evaluated children with hemiplegic, diplegic and quadriplegic CP. The results of our current study supported the findings of Romeo et al. (16) and our results proved that girls with diplegic CP had better fine and gross motor skills than boys.

Overall, research in the literature reflects that girls with CP have better fine and gross motor skills than boys (16,25). Romeo et al. (25) concluded that girls were 89% better than boys in the standing subdivision of GMFM in another study of them where they investigated the gross motor functions of boys and girls with CP based on GMFCS levels. In our study, in parallel with these studies, there was an increase in favor of girls by 40.80% in the fine motor precision subtest, 70.27% in the bilateral coordination subtest, 81.81% in the upper-limb coordination subtest, and 35% in the total score of BOT2-SF. Possible explanations for this situation by Romeo et al. (16) were the neuroprotective effect of female hormones and different histomorphological features between the two genders. The fact that women have larger neuropil areas with more synaptic connections and more common dendritic arborization than men which can mediate better reorganization after a lesion and thus, girls with CP may have better fine and gross motor skills than boys, is supported by studies (23,26,27).

Study Limitations

The limitations of our study were not including children with diplegic CP with GMFCS levels IV and V and lack of control group consisting of healthy children. In the future, there is a need for studies that present the difference in the development of children with CP by gender by comparing them with healthy peers in larger groups.

In children with CP, the limitation in fine and gross motor skills affects the child's relationship with the environment and his/her physical abilities. This problem can lead to a decrease in the learning and experiencing of the child with diplegic CP and as a result may affect the child's ability to live independently (28,29). In the light of our current findings, it is important to consider the differences between girls and boys in rehabilitation programs so that children with diplegic CP can increase their participation in daily life activities.

Conclusion

As a result, physiotherapists need to make a good assessment about the problems of children with CP in fine and gross motor skills and collect evidence so that they can offer a multi-factor integrated therapeutic approach for children with diplegic CP. According to our current study, where we revealed gender-specific differences in children with diplegic CP; evaluating the development of fine and gross motor skills in children with diplegic SP would be the main building block for planning appropriate rehabilitation programs specific to the child.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Health Sciences University, Non-Interventional Research Ethics Committee (Date: 16.10.2018, number: 18/249).

Informed Consent: The children and their families included in the study were given detailed information about the study and were informed.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: K.K., Concept: Ö.K.K., S.Ş., Design: Ö.K.K, S.Ş., K.K., Data Collection or Processing: B.K., H.A.T., Analysis or Interpretation: K.K., B.K., S.Ş., Ö.K.K., Literature Search: B.K., H.A.T., Writing: Ö.K.K.

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Original Article

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The Effect of Serum Bone Sialoprotein Levels on Tympanosclerosis

Serum Kemik Sialoprotein Seviyelerinin Timpanoskleroza Etkisi

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ABSTRACT

Objective: This study aimed to investigate serum bone sialoprotein (BSP) levels in patients with tympanosclerosis (TS).

Methods: We included into this study 24 patients with TS and 24 asymptomatic healthy volunteers. Our study consisted of two groups: TS group (n=24), comprising of patients who underwent surgery for chronic otitis media and had tympanosclerotic plaques; and a control group (n=24), comprising of healthy individuals without ear problems. The serum BSP levels were measured and the results were compared between the two groups.

Results: In the TS group, there were 15 female and nine male patients. The ages of the females ranged from 24 to 54 years, while those of the males ranged from 34 to 55 years; the average age was 40.46±9.75 and 43.11±6.77, respectively. In the control group, there were 14 females and ten males. The ages of the females ranged from 30 to 48 years, while those of the males ranged from 27 to 47 years; the average age was 40.25±5.28 and 38.4±27.08, respectively. There was a statistically significant difference in BSP levels between the two groups (p=0.001). In addition, there was a moderate positive correlation between BSP and hearing levels.

Conclusion: The serum BSP levels were higher in the TS group than in the control group and might have some effect on TS. Further studies on a large number of subjects using serum and tissue BSP levels should be designed to affirm the effects of BSP on TS.

Keywords: Timpanosclerosis, bone sialoprotein, calcification

ÖZ

Amaç: Bu çalışmanın amacı timpanoskleroz (TS) hastalarında serum bone sialoprotein (BSP) seviyelerini araştırmaktır.

Yöntemler: Yirmi dört TS hastası ve 24 asemptomatik sağlıklı gönüllü çalışmaya dahil edildi. Çalışmamızda iki grup vardı: kronik otitis media ameliyatı geçirmiş ve timpanosklerotik plakları olan hastalardan oluşan TS grubu (24); ve kulak problemi olmayan sağlıklı bireylerden oluşan kontrol grubu (n=24). Serum BSP seviyeleri ölçüldü ve sonuçlar iki grup arasında karşılaştırıldı.

Bulgular: Timpanoskleroz grubunda 15 kadın ve 9 erkek hasta vardı. Kadınların yaşları 24 ile 54 arasında değişirken, erkeklerin yaşları 34 ile 55 arasında değişmekteydi ve yaş ortalaması sırasıyla 40,46±9,75 ve 43,11±6,77 idi. Kontrol grubunda 14 kadın ve 10 erkek vardı. Kadınların yaşları 30 ile 48 arasında değişirken, erkeklerin yaşları 27 ile 47 arasında değişmekteydi ve yaş ortalaması sırasıyla 40,25±5,28 ve 38,4±27,08 olarak saptandı. BSP düzeyleri karşılaştırıldığında iki grup arasında istatistiksel olarak anlamlı fark bulundu (p=0,001). Ek olarak, BSP ile işitme seviyeleri arasında pozitif orta düzeyde bir korelasyon vardı.

Sonuç: Serum BSP düzeyleri TS grubunda kontrol grubundan daha yüksekti ve TS üzerinde bir etkisi olabilir. Çok sayıda hasta üzerinde serum ve doku BSP seviyelerini araştıran yeni çalışmalar, BSP'nin TS üzerindeki etkilerini doğrulamak için tasarlanmalıdır.

Anahtar Sözcükler: Timpanoskleroz, kemik sialoprotein, kalsifikasyon

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Introduction

Tympanosclerosis (TS) is a chronic middle ear disease that manifests as collagen accumulation in the tympanic membrane lamina propria and mastoid cavity submucosa and also affecting auditory ossicles (1). This disease involves the development of calcified plaques in the submucosal area of the middle ear, due to calcification of the connective tissue layer pathologically. Regarding the situation of calcification, we can observe by electron microscopy a network of intense collagen fibers with scattered crystalline material, which is fundamentally calcium phosphate. It is thought that the calcium phosphate clusters are formed by deposition of the mineral on the surface of matrix vesicles, which acts as primary sites of calcification (1,2). These changes often disrupt the movement of the eardrum and the ossicular chain, leading to hearing loss.

Although the etiology of TS is still not fully understood, it is widely believed that it commonly develops secondary to acute or chronic inflammation of the middle ear and as a result of other factors such as myringotomy, ventilation tube insertion, physical trauma, various chemical agent exposure, genetic predispositions, immunological processes and hypercalcemia (3).

Bone sialoprotein (BSP) is one of the most important extracellular matrix (ECM) proteins of the bone and belongs to the small integrin-binding ligand N-linked glycoprotein family. This family consists of BSP, dentin sialophosphoprotein, osteopontin (OPN), matrix extracellular phosphoglycoprotein and dentin matrix protein-1 that are believed to play crucial biological roles in the turnover, improvement and mineralization of dentin and bone (4,5). Although BSP is usually expressed in mineralized tissues and has been proposed to have a direct role in mineralization, the protein has currently been shown to be expressed in varied tissues including renal tissues, salivary glands and in pathological conditions such as tumours (6-8).

OPN is a hormone that is a regulator of biomineralization and inflammation and is also known as BSP I. Several studies have shown that OPN is upregulated in pathological ectopic calcification and tympanosclerotic focusing regions (9,10). Although the relationship between osteopontin and TS is known, the relationship between BSP and TS has not been investigated before. In this study, the serum BSP levels were evaluated in TS patients.

Methods

Following approval by the local ethics committee (Protocol number: 110, Date: 27.06.2018), the study was conducted in the Uskudar State Hospital Otolaryngology Clinic. Twenty-four patients who were diagnosed with chronic otitis media between July 2018 and March 2019 were included in the study. Patients with otorrhea, otitis media with effusion, acute otitis media, and chronic systemic disease were excluded. There were 48 participants: groups of 24 patients and 24 controls. The control group had no ear problems and no chronic systemic disease. There were 15 females and nine males in the patient group and the mean age was 40.46±9.75 and 43.11±6.77 years, respectively. There were 14 females and ten males in the control group and the mean age was 40.25±5.28 and 38.4±27.08, respectively (Table 1).

Sampling

Serum Bone Sialoprotein Levels

Serum BSP levels were evaluated using with a human enzyme-linked immunosorbent assay kit (lot no.: AK0018JAN10047; Elabscience, Wuhan, Hubei, PRC) and a Multiskan plate reader. (Thermo Scientific, Waltham, MA, USA). Anti-Human BSP antibodies in pre-covered 96-well plates were used. The biotin-conjugated anti-Human BSP antibodies were used as detection antibodies. Test samples, biotin-conjugate detection antibodies and standards were washed with the wash buffer after addition to wells. The samples and standards were analysed in duplicates as demonstrated in the kit package suffix.

Horseradish peroxidase (HRP)-Streptavidin was added to the unconjugated conjugates and further washed with washing buffer. TMB (tetramethylbenzidine) was catalysed with HRP to generate a blue colour product that turned yellow when the acidic stop solution was added. The quantity of Human BSP captured on the plate is proportional to the intensity of the yellow colour. The absorbances were read at 450 nm in a microplate reader and then the Human BSP concentrations were calculated according to the standard curve. The other serum parameters were examined using a Beckman Coulter AU 2700 Device (California, USA) and the spectrophotometric method.

Calibration was done with seven standards in the kit. The standards at 40, 20, 10, 5, 2.5, 1.25 and 0.63 ng/mL concentrations were ran twice and the standard curve was created. The standard curve was obtained in a similar manner to the shape recommended in the kit package insert. A well was separated as a blank well.

Biochemical Analysis: Total BSP (ng/mL) levels were measured from the serum samples of the patients.

The blood of the patients and the control group were centrifuged (10 min at 2,500 × g, 4 °C). Serum samples were stored in Eppendorf tubes at −80 °C until tested.

Statistical Analysis

In this study, IBM SPSS Statistics Version 22 software package was used for the statistical analysis. Shapiro–Wilks test was used for the normal distribution suitability of the parameters. Descriptive statistical methods (Mean, standard deviations and median values) were calculated. Mann–Whitney U test was used in the comparison of nonparametric data between groups. Significance was assessed at $p<0.05$ level. Spearman's correlation test was used in the correlation test performed between the hearing level and BSP level.

Results

The right side air and bone hearing levels of the patient group were 45.7±20.37 dB and 19.04±11.29 dB and the left side air and bone hearing levels were 40.54±21.69 dB and 17.54±12 dB, respectively (Table 1).

The right side air and bone hearing levels of the control group were 12.59±5.01 dB and 9.86±4.27 dB and left side air, and bone hearing levels were 13.31±5.42 dB and 9.77±4.51 dB, respectively (Table 1).

The mean serum BSP levels of the patient and control groups were 28.8±4.4 (ng/mL) and 24.1±4.9 (ng/mL), respectively. Statistical analysis of the patient and control groups revealed that serum BSP levels were significantly higher in the patient group compared to the control group ($p \leq 0.001$) (Table 2).

There was a moderate positive correlation between BSP and severity of hearing loss in the patient group ($r=0.49$; $r^2=0.319$; $p=0.01$) (Graphic 1).

Discussion

TS is a disease characterised by hyaline calcareous plaques in the tympanic membrane and tympanic space. It may be located in the ossicular chain, ligaments and sometimes in the mastoid. It is an irreversible disease that occurs as a sequelae of a poor inflammatory process in the case of a long-lasting chronic otitis media (11). The inflammatory state occurring in the middle ear mucosa progresses towards an abnormal scarring process characterised by hyalinisation, calcification and osteogenesis. These changes often disrupt the movement of the eardrum and ossicular chain, leading to hearing loss (12).

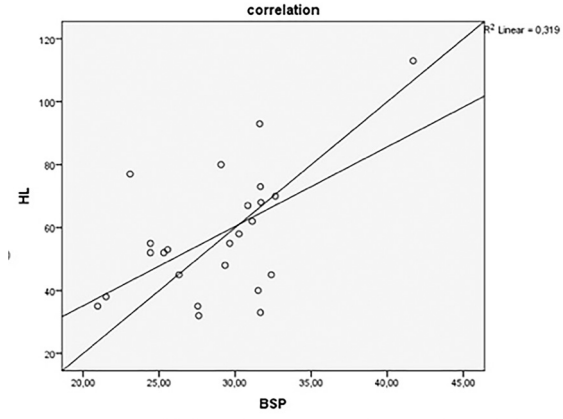
Table 1. Demographic data of the patient and control groups

Patient group	N	min - max	Mean ± SD
Female age	15	24-54	40.46±9.75
Male age	9	34-55	43,11 ± 6,77
Right air	24	10-87 dB	45.7±20.37 dB
Right bone	24	2-57 dB	19.04±11.29 dB
Left air	24	7-73 dB	40.54±21.69 dB
Left bone	24	0-50 dB	17.54±12 dB
Control group	N	min - max	Mean ± SD
Female age	14	30-48	40.25±5.28
Male age	10	27-47	38.4±27.08
Right air	24	3-20 dB	12.59±5.01 dB
Right bone	24	2-20 dB	9.86±4.27 dB
Left air	24	2-20 dB	13.31±5.42 dB
Left bone	24	2-17 dB	9.7±4.51 dB

N: Number of patients, SD: Standard deviation, dB: Decibel, min: Minimum, Max: Maximum

BSP is produced by osteoclasts, chondrocytes and osteoblasts and it is an important ECM protein (13-15). It was suggested to be physiologically significant for hydroxyapatite nucleation and mineralization (16,17). Although BSP does not contain different structural areas, the protein is highly modular, comprising spatially segmented motifs that can bind varied distinct ECM components with various biological roles, including collagen, matrix metalloproteinases, hydroxyapatite, as well as integrins present on many cell types (18-21). BSP might have a versatile act in the progress of the mineralized tissue. Spatiotemporal expression of BSP in *de novo* mineralization areas correlated with BSP at the start of mineralization (14,22). In addition, BSP is expressed at pathological areas of mineralization such as microcalcifications in the breast, atherosclerotic plaques, prostate and thyroid neoplasms (8,23-25). It is known that the basic pathology in tympanosclerotic tissues is excessive calcified hyaline plaques and pathological mineralization. There is no previous study in the literature investigating BSP levels in patients with TS. In our study, serum BSP levels were remarkably higher in the TS group than in the control group.

BSP is a highly post-translationally modified acidic phosphoprotein normally expressed in mineralized tissues such as dentin and bone (26). BSP was suggested to be physiologically important for hydroxyapatite nucleation, cell cohesion and collagen binding (16,17). BSP gene ablated mice with various skeletal and dental defects had decreased bone length and decreased cortical density (27,28). BSP gene-ablated mice also showed a delay in bone repair in cortical injury models; bone formation and absorption were also found to be impaired in bone marrow ablation models (29,30). Cementum is a mineralized tissue in the



Graphic 1. BSP: Bone sialoprotein, HL: Hearing level (moderate positive correlation between BSP and HL)

Table 2. Comparison of serum bone sialoprotein levels between patient and control groups

	N	Min	Max	Mean ± SD	p
Patient	24	20.96 (ng/mL)	41.7 (ng/mL)	28.8±4.4 (ng/mL)	0.001
Control	24	6.01 (ng/mL)	29.62 (ng/mL)	24.1±4.9 (ng/mL)	

Mann-Whitney U test $p \leq 0.05$, SD: Standard deviation, ng: Nanogram

cervical part of the root of the tooth. In immunohistochemical studies, a significant reduction in cementum accumulation was observed in BSP gene ablation mice (31).

BSP has been involved in the reparation of several mineralized tissues. Bone formation was observed when BSP and collagen implantation were performed in 7-8-week old rats with calvarial deficiency (32). Cortical default drilled into the femurs of BSP-ablated mice gets well slowly when compared to controls (33).

In a study comparing patients with metabolic bone disease and a healthy control group, serum BSP concentrations were found to be remarkably higher in patients with the metabolic disease. The highest concentrations were found in patients with active Paget's disease and secondary renal hyperparathyroidism (34).

In some studies, it has been suggested that osteoblast cultures can interfere with osteoblast binding through the selection of low-expressing clones or by the addition of an anti-BSP and that the antibody may have a negative effect on osteoblast distinction by changing BSP levels. This condition is presumably due to the breaking down of osteoblast differentiation (35-38).

In our study, we compared the serum BSP levels between the patient and the control group because we think that BSP plays an active role in tissue mineralization and calcification. In this study, serum BSP levels were significantly higher in the TS group than in the control group and there was a moderate positive correlation between BSP and hearing levels. The limitations of our study were that the number of patients was low and the amount of BSP at the tissue level was not measured.

Conclusion

The serum BSP levels were significantly higher in the TS group than in the control group. There was a moderate positive correlation between BSP and hearing levels. In the future, the manipulation of local BSP levels may be useful in the treatment of TS.

Ethics

Ethics Committee Approval: Following approval by the Local Ethics Committee (Protocol number: 110, Date: 27.06.2018), the study was conducted in the Uskudar State Hospital Otolaryngology Clinic.

Informed Consent: Written informed consent was obtained from the patients.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.B., Concept: A.B., Design: A.B., Data Collection or Processing: A.B., Ö.F.Ö., H.G.Ç., Analysis or Interpretation: A.B., M.Y., Ö.F.Ö., H.G.Ç., Literature Search: A.B., M.Y., Writing: A.B., M.Y.

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Original Article

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Serum Melatonin Levels in Patients with Sudden Sensorineural Hearing Loss

Ani Sensörinöral İşitme Kaybında Serum Melatonin Düzeyleri

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ABSTRACT

Objective: This study aimed to investigate the serum melatonin levels of patients with idiopathic sudden sensorineural hearing loss (ISSNHL).

Methods: This study enrolled 22 patients with ISSNHL and 22 asymptomatic healthy volunteers. The subjects underwent pure tone audiometry and serum melatonin levels were measured.

Results: The patient group was composed of 12 women (mean age, 46.41±7.8) and 10 men (mean age, 48±6.46), and the control group was composed of 12 women (mean age, 40.25±5.28) and 10 men (mean age, 38.4±27.08). The serum melatonin levels were significantly lower in the patient group than in the control group (p≤0.001). A statistically significant strong negative correlation was found between serum melatonin level and severity of hearing loss (r=–0.644; p=0.001).

Conclusion: Serum melatonin levels of patients with ISSNHL were lower than controls. A statistically significant strong negative correlation was found between serum melatonin level and the severity of hearing loss.

Keywords: Sudden hearing loss, melatonin, antioxidant

ÖZ

Amaç: Bu çalışmanın amacı, idiyopatik ani sensörinöral işitme kaybı (İASİK) olan hastaların serum melatonin düzeylerini ortaya koymaktır.

Yöntemler: İASİK olan 22 hasta ve 22 asemptomatik sağlıklı gönüllü çalışmaya dahil edildi. Katılımcılara saf ses odyometrisi uygulandı ve katılımcıların serum melatonin seviyeleri ölçüldü.

Bulgular: Hasta grubunda 12 kadın [ortalama (ort.) yaş: 46,41±7,8] ve 10 erkek (ort. yaş: 48±6,46) vardı. Kontrol grubunda 12 kadın (ort. yaş: 40,25±5,28) ve 10 erkek (ort. yaş: 38,4±27,08) vardı. Serum melatonin düzeylerinin hasta grubunda kontrol grubuna göre anlamlı derecede düşük olduğu saptandı (p≤0,001). Serum melatonin seviyesi ile işitme kaybının şiddeti arasında istatistiksel olarak anlamlı güçlü negatif bir korelasyon vardı (r=-0,644; p=0,001).

Sonuç: İASİK olan hastaların serum melatonin düzeyleri kontrol grubundan daha düşüktü. Serum melatonin seviyesi ile işitme kaybının şiddeti arasında istatistiksel olarak anlamlı güçlü negatif bir korelasyon vardı.

Anahtar Sözcükler: Ani işitme kaybı, melatonin, antioksidan

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Introduction

The etiology of sudden hearing loss is only known in 10% of the cases, and it is still classified as idiopathic in 90% of the cases. Although idiopathic sudden sensorineural hearing loss (ISSNHL) is an otologic emergency, its etiopathogenesis is not known exactly. Although some theories attempt to explain the pathogenesis of ISSNHL, such as viral infections, membrane rupture, immune-mediated inner ear disease, vascular events, genetic and acquired factors, none of these theories have yet been proven (1).

Hair cells are high-energy and oxygen-consuming cells, and the most important factor for this is the mitochondrial electron transport chain. Reactive oxygen species (ROS), which appears as a result of mitochondrial changes during hypoxia, can trigger cell death by damaging lipids, proteins and deoxyribonucleic acid (2).

ROS causes apoptosis by damaging the inner hair cells. This hypothesis has been verified by showing ROS in the perilymphatic fluid of the inner ear of patients with deep sensorineural hearing loss throughout cochlear implantation surgery (3). Many studies have demonstrated that ROS is linked to many diseases that may cause hearing loss, including noise, drug use, genetic hearing loss, presbycusis, and Meniere syndrome (4-7).

Melatonin is a hormone secreted by the pineal gland, has a direct antioxidant effect, is a potent scavenger of ROS and enhances the activity of antioxidant enzymes (8).

Melatonin is also detected in the organ of Corti, basilar membrane, spiral ligament, stria vascularis and cochlear nerve (9). Lasisi and Fehintala (10) had shown that low plasma melatonin level is important in the development of age-related high-frequency hearing loss.

In this study, we aimed to investigate the serum melatonin levels in patients with ISSNHL to determine whether serum melatonin levels have an effect on the pathophysiology of ISSNHL.

Methods

Study Population

The study was planned with 31 patients diagnosed with ISSNHL and 22 healthy volunteers in Uskudar State Hospital Otolaryngology Clinic. The diagnosis of ISSNHL was made according to criteria of the American Academy of Otolaryngology-Head and Neck Surgery (11). Patients with conductive hearing loss, a history of otologic surgery, head trauma, or barotrauma during the previous 4 weeks, neurologic disorders predisposing to hearing loss, accompanying upper respiratory tract infection, autoimmune diseases, vestibular symptoms, fluctuating hearing loss in the last 4 weeks and hearing loss due to pathological brain mass in magnetic resonance imaging were excluded from the study. Following patient screening, nine patients were excluded from the study. The study included 22 patients diagnosed with ISSNHL. The control group was composed of 22 healthy volunteers, i.e. had no ear problems and no chronic systemic disease. Complete history taking, physical examination, laboratory workup, bleeding profile, venereal diseases research laboratory test and antinuclear antibody test were performed in both groups. None of the subjects were taking any antioxidant vitamins.

The study was approved by the ethics committee of Zeynep Kamil Women's and Children's Diseases Training and Research Hospital (Protocol number: 109, date: 27.06.2018).

Audiological Evaluation

All patients were tested for pure tone audiometry for both ears up to 8000 Hz frequency starting at 250 Hz frequency by international standards. Pure-tone average was determined by calculating the mean of the 500, 1000, 2000 and 4000 Hz thresholds. All patients underwent a tympanogram test. Hearing impairment was assessed according to the international standard criteria defined by the World Health Organization Prevention of Deafness and Hearing Impairment standard 97.3 (12).

Laboratory Study

The human melatonin levels were measured with a competitive enzyme-linked immunosorbent assay (ELISA) using commercial kits (Elabscience; lot no. QQQB5LYL, PRC) and an ELISA reader (Multiskan FC® Microplate Photometer; Thermo Scientific, USA).

In this study, 96-well ELISA plates precoated with anti-human melatonin antibodies were used. The standards and samples were added to the micro ELISA plate wells for binding to the specific antibody. Then, biotinylated detection antibody was added immediately. During the reaction, human melatonin in the sample or standards compete for binding with human melatonin antibody. After a specific incubation period, excess conjugate and independent sample or standards were washed from the plate, and avidin that conjugated to horseradish peroxidase was annexed to every well and incubated. After these procedures, a tetramethylbenzidine substrate solution was supplemented to each well. The enzyme-substrate reaction was finished by the supplement of a stop solution, and the colour shift was measured spectrophotometrically at a wavelength of 450 nm. The human melatonin concentrations in the samples were calculated according to the optical density (OD) in the standard curve and then determined by comparing the OD of the samples to the classical curve. The results were demonstrated using the pg/mL unit. For sensitivity levels, the minimum definable dose of melatonin was 9.38 pg/mL, and the detection range was 15.63-1000 pg/mL.

Statistical Analysis

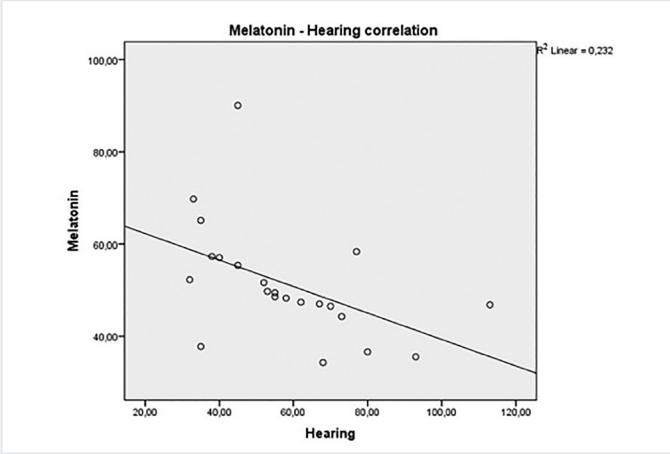
In this study, IBM SPSS Statistics version 22 was used for statistical analysis. Shapiro-Wilk test was used to evaluate the normal distribution of the parameters. Descriptive statistical methods (mean, standard deviations and median value) were calculated. Mann-Whitney U test was used to compare nonparametric data between groups. Spearman correlation test was used to determine the correlation of nonparametric data between two groups. The r value was evaluated between –1 and +1. Significance was assessed at $p<0.05$ level.

Results

This study enrolled 22 patients with ISSNHL and 22 asymptomatic healthy volunteers. The patient group was composed of 12 women and 10 men. The female patients were 32-62 years old (mean age, 46.41±7.80 years). The male patients were 38-55 years old (mean age, 48±6.46 years). The control group was composed of 12 women and 10 men. The female volunteers were 30–48 years old (mean age, 40.25±5.28 years). The male volunteers were 27–47 years old (mean age, 38.4±27.08 years) (Table 1).

Type A tympanogram was obtained in both groups. In the pure tone audiometry test, the mean values of the right air, right bone, left air and left bone were 34.36±21.66 dB, 29.40±20.88 dB, 40.72±30.33 dB and 35.09±27.77 dB, respectively (Table 1). The serum melatonin level averages of the patients and controls were 51.32 ± 12.45 and 78.79 ± 29.39 pg/mL, respectively. The serum melatonin levels were significantly lower in the patient group than in the control group (p≤0.001) (Table 2).

A statistically significant strong negative correlation was found between serum melatonin and severity of hearing loss in the patient group (r=–0.644; p=0.001). The coefficient of determination (r^2) between these two variables was 0.232 (Table 3) (Graphic 1).



Graphic 1. Correlation between melatonin and hearing level (strong negative correlation is present)

Table 1. Demographic data of the patient and control group

Patient group	N	Min - Max	Mean ± SD
Female age	12	32-62	46.41±7.80
Male age	10	38-55	48±6.46
Right air	22	7-77 dB	34.36±21.66 dB
Right bone	22	3-70 dB	29.40±20.88 dB
Left air	22	10-113 dB	40.72±30.33 dB
Left bone	22	8-100 dB	35.09±27.77 dB
Control group	N	Min - Max	Mean ± SD
Female age	12	30-48	40.25±5.28
Male age	10	27-47	38.4±27.08
Right air	22	3-20 dB	12.59±5.01 dB
Right bone	22	2-20 dB	9.86±4.27 dB
Left air	22	2-20 dB	13.31±5.42 dB
Left bone	22	2-17 dB	9.77±4.51 dB

dB: Decibel, N: Number of patients, SD: Standard deviation, min: Minimum, max: Maximum

Table 2. Comparison of the serum melatonin levels between the patient group and control group

	N	Min	Max	Mean ± SD	p
Patient	22	34.28	90.06	51.32±12.45	0.001
Control	22	11.69	136.03	78.79±29.39	

Mann-Whitney U test, p≤0.05, min: Minimum, max: Maximum

Table 3. Correlation between serum melatonin levels and hearing loss levels in the patient group

	N	Min	Max	Mean ± SD	p	r	r^2
Melatonin level	22	34.28	90.06	51.3±12.45	0.001	-0.644	0.232
Hearing level	22	32	113	58.13±20.88			

Spearman's test p value ≤0.01, r value (–1, 0,+1), coefficient of determination (r^2), min: Minimum, max: Maximum

Discussion

The pathogenesis of ISSNHL can not be clearly identified because histopathological examination was not possible. Its causes include viral infections, autoimmune inner ear diseases, cochlear vascular pathologies or a combination of these mechanisms (13,14).

Merchant et al. (15) demonstrated that ISSNHL may be the result of the abnormal activation of cellular stress pathways within the cochlea and that nuclear factor kappa B (NF-kB) induces oxidative stress, inflammatory cytokines and other stress-related proteins. This hypothesis was supported by the pathological activation of NF-kB, which stimulated the production of inflammatory cytokines and other proteins due to oxidative stress since the cochlear microcirculation is very sensitive to changes in blood flow velocity, and dysfunction of the cortical organ occurs very quickly even in limited perfusion disorders (16).

Different models of experimentally induced reperfusion injury confirm that free radicals originating from oxygen play a significant role. Clerici and Yang (17) found high-frequency compound action potential threshold shifts in an animal study examining the specific effects of ROS production on cochlear function. Bielefeld et al. (18) found similar findings in a study evaluating the effect of superoxides on inferior colliculus-induced potential thresholds and hair cell damage. In a study comparing the ROS and total antioxidant status (TAS) concentrations on the effect of oxidative stress on ISSNHL, ROS levels were considerably higher in the patient group than in the healthy group, while no significant difference was found between the TAS levels (19).

Dysfunction of endothelial cells leads to an increase in ROS and may result in apoptosis or sudden death of endothelial cells (20). Guo et al. (21) showed that the increase in superoxide radicals and decreased endothelial nitric oxide synthetase activity caused hair cell loss, thickening of the vascular intima and luminal stenosis in the spiral modiolus. Haubner et al. (22) also showed increased adhesion molecules in the vascular circulation of patients with ISSNHL. These studies found that endothelial dysfunction leads to impaired labyrinth perfusion and hearing loss in patients with ISSNHL, indicating the presence of vascular pathology in the etiopathogenesis of the disease.

Melatonin, a pineal secretory product of vertebrates, can be produce in many tissues and cells such as the cochlea (23,24). Melatonin has a neuroendocrinoimmunological role at the tissue level. It has both indirect antioxidant and direct free radical scavenger activity (24). Melatonin ensures these effects by transforming its metabolites, such as cyclic N-1-acetyl-5-methoxy kynuramine, 3-hydroxymelatonin and N-1-acetyl-N2-formyl-5-methoxykynuramine (25-27). All these metabolites neutralise free radicals. Moreover, studies demonstrated that melatonin induced several antioxidative enzymes, such as glutathione peroxidase, glutathione transferase and superoxide dismutase (28-32).

Melatonin has also been deliberated as a potent antihypertensive treatment. It may also enhance endothelial function by increasing the presence of nitric oxide, thereby exerting vasodilatory and hypotensive effects. Furthermore, it appears to be effective in disorders of the peripheral and central autonomic system by causing a decrease in the function of the adrenergic system and an increase in the cholinergic system (33). Melatonin application reduces the mean pulsatility sign of the internal carotid artery, systolic and diastolic blood pressure and norepinephrine levels (34). It also reduces blood pressure and decreases the catecholamine level in human subjects (35).

A study observed that aminoglycoside ototoxicity improved within 2 weeks, but when melatonin was added, it decreased to 5 days in rats (36). Melatonin as an antioxidant and immune modulator can be also used to treat cisplatin ototoxicity by transtympanic local administration in lower doses (37). Another study showed that free oxygen radicals are effective in the treatment of cochlear damage caused by noise, and melatonin plays a strong role in the protection of cochlear damage (38).

In this study, we investigated the relationship between serum melatonin levels and ISSNHL by taking into account the presence of antioxidant property, direct free radical scavenging activity and antihypertensive property of melatonin. In this study, we found that melatonin levels were significantly lower in patients with ISSNHL than in the control group, and a statistically significant result was obtained. Moreover, a statistically significant strong negative correlation was found between serum melatonin level and the severity of hearing loss.

The results of this study were limited by the small sample size. Nevertheless, we think that the study findings will help in the development of future treatment methods for ISSNHL.

Conclusion

This study indicates that low serum melatonin levels may be associated with ISSNHL. Serum melatonin levels of patients with ISSNHL were lower than controls. A larger series of studies are required to elaborate on this relationship.

Ethics

Ethics Committee Approval: The study was approved by the ethics committee of Zeynep Kamil Women's and Children's Diseases Training and Research Hospital (Protocol number: 109, date: 27.06.2018).

Informed Consent: Written informed consent was obtained from the patients.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.B., Ö.F.Ö., Concept: A.B., Ö.F.Ö., M.Y., Design: A.B., Ö.F.Ö., M.Y., Data Collection or Processing: A.B., Ö.F.Ö., M.Y., F.K., Analysis or Interpretation: A.B., M.Y., F.K., Literature Search: A.B., Writing: A.B.

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

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Original Article

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Effect of Flavopiridol on Cell Cycle, Apoptosis and Biomolecule Structure Changes in Breast Cancer Stem Cells

Meme Kanseri Kök Hücrelerinde Flavopiridolün Hücre Döngüsü, Apoptozis ve Biyomolekül Yapı Değişimleri Üzerine Etkisi

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ABSTRACT

Objective: Cancer stem cells (CSCs) are a small population in cancer, which are responsible for therapeutic resistance, relapse and metastasis. Flavopiridol has antitumor activity against various types of cancer cells. The mechanism of action of flavopiridol on CD44+/CD24- breast CSCs has not yet been fully elucidated. The aim of this study was to evaluate the mechanism of action of flavopiridol on breast CSCs (BCSC) in terms of apoptosis, cell cycle and biomolecular changes.

Methods: In human breast cancer, cells with CD44+/CD24– markers were isolated from MCF-7 cell line using flow cytometry. The induction of apoptosis was investigated by Annexin-V. The effect of flavopiridol on cell cycle arrest was determined and the percent of cell populations at G0/G1, S and G2/M cycles were identified. The effect of the drug on three-dimensional cell cultures was investigated using a multicellular tumor spheroid model. In addition, the effect of flavopiridol on biomolecules has been evaluated using Fourier transform infrared (FTIR) spectroscopy, which has recently been used effectively in various scientific fields.

Results: Flavopiridol especially induced early apoptosis. Cell cycle analyses revealed that flavopiridol induced cell cycle arrest in G0/G1 phase. Decreased number and diameter of spheroids was observed following flavopiridol treatment. ATR-FTIR data showed that treatment with flavopiridol led to significant changes in nucleic acids.

ÖZ

Amaç: Kanser kök hücreleri (KKH) terapötik direnç, relaps ve metastazdan sorumlu olan oldukça küçük bir hücre popülasyondan oluşmaktadır. Flavopiridol (Alvocidib), çeşitli KKH'lerine karşı anti-tümör aktiviteye sahiptir. Flavopiridolün CD44+/CD24- meme KKH (MKKH) üzerindeki etki mekanizması henüz tam olarak aydınlatılamamıştır. Bu çalışmada, apoptozis, hücre döngüsü ve biyomoleküler değişiklikler dahil olmak üzere flavopiridolün MKKH üzerindeki etki mekanizmasının çeşitli şekillerde değerlendirilmesi amaçlanmıştır.

Yöntemler: MCF-7 KKH hattı içerisindeki CD44+/CD24- yüzey belirteç özelliklerine sahip MKKH, akış sitometrisi kullanılarak izole edilmiştir. Apoptozis indüksiyonu Annexin-V yöntemi ile incelenmiştir. Flavopiridolün hücre döngüsü tutulumu üzerine etkisi Muse Cell Analyzer ile belirlenmiş ve G0/G1, S ve G2/M döngüsündeki hücre populasyonları yüzde olarak ifade edilmiştir. İlacın üç boyutlu hücre kültürlerindeki etkisi multiselüler tümör sferoid modeli kullanılarak incelenmiştir. Buna ek olarak, flavopiridolün biyomoleküller üzerindeki etkisi, son zamanlarda çeşitli alanlarda oldukça etkin bir şekilde kullanılan Fourier dönüşüm kızılötesi (FTIR) spektroskopisi kullanılarak değerlendirilmiştir.

Bulgular: Flavopiridol spesifik olarak erken apoptozu indüklemiştir. Hücre döngü analizleri, flavopiridolün G0/G1 arrestine yol açtığını ortaya koymuştur. Flavopiridol uygulamasından sonra sferoid sayısı ve çapında azalma tespit edilmiştir. ATR-FTIR verileri, flavopiridol

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Conclusion: According to the data obtained in this study, flavopiridol exhibits anticancer effects by altering the structure/expression level of nucleic acids and changing cell cycle progression and inducing apoptosis. These finding reveals that flavopiridol can be an effective antitumor agent for the treatment of breast cancer after *in vivo* and phase studies are completed.

Keywords: Flavopiridol, breast cancer, cancer stem cell, apoptosis, cell cycle, FTIR spectroscopy

uygulamasının hücre içindeki nükleik asitlerde önemli değişimlere yol açtığını göstermiştir.

Sonuç: Elde edilen bulgular, flavopiridolün nükleik asitlerin yapısını/expresyon seviyesini ve hücre döngüsünü değiştirdiğini ve apoptozu indükleyerek anti-kanser etkiler sergilediğini göstermektedir. Bu veriler, *in vivo* ve faz çalışmaları tamamlandıktan sonra flavopiridolün meme kanser tedavisi için etkili bir terapötik molekül olabileceğini ortaya koymaktadır.

Anahtar Sözcükler: Flavopiridol, meme kanseri, kanser kök hücresi, apoptoz, hücre siklusu, FTIR spektroskopisi

Introduction

Cancer consists of subpopulations of heterogeneous cells in terms of morphology, phenotype and function (1). Cancer stem cells (CSCs) are expressed as a small subpopulation within the heterogeneous population, which have the ability to create a high degree of tumor, self-renewal and differentiation (2). Studies on cancer treatment show that CSCs are resistant to standard therapies, including chemotherapy, radiotherapy and molecular targeting therapy (3). The main goal in new treatment methods is to target and eliminate CSCs.

Breast CSCs (BCSCs) were first shown in 2003 in a study in NOD/SCID (Nonobese diabetic/severe combined immunodeficiency) mice by Al Hajj et al. (4). In the study, cells with CD44 + CD24- phenotype in breast tissue have been shown to be more tumorogenic and exhibit similar characteristics with normal stem cells. CD44 adhesion molecule, one of the cell surface transmembrane glycoproteins, plays an important role in the proliferation, differentiation, motility and migration of CSCs (5). Compared to other cells in breast tumor tissue, the resistance of CSCs to standard therapies and features similar to stem cells highlights the need for new treatments targeting CSCs.

Among many new drugs developed for cancer-targeted treatments in recent years, cyclin-dependent kinase (CDK) inhibitors have shown unique advantages in targeting various cancers (6). Flavopiridol, one of the best compounds studied, is the first CDK inhibitor evaluated in phase I/II clinical studies (7). Flavopiridol shows strong antitumor activity through many mechanisms, including cell cycle arrest, apoptosis induction and modulation of transcriptional regulation (7). Previous studies of our study team have shown that flavopiridol has cytotoxic and apoptotic effects on breast, lung and prostate CSCs (8-10). The aim of this study was to illuminate the cytotoxic effects of flavopiridol on CD44 +/CD24 BCSCs by molecular mechanisms.

Methods

Production and Reproduction of MCF-7 Breast Cell Line

The RPMI 1640 medium was used to reproduce and maintain the MCF-7 human breast cancer cell line. To the 500 mL sterile medium, 1% penicillin/streptomycin, fetal bovine serum inactivated by 10% heat, 1% amphotericin B and 1% L-glutamine were added. Cells planted in the medium were incubated at 37 ^{0}C, 5% CO_2 and humid environment. The cell line was monitored daily with an inverted microscope for viability, proliferation and infection. When more than 80% cell density was observed in flasks, cells were multiplied by passaging. Ethics committee approval was not required since our study was a cell culture study.

Isolation of CD44 +/CD24- Breast Cancer Stem Cells

Isolation of CD44 +/CD24- subpopulation in MCF-7 breast cancer cells was done using flow cytometry. Cells were kept in the dark for 15 minutes at + 4 ºC by adding 10 µL CD44-FITC and 10 µL CD24-PE. At the end of the incubation period, the cell population with CD44 +/CD24- surface feature was sorted using the FACS Aria II (Beckton Dickinson) device. Cells were selected primarily from forward scatter and side scatter charts according to their size and granularity. The selection gate of the cells showing CD44 +/CD24- feature was created over the selected population. Cells were separated from the selected gate.

Apoptotic Cell Measurement with Annexin-V Method

Apoptotic cell analyzes were performed with Muse™ Cell Analyzer using Muse™ Annexin V & Dead Cell. MCF-7 CSCs were planted in 6-well plates. The IC50 dose (500 nM) of flavopiridol obtained from our previous study (8) was added to the cells and they were incubated in a humid environment with 5% CO_2 for 72 h at 37 ^{0}C. At the end of the incubation period, the cells were removed from the plate surface with trypsin and centrifuged at 1000 rpm for 5 minutes. Muse™ Annexin V & Dead Cell reagent was added to the cell pellet obtained and kept at room temperature for 20 minutes. Cells were analyzed at the end of the period.

Cell Cycle Analysis

Cell cycle analysis was done with the Muse™ Cell Analyzer using the Muse™ Cell Cycle Kit. MCF-7 CSCs were planted in 6-well plates. The IC50 dose (500 nM) of flavopiridol obtained from our previous study (8) was added to the cells and they were incubated for 72 h at 37 ^{0}C in 5% CO_2 and humid environment. At the end of the incubation period, the cells were removed from the plate surface with trypsin and centrifuged at 1000 rpm for 5 minutes. The cells were washed with cold 1x PBS by removing the supernatant. Cells were incubated in 70% ethanol for approximately three hours at -20 ^{0}C. After the time expired,

Muse™ Cell Cycle reagent was added to the cells and they were kept in the dark for 30 minutes. Cells were then measured on the Muse™ Cell Analyzer instrument.

Multicellular Tumor Spheroid Model

Culture plates coated with agar were used to obtain tumor spheroids. RPMI-1640 medium without serum was added to the stock solution prepared as 3% agar. The agar-medium mixture prepared in a final concentration of 1% was poured into 6-well containers. After coating, the CD44 +/CD24- cells were suspended in serum-free RPMI-1640 medium at a concentration of $1x10^4$ cells/well and seeded to the wells.

Preparation of Cell Samples for FTIR Analysis

The CD44 +/CD24- cells isolated from the MCF-7 breast cancer cell line were seeded in a 25 cm^2 flask. The cells outside the control group were incubated for 72h by adding the IC50 dose (500 nM) of flavopiridol. At the end of the incubation period, cells were washed. The cells obtained were re-suspended in isotonic solution (0.9% NaCl) with a final cell concentration of approximately $1x10^6$ cells/mL. In all sample groups, shots were taken with the same number of cells. Therefore, the number of cells placed in the attenuated total reflection (ATR) unit was expected to be the same.

FTIR Spectroscopic Measurements

FTIR analyzes were performed using the IRTracer-100 FTIR spectrometer (Shimadzu, Japan) combined with the ATR unit and equipped with a DLATGS detector. As stated and applied in recent literature (11-13), a few µl of cell samples are sufficient for the shot and to form enough cell layer to cover the ATR crystal. In this study, 2 µl of cell sample ($1x10^6$ cells/mL) was placed in the crystal unit and left to stand for 12 minutes under dry air cleaning conditions at room temperature. Thus, the free water molecules in the cell sample were expected to evaporate. It was observed that the intensity in the range of 4000-3000 cm^{-1} caused by O-H tension vibration was reduced in the spectra taken successively during the drying period, and then, when the dry cell sample was obtained, the intensity was balanced. It was measured by taking samples from each sample three times. A minimum of four spectra were recorded per sample in the range of 4000-800 cm^{-1}. A total of 128 scanning averages of 4 cm^{-1} spectral resolution were obtained for each interferogram. In this study, air measurement was taken while the ATR unit as the background spectrum was empty. All cells were measured under the same conditions and parameters. Low concentration NaCl salts used as buffer solution did not affect the cell sample spectrum after drying.

Processing of FTIR Data

Spectral pretreatment, derivative spectrum of second degree, difference spectrum and Student t-tests were performed with 'Kinetics' (provided by Prof. Dr. Erik Goormaghtigh at Université Librede Bruxelles in Belgium) operating under MATLAB. FTIR cell sample shots (spectrum recording) were performed with the software software LabSolutions (Shimadzu, Japan). As is known, in the amide II region, a sharp IR peak originating from atmospheric water vapor is taken at ~1559 cm^{-1} (12). As in previous studies (12-16), the contributions from the water vapor in the atmosphere were removed in this study with reference to the IR peak between 1562 and 1555 cm^{-1}. For this purpose, the water vapor spectrum in the atmosphere was introduced to the "Kinetics" program and the cells were extracted from the sample spectrum automatically. After baseline arrangement of the spectra, it was normalized in the Amid II region for an equal area between 1580 and 1485 cm^{-1}. The absorbance spectra (at least 12 spectra recorded for each cell condition) with full pre-processing were averaged for all samples (baseline corrected and normalized). In order to calculate FTIR difference spectra, the average absorbance spectra of the control group and the flavopiridol applied cell group were subtracted from each other. In order to make statistical comparisons between two different cell states, Student t-test was performed at each wavelength. The red dots here show standard deviations in wave numbers where significant differences occur (with α =0.1% significance). For different cell conditions, the B-method in OPUS 6.5 software (Bruker, Germany) was used to calculate band ratios in the mean absorbance spectra.

Statistical Analysis

Consecutive concentrations of flavopiridol were tested in three wells in experiments, and each experiment was repeated three times. SPSS Windows version 10.0 (SPSS Inc. Chicago, IL) was used for statistical evaluation of the data. Whether there was a significant difference in the results was examined using one-way ANOVA followed by Tukey's or Dunett's post-hoc test. A p value <0.05 was accepted as statistically significant.

Results

Breast Cancer Stem Cells Isolation

According to FACS-Aria flow cytometry results, the average percentages of MCF-7 CSCs and non-CSCs (bulk population) were 1.4% and 98.6%, respectively (Figure 1).

Effect of Flavopiridol on Cell Morphology

It was noted that after applying flavopiridol, the number of BCSC decreased and some of the cells shrank, separated from

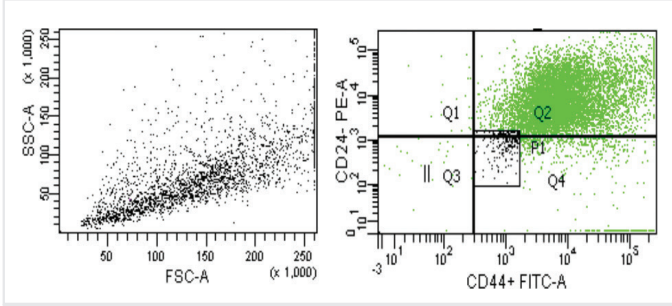

Figure 1. Breast cancer stem cell isolation. Flow cytometry showing the distribution of CD44 +/CD24 cells isolated from the MCF-7 breast cancer cell line. CD44 +/CD24 population is shown with "P1"

the culture plate and rounded. In addition, it was observed that apoptotic bodies formed, some of the cells swelled and most of the cells lost their membrane integrity (Figure 2).

Apoptotic Effect of Flavopiridol

It was determined that flavopiridol had an apoptotic effect with the IC_{50} value (500 nM) at the 72nd hour determined according to the cytotoxic effect on BCSCs (Figure 3). When compared with the control group, a statistically significant difference in terms of early apoptotic cell ratios was determined ($p<0.05$).

Effects of Flavopiridol on Cell Cycle

After flavopiridol treatment, significant changes were found in cell cycle distribution. Compared with the control group, flavopiridol was found to specifically cause G0/G1 arrest (Figure 4).

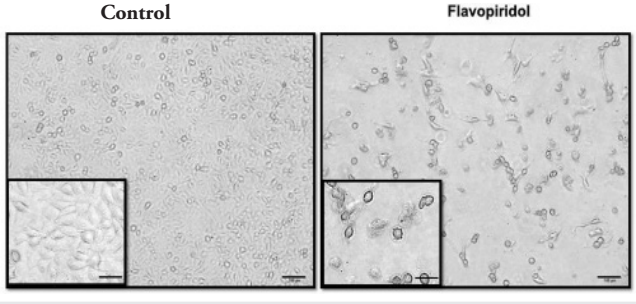

Figure 2. Morphological changes due to flavopiridol in MCF-7 cancer stem cells [Scale bar: 100 µm (Outer); 50 µm (Inner)]

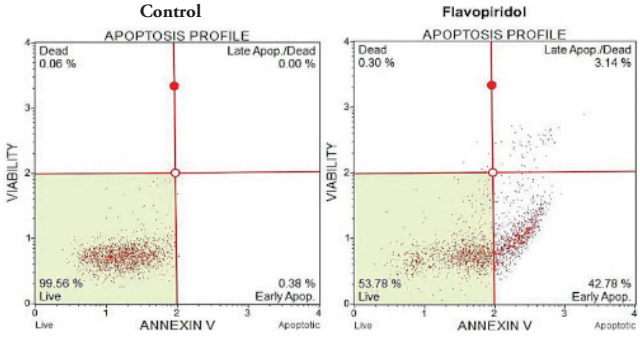

Figure 3. Live, dead, early apoptosis and late apoptosis values (%) of flavopiridol in breast cancer stem cells

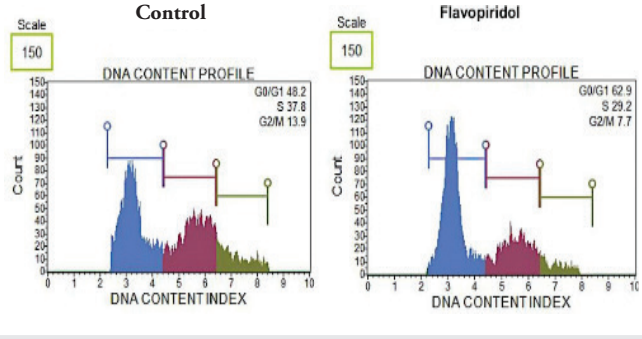

Figure 4. Effects of flavopiridol on cell cycle

Effect of Flavopiridol on Spheroid Number and Diameter

Multicellular tumor spheroid model studies used in the study of the effects of flavopiridol on the three-dimensional system showed that there was a statistically significant decrease in spheroid count ($p<0.01$) and spheroid diameter in the group given flavopiridol compared to the control group ($p<0.05$) (Figure 5).

ATR-FTIR Results

FTIR spectroscopy has been used very effectively in cell studies and biophysical research fields recently (11-17). In this study, the effect of flavopiridol molecule on biomolecules of MCF-7 CSCs was investigated using FTIR spectroscopy technique. As can be seen in the FTIR absorbance spectra of MCF-7 CSCs with control and flavopridol application (Figure 6), information about the biochemical components of the cell can be obtained quickly. Specific changes were seen in nucleic acids and carbohydrate regions (1250-900 cm^{-1}) in MCF-7 CSCs where flavopridol was applied.

The FTIR-difference spectrum was calculated to more precisely reveal the spectral changes observed in the absorbance graph in Figure 6 (Figure 7). The FTIR-difference spectrum shows significant differences between 1250 and 900 cm^{-1}. IR signals

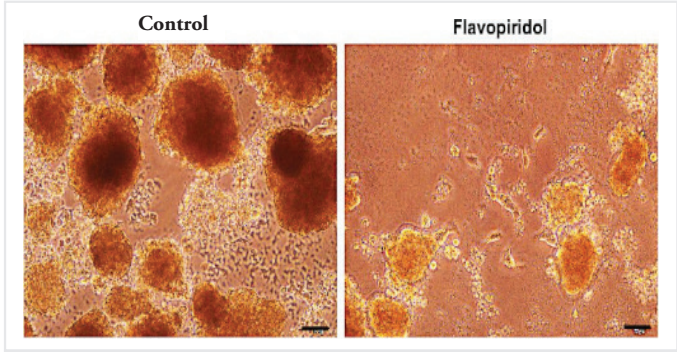

Figure 5. Changes in spheroid diameter (Scale bar: 50µm) in breast cancer stem cells incubated with IC50 dose of flavopiridol

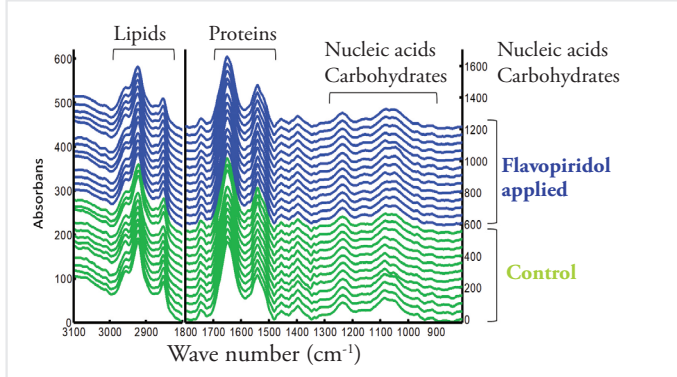

Figure 6. Fourier transform infrared absorbance spectra of MCF-7 cancer stem cells. Flavopiridol applied cell group is shown as "blue" and control cell group is "green"

appear in this region of carbohydrates and phosphates, especially phosphate groups associated with nucleic acids (DNA, RNA) (16-19). In Figure 7, while significant changes were not observed for lipid and protein regions, IR signals in the region of 1250-1200 cm^{-1} and IR signal in 970 cm^{-1} decreased. This indicated that there was a decrease in the amount of DNA. On the other hand, an increase in absorbance was observed in IR peaks at 1157, 1028 and 1005 cm^{-1}. This emphasized the increase in the amount of glycogen in the cell. DNA/Amide II and glycogen/Amide II ratios were calculated to reveal the effect of flavopiridol on changes in cell content (Table 1). The area in the range of 1280-1192 cm^{-1} (DNA) calculated on the average absorbance spectra for the DNA/Amide II ratio was divided into the area calculated in the range of 1580-1485 cm^{-1} (Amide II). The DNA/Amide II ratio was 0.28±0.006 for the flavopiridol-treated cell group, and 0.30±0.003 for the control group. In order to find the glycogen/Amide II ratio, the area between 1180-985 cm^{-1} (glycogen) was divided into the area of the Amide II region. The glycogen/Amide II ratio was 0.93±0.06 for the flavopiridol-treated cell group and 0.78±0.06 for the control group (Table 1). Therefore, there was a decrease in the DNA content of the cell group administered flavopiridol while there was an increase in the amount of glycogen.

In FTIR-second order spectrum, frequency shifts indicating structural changes in DNA were observed (Figure 8). The peaks originating from the DNA-related phosphate (1237, 1222, 1085, 967 cm^{-1}) and glucose (900-950 cm^{-1}) groups in the control cell group tended to shift to lower wave number (downshift: 1236, 1221, 1083, 965) (946, 912 cm^{-1}), but a new peak appeared at 1251 cm^{-1}. These frequency changes clearly showed that the applied flavopiridol caused structural changes due to its binding and interaction with the cell DNA.

As a result, according to FTIR data, when the flavopiridol molecule is applied to MCF-7 CSCs, it causes changes in the cell's DNA. Thus, the mechanism of action of the flavopiridol molecule may be related to a decrease in the level of expression of nucleic acids and/or DNA damage.

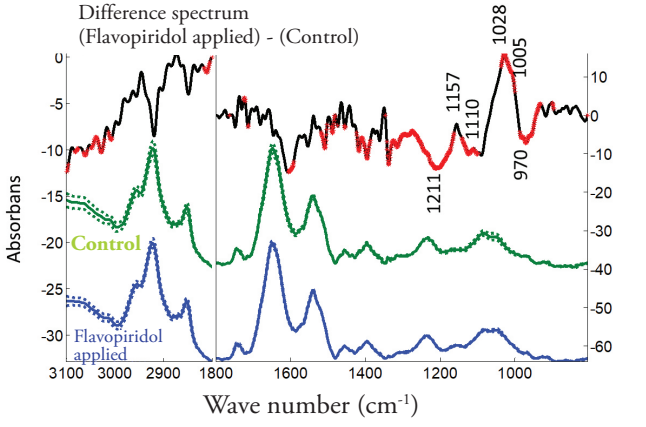

Figure 7. The Fourier transform infrared (FTIR) -difference spectrum and Student's t-test, expressed as "(Flavopiridol applied) - (control)" with MCF-7 cancer stem cells' flavopiridol applied cell group (blue) and control cell group (green) average absorbance spectra. The FTIR-difference spectrum was obtained by subtracting the mean absorbance spectrum of the control group cells from the mean absorbance spectrum of the Flavopiridol-treated cells. The Student t-test with a significance level of α =0.1% at each wavelength was calculated. Thick dotted marks on the spectrum show statistically significant differences. The spectra are balanced for better readability

Discussion

Breast cancer is among the leading causes of cancer-related deaths in women worldwide (20). While new treatment methods and advances in early diagnosis improve breast cancer mortality statistics, CSCs within the heterogeneous tumor mass are among the important causes of treatment failure with their features such as resistance to treatment, relapse and metastasis (2). For this reason, the development of new treatment strategies targeting the "CSCs", which are called the root of the tumor, gains great importance at this point. In this study, the effect of flavopiridol, which had highly cytotoxic properties on cancer cells, on BCSCs and the mechanisms underlying this effect were aimed to be elucidated. The obtained results showed that flavopiridol was effective on apoptosis, cell cycle and nucleic acid structure changes in the cell.

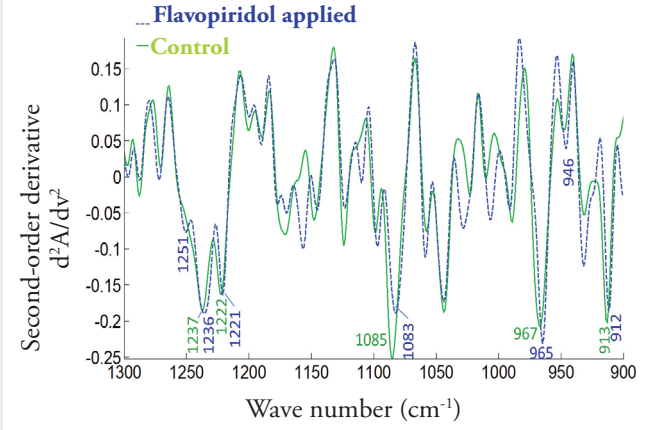

Figure 8. (a) The Fourier transform infrared second order derivative spectra (1300-900 cm-1 spectral range) of MCF-7 cancer stem cells flavopiridol-administered cell group (blue) and control cell group (green). Second order derivative spectra are obtained from the average absorbance spectra in Figure 7

Table 1. Calculated band area ratios for flavopiridol applied cell group and control group. The mean ± standard error value was given for each cell group (p<0.05)

Band ratio	Control cell group	Flavopiridol applied cell group
DNA/Amide II	0.30±0.003	0.28±0.006
Glycogen/Amide II	0.78±0.06	0.93±0.06

Specific cell surface markers are used for identification and isolation of BCSC. In this study, CD44 +/CD24- cell phenotype was used to obtain BCSCs. Combinations of transmembrane proteins CD44 and CD24 are frequently used in isolation of BCSCs (4,21,22). Al-Hajj et al. (4) reported in a study conducted in breast cancer that CD44 +/CD24- cells were more tumorogenic than CD44 +/CD24 + cells and this feature might be a marker of CSCs.

Flavopiridol, which is under investigation in different clinical and phase studies, exhibits antitumor activity with various mechanisms including apoptosis, cell cycle blockade, translation and inhibition of ribosome biogenesis. In a study on breast cancer cell lines (SKBR-3 and MB-468), it has been reported that flavopiridol causes G1 cell arrest and induces apoptosis (23). In a previous study, flavopiridol has been shown to have cytotoxic effects on BCSCs and cause inhibition of translation and ribosome biogenesis (8).

The results we obtained from this study showed that flavopiridol caused apoptotic effect in BCSCs. It has been shown in studies that the treatment of CSCs, which can survive with their anti-apoptotic mechanisms, with flavopiridol causes apoptotic effect. In a study by Soner et al. (9) flavopiridol was shown to induce both early and late apoptosis in prostate CSCs. In addition, it was determined in that study that flavopiridol caused an increase in caspase-3, caspase-8 and p53 expressions.

The discovery of CDKs, which were considered the main regulators of the cell cycle, paved the way for the design of potential inhibitors. Flavopiridol, a synthetic antitumor flavone derivative, was reported to significantly block cell cycle progression at the G1/S and G2/M points (24) by inhibition of some CDKs (1,2,4,7). In this study, it was found that flavopiridol caused G0/G1 cell arrest in BCSCs. Shao et al. (25) reported that the ratio of MCF-7 cells in the G1 stage was 59% as a result of the application of 300 nM flavopiridol, and this ratio was increased to 65% when 500 nM flavopiridol was applied and it was stated that flavopiridol could block the cell cycle in the G1 stage.

There is an increasing interest in screening anti-tumor drugs in terms of their mechanism of action on cancer cells. However, revealing the mechanism of action of drugs at the cellular and molecular level provides important advantages in developing cancer treatment strategies. Recently, FTIR spectroscopy has been seen as a highly effective tool in defining the mechanism of action of drugs (11). In this study, the FTIR results we obtained with the difference spectrum, band frequency shifts and band field ratio calculations showed that flavopiridol had important effects on the nucleic acid structure and level. The downshift of the IR band originating from the phosphate group to low frequency shows that the phosphate group makes a strong H-bond (15). The band frequency shifts observed with the decrease in the amount of DNA in the flavopiridol-treated cell group and the new peak obtained reveal that the DNA has undergone structural and conformational changes as a result of the interaction of flavopiridol with DNA's phosphate groups. The fact that flavopiridol caused changes in DNA structure in particular suggests that its lethal effect on cancer cells may be related to its interaction with DNA. In accordance with the results obtained, it has been shown that flavopiridol interacts with the DNA structure and that nucleic acids are among the possible targets of flavopiridol (26,27). In a study conducted by Bible et al. (26) in A549 human lung cancer cell line, it was revealed that flavopiridol had effects on DNA and RNA structure and synthesis. Researchers have been shown that RNA synthesis is inhibited at 500 nM flavopiridol concentrations and that it binds to DNA similar to binding to ethidium bromide and Hoechst 33258 (26). Similarly, Ray and his team used various spectroscopic and calorimetric techniques to describe the direct effect of flavopiridol on the structural and conformational changes and thermodynamic orientation of DNA (27). The team's ATR-FTIR results showed that flavopiridol interacted with the corrugated structure of DNA (27). Collectively, all of these results emphasize that nucleic acids may be the target of flavopiridol.

Study Limitations

Our study shows that flavopiridol is effective in breast CSCs *in vitro*. However, the effects of flavopiridol on breast cancer should be supported by *in vivo* studies.

Conclusion

The findings revealed that flavopiridol caused cell cycle arrest and effectively induced apoptosis. Results from the multicellular spheroid model showed that flavopiridol significantly suppressed the formation of spheroids specific for CSCs. Our FTIR findings, obtained with the difference spectrum, band area ratio and frequency shift calculations, revealed a potential view that flavopiridol interacted with the nucleic acid construct and that DNA might be the secondary target of flavopiridol. These findings obtained as a result of *in vitro* studies showed that flavopiridol might have a potential therapeutic value against breast CSCs. However, there is a need to support the effective roles of flavopiridol in targeting breast CSCs with *in vivo* and clinical studies.

Ethics

Ethics Committee Approval: Ethics committee approval was not required since our study was a cell culture study.

Peer-review: Externally peer reviewed.

Authorship Contributions

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

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

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Original Article

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Management and Outcomes of Paediatric Patients with Palpitations Examined in Our Clinic

Çarpıntı Şikayeti ile Kliniğimizde İncelenen Çocuk Hastaların Sonuçları ve Tedavi Yönetimi

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ABSTRACT

Objective: We retrospectively reviewed the data of patients who presented to the paediatric cardiology clinic with complaints of palpitations. We aimed to describe the characteristics of these patients, the rhythm disorders that were detected, and the treatment methods with a particular attention on rare and vital diseases.

Methods: In total, 1,680 patients aged 5-18 years who presented with palpitations at the paediatric cardiology clinic between January 2016 and June 2019 were enrolled. Of these, 714 (42.5%) were male and 966 (57.5%) were female. All the hospital records including electrocardiography, echocardiography, cardiovascular stress test, 24-h Holter monitoring, event recorder and genetic analysis results were reviewed.

Results: The mean age of the patients was 13.5±3.2 years (range: 5-17.8 years). Palpitation was accompanied with chest pain in 218 patients, shortness of breath in 152 patients and weakness in 67 patients. Also, 726 Holter monitoring, 165 event recorder and 104 cardiovascular stress test results were evaluated. Dysrhythmia was detected in 306 patients (18.2%). The most common dysrhythmias were supraventricular extrasystoles (n=171, 55.8%) and ventricular extrasystoles (n=82, 26.8%). Five patients were diagnosed with non-sustained ventricular tachycardia (VT) episodes, one with long QTc syndrome and one with catecholaminergic polymorphic VT. Two patients were followed-up for arrhythmogenic right ventricular dysplasia (ARVD), 12 patients had mitral valve prolapsed (MVP), 8 had valvular heart disease caused by acute rheumatic fever (ARF) and 7 had bicuspid aortic valve (BAV).

ÖZ

Amaç: Bu çalışmada, çocuk kardiyoloji polikliniğine çarpıntı şikayeti ile başvuran hastaların bilgileri retrospektif olarak incelendi. Bu konu ile ilgili güncel yaklaşımlar derlendi, ayrıca seyrek görülen ve hayati önemi olan hastalıklara dikkat çekilmeye çalışıldı.

Yöntemler: Ocak 2016 - Haziran 2019 tarihleri arasında 5-18 yaş arasında olan ve çarpıntı şikayeti ile çocuk kardiyoloji polikliniğine başvuran 1680 hasta çalışmaya dahil edildi. Hastaların 714'ü erkek (%42,5) ve 966'sı (%57,5) kız idi. Hastaların elektrokardiyografi (EKG), ekokardiyografi, kardiyovasküler stres test, 24 saat ritim Holter, olay kaydedici ve genetik analiz bilgilerini içeren tüm hastane kayıtları incelendi.

Bulgular: Hastaların yaş ortalaması 13,5±3,2 yıl (minimum/maksimum: 5-17,8 yıl) idi. Çarpıntı şikayetine 218 hastada göğüs ağrısı, 152'sinde nefes darlığı ve 67'sinde halsizlik şikayeti eşlik ediyordu. Hastalara ait 726 ritim Holter, 165 olay kaydedici, 104 kardiyovasküler stres test incelendi. Hastaların 306'sında (%18,2) disritmi belirlendi. En sık belirlenen disritmiler supraventriküler ekstrasistol (n=171, %55,8) ve ventriküler ekstrasistol (n=82 %26,8) idi. Beş hasta ventriküler taşikardi, bir hasta uzun QTC sendromu, bir hasta katekolaminerjik polimorfik ventriküler taşikardi (VT) tanısı aldı. İki hasta aritmojenik sağ ventrikül displasizi açısından izleme alındı. Hastaların 12'sinde mitral kapak prolapsusu, 8'inde akut romatizmal ateşe bağlı kalp kapak hastalığı ve 7'sinde biküspit aortik kapak belirlendi.

Sonuç: Çocuklarda yaygın poliklinik başvuru sebeplerinden olan çarpıntı şikayeti sıklıkla iyi huylu patolojilerle ilişkili olsa da ciddi

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Conclusion: Palpitation is one of the common causes of outpatient clinic visits in children and it may be the first symptom of serious arrhythmias, although it is frequently associated with benign pathologies. Most life-threatening dysrhythmias can be detected by a thorough analysis of the patient using basic cardiological examination methods.

Keywords: Palpitation, electrocardiogram, rhythm holter, symptoms, child

aritmilerin ilk semptomu olabileceği mutlaka akla getirilmelidir. Hayatı tehdit edebilecek çoğu ritim bozukluklarını hastaların iyi bir şekilde analiz edilmesi ve temel kardiyolojik inceleme metodlarının kullanılması ile saptamak mümkündür.

Anahtar Sözcükler: Çarpıntı, elektrokardiyografi, ritim holter, semptomlar, çocuk

Introduction

Palpitation is a challenging symptom that is often encountered by paediatric cardiologists. The challenging factors include the pathological findings frequently occurring with the symptoms and symptoms disappearing in most patients during hospital visits. Basal electrocardiography (ECG) rarely provides clues regarding the pathology, usually showing normal findings. Normal findings observed in the first evaluation should not mislead the physician, who should carefully run further tests considering that the patient may be experiencing a rhythm disorder. This study describes the characteristics of patients who presented with palpitation at our clinic, rhythm disorders that were detected, and the treatment methods.

Methods

Children aged 5-18 years who presented to the paediatric cardiology clinic with complaints of palpitation were included in this study. ECG and echocardiographic examination were performed for all patients. Cardiovascular stress test, 24-h Holter monitoring, event recorder monitoring, cardiac magnetic resonance imaging (MRI) and genetic analyses were performed when necessary. In this study, 726 Holter monitoring, 165 event recorder monitoring, and 104 cardiovascular stress test recordings were evaluated. Patients with complex congenital heart disease were excluded from this study. In addition, patients who did not regularly attend follow-up visits were excluded from the study.

Statistical Analysis

Statistical analysis was performed using the PASW version 17.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed in mean ± standard deviation (SD), median (minimum-maximum), or number and frequency. Chi-square test was used to compare the categorical variables. A p value <0.05 was considered statistically significant.

Results

The mean age of the children included in the study was 13.5±3.2 years (range: 5-17.8 years). Palpitation was accompanied with chest pain in 218 patients, shortness of breath in 152 patients, weakness in 67 patients, numbness of the hands and face in 21 patients, nausea in 16 patients, dizziness in 12 patients and fainting in three patients. Dysrhythmia was detected in 306 patients (18.2%). Of the patients with dysrhythmia, 171 (55.8%) had supraventricular extrasystole (SVE), 82 (26.8%) had ventricular extrasystole (VES), 22 (7.2%) had ectopic atrial rhythm, 12 (4%) had Wolff-Parkinson-White syndrome (WPW), 9 (3%) had supraventricular tachycardia (SVT), five (1.6%) had VT episodes, one had long QTc syndrome, one had hyperthyroidism-induced sinus tachycardia, one had atrial flutter (AF), one had focal atrial tachycardia (FAT) and one had catecholaminergic polymorphic VT. Genetic testing was performed in four patients to evaluate their genetic dysrhythmia. Two patients with suspected arrhythmogenic right ventricular dysplasia (ARVD) (Figure 1) were evaluated using cardiac MRI. Of the patients with SVE, 82 (48%) were male and 89 (52%) were female. Of the patients with premature VES, 39 (47.6%) were male and 43 (52.4%) were female. Although no statistically significant difference was noted, the incidence of SVE and VES in males was slightly higher than in females ($p>0.05$). Supraventricular extrasystoles identified on Holter monitoring or ECG were considered to be benign dysrhythmias and were followed-up without any treatment. Similarly, 22 patients with ectopic atrial rhythms did not require any treatment. Medical treatment was commenced in 13 of the 82 patients with ventricular extrasystole due to frequent VESs (Figure 2). The

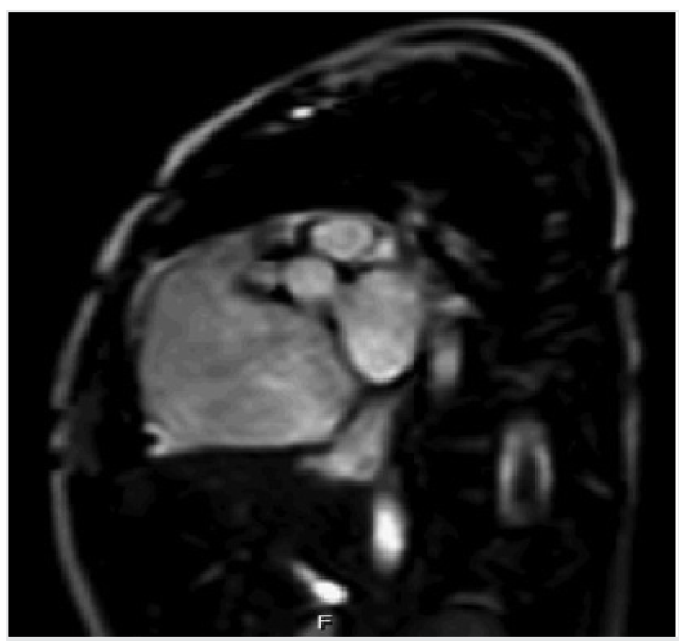

Figure 1. Magnetic resonance imaging of a 3-year-old patient with suspected ARVD shows enlargement of right ventricular outflow tract

ARVD: Arrhythmogenic right ventricular dysplasia

follow-up Holter monitor recordings performed in all but two of the treated patients showed a significant reduction in VES frequency.

We found that the VES rates were reduced after rearranging the medical treatment in two patients whose first-line treatments were unsuccessful. Sixty-nine patients who were found to have a low VES frequency in the Holter monitoring and who had no increase in VES in the cardiovascular stress test, were considered to have a low risk and followed-up without treatment. Electrophysiological studies (EPS) and catheter ablation were not required in any of the patients with VES. Of the five patients with non-sustained VT episodes, one is currently being followed-up with medical treatment. The remaining four patients who were found to have a short coupling interval and frequent VES were referred to undergo risk analysis for EPS and catheter ablation.

Seven out of twelve patients who were found to have WPW syndrome on ECG were referred for EPS and catheter ablation risk analysis (Figure 3). The other five patients with WPW were younger and had no documented episodes of SVT. Therefore, these patients were placed under clinical follow-up after their families were informed and educated about SVT episodes. Eight of the nine patients with supraventricular tachycardia were referred for catheter ablation. One patient with a slow-fast SVT episode of 10-15 beats in the Holter monitoring was placed under follow-up with medical treatment due to the young age. One patient with hyperthyroidism-induced sinus tachycardia was put on beta-blocker therapy until the results of the thyroid function tests returned to normal. In this patient, sinus tachycardia resolved after the patient's thyroid functions improved. In one patient, FAT was controlled with medical treatment at the acute stage and tachycardia did not recur during the follow-up period. In a patient with a history of exercise-induced syncope, an episode of bidirectional VT developed during the cardiac stress test (Figure 4) and the patient was diagnosed with catecholaminergic polymorphic VT. The patient's symptoms improved after receiving therapy a beta-blocker therapy. Flecainide was also initiated and left sympathetic denervation was performed. One patient diagnosed with long QTc (QTc: 480 msec) syndrome was placed under beta-blocker therapy and followed-up. Another

Figure 2. Three-channel 24-h Holter monitoring shows monomorphic VES in a 15-year-old patient

VES: Ventricular extrasystole

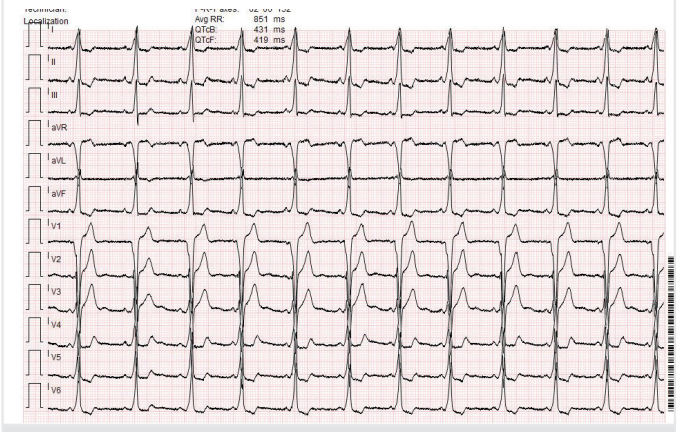

Figure 3. The basal ECG of a 10-year-old patient diagnosed with Wolff-Parkinson-White syndrome who underwent catheter ablation shows a short PR interval, delta wave, and wide QRS

ECG: Electrocardiography

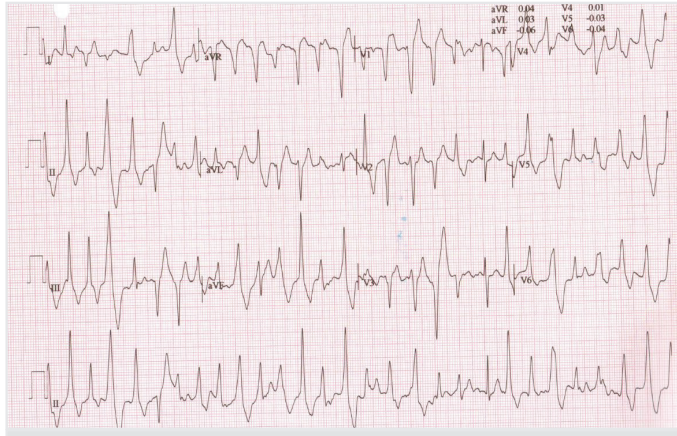

Figure 4. A patient with a history of exercise-induced syncope who had a bidirectional VT episode at the fifth minute of the cardiac stress test was diagnosed with catecholaminergic polymorphic VT

VT: Ventricular tachycardia

patient diagnosed with atrial flutter started receiving therapy with sodium warfarin (with an INR range of 2-3) and a beta-blocker to control the heart rate. Sodium warfarin therapy was continued for three weeks and then synchronised cardioversion followed by transoesophageal echocardiography was performed. One month after the cardioversion, the atrial flutter recurred and the patient was referred for catheter ablation therapy.

In addition, MVP was detected in 12, ARF-induced heart valve disease in 8 and BAV in 7 patients included in this study (Table 1). Clinical follow-up of all the patients was continued periodically.

Discussion

Palpitation is defined as a disturbing sensation of flutter in the chest. Patients may often describe sinus tachycardia when they present with complaints of palpitation. Conditions such as panic disorders, anaemia, hyperthyroidism, obesity and non-cardiac sinus tachycardia such as postural orthostatic tachycardia syndrome may also lead to the complaint of palpitation. Dysrhythmias other than these are also important causes of palpitation. Palpitation is a feeling of discomfort caused by dysrhythmias. The present study primarily focused on dysrhythmias. Patients may express their feeling of palpitation in several ways: by saying that sometimes their heart beats quickly, sometimes there is a feeling of fluttering wings in their chest, sometimes there is a short-term twisting sensation in their chest that repeats from time to time and sometimes it feels as if they felt their heartbeat in their mouth. A detailed history should be obtained before assessing the possibility of dysrhythmia and the need for further examination in a child presenting with a complaint of palpitation. It should be kept in mind that young children may find it difficult to express their feeling of palpitations and it should be known that the underlying causes of fainting and chest pain in paediatric patients may be serious dysrhythmias. Similar to our study, complaints such as chest pain, shortness of breath and fatigue are frequently reported in addition to palpitations (1). SVE and ectopic atrial rhythm are frequently observed in children using 24-h Holter monitoring, although they rarely present with symptoms. They are usually of no clinical significance and do not require treatment (1). The clinical significance of supraventricular extrasystoles is that they can trigger some re-entrant tachycardias. In our study, SVE was the most common dysrhythmia and no patient with SVE required treatment. The nature of the palpitation, its onset and whether or not it is sustained can give us a clue about the cause of the palpitation. One of our patients reported experiencing palpitations for 15 days and that this complaint has been persisting. The patient's ECG showed sinus tachycardia that was incompatible with symptoms and hyperthyroidism was detected in the patient's thyroid function tests. Beta-blocker therapy was commenced for tachycardia and tachycardia resolved after controlling hyperthyroidism.

Table 1. Demographic characteristics and diagnosis of patients

	N=1680
Mean age (min - max) years	13.5±3.2 (5-17.8)
Gender	
Male/female	714 (42.5%)/966 (57.5%)
Chest pain	218 (13%)
Respiratory distress	152 (9%)
Debility	67 (3%)
Hands and face numbness	21 (1%)
Nausea	16
Dizziness	12
Syncope	3
Premature supraventricular extrasystole	171 (10.2%)
Premature ventricular extrasystole	82 (4.8%)
Ectopic atrial rhythm	22 (1.3%)
Wolff-Parkinson-White syndrome	12
Supraventricular tachycardia	9
Non-sustained ventricular tachycardia	5
Long QTc syndrome	1
Catecholaminergic polymorphic VT	1
Sinus tachycardia due to hyperthyroidism	1
Atrial flutter	1
Focal atrial tachycardia	1
Mitral valve prolapse	12
Heart valve disease due to ARF	7
Atrial septal defect	5
Coronary artery fistula	3
Patent ductus arteriosus	3
Ventricular septal defect	1

ARF: Acute rheumatic fever, VT: Ventricular tachycardia

Nodal premature beats are narrow QRS complexes with no P wave as the excitation originates from the AV node. Rarely, there may be an inverse P wave just in front of or behind the narrow QRS complexes. Nodal premature beats are mostly benign and do not require treatment.

The duration of the palpitation with other accompanying symptoms such as fainting and the patient's age facilitates the identification of the underlying cause. Premature VESs are described as occasional twisting and short-term compression in the chest or short-term shortness of breath. When a thorough history is taken, it may be possible to obtain this information from the paediatric patients. Premature VES is common in healthy children as well as in children with heart disease. Without significant heart disease, isolated premature VESs occur in 10-15% of infants and 20-35% of adolescents, whereas ventricular tachycardias are rare (2-5%). Most are benign and few require treatment (6-8). Consistent with the literature, medical therapy with good response was initiated in very few patients in the present study and none of the patients required EPS and catheter ablation.

Although ventricular extrasystoles are often idiopathic, they may be associated with cardiomyopathy, myocarditis, diffuse myocardial damage, coronary artery pathologies, hypokalaemia, hypocalcaemia, acidosis, or hypoxemia (9,10). Most of the premature VESs that require medical therapy can be suppressed using drug therapy and catheter ablation may rarely be needed (10). Medical treatment alone was sufficient without the need for catheter ablation in all of our patients with premature VES. A VES rate higher than 20% of the 24-h total QRS complex is described as very frequent VES and because this is considered a risk factor for cardiomyopathy, it is recommended that patients be placed on medical therapy or undergo catheter ablation (8,11-13). As reported in the literature, four of our patients with frequent VES who experienced episodes of non-sustained VT were referred for catheter ablation and the VT episodes of one patient were controlled with medical treatment.

The treatment of WPW syndrome depends on the type of dysrhythmia, clinical condition and age of the child. Catheter ablation is the recommended treatment for older children (14-18). Catheter ablation has a high success rate and the long-term use of medications is not required (14-18). In our study, in accordance with the recommendations in the literature, older children with WPW syndrome were referred for EPS and catheter ablation. Families of younger patients who had no documented episodes of SVT were taught on how to check the pulse in order to recognise an SVT episode and the patients were placed under clinical follow-up.

The risk of recurrence of SVT in infants is high in the short term; thus, prophylactic antiarrhythmic drug use is required. Prophylactic drugs are usually given for 6-12 months and most infants do not experience recurrence after this period (19,20). The persistence of pre-excitation findings on ECG significantly increases the risk of SVT recurrence. If SVT occurs or persists in older children, catheter ablation is recommended since spontaneous recovery is unlikely (19-22). In the case of SVTs that are resistant to medical therapy, catheter ablation can be performed with high success and low complication rates at any age including new born infants (21-29). In our study, all but one patient with SVT were referred for catheter ablation. One young patient with SVT was followed-up with medical therapy.

Although catecholaminergic polymorphic VT is rare in children, it is one of the dangerous ventricular dysrhythmias with a high mortality risk (30,31). The observation of bidirectional ventricular premature beats and/or polymorphic VT episodes in ECG recordings during exercise or during Holter monitoring are characteristic findings for diagnosis (30,31). Similarly, bidirectional VT episodes were detected in one patient with exercise-induced syncope during the cardiac stress test in our study. In this patient, syncope attacks were not observed after the initiation of beta-blocker plus flecainide therapy together with left cardiac sympathetic denervation.

Arrhythmogenic right ventricular dysplasia is a disease characterised by the replacement of the myocardium of both ventricles, usually the right ventricle by fat and fibrous tissues (32,33). It occurs in a wide clinical spectrum and the patients may be asymptomatic; however, heart failure, dysrhythmia, or sudden death may be the first sign of the disease (32,33). It is a genetic disease and early diagnosis and treatment increases the quality of life and duration. There is no standalone diagnostic tool for ARVD. Diagnosis is made by clinical, electrocardiographic and radiological features. According to the diagnostic criteria updated in 2010, two major or one major and two minor criteria are required for the definitive diagnosis (33). The two patients in our study did not fully meet the diagnostic criteria but were followed-up as suspicious cases.

The main concerns in patients examined for palpitations are the identification of patients who are at risk of sudden cardiac death and making efforts to reduce this risk; this is a crucial reason for the diagnosis and treatment of dysrhythmias that trigger cardiomyopathies. In our study, a patient with catecholaminergic polymorphic VT and another patient with long QTc syndrome at risk of sudden cardiac death were placed on a therapy. In addition, one patient with AF, one with FAT and patients with frequent polymorphic VES who were considered to be at risk for cardiomyopathy were placed on a therapy.

Study Limitations

The retrospective design of this study is an important disadvantage with regard to data collection and analysis. The retrospective study design also complicates the testing of the accuracy of diagnosis by questioning the palpitation complaints. The large sample size screened in this study is considered to be an important strength.

Conclusion

Palpitation is the most important symptom of dysrhythmias in children. In patients presenting with palpitations, the possibility of a cardiac disease that can be fatal and result in sudden death should not be overlooked. Reducing the families' anxiety can only be possible by determining the causes of the palpitations. The most important step for starting treatment is to first detect these dysrhythmias.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

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Original Article

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Validation and Reliability of the Turkish Premenstrual Coping Measure

Premenstrual Semptomlarla Baş Etme Ölçeği'nin Türkçe Geçerlik ve Güvenirlik Çalışması

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ABSTRACT

Objective: The aim of this study is to evaluate the Turkish validity and reliability of the premenstrual coping measure (PCM) among university students.

Methods: The universe of this methodological study consisted of 364 university students who were found to meet the inclusion criteria in a university in the spring semester of the 2016-2017 academic year. In the study, stratified sampling method was used and stratified weights were determined according to the education field (health, social and natural sciences). Data were collected by using the Inclusion Criteria Questionnaire, Premenstrual Symptoms Screening Tool, Personal Information Form, and PCM. In the study, scale validity was determined by language, content and construct validity methods; scale reliability was evaluated by Cronbach alpha reliability coefficient calculation and test- retest method.

Results: In the study, the content validity index of the PCM was determined as 0.997. As a result of confirmatory factor analysis, 5 items were removed from the scale. The fit index values obtained for the 27-item measurement model was found to be acceptable. Cronbach's alpha reliability coefficients of the scale sub-dimensions were found to be highly reliable. The correlation between the re-test and the first test was calculated for the sub-dimensions of the PCM, and it was found that the correlation coefficients and the scale did not show a time-dependent change.

Conclusion: In the study, it is concluded that PCM is a valid and reliable instrument that can be used to evaluate the premenstrual symptoms coping status of university students with premenstrual symptoms.

Keywords: Premenstrual coping measure, validity, reliability

ÖZ

Amaç: Çalışmada Premenstrual Semptomlarla Baş Etme Ölçeği'nin (PSBÖ) üniversite öğrencilerinde Türkçe geçerlik ve güvenirliğinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Metodolojik tipte olan bu çalışmanın örneklemini 2016-2017 eğitim-öğretim yılı bahar döneminde bir üniversitede öğrenim gören öğrencilerden araştırmaya dahil edilme kriterlerine uygun 364 öğrenci oluşturmuştur. Çalışmada tabakalı örnekleme yöntemi kullanılmış olup, öğrenim alanına (sağlık, sosyal ve fen bilimleri) göre tabaka ağırlıkları belirlenmiştir. Veriler Araştırmaya Dahil Edilme Kriterleri Soru Formu, aybaşı öncesi belirtileri tarama gereci, kişisel bilgi formu ve PSBÖ kullanılarak toplanmıştır. Çalışmada ölçek geçerliği dil, kapsam ve yapı geçerliği yöntemi ile; ölçek güvenirliği ise Cronbach alfa güvenirlik katsayılarının hesaplanması ve test-tekrar test yöntemi ile değerlendirilmiştir.

Bulgular: Çalışmada PSBÖ'nün kapsam geçerlik indeksi 0,997 olarak belirlenmiştir. Doğrulayıcı faktör analizi sonucunda ölçekten 5 madde çıkarılmıştır. Yirmi yedi madde ile oluşturulan ölçüm modeli için elde edilen uyum indeks değerlerinin kabul edilebilir düzeyde olduğu saptanmıştır. Ölçek alt boyutlarına ait Cronbach alfa güvenirlik katsayılarının yüksek derecede güvenilir olduğu belirlenmiştir. PSBÖ'nün alt boyutları için tekrar test ile ilk test arasında korelasyon hesaplanmış olup, sınıf içi korelasyon katsayıları ile ölçeğin zamana bağlı bir değişim göstermediği tespit edilmiştir.

Sonuç: Çalışmada PSBÖ'nün üniversitede öğrenim gören ve premenstrual semptom yaşayan kız öğrencilerin premenstrual semptomlarla baş etme durumlarını değerlendirmede kullanılabilecek geçerli ve güvenilir bir ölçüm aracı olduğu sonucuna ulaşılmıştır.

Anahtar Sözcükler: Premenstrual semptomlarla baş etme ölçeği, geçerlik, güvenirlik

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Introduction

Menstruation in women's life is a period that starts with puberty and repeats every month until menopause. Hormonal changes in the menstrual cycle can cause problems such as anxiety, irritability, depressive mood, sudden change in mood, sleep disturbance, fatigue, change in sexual desire, breast swelling and tenderness, weight gain, headache, appetite change, general body aches and edema (1-4). The American College of Obstetricians and Gynecologists defines the condition where these physical and emotional symptoms appear about five days before menstruation and end within a few days with the onset of menstruation, as premenstrual syndrome (PMS) (3).

Of women at reproductive age in the world, 90-95% experience premenstrual changes (2). In a systematic analysis study, it was determined that the prevalence of PMS in the world was 47.8% and that the prevalence of PMS was lowest in France (12%) and highest in Iran (98%) (5). Studies show that PMS prevalence is quite common in our country (6-9). It is noteworthy that the prevalence of PMS varies between 66% (10) and 91.8% (11), especially in young women.

Premenstrual symptoms can cause a change in body perception, decrease in self-confidence, deterioration in family and social relationships, sleep problems, substance abuse, increased tendency to commit crime, increased tendency to accidents, loss of labor and economic losses (12,13). In addition to all these problems, PMS negatively affects the future general health, reproductive health and quality of life of young women aged 15-24. In particular, it prevents students from attending classes and reduces their academic success (14,15).

The etiology of PMS is thought to be multifactorial. Studies show that estrogen, progesterone, serotonin, gamma-aminobutyric acid levels, genetic properties, nutrition, body mass index, and exercise are associated with PMS (16-19).

Thyroid diseases, irritable bowel syndrome, symptoms related to climacteric syndrome, anxiety, fatigue, depression can often be confused with premenstrual symptoms (3,19). Half of those who experience PMS experience one or more of these health problems. In this regard, it is important to evaluate women thought to experience PMS in terms of these diseases (17). PMS cannot be diagnosed by laboratory tests, but it can be distinguished from other diseases by blood and urine analyzes (4,19). At the same time, posttraumatic stress disorder and sexual abuse were found to be associated with PMS (20). In this regard, the menstrual, reproductive and medical history of the woman should be evaluated in detail (17,21).

The time and type of premenstrual symptoms are important for the diagnosis of PMS (4). The severity of symptoms seen in the luteal phase increases before menstruation and decreases at the end of menstruation (17). In addition, the diagnosis of PMS should be confirmed by healthcare professionals using PMS scales and by reviewing the two-month daily records (3,17,21,22).

When the literature is examined, the importance of individualized treatment approach by a multidisciplinary team is remarkable in reducing premenstrual symptoms (14,15). It is also recommended to adopt a holistic and gradual approach to dealing with premenstrual symptoms (15,21,23). In this context, it is recommended to provide life modification by teaching self-care practices such as raising awareness through training and counseling, providing self-monitoring (keeping PMS diary), lifestyle changes (regular exercise, adequate and quality sleep, quitting smoking, communicating, choosing the appropriate clothing), diet regulation, methods of dealing with stress (relaxation exercise such as breathing exercise, meditation and yoga, bathing, hobbying, massage, biofeedback, autohypnosis), dietary modification, methods of coping with stress (breathing exercises, a relaxation exercise such as meditation and yoga, taking a bath, dealing with a hobby, massage, biofeedback and other methods such as autohypnosis). In the second step approach, non-pharmacological methods including traditional and complementary medicine practices (calcium + vitamin D, magnesium supplement) and cognitive behavioral therapy are recommended. Pharmacological strategies such as hormonal (estrogen, danazol, gonadotropin releasing hormone analogues), non-hormonal (selective serotonin reuptake inhibitors) and symptomatic therapies (non-steroidal anti-inflammatory drug and diuretic) are recommended in cases where the problem persists (3,21-26) .

Health professionals have roles and responsibilities in determining women's PMS status and coping levels with premenstrual symptoms and in gaining coping behaviors (3,21). When the literature is analyzed, it is determined that there is no standard Turkish measurement tool to evaluate how women can cope with premenstrual symptoms. In this study, it was aimed to evaluate the validity and reliability of the Premenstrual Coping Measure (PCM) developed by Read et al. (2) for Australian women.

Methods

In this study, the first stage of the doctorate thesis titled "Evaluation of the Effectiveness of Coping with Premenstrual Symptoms Education Program based on Information-Motivation-Behavioural Skills (IMB) Model in University Students", which examined the Turkish validity and reliability of PCM, was presented.

The Universe and the Sampling of the Research

The universe of the study was composed of all students studying at Ankara Yıldırım Beyazıt University in the spring term of 2016-2017 academic year (n=5757). In scale validity and reliability studies, it is recommended that the sample volume be 5-10 times the total number of scale items (27). In this context, the sample of the study was intended to be composed of at least 224 students who were studying at the university in the spring semester of 2016-2017 academic year (Scale number of items =32, 7 times of number of items =224). The stratified sampling method was used in the study, considering that students' behavior to cope with premenstrual symptoms might differ depending on the area they were getting education. Layer weights were determined according to the state of education in health, social and science.

It was aimed to reach at least 61 students in the field of Health Sciences, at least 142 students in the field of Social Sciences and at least 21 students in the field of Natural Sciences. At the same time, it was aimed to reach at least 45 students from each class including preparatory class, first, second, third and fourth year classes (n=224). In the study, more students were reached with the prediction of data losses. When 344 students were reached, the number of students to enter the teaching area layers was completed ($n_{health\ sciences}$ =69, $n_{social\ sciences}$ =242, $n_{natural\ sciences}$ =33). However, since the targeted number of students according to class level could not be reached, it was continued to collect data from the first year class, which had missing number. Twenty seven more students were reached and seven of these students were found to fill the data collection forms incompletely. The study was completed with 364 students ($n_{preparatory}$ =87, $n_{first\ year}$ =65, $n_{second\ year}$ =66, $n_{third\ year}$ =69, $n_{fourth\ year}$ =77).

Criteria For Inclusion In the Study

The inclusion criteria of the study; 1) Students having premenstrual symptoms (Students marking at least one of the items of 1st-14th items of the Premenstrual Symptoms Screening Tool (PSST) as "mild", "moderate" or "severe"), 2) students having regular menstruation every 24-35 days (22), 3) students who did not have pregnancy or lactation for the past 12 months, 4) students who did not use oral contraceptives, 5) students who were literate in Turkish, and 6) students who volunteered to participate in the study.

Data Collection Tools

The Inclusion Criteria Questionnaire: The Inclusion Criteria Questionnaire prepared by the researchers in line with the literature review (1,2,5,14) consisted of 6 items containing the inclusion criteria of the study. The students who stated the 1st, 2nd, 5th and 6th questions of the Inclusion Criteria Questionnaire as "yes", and the 3rd, 4th questions as "no" were included in the study.

The Premenstrual Symptoms Screening Tool (PSST): The PSST was developed by Steiner et al. (28) to identify premenstrual symptom, PMS or premenstrual dysphoric disorder. The scale, which is a four-point Likert type scale and consists of 22 items, determines the degree of premenstrual symptoms and how much they affect life. Marking at least one of the items of 1st-14th items of the scale as "mild" or "moderate" or "severe" is considered as "having premenstrual symptom". The Turkish validity and reliability study of the scale was done by Özdel et al. (29) and Cronbach's alpha reliability coefficient was determined as 0.92. In our study, Cronbach alpha reliability coefficient was calculated as 0.92.

Personal Information Form (PIF): PIF was prepared by researchers in line with the literature review (1,2,5,14) and opinions were received from three experts. The form contained a total of 12 items related to the individual and sociodemographic characteristics of the students such as education area, class, age, residential area, and family type.

Premenstrual Coping Measure (PCM): The PCM was developed by Read et al. (2) to evaluate the coping status of Australian women aged 18-49 with symptoms in the premenstrual period. Each item of the scale, which consists of 5 sub-dimensions in five-point Likert type, is scored between 1-5. There is no evaluation on the total score of PCM. As the score obtained from the sub-dimensions of the measure increases, the ability to cope with premenstrual symptoms increases. With the measure structure consisting of 32 items, 38.9% of the variance is explained. In addition, the sub-dimensions of the measure are in a meaningful relationship with each other, and the coefficients of coherence vary between 0.188 -0.518. The items in the measure sub-dimensions, the lowest and highest scores that can be obtained from the sub-dimensions and the Cronbach alpha reliability coefficients of the sub-dimensions are given in Table 1 (2).

Application of the Research

The measure validity was evaluated by language, scope and construct validity methods, and the measure reliability was evaluated by calculating Cronbach alpha reliability coefficients and test-retest method (Figure 1).

Language Validity: The measure items were translated from English to Turkish by three different foreign language experts and from Turkish to English by three different foreign language experts for the language validity. A single Turkish draft measure form was prepared by comparing the English translations with the original measure and selecting the most appropriate expressions from the Turkish translations.

Scope Validity: Davis Technique was used to evaluate the scope validity of the study. For the Turkish draft measure form, it was sent to 13 experts in the field of women's health, mental health, child health, public health and measurement-evaluation and a Turkish language expert (n=14). The experts were asked to evaluate each measure item in the range of 1-4 points in terms of language, expression, understandability, and suitability, and the

Table 1. Features related to the sub-dimensions of PCM (2)

Sub-dimensions	Items	Min. point	Max. point	Cronbach alpha
1. Avoiding harm	1-8	8	40	0.89
2. Awareness and Acceptance of premenstrual change	9-18	10	50	0.86
3. Adjusting energy	19-23	5	25	0.73
4. Self-care	24-27	4	20	0.81
5. Communicating	28-32	5	25	0.68

Min: Minimum, Max: Maximum, PCM: Premenstrual coping measure

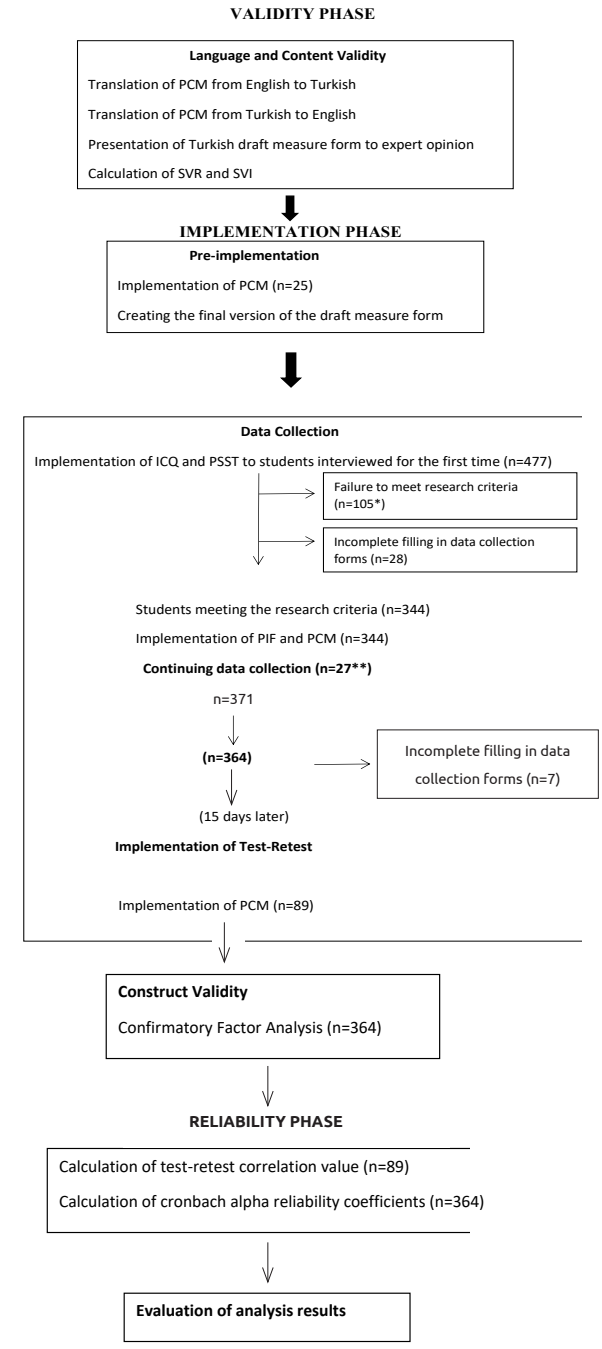

Figure 1. Flow chart of the research

Turkish language specialist was asked to evaluate the final version of the Turkish measure in terms of compliance with Turkish language rules. According to the evaluations from the experts, the scope validity ratio (SVR) of each item was calculated and Scope Validity index (SVI) was calculated for the requirement and eligibility level of each item.

Pre-Application: In order to evaluate the comprehensibility of PCM and whether there was any change in perception while applying the measure, 25 students in accordance with the research criteria were reached and the measure was pre-applied. The data obtained in the pre-application were not included in the study. In this context, some structural changes were made in the sentences, and the draft measure form was rearranged.

Data Collection: Within the scope of the study, students were informed about the research at a time when they did not have lessons in the classroom. PSST, PIF and PCM were given to the students who volunteered to participate in the study and students who answered "yes" to 1st, 2nd, 5th and 6th items of the Inclusion Criteria Questionnaire and "no" to 3rd and 4th items were asked to continue to fill the forms. The students were asked to continue filling out the data collection forms. Of the 477 students interviewed, 372 students met the inclusion criteria. As 28 of these students filled the data collection forms incomplete, the study was completed with 344 students.

Test-retest Application: The reliability of the measure was evaluated with the test-retest method. The test-retest application of the study was carried out after 15 days by reaching students (25% of 224=56). In this context, PSST was sent to 364 students via e-mail. Eighty nine students sent back the PSST, which they filled in, and the test-retest application of the study was completed.

Construct Validity: Confirmatory Factor Analysis (CFA) method was used to evaluate the construct validity of PSST. With this method, the suitability of the measure's factor and item structure to the Turkish culture and the verification of the measure model were evaluated. The measurement model established to verify the structure consisting of 32 items was analyzed and item factor loads and fit index values were examined.

Measure Reliability: Cronbach alpha reliability coefficients of the measure sub-dimensions in evaluating the internal consistency of PSST were used and in determining the stability, Intraclass Correlation Coefficient (ICC) was calculated by looking at the correlation between the retest and the first test.

Ethical Aspect of the Study

In order to carry out the validity and reliability study of PCM in Turkish, written permission was obtained from the measure owner and the author for the use of PMST. Ethical approval (date/number: 10.09.2017/08) was obtained from Ankara Yıldırım Beyazıt University Ethics Committee and institutional permission was obtained from the faculties. Volunteerism was used in participation in the study and informed written consents of those who agreed to participate were obtained. In the study,

the ethical principles of "Confidentiality and protection of confidentiality", "Respect for autonomy" and "Do not harm/ benefit" were followed (30). This research was carried out outside the course hours of the students and education was not disrupted. There was no relationship of interest between researchers and students.

Evaluation of the Data

Data were transferred to IBM SPSS Statistics 23 package program and analyzes were done. While analyzing the data, frequencies (number, percentage) were given for categorical variables and descriptive statistics [mean ($\bar{X}$), standard deviation (SD)] were given for numerical variables. Language, scope and construct validities of the study within the scope of measure validity were evaluated and within the scope of measure reliability, test-retest method was used and Cronbach alpha reliability coefficients were calculated.

Results

The average age of students was 21.42±1.82, 65% of them were in the field of social sciences and 24% in preparatory class. Of the students 63% lived in the Central Anatolia Region and 66% lived in the city centers. Of the students 79% stated that their income covered the expenses of their income and 87 of them had nuclear families. The education level of the mother of 50% of the students was primary school and the education level of 66% was high school and above. According to the statements of the students and the results of PSST, 58% of the students experienced PMS and 14% had premenstrual dysphoric disorder (Table 2).

When the scope validity results of PCM were examined, it was determined that the SVR value of item 8 was 0.923 and the SVR values of other items were 1. In addition, the measure's SVI value was found to be 0.997.

The measurement model established to verify the structure consisting of 32 items was analyzed with CFA which was used in evaluation of the structure. As a result of the analysis, it was seen that the model did not show enough compliance. For this reason, model improvement studies were carried out. Firstly, by looking at the modification index table, Chi-Square drop values ("M.I." values) for possible changes in the model were examined. The modification demonstrated by highest "M.I." was tied to situations that were conceptually appropriate and the model was executed. "Item 8" which was loaded with too many modifications, and "item 9", "item 19", "item 23" and "item 31" of which factor loads were low, were removed from the structure. As a result, the model was confirmed. It is seen in Figure 2 and Table 3 that with which items the measurement model confirmed with 27 items are formed. In Figure 2 and Table 3, there are standardized regression coefficients, namely factor loads, that are belong to ways on One-Way arrows.

The fit index values of PCM are as follows: The ratio of chi-square to degrees of freedom (χ^2/SD) is 2.353, Goodness of Fit Index (GFI) is 0.868, Incremental Fit index (IFI) is 0.920,

Table 2. Individual characteristics of students

Individual characteristics	n	%
Age ($\bar{X}$ ± SD =21.42±1.82)		
Educational field		
Social sciences	237	65.1
Health sciences	86	23.6
Natural sciences	41	11.3
Class		
Preparatory class	87	23.9
First year	65	17.9
Second year	66	18.1
Third year	69	19.0
Fourth year	77	21.2
Region in which the individual lived longest		
Mediterranean Region	36	9.9
Eastern Anatolia Region	14	3.8
Aegean Region	15	4.1
Southeast Anatolia Region	8	2.2
Central Anatolian Region	230	63.2
Marmara Region	28	7.7
Black Sea Region	33	9.1
Residential area		
Provincial Center	240	65.9
District center, parish, village, abroad	124	34.1
Economical status		
Income more than expense	45	12.4
Income equal to expense	286	78.6
Income less than expense	33	9.1
Family type		
Nuclear family	318	87.4
Extended family, mother-father divorced	46	12.6
Educational status of the mother		
Illiterate, literate	33	9.1
Primary school	184	50.5
High school and ↑	147	40.4
Educational status of the father		
Illiterate, literate	12	3.3
Primary school	113	31.1
High school and ↑	239	65.6
Menarche age ($\bar{X}$ ± SD =13.19±1.246)		
Experiencing PMC (According to PSST)		
Yes	210	57.7
No	154	42.3
Experiencing premenstrual dysphoric disorder (According to PSST)		
Yes	51	14.0
No	313	86.0

PMS: Premenstrual syndrome, PSST: Premenstrual Symptoms Screening Tool

Tucker-Lewis index (TLI) is 0.909, Comparative Fit index (CFI) is 0.920, The Root Mean Square Error of Approximation (RMSEA) is 0.061 and Standardized Root Mean Square Residual (SRMR) is 0.063 (Table 4).

Table 5 shows the item statistics for the measurement model created with 27 items. Since no reliability of the items was negatively affected, no other item was removed from the measure.

As a result of the reliability analysis of PCM, the Cronbach alpha reliability coefficient of the 7-item "Avoiding Harm" sub-dimension is 0.885. The Cronbach's alpha reliability coefficient for the sub-dimension of "Awareness and Acceptance of Premenstrual Change", consisting of 9 items, is 0.890. The Cronbach alpha reliability coefficient of the "Adjusting Energy" sub-dimension consisting of 3 items is 0.775. The Cronbach alpha reliability coefficient for the "Self Care" sub-dimension consisting of 4 items is 0.831 and the Cronbach alpha reliability coefficient for the "Communicating" sub-dimension consisting of 4 items is 0.860 (Table 6).

When the correlation between retest and first test for the subdimensions of PCM is examined, the ICC value of the sub-dimension of "Avoiding Harm" and "Awareness and Acceptance of Premenstrual Change" is 0.713, the ICC value of the sub-dimension of "self-care" is 0.734, and the ICC value of the "Communicating" sub-dimension is 0.719 (Table 7).

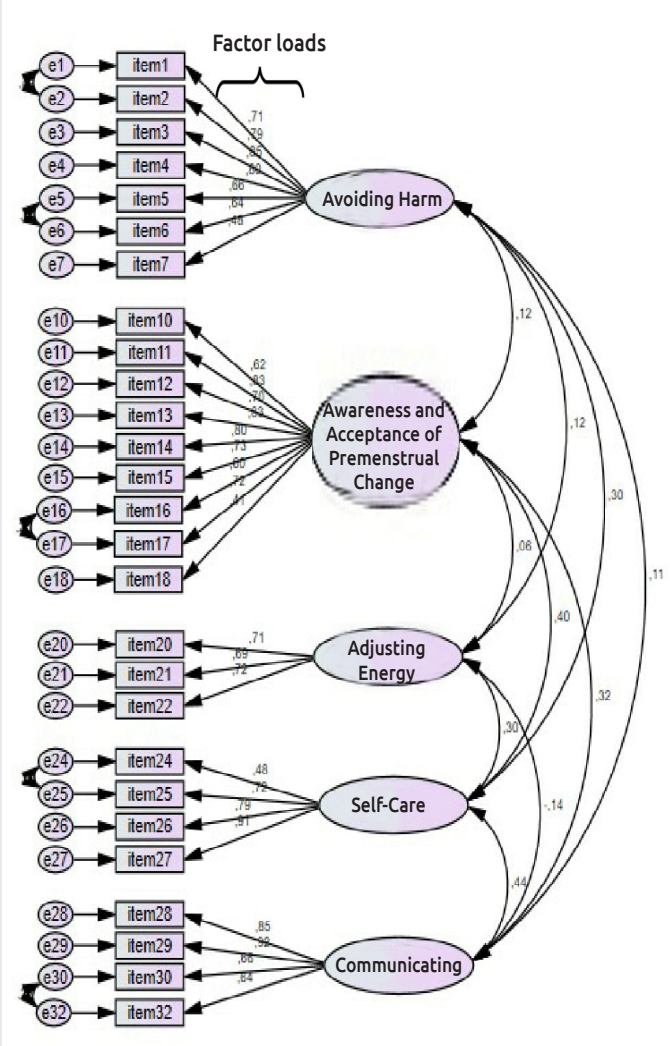

Figure 2. Measurement model of PCM

Discussion

Premenstrual symptoms experienced by women negatively affect the quality of life. For this reason, it is important to determine the coping status of women experiencing PMS and develop a coping approach accordingly. In this study, Turkish validity-reliability of PCM, which evaluated the individual's behavior to cope with PMS in five basic areas, such as harm avoidance, awareness and acceptance of premenstrual symptoms, adapting energy, self-care and communication, was evaluated in university students.

It is expected from a scale to have two characteristics: Validity and reliability. In the study, validity of PCM was evaluated by using content validity and construct validity methods. Scope validity is determined by the scale's inclusion of all important subtopics of the subject studied. It is recommended that the number of experts consulted for this evaluation should be between 5 and 40 (31). In our study, the draft measure form was sent to 13 experts and their opinions were received. When the smallest acceptable SVR are examined according to the number of experts, if the opinions of 13 experts are received, the SVR values should be above 0.54 (32). According to the results of the analysis of expert evaluations, the SVR values of all items were found to be greater than 0.80. It is recommended that the SVI value of multidimensional scales should be greater than 0.80 (33). In the study, the SVI value of the scale was calculated as 0.997. The SVI represents the dimensions of the overlap detected between the functional capacity of a defined task performance area and the performance observed in the test under examination. Functionally, the SVI is the average percentage of overlap between test items and the task performance area (34,35). The high SVI value in the study indicated that the measure items were good at measuring the coping behaviors with premenstrual symptoms.

In our study, the construct validity of PCM was evaluated with CFA and five items (item 8, item 9, item 19, item 23, item 31) were removed from the measurement model established to confirm the structure consisting of 32 items. Thus, all of the item factor loads were found above 0.40. Regardless of the sign in the literature, load values of 0.60 and above are defined as high, and load values between 0.30 and 0.59 are defined as medium values (36). Factor load, which was a coefficient that explains the relationship of items with factors, was sufficient for each item in the measurement model, which was confirmed with 27 items in our study. Thus, it could be said that the items were related to the factor they were involved in.

When determining whether the measurement model is compatible with the theory, fit indices are used (37). Among the fit indices, it is recommended that χ^2/SD should be ≤3, GFI ≥0.90 (0.85-0.90), IFI ≥0.95 (0.90-0.95), TLI (NNFI) ≥0.95 (0.90-0.95), CFI ≥0.95 (0.90-0.95), RMSEA ≤0.05 (0.05-0.08)

Table 3. Item factor loads

		Factor load
Avoiding harm		
Item 1	I avoid situations that have the potential to provoke me	0.715
Item 2	I avoid people that have the potential to provoke me	0.786
Item 3	I avoid raising topics that have the potential to create conflict	0.852
Item 4	I remove myself from a situation if it starts to provoke me	0.799
Item 5	I avoid situations where I know I will feel vulnerable	0.658
Item 6	I avoid having conversations that are liable to upset me	0.644
Item 7	I try to avoid dealing with difficult family issues	0.477
Awareness and acceptance of premenstrual change		
Item 10	I am aware that my premenstrual changes are only temporary	0.620
Item 11	I think it is okay to be feeling differently when I am premenstrual	0.827
Item 12	I am aware of my bodily changes	0.700
Item 13	I think it is okay to be more emotional or sensitive when I am premenstrual	0.830
Item 14	I am aware of my emotional changes	0.804
Item 15	I think that my premenstrual changes are a normal part of a woman's experience	0.731
Item 16	I know that other women go through this	0.596
Item 17	I think it is okay that my physical needs may be different	0.715
Item 18	I know what I need to do to support myself	0.406
Adjusting energy		
Item 20	I decrease my social activities	0.713
Item 21	I focus less on the needs of others	0.693
Item 22	I exercise less	0.719
Self-care		
Item 24	I spend time doing things that help me relax e.g. have a bath, massage, read a book	0.481
Item 25	I take time to focus on my own needs	0.718
Item 26	I allow myself extra time to rest	0.793
Item 27	I do things to make myself more comfortable	0.913
Communicating		
Item 28	I feel confident to tell people how I feel	0.845
Item 29	I feel confident to tell people what I need	0.918
Item 30	I tell others about how I am feeling	0.656
Item 32	I feel comfortable when asking for help from others	0.636

and SRMR ≤0.05 (0.05-0.10) (36,37). In this study, χ^2/SD was below 3, GFI was above 0.85, IFI, TLI and CFI values were above 0.90, RMSEA was below 0.08 and SRMR was below 0.10. The results provided acceptable fit values and the measurement model appeared to be compatible with the theory.

In our study, the reliability of PBSS was evaluated using the Cronbach alpha reliability coefficients and test-retest methods. In our study, PCM's "Harm Avoidance" sub-dimension was highly reliable (α=0.885), "Awareness and Acceptance of Premenstrual Change" sub-dimension was highly reliable (α=0.890), "Adjusting Energy" sub-dimension was reliable (α=0.751), "self-care" sub-dimension was highly reliable (α=0.831), and "Communicating" sub-dimension was highly reliable (α=0.860) (31). This showed that PCM was a consistent measurement tool.

Table 4. Fit index values of the measurement model and acceptable fit values

	Fit index values	Acceptable fit values
x^2/df (Ratio of chi-square to degree of freedom)	2.353	≤3
GFI (Goodness of Fit index)	0.868	≥0.90 (0.85-0.90)
IFI (Incremental Fit index)	0.920	≥0.95 (0.90-0.95)
TLI (Tucker-lewis index)	0.909	≥0.95 (0.90-0.95)
CFI (Comparative Fit index)	0.920	≥0.95(0.90-0.95)
RMSEA (The root mean square error of approximation)	0.061	≤0.05 (0.05-0.08)
SRMR (Standardized root mean square residual)	0.063	≤0.05 (0.05-0.10)

Table 5. Item statistics

	Scale mean if item deleted	Scale variance if item deleted	Corrected item-total correlation	Squared multiple correlation	Cronbach's alpha if ıtem deleted
Item 1	88.86	194.163	0.457	0.637	0.863
Item 2	88.78	193.169	0.469	0.721	0.862
Item 3	88.80	194.712	0.425	0.679	0.864
Item 4	88.89	193.768	0.440	0.611	0.863
Item 5	88.75	192.045	0.487	0.695	0.862
Item 6	88.83	193.010	0.447	0.692	0.863
Item 7	88.88	196.389	0.331	0.375	0.867
Item 10	87.66	197.565	0.396	0.467	0.864
Item 11	87.68	194.263	0.526	0.673	0.861
Item 12	87.57	195.667	0.492	0.554	0.862
Item 13	87.62	194.875	0.537	0.652	0.861
Item 14	87.58	196.338	0.479	0.636	0.862
Item 15	87.74	196.060	0.432	0.580	0.863
Item 16	87.62	198.303	0.395	0.482	0.864
Item 17	87.68	195.667	0.502	0.598	0.862
Item 18	88.29	193.530	0.459	0.364	0.863
Item 20	89.04	202.979	0.156	0.425	0.871
Item 21	89.05	203.213	0.153	0.394	0.871
Item 22	88.75	203.462	0.129	0.421	0.873
Item 24	88.02	195.421	0.419	0.436	0.864
Item 25	88.15	191.958	0.564	0.626	0.860
Item 26	87.93	193.698	0.501	0.601	0.862
Item 27	87.88	191.989	0.600	0.666	0.859
Item 28	88.70	194.568	0.413	0.648	0.864
Item 29	88.72	193.821	0.433	0.692	0.863
Item 30	88.85	195.682	0.390	0.500	0.865
Item 32	88.88	197.286	0.339	0.485	0.866

Table 6. Reliability analysis results of PCM sub-dimensions

	Items	Cronbach alpha	Reliability level
Avoiding harm	1-7	0.885	Highly reliable
Awareness and acceptance of premenstrual change	8-16	0.890	Highly reliable
Adjusting energy	17-19	0.751	Reliable
Self-care	20-23	0.831	Highly reliable
Communicating	24-27	0.860	Highly reliable

PCM: Premenstrual coping measure

Table 7. Compliance of sub-dimensions of PCM between test and retest

	ICC	95% confidence ınterval
Avoiding harm	0.712	0.561-0.811
Awareness and acceptance of premenstrual change	0.712	0.562-0.811
Adjusting energy	0.713	0.561-0.811
Self-care	0.734	0.595-0.825
Communicating	0.719	0.572-0.815

ICC: Intraclass correlation coefficient

Supplementary 1. The premenstrual coping measure

Women cope with their premenstrual experience in a variety of ways. We are interested in what you do when you are premenstrual. Tick the response choice which indicates how the following statements apply to your premenstrual experience

Coping statements	Doesn't apply to me	Seldom applies to me	Sometimes applies to me	Applies to me	Almost always applies to me
1. I avoid situations that have the potential to provoke me					
2. I avoid people that have the potential to provoke me					
3. I avoid raising topics that have the potential to create conflict					
4. I remove myself from a situation if it starts to provoke me					
5. I avoid situations where I know I will feel vulnerable					
6. I avoid having conversations that are liable to upset me					
7. I try to avoid dealing with difficult family issues					
*8. I challenge my negative thoughts					
*9. I accept my changeable moods					
10. I am aware that my premenstrual changes are only temporary					
11. I think it is okay to be feeling differently when I am premenstrual					
12. I am aware of my bodily changes					
13. I think it is okay to be more emotional or sensitive when I am premenstrual					
14. I am aware of my emotional changes					
15. I think that my premenstrual changes are a normal part of a woman's experience					
16. I know that other women go through this					
17. I think it is okay that my physical needs may be different					
18. I know what I need to do to support myself					
*19. I vent my feelings through emotional outbursts					
20. I decrease my social activities					
21. I focus less on the needs of others					
22. I exercise less					
*23. I eat more sugary foods					
24. I spend time doing things that help me relax e.g. have a bath, massage, read a book					
25. I take time to focus on my own needs					
26. I allow myself extra time to rest					
27.I do things to make myself more comfortable					
28. I feel confident to tell people how I feel					
29. I feel confident to tell people what I need					
30. I tell others about how I am feeling					
*31. I try not to express how I am feeling					
32. I ask for help from others					

* These items were removed in the Turkish version of the measure

In the study of Read et al., where PCM was developed, "Avoiding Harm" sub-dimension was highly reliable (α=0.89), "Awareness and Acceptance of Premenstrual Change" sub-dimension was highly reliable (α=0.86), "Adjusting Energy" sub-dimension was reliable (α=0.73), "self-care" sub-dimension was highly reliable (α=0.81) and "Communicating" sub-dimension was reliable (α=0.68) (2). It was determined that the results reached by Read et al. (2) were similar to our study's findings. Therefore, it can be said that PCM is open to international use.

Another method in which scale reliability is evaluated is the test-retest method. This method is based on determining the stability of a scale by applying it again in the same individuals, in the same conditions, but with a certain time interval. In this context, the ICC, which is sensitive to changes in the averages, is calculated. Values in the behavioral sciences in the range of 0.70-0.80 are considered "acceptable" (31). In this study, it was determined that the ICC of the measure sub-dimensions ranged between 0.712 and 0.734. It was concluded that the retest and the first test averages of the sub-dimensions of the measure were compatible and did not show a change in time.

Study Limitations

This measure adaptation study was conducted at a university where students came from different regions of Turkey, and adopted different aspects of Turkish culture. This situation constituted the limitation of the study. At the same time, the validity and reliability study of PCM was carried out to be used in the second stage of the doctorate thesis titled "Evaluation of the Effectiveness of the Training Program for Coping with the Premenstrual Symptoms in the University Students Based on the IMB Model". As the sample of this study consisted of only female students studying at the university, the validity and reliability of PCM in university students were evaluated. This was the other limitation of the study.

Conclusion

In this study, it was concluded that PCM is a valid and reliable measurement tool that can be used to evaluate the coping situation of female students studying at university and experiencing premenstrual symptoms. PCM is recommended for evaluation of coping with PMS consultancy given to female students studying at the university. Since the measure makes a comprehensive assessment in determining the individual's approaches to coping with PMS, routine use is recommended by healthcare professionals working in primary care by evaluating the validity-reliability in different populations.

Ethics

Ethics Committee Approval: Ethical approval (date/number: 10.09.2017/08) was obtained from Ankara Yıldırım Beyazıt University Ethics Committee and institutional permission was obtained from the faculties.

Informed Consent: Obtained.

Peer-review: Internally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: H.A., Concept: H.B., S.K., Design: H.A., S.K., Data Collection or Processing: H.A., Analysis or Interpretation: H.A., S.K., Literature Search: H.A., Writing: H.A.

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Original Article

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Evaluation of Community Based Medical Education Program in Bezmialem Vakıf University Faculty of Medicine Education

Bezmialem Vakıf Üniversitesi Tıp Fakültesi Eğitiminde Topluma Dayalı Tıp Eğitimi Program Uygulamalarının Değerlendirilmesi

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ABSTRACT

Objective: The World Health Organization, National and international accreditation bodies emphasize that physician candidates should also receive training in environments where they can see and recognize the health problems and health system of the society in which they live. The aim of this study is to evaluate community-based medical education practices in Bezmialem Vakıf Faculty of Medicine education program.

Methods: Beginning from the first period of our medical education for community based medical education and community recognition program practices; visits to community health centers, family health centers, childrens' houses from social work instutitions, hospice, tuberculosis dispensary, as well as Bezmialem Public Health Days as an education and service project in society and the Forensic Medicine Institute has been planned as application areas. All applications were made in the training program on predetermined dates and the feedbacks received from the students were evaluated using the thematic analysis method. The feedback of each program was evaluated as a separate category and analyzed on the themes of education efficiency, fitness for purpose, adequacy of the organization.

Results: The students expressed their satisfaction with these educational activities and community visits to the community. However, they stated that the applications in the pre-clinical period were close to exam dates, problems such as disruptions in transportation, that they wanted to communicate with more people in the institutions they went to and that the applications should be extended for a longer period of time.

ÖZ

Amaç: Dünya Sağlık Örgütü, Ulusal ve Uluslararası Akreditasyon Kuruluşları, hekim adaylarının yaşadıkları toplumun sağlık sorunlarını ve sağlık sistemini görebilecekleri, tanıyabilecekleri ortamlarda da eğitim almaları gerektiğini vurgulamaktadır. Bu çalışmada, Bezmialem Vakıf Üniversitesi Tıp Fakültesi eğitim programında yer alan topluma dayalı tıp eğitimi uygulamalarının değerlendirilmesi amaçlanmıştır.

Yöntemler: Topluma dayalı tıp eğitimi ve toplumu tanıma program uygulamaları için tıp eğitimimizin ilk döneminden itibaren; toplum sağlığı merkezleri, aile sağlığı merkezleri, sosyal hizmet kurumlarından çocuk evleri, darülaceze, verem savaş dispanseri ziyaretleri yanı sıra toplum içinde eğitim ve hizmet projesi olarak; Bezmialem Halk Sağlığı Günleri ve Adli Tıp Kurumu uygulama alanları olarak planlanmıştır. Tüm uygulamalar eğitim programında önceden belirlenen tarihlerde yapılmış ve öğrencilerden alınan geri bildirimler tematik analiz yöntemiyle değerlendirilmiştir. Her bir programın geri bildirimi ayrı bir kategori olarak değerlendirilmiş ve eğitimin verimliliği, amaca uygunluğu, organizasyonun yeterliliği temalarında analiz edilmiştir.

Bulgular: Öğrenciler, toplum içinde yapılan bu eğitim etkinliklerinden ve toplum ziyaretlerinden memnun olduklarını ifade etmişlerdir. Ancak, klinik öncesi dönemdeki uygulamaların sınav tarihlerine yakın olması, ulaşımdaki aksaklıklar gibi sorunlar bulunduğunu, gittikleri kurumlarda daha fazla kişiyle iletişim kurmak istediklerini, uygulamaların daha uzun bir süreye yayılması gerektiğini belirtmişlerdir.

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Conclusion: Physicians need to be aware of the health and social problems of the society in which they live and to be aware of them. It has been determined that the applications of our faculty are well integrated into the educational programs and that many of the knowledge they have gained in theory has strengthened in the application areas in the primary care. Children's Houses and Darülaceze visits have been found to be beneficial for preclinical students in terms of getting to know the community and raising awareness. The students' suggestions were discussed in the relevant boards and reflected in the next year's curriculum.

Keywords: Community based medical education, community recognition programs, community visits

Sonuç: Hekimlerinin yaşadıkları toplumun sağlık ve sosyal sorunlarını bilerek ve farkında olarak yetişmeleri gerekmektedir. Fakültemizdeki uygulamalarının eğitim programlarına iyi entegre olduğu, teorikte edindikleri birçok bilginin birinci basamaktaki uygulama alanlarında pekiştiği saptanmıştır. Çocuk evleri ve darülaceze ziyaretlerinin ise klinik öncesi öğrencileri için toplumu tanımak ve farkındalık oluşturma açısından faydalı olduğu gözlenmiştir. Öğrencilerin önerileri, ilgili kurullarda görüşülerek bir sonraki yılın ders programına yansıtılmıştır.

Anahtar Sözcükler: Topluma dayalı tıp eğitimi, toplumu tanıma programları, toplum ziyaretleri

Introduction

In order to be aware of the society in which they live, it is suggested that the candidates of physicians trained in medical education should be educated in environments where they can see the health problems and the health system of the society (1). In line with these recommendations, programs have been made in many medical schools in order to receive education outside of the tertiary education environment, and efforts have been made to ensure the recognition of the sociocultural diversity of the society and the communication with a large number of people. This suggestion is included in the National Standards of the World Health Organization, World Medical Education Federation and the National Medical Education Accreditation Board (1,2). In World Health Organization reports, in the declarations of institutions such as Medical Councel, CanMed, World Medical Education Federation; there are decisions in the form of "Medical education should primarily be able to reflect the changing nature of healthcare services and provide experience in different settings such as hospitals, primary care and community healthcare. From the beginning of the education, students should be able to interact with different people socially, culturally and ethnically" (1). On the other hand, in our country, the National Board of Accreditation for Medical Education (2018) standards include: "Medical schools must construct the education program to include the primary health problems of the society", "Medical schools must perform some of the educational activities during medical education in health institutions other than third level and in the community", "Medical schools education program should include local priority health problems of the community" (2). Education programs in medical schools in our country are prepared by taking into account the health problems that society needs and are also determined and supported by the National Core Education Program. In addition to these programs, which are planned as community-oriented education, there is also a need to achieve gains related to the needs of society through community-based medical education programs. In these programs, learning activities are expected to actively participate in the learning experiences of educators, community members, public and sector workers, not just students as a learning universe (3).

There are important reasons why institutions that train future physicians should include community-based educational practices. Students have the opportunity to learn about similar situations in their professional lives beforehand, have the opportunity to work with medical staff in different institutions and organizations such as primary care institutions, and have the opportunity to apply competencies that they can not learn elsewhere, such as leadership, teamwork, communication skills. These practices strengthen cooperation between the university, the community, and those who form health policies (3,4).

By reason of university hospitals where medical education is provided are more concerned with more specific diseases than common diseases in the society, having higher technological opportunities in diagnosis and treatment than primary and secondary care settings, lack of holistic approach in health services, and limited possibility to realize the relationship between diseases and social factors, it becomes compulsory to carry out applications in the community.

It has also been seen that early initiation of community-based medical education promotes learning and professional attitude development (4). For this purpose, many environments can be selected as application areas. For example, community health centers (CHS), family health centers (FHC), tuberculosis dispensaries, workplaces, schools, elderly hospices, secondary hospitals, health-related non-governmental organizations can be counted (2-4). In the studies related to the subject, it is also emphasized that it is important for these trainings to be given in the society in medical education to be carried out in cooperation with different disciplines. It is stated that such practices are beneficial not only for medical students, but also for other students studying in the field of health (2-5).

Currently, in order to train physicians for Primary Health Services, which are the priority of medical education in our country, attention is paid to this issue and studies and evaluations highlighting the importance of the issue are published (5-9). At the end of the applications, feedback should be received from the students, field trainers, lecturers and field health personnel in the program and all components should be observed and evaluated.

With this view in our study; it is aimed to evaluate the reports based on community-based programs in Bezmialem Vakıf University (BFU) Faculty of Medicine Education Program and the feedbacks received from students after these practices and the program we implemented.

Methods

In the BFU Faculty of Medicine Education Program, practices have been established to inform physician candidates about the structure of the health system, to raise awareness about the activities of non-governmental organizations that are involved in health and/or social assistance, and to enable them to take part in social responsibility projects. Attention was given to giving priority to these practices at all stages of education, and importance was given to meeting with the society from the early stages of education.

When these applications are mapped by periods (classes) ;

a. Raising awareness about FHC, Red Crescent and its activities in term I,

b. Visits to children's homes from social work institutions in term II,

c. Visit to hospice and education and service project in the community with the name "Bezmialem Public Health Days" in term III

d. Tuberculosis Dispensary in term IV,

e. Forensic Medicine Institution in term V,

f. Term VI is planned as training in CHS and FHCs.

Regarding the applications, official correspondence was made with the institutions, necessary information was made by contacting the municipalities and Health Directorates, permits were obtained and student lists were reported to the relevant institutions prior to the activities. All meetings and correspondence with the institutions were made by The Deanery and clear information was obtained about who to contact. Students were informed by meeting before each event and asked to carefully fill out the activity and feedback forms given to them.

In the FHC visit program implemented in period I, approximately thirteen ASM visits were made, directed by the District Health Directorates in Bayrampaşa and Zeytinburnu. Students are divided according to unit numbers (physician numbers) in FHCs. Some FHCs had 2-3 students while others had 8-9 students. These groups are divided by the respective District Health directorates such that one student is assigned to each FHC physician. The students who were divided into groups and taken to these centers received information from the physicians responsible for the center and observed the work of the physician. Students observed the functioning of FHC during their stay and were asked to write their learning about the functioning and their feedback on the program in free text. They submitted these reports to the Department of Medical Education and Informatics. Red Crescent, another activity in term I, attempted to raise awareness about the activities of this institution and the benefits they provide to the society. The presentations made by the authorities were interactive with the students and the students were asked to give a report containing their feelings and thoughts on the subject. A total of 146 students attended the event in the 2018-2019 academic year, having attended the first grade.

Students visited four different FHCs in groups in the FHC visiting program which was implemented in term II. Similar to the visit schedule in term I, the visit of FHCs in Bayrampaşa and Zeytinburnu consists of receiving information from the responsible persons and monitoring the services in FHCs. In the term II, there was also a visit to children's houses from the important social service institutions of our country and three different children's houses (Kasımpaşa, Bahçelievler and Zeytinburnu children's houses) close to our campus area. The students were shared equally among these three institutions, and one person from the term II coordinator and assistant and the Dean's Office of Student Affairs went to the institutions with the students. During the visit, students were informed about the activities of the institution and its benefits to society, asked to make observations and give feedback by writing reports. A total of 120 students attended the event in the 2018-2019 academic year, having attended the second grade.

In the program of visit to the aged care homes, which was implemented in the term III, Darülaceze, an old institution known since the Ottoman period, was visited, the institution officials provided detailed information to the students, and the students were allowed to communicate with the elderly, make observations, prepare reports and provide feedback. In this collective visit, the students were accompanied by a semester III coordinator and an officer in charge of Student Affairs of the Dean's office.

In order to organize the social responsibility activity implemented in term III, (Bezmialem Public Health Days), term III Coordinator and Assistant, as well as Medical Education and Informatics, Public Health, Child Health and Diseases, General Surgery, Gynecology and Obstetrics, Chest Diseases and Family Medicine assistant professors and/or research assistants and interns' assignments were made. An organizational team was established with the participation of faculty members and/or senior students from the Physiotherapy and Nutrition and Dietetics Departments from the Faculty of Health Sciences. The aim of the program is to provide students with practical learning to serve in the community. The learning objectives of this event are to develop communication skills in society, to learn common health problems in society, to recognize other institutions, staff and functions in the field of Community Health and to develop their knowledge and experience about these issues. During the preliminary preparation process, numerous meetings were held regarding the content of the program. During the meetings, the lecturers responsible for the control of the tents, their duties and days were determined. In addition, the contents of the brochures were prepared by the departments and the organization team related to the determined activities and printed by The Deanery. According to the program, in Eyüp Square, students

provided services for the public in six tents where some basic measurements, trainings and brochure distribution were carried out in the fields of women's cancers, nutrition, physical activity, diabetes, blood pressure, respiratory disorders. In these tents, informations about breast and cervical cancers, self-examination of breast examination, healthy nutrition education, body mass index measurement, spirometry measurement, glucose and blood pressure measurements and informations were made and brochures were distributed. In each tent, a faculty member and a research assistant were responsible for their own subject everyday and checked the information and measurement of the students. In all activities, students have gained skills by communicating with the community, directing and informing people on common health problems. Students had the opportunity to practice in this program what they had previously learned during basic medical skill hours when they were in first and second grade. The students were informed about the program in advance and the class representative was invited to all the meetings held before the program and their opinions were received. Tents provided from various institutions were set up in the very crowded square of Eyüp district. Transfer of students to the field was provided with the necessary tools and equipment. The practice started at 9:00 for five days and lasted until 17:00.

Selected topics at the beginning of the project;

a. Information about common cancers in women,

b. Breast examination,

c. Family Practice (blood pressure, glucose measurements etc.)

d. Body mass index calculation,

e. Doing respiratory function testing with spirometry.

The rotation of the students to take part in each topic is planned and thus it is aimed that each student will gain skills with the applications he/she performs in each activity. Students were asked to communicate directly with the people who visited the tents and to record every action they performed. In some applications, students in Physiotherapy and Nutrition and Dietetics also participated in the work in tents. Eyüp district Health Directorate observed the activity and informed them again about what was being done. The event was attended by all 98 students who were in third grade during the 2018-2019 academic year.

In term IV, our students are grouped together to attend Tuberculosis dispensary every week as one day per week during the internship of the Department of Child Health and diseases. The students are informed about the operation and the procedures. It is practiced as a primary care rotation within the internship. Feedback from students about their observations here is taken together with internship feedback and evaluated. A total of 131 students enrolled in fourth grade during the 2018-2019 school year participated in this rotation.

In term V, our students go to Forensic Medicine Institution in forensic medicine internship and receive education and information about the functioning of the forensic medicine applications in their own place. It is the practice of rotation within the internship. A total of 131 students enrolled in fifth grade during the 2018-2019 academic year.

In the training of term VI, interns in Public Health Applications are provided to do rotation internships in Provincial Public Health Services and District Health Directorate/Community Health Centers. Family medicine practices are carried out in all Family Health Centers within the District Health Directorate/ Community Health Center. During the 2018-2019 academic year, a total of 132 students enrolled in the sixth grade attended these practices.

In public health internships, students were trained in the Public Health Services Department of the Provincial Health Directorate for one week. During these practices, students were distributed to different units each day from Family Medicine Environmental Health Infectious Diseases, Child, Adolescent and female reproductive health, vaccine programs, cancer, mental health departments and received seminars about what works are done and how they are done. In cancer early diagnosis screening and education center, child, adolescent, woman and reproductive health, healthy life center, infection control, occupational health safety, diabetes and obesity, migrant health center and health center in Bayrampaşa and Zeytinburnu District Health Directorates, they learned the work done in their units in the form of a seminar for one week. Also infectious diseases, immunization and outbreak control, tuberculosis control services, non-communicable diseases and services for the control of obesity, women's health and reproductive health services, environmental health services, in-service training services in the areas of public life, and school health services, oral health services, child and adolescent health services, early detection of cancer, screening and education services in terms of field studies participated in this survey.

In the study, feedback from the students reached all community-based activity evaluations in the BFU Faculty of Medicine Program. The reports were prepared at the end of the program in a free-form text, not through specific questions, in which the students' opinions on the program were taken and their observations summarized. The effects of these educational activities in the community on the students, their feelings, thoughts and suggestions regarding these programs, were obtained by the observation reports they prepared.

Verbal feedback is always received from the institutions related to the practices and from the trainers and observers involved in the trainings.

Reports were taken separately for each program and each program was considered a different category. The contents of the reports are discussed in the headings: efficiency of applications and observations in terms of content, fitness for purpose in terms of teaching practices and observations, competence of the organization.

Results

1. FHC Visits (Term I and II)

FHCs, as primary health care institutions, aims to ensure that medical school students can learn preventive health services from a societal perspective. FHC visits were based on the "Cooperation Protocol between the İstanbul Governorship and BFU (SEAB Protocol)" signed between the ministry of health and our university, official correspondences were made beforehand and the areas of application were tried to be close to the campus area and students were grouped and visit was accompanied by a responsible person.

Information such as the characteristics of ASMs, working principles, competencies, job descriptions of the staff were explained by ASM personnel and then distributed to the physicians who performed the outpatient clinic examination for observation. Physicians transferred their procedures, Anamnesis and patient examinations to the students according to the status of the incoming patients and chatted with the young people to learn from their experiences and some of the events they had experienced before. The students have learned a lot during the visit and have reported that their education has been productive.

"*I think it was very useful. I think it was very important to be able to watch and observe what he did next to a family physician and even experience it with the help of a substitute. Personally, I'd like to come for longer periods of time*"

The main purpose of FHC visits; in general, it is aimed to enable students to learn the objectives, management and scope of community based health services. Students' feedback on the suitability of FHC visits for their purpose, "*I learned information such as who managed FHC, where it gets its budget*", are included in the statements. It is understood that they can develop awareness about the operation and management in FHCs. FHCs contain different diseases and patient profiles as the first health centers that the society applies to. Other special services of FHC outpatient clinics are that family physicians serve a certain population in FHCs.

In addition to functioning and management, students also observed special situations in the outpatient services of the family physician. Students who stated that they can get the information about the functioning of the instution, which is one of the most important goals of the visits, "*I had the opportunity to see how FHC works and serves*" as stated, the visits showed that the students gained information suitable for the purposes.

Family physicians working in FHC have administrative responsibilities such as information transfer, management and training responsibilities in addition to performing medicine related to outpatient procedures. It is seen that students also benefit from these educator roles of Family Physicians.

"*I had the opportunity to observe my profession at the FHC where I came from. The most conspicuous features are that the physician greets his patients with a smiling face, questions their complaints and examines them with great care. He responded meticulously to the questions I asked, and invited me to attend a one-to-one examination. There were too many patients. The doctor saw me as a colleague and said I could come by whenever I wanted. I had an observation that I enjoyed. I had fun, learning new information. It was a beautiful day*".

Observations on the patient-physician relationship that all physicians have to internalize have also benefited students.

"*During the visit we saw what the patient-doctor relationship should be like. We listened to the experiences of Physicians. This visit has given us so much. We have seen our profession in the field*".

In the feedback received from the students, there were also suggestions to be taken into consideration, such as determining the dates of visits and strengthening the transportation planning, while the FHC visits carried out within the scope of social responsibility could be carried out more efficiently and effectively.

"*We had a service problem. Driver had difficulty finding FHC*".

"*It was very bad that this practice was close to our committee exam*".

He said: "*I think it was unnecessary, it was never good to have it in committee exam week*".

In all FHC practise, team I and II visited on separate dates. The students did not have any criticism other than timing. On the contrary, the vast majority stated that this practice was beneficial and their satisfaction with the observations they made on the spot. The decision to continue this practice next year, but not to exam weeks, was taken in the relevant boards.

2. The Red Crescent Awareness Study

The Red Crescent is an international and ancient institution of Turkey that provides social assistance in terms of social determinants of health. This institution has studies that have direct or indirect effects on health in many areas such as fundraising, awareness, humanitarian aid, disaster relief. While determining the program to be carried out in The Red Crescent, correspondences were made with the Fatih branch of the institution. It was decided by discussing with the officials of the institution what things can be done to get the Term I students to have detailed information about this institution works in the public interest. Due to the large number of students, it was decided to inform the students with an interactive presentation. 129 students participated in the activity and provided feedback reports.

Five people from the physician and administrative staff who are in charge of Kızılay Fatih Branch Presidency informed our students with this interactive presentation. In students' reports, it is reported that in this meeting they were both informed and received their answers under various topics such as the history of the Red Crescent, its activities, blood donation, stem cell donation, volunteering, scholarships, and the Young Red Crescent.

Students expressed their opinions regarding the efficiency of the activity;

"*Although it is an impressive and informative event, I can say that it has increased my willingness to volunteer at the Red Crescent in the future*".

The purpose of social responsibility projects is to enable students to realize their social responsibilities from the public health perspective while performing their medical duties and to guide their patients with this awareness while performing the medical profession. It was understood that this learning goal was achieved with the feedback of the students. As Demirören stated in their study, the students in faculty of medicine should be able to understand social responsibility in depth (6). One of the goals of the Red Crescent visit is to enable students to see the health-related social service activities on site in order to gain social responsibility. Students expressed their views on the suitability of the visit to their learning goals as follows;

"*First of all, I am aware that I have learned better the duties and the points of the Red Crescent. I was impressed and proud of the development of the Red Crescent. As a human being, I realized that I should be more sensitive about these issues. Thank you*".

Sensitivity to social problems and issues is a merit that should be developed in accordance with the physicians' missions to protect public health. Students stated that their sensitivity towards social problems increased during the activity. The role of the health defender, which is among the graduate qualifications of the BVU Faculty of Medicine; is "to improve the health of individuals and society, to understand their needs, to work with them to meet their needs, to advocate when necessary, and to contribute to creating resources to create a change or to be a driving force". It is revealed from the following statements that students develop social sensitivity with this visit and make internalized decisions towards health advocacy;

"*My friends and I decided to volunteer for blood donation and bone marrow donation*".

"*I liked the event very much. Thanks to this activity, I learned a lot about the Red Crescent. I learned how to volunteer and decided to volunteer. The speeches were very friendly and sincere, I could watch it carefully*".

Developing students' sensitivity is very important in terms of medical education, community based medical education practices as a learning objective.

3. Children's Shelter Site Visits

Children's shelters are institutions where children under the age of 18 need protection and care sheltered. Within the scope of social responsibility programs, it is aimed that the students can see the health service needs of the children's shelter site and the areas where the physicians can fulfill their social role.

After the official correspondence, the students were taken to the three different children's shelters with shuttle services. Kasımpaşa, Bahçelievler and Zeytinburnu Children's Shelter Sites, which are close to the University Campus area, were visited together with the responsible lecturers. An informative meeting was held for our students by the officers, teachers and physicians of the institutions, and the students were enlightened with the answers to their questions. The students stated that the program was efficient with the excess of information they learned during the visit.

"*It was an interactive practice. I learned a lot about children's homes, my prejudice was broken*".

It is also understood from the feedback received that the students' sensitivity and awareness about children in the children's shelters has increased.

"*We encountered a very cute and warm environment. Although we could not meet with the children directly, we observed the environment they stayed in, social activities and the areas they had fun*",

It is understood from what they say that students have mastered the studies of health-related institutions. The details they give about the content of the visit shows that it is effective for students to gain awareness, which is the purpose of education.

"*I saw that children's shelters are very different from those pictured in the media. All kinds of their needs are considered, they even have clinical psychologists.*"

Students also had some suggestions about the organization. This shows that students' participation in the education program is strong.

"*We couldn't meet the kids. I wish it was a different organization like picnic*".

It is seen that they have requests to communicate directly with the society that they are likely to serve. This makes us think that students' social sensibilities are also improving.

4. Darülaceze (Poorhouse) Visit

Darulaceze is an institution that carries out the duty of caring for people in need since its foundation. Information about the location of the institution, where basic needs were met and health support was received, and how the health and social needs are met, and awareness was raised.

Students studying in Term III visited Darülaceze, one of the well-established institutions of our country, based on a voluntary basis. On the specified day after the official correspondence with the institution, 25 students were taken to the visit with their coordinators. The students were informed by the institution officials about the purpose of the institution, who benefited from them, their accommodation opportunities, job and skill activities, and they were allowed to communicate with the individuals living in the institution. The aim of the program is to increase social sensitivity and awareness and to make students aware of the social responsibilities of physicians in environments where social service and support are collectively provided to individuals at different stages of life. The students provided feedback about the efficiency of the program, thus gaining this awareness. Students have provided feedback on gaining this awareness and therefore the efficiency of the program.

"*As a candidate for physician, it was very important for me to communicate with the elderly in this institution. I recommend it to be more comprehensive and done every year.*"

Students have started to present new ideas and projects with the responsibilities they undertook under favour of the visits. It seems possible that these ideas can be realized later as student club activities.

"Darülaceze is an institution established by Abdülhamid the 2nd, for the protection of people in need due to the intense migration after the Ottoman-Russian war. We met some of the remaining residents. They make handcrafts and they sell them. Every resident takes place at an event. I learned a lot that I had not not know before, in this activity. But we need to communicate more with the individuals there. I had an idea; we have to create a project and spread it over the whole year. We can work all day at the Darulaceze event building. I would like such events to be more frequent".

The fact that students have developed social sensitivity and awareness of the working objectives of the institutions shows that the learning objectives of the program have been reached.

5. Social Responsibility Week

This activity, which was initiated under the name of Bezmialem Public Health Days and traditionally planned every year, was carried out with the participation of all Term III students (Figure 1).

The content of our event was announced and the necessary permits were obtained from the authorized institutions such as the Provincial and District Health Directorate and Eyüp Municipality. Public examinations and trainings were held in Eyüp Square in line with the program details determined as one week in our training program. Brochures prepared in these trainings were distributed to the public (Figure 2).

In the tents set up in the Eyüp District Square, for a week, examinations and information were provided for protection against diseases of different themes (*briefing about the common cancers in women, breast examination, family medicine practices, blood pressure and diabetes measurements, body mass index calculation, spirometry and respiratory function test*). These include physical examinations and respiratory function tests, blood pressure, sugar and weight measurements, diabetes, growth and development in children, nutrition and vaccine information, and briefing on the importance of cancer screening.

Figure 1. Students and faculty members in Bezmialem public health days event

The efficiency of the program;

"*Helping people and raising their awareness about healthy living made me happy*".

Dilekmen stated that according to the learning theory, students acquire problem solving skills in real life while in social interaction (8). It can be thought that basic medical skills also developed in this context.

"*It helped me gain basic medical skills*".

The aim of this program is to teach students how to serve in the community. Figure 2 shows students' pictures in the activity (Figure 2).

It is understood from the achievements that the education program contributes to the development of skills such as communication, teamwork, and social sensitivity, which are aimed in the Public Health Days program, and that the students stated they especially developed;

Figure 2. Student practices in Bezmialem public health days events

"*I made gains in terms of patient physician dialogues*".

"*It was a beautiful environment where we implemented teamwork and cooperation*".

"*I think my communication with both the community and my group friends has improved*".

In their feedback, the students stated that they could learn to be able to serve in the community and learn about communication, and made suggestions that would contribute to the development of the program.

Students show that in their feedback to the organization, a participatory training was carried out with some criticism of inventory and planning.

"*It was a very nice event, I wish it was held every year. But there were some shortcomings. The division of labor should be made to students in advance*".

"The system should maturate bit longer".

"*The number of spirometers should be high*".

"*It can be measured in BMI in child nutrition department*".

6. Tuberculosis Dispensary

Today, Tuberculosis Dispensaries are service units that stand at a key point in terms of preventive medicine and public health. This rotation, which is placed in the program with the permission of the relevant institutions, provides awareness of the operation in the units providing primary health care.

Term IV students performs rotation at Fatih Verem Savas Dispensary every Friday within the internship of the Department of Pediatric Health and Diseases. Students are sent regularly by grouping beforehand and reporting their names to the relevant institution. In this institution, they follow-up patients with tuberculosis with the responsible physician, interpret chest X-rays, observe the treatments given, and they can apply the measurements of the PPD tests, and etc. under the supervision of the principals and in limited numbers.

Feedback from students about this rotation is taken with emphasis on this rotation in Pediatric Health and Diseases internship feedback. Positive notes are taken about this training. It is understood that students are satisfied with the experience gained from this primary health care service.

7. Forensic Medicine Institute

With the official protocols made, in the rotation of the Forensic Medicine Institution applied in the Forensic Medicine internship in Term V, all students, in groups, observe and experience the operations performed at the institution for two days.

Students, as part of our education, while they are at the Forensic Medicine Institute; they can monitor and/or apply skills such as "Forensic case examination", "Examination of deceased", "Preparing a forensic report" in the National CEP (Core Education Program).

Feedback on this rotation is taken by referring to this rotation in Forensic Medicine internship feedback. Students express very positive opinions about this experience. It is understood that the students are satisfied with the experience gained from the relevant institution.

8. Provincial Public Health Services Presidency, District Health Directorate and Primary Care Clinic Applications

With the protocol between the Turkish Ministry of Health and our University, "T.C. The cooperation protocol (SEAB protocol) between the governorship of Istanbul and Bezmialem Vakıf University on the establishment of a health, education and research zone", the educational zone of our university is determined as Bayrampasa and Zeytinburnu districts of Istanbul province. For this reason, the studies regarding the education and research that our Faculty of Medicine will conduct with the Ministry of Health are carried out in Bayrampaşa and Zeytinburnu District Health Directorate/Community Health Center Region. Our interns, in groups, go to the internship in Provincial Public Health Services for a week and in Zeytinburnu and Bayrampaşa District Health Directorates/Community Health Center for a week in correspondence within the scope of the Protocol. Family Medicine internships are carried out for two weeks in Training and Research Family Health Centers (TRFHC), that is, in all Family Health Centers in Education Research District Health Directorate/Community Health Center.

Students are sent to the units that provide public health services (*Vaccine Programs Unit, Contagious Diseases Unit, Employee Health Unit, Environmental Health Unit, Cancer Unit, Mental Health Unit, Healthy Nutrition and Active Life Unit*) within the Provincial Public Health Services Directorate. The internships are related to the functioning of the units they are sent in line with the pre-determined learning objectives, the related units, the reflections of the unit studies in the national health system, etc. and they include the acquisition of information and the learning of the duties of physicians in the relevant institutions and units. Thus, our students learn the duties, responsibilities and authority that a physician who work at the Provincial Public Health Services Directorate should undertake.

Within the scope of the services provided in Zeytinburnu and Bayrampaşa District Health Directorates/Community Health Center; students also observed Infectious Diseases, Immunization and Outbreak Control Services, Non-communicable Diseases and Obesity Control Services, Women and Reproductive Health Services, Environmental Health Services, Mental Health Programs, Pediatric Health and Safety Services, Public Living Areas and School Health Services, Children and Adolescent Health Services, Cancer Early Diagnosis Services, as well as KETEM (Early Detection, Screening and Education Center for Cancer) Unit, ÇEKÜS (Child, Adolescent, women and Reproductive Health) Unit, Healthy Life Center, Occupational Health and Safety Unit, Diabetes and Obesity Unit, Migrant Health Center and Health House Units.

Students have the opportunity to make many observations and obtain information in the field internships they perform during

Public Health internships. The ability of students to bring critical comments reveals the efficiency of education.

"*I got an idea about the work in the field. I noticed the aspects of primary level applications that need to be improved. Family medicine assignment was efficient. DHD (District Health Directorate) was generally effective and efficient*".

"*My visit to District Health Directorate (DHD) was the first. I observed the functioning of the working units. I have observed that its productivity is good in units such as screening programs, family and follow-up*".

The internship is considered to be more efficient because students think they have acquired the information they will benefit from in their professional lives.

"*I think it is very useful. In particular, we had the opportunity to observe the Environmental Health, Cancer Unit and Mental Health as prospective general practitioners*".

Students' opinions that they contribute to the awareness of their responsibilities towards the society as a physician in their professional lives are also important in terms of demonstrating the efficiency of education (6).

"*When we needed to see that the Migrant Health Center was working efficiently, it was a good achievement in terms of our guidance*".

"*The infectious diseases unit was good. Everything was in consistency. The adolescent unit was also useful. Education was good… The education and system in the vaccine was good*".

Students also evaluated the training in terms of the attitudes and knowledge of the trainers during the internship. It is seen that the trainer-student relationship, which is one of the factors affecting the efficiency of education, and the dominance of the trainer increases the efficiency of the internships.

"*Vaccination, environmental and cancer units were very useful and informative. Most importantly, it was very important that they regard us as the doctors of the future and respect us*".

"*Those in the vaccination and environmental health units were people who had a good command of their jobs, treated us with respect and earned our respect with their interests and competencies. I felt that our time was valued, not wasted*".

Students found screening programs that they actively participated in during their internships efficient. Applied trainings speed up students' learning. Students' views have also been this way.

"*Newborn (NB) screening program was good and efficient*".

"*We learned the screenings performed in the cancer unit, we learned the role of the family doctor in this process. We learned how they monitor drinking water in the peripheral unit. We learned how to follow the cold chain and get the records in the vaccine unit*".

"*We were pleased with the people who were interested in us for neonatal screening program (NCP) and hearing screening*".

Other opinions of students about the efficiency of the internship are as follows:

"*Obesity department was productive*".

"*Information about heel blood monitoring and vaccination; especially the Family Medicine unit was efficient*".

In this internship, our students have gained a Public Health perspective by going out of the clinic-oriented trainings and observing the duties taken by the physicians in the health services offered for protecting and improving health in the field.

Family Medicine internships are carried out for two weeks in Training and Research Family Health Centers (TRFHC), that is, in all Family Health Centers (ASM) in Education Research District Health Directorate/Community Health Center. Students were provided to learn how health data is processed and how our health system works in primary care.

It is understood from the following expressions of the students that internships can reach their learning goals:

"*We had the opportunity to examine the units in the units we see in the Provincial Health Directorate on a district basis and we saw the places where the doctors worked*".

"*We learned about the issues covered by DHDs (District Health Directorate)*".

The efficiency of the trainings increases with the motivation of the students and their motivation by believing in the benefit of the educational content (8). In a study carried out at Suleyman Demirel University, the results of the scores given over 1 to 10 points in the question about "the status of the medical education they have received is serving the duty they are doing now" have been obtained over 6.4 points (9). BVU Faculty of Medicine Term IV students also reported that the efficiency of their education was quite high due to their internship in an institution where there is a possibility of working in after their graduation.

"*What does a general practitioner do at DHD (District Health Directorate) and what are their daily routines, it is much better to observe these live than to hear them. After all, even if we pass TUS (Examination for Specialty in Medicine), we will have to do these work for a while. It was good to see in advance, it would be better if the physical conditions were sufficient. I think that the field duties are very useful and contribute a lot at the professional point. This period could be increased a little more*".

The students' interest in this internship was intense because they had performed an internship while they were students in the institutions where they will be assigned to after their graduation. The observation of students about the environment they will encounter in post-graduate assignments and the work they will do reduce their anxiety about post-graduation period.

"*Seeing the functioning of an institution that we are most likely to be appointed to*".

"*I learned how to track and keep statistics on contagious diseases. I have seen the rehabilitation center facilities on site*".

"*Learning our professional obligations, especially in contagious diseases, office work may be a small but an important detail that was ignored throughout our education*".

The fact that students give unit names, observations and information they have learned in the feedback is an indication that students have had an efficient internship. It is seen that our students comprehend the studies they observe in every units and their importance in our health system and understand the importance of primary health care services as physicians.

"*I was in the immigrant department. Such a service for foreigners was quite satisfying*".

During the internships at Provincial Public Health Services Directorate and the District Health Directorate, students have the opportunity to observe the institutions and areas where their post-graduate appointments will take place, where preventive studies and health advocacy are carried out. It is understood that students have mastered their learning goals in internships and benefited from trainings for these purposes. Compilation or meta-analysis studies obtained from studies dealing with community based medical education practices also support these findings. In the data obtained from a compilation study evaluating 72 single cohort or cohort studies, it was determined that "the majority of the graduates and students receiving education from the education programs that include community based education practices were positively affected by the rural medicine experience and the education they received in primary care units". It is understood from the feedback that these students value their primary care areas (10). We believe that the reflections and benefits of our practices will be better determined with BVU Alumni feedback.

In another review study evaluating fifteen studies published between 2000 and 2009, it was stated that students self-assessed in primary education settings, and this contributed to their professionalism development with reflection (11). In the feedback reports of BVU students, similar expressions were included in which the students expressed themselves, the quality of their education, their perceptions and feelings.

There is no single concept for Community Based Education. "Educational programs", which are among the subgroups of community based education, consist of two main items: 1. Programs for primary health care and 2. Community recognition programs (12). Both were included in the BVU Faculty of Medicine education program. In the Public Recognition Programs, students are often required to observe or participate in data collection within a limited time. For this purpose, places close to university, community or primary level institutions are preferred for this purpose. This approach was also used in the education program of BVU Faculty of Medicine.

Results

Regarding all of the community based learning practices carried out in the BVU Faculty of Medicine education program;

1. A significant awareness has been raised by encountering the health and social problems of the society in the early periods,
2. Based on their experiences, they have confidence in their communication skills,
3. They will be able to comply with team work in activities they have done together with professional groups such as nutrition and dietetics and physiotherapy,
4. We found that student-faculty communication increased in all activities with the support and participation of faculty members.

Conclusion

As a result of the positive feedbacks and evaluations received from these practices, we believe that the community based medical education activities and community recognition programs implemented in our faculty should be maintained, extended and continued.

Ethics

Peer-review: Externally peer reviewed.

Authorship Contributions

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Review

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The Effects of Abdominal Massage on the Management of Constipation: A Systematic Review of Randomised Controlled Trials

Konstipasyonun Yönetiminde Abdominal Masajın Etkisi: Randomize Kontrollü Çalışmaların Sistematik Derlemesi

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ABSTRACT

This study aimed to assess the effectiveness of abdominal massage in the management of constipation.

We conducted this systematic review by scanning Pubmed, CINAHL, EBSCOhost, ScienceDirect, Ovi, ProQuest, Web of Science and ULAKBIM National Databases without any time restriction. To search the literature, we used the following keywords: "constipation", "constipation management" and "abdominal massage". We included into the systematic review randomised controlled trials on constipation management whose full texts were available both in English and Turkish, while studies without the full text and/or ongoing studies were excluded. A total of 31 articles were found; however, only 9 of these studies met the inclusion criteria.

The effects of abdominal massage on constipation management have been assessed in different randomised controlled trials, with the participation of cancer, parkinson, multiple sclerosis and orthopedics and traumatology patients. The abdominal massage was applied to the patients in the supine position and in the direction of the colon, with different techniques of circular movements (kneading, vibration, effleurage, superficial or deep stroking techniques) for different periods (10-40 minutes) and at different frequencies (1 to 2 times in a day or week). In six trials, abdominal massage and laxatives were applied to the experimental group,

ÖZ

Çalışmanın amacı konstipasyonun yönetiminde abdominal masajın etkinliğini değerlendirmekti. Sistematik derleme nitelikte olan bu çalışma, yıl sınırlaması olmaksızın, Pubmed, CINAHL, EBSCOhost, ScienceDirect, Ovi, ProQuest, Web of Science, ULAKBİM Ulusal Veri Tabanları taranarak gerçekleştirildi. Literatür taraması "konstipasyon", "konstipasyon yönetimi", "abdominal masaj" anahtar kelimeleri kullanılarak gerçekleştirildi. Çalışmaya konstipasyonun yönetiminde İngilizce ya da Türkçe tam metnine ulaşılabilen randomize kontrollü araştırmalar dahil edildi, tam metin olmayan ve/veya devam eden çalışmalar kapsam dışı bırakıldı. Toplam 31 araştırma makalesine ulaşıldı, bu çalışmaların sadece 9 tanesi araştırmaya dahil edilme kriterlerine uygun olduğu belirlendi. Konstipasyonun yönetiminde abdominal masajının etkisi kanser, parkinson, multiple skleroz ve ortopedi ve travmatoloji hastalarının katılımı ile gerçekleştirilen farklı randomize kontrollü çalışmalarda değerlendirilmiştir. Bu hastalara karın masajı, hasta supine pozisyonunda iken, kolon yönünde dairesel hareketler ile farklı teknikler (yoğurma, vibrasyon, efloraj, yüzeyel veya derin vuruş) kullanılarak, farklı sürelerde (10-40 dk), farklı sıklıkta (günlük veya haftada 1-2 kez) yapılmıştır. Altı çalışmada deney grubuna abdominal masaj ve laksatif, kontrol grubuna ise kliniğin standart protokolü (laksatif ve/veya yaşam

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whereas the standard clinical protocol (laxative and/or change in the lifestyle) was applied to the control group. In a study, massage based on the tensegrity principle (balance the tension of muscles, fasciae and ligaments that are structurally associated) was applied to the control group. In another study, the classical abdominal massage was applied to one group, the aroma massage was applied to the second group and only laxatives were administered to the third group. To assess constipation, the Gastrointestinal Symptom Rating scale, Constipation Severity index, Bristol Visual Stool scale, Constipation Quality of Life Questionnaire and Neurogenic Bowel Dysfunction or bowel diary were used in these studies.

Our results showed that abdominal massages were effective in reducing constipation-related symptoms, increasing the frequency of defaecation and enhancing the quality of life of patients.

Keywords: Constipation, constipation management, abdominal massage

şekli değişikliği) uygulanmıştır. Bir çalışmada, kontrol grubuna tensegrity ilkesine dayalı masaj (yapısal olarak bağlantılı kas, fasya ve bağların gerginliğini dengeleme) uygulanmıştır. Diğer bir çalışmada ise bir gruba klasik karın masajı, bir gruba aroma masajı, üçüncü gruba ise laksatif uygulanmıştır. Konstipasyonun değerlendirilmesinde ise çalışmalarda Gastrointestinal Semptom Derecelendirme ölçeği, Konstipasyon Şiddeti ölçeği, Bristol Görsel Dışkı ölçeği, Konstipasyon Yaşam Kalitesi ölçeği, Nörojenik Barsak Disfonksiyonu ya da barsak günlüğü kullanılmıştır. Çalışmadan elde edilen sonuçlar, abdominal masajın konstipasyon ilişkili semptomları azaltmada, defekasyon sıklığını arttırmada ve yaşam kalitesini iyileştirmede etkili olduğunu göstermiştir.

Anahtar Sözcükler: Konstipasyon, konstipasyon yönetimi, abdominal masaj

Introduction

Constipation is currently one of the most common symptoms related to the digestive system. It does not only negatively affect the quality of life, well-being, social life and daily life activities of individuals, but also causes economic losses. Constipation may be idiopathic, although neurogenic or non-neurogenic diseases like irritable bowel syndrome, hypothyroidism, hypocalcemia as well as drugs and pregnancy may play a role in its etiology (1). In addition, changes in the diet, patient exercises, acute emotional stress, abdominal surgery and the disease course are also among the causative factors of constipation (2,3).

In previous studies, the prevalence of constipation has been determined to be between 0.7%-79% across the world, with an average of 16% and a rate of 35% in elderly people. It is more frequent in women, elderly people, home care patients and terminal patients (4-6).

Today, pharmacological and non-pharmacological approaches are used in constipation management; however, the pharmacological methods are more frequently used. The most commonly used pharmacological approaches are laxatives, enema and suppositories (7), which leads to an increase in cost. Regarding the non-pharmacological approach, lifestyle changes like diet, fluid intake and increasing physical activity are applied (8). Apart from this, many other non-pharmacological approaches like abdominal massage, meditation, the use of probiotics, biofeedback, reflexology and acupuncture are used (9).

Abdominal massage is one of the non-pharmacological approaches used in the management of constipation. It is a cheap non-invasive method that has no side effects and can be easily applied by patients and their relatives (10). The use of abdominal massage in constipation management dates back before the 1870s. Abdominal massage is performed by placing the patient in a semi-Fowler or supine position, applying circular movements in the direction of colon and in the bowel region over the abdominal wall, using kneading, vibration, effleurage and superficial or deep stroking techniques. It has been reported in the literature that abdominal massage increases parasympathetic stimulation, muscle motility, and the release of digestive secretions (10,11). It has also been reported that abdominal massage exerts mechanical and reflexive effects on digestive system organs by enabling the relaxation of the sphincters in the gastrointestinal system. Based on these effects, abdominal massage provides a bowel purge by accelerating gastric emptying and bowel peristalsis (12). There is no review that has evaluated the effectiveness of abdominal massage on constipation management. Therefore, the purpose of this study was to systematically examine scientific evidences regarding the effectiveness of abdominal massage on constipation management.

Method

This study was a systematic review examining randomised controlled trials that were conducted to determine the efficacy of abdominal massage on constipation management. Two researchers conducted the literature search in Turkish and English by scanning Pubmed, CINAHL, EBSCOhost, ScienceDirect, Ovi, ProQuest, Web of Science and ULAKBIM National Databases, without any time restrictions. The following keywords were used: “constipation”, “constipation management”, “abdominal massage” and their Turkish translations.

Inclusion and Exclusion Criteria

Studies on constipation management whose full texts were available both in English and Turkish were included into the systematic review. There was no randomised controlled trial in Turkish that had been conducted on this subject.

Studies without the full texts, ongoing studies, studies conducted in languages other than Turkish and English, qualitative, quantitative, review and case studies were excluded from the systematic review.

Assessing the Quality of the Studies

The studies were assessed by a researcher in terms of the sample size, study groups, characteristics of the interventions applied, assessment scales and results. In addition, two researchers independently assessed each study using the Jadad scoring system.

The Jadad Scale is one of the scoring systems that is reported to have the best validity and reliability in the methodological assessment of the quality of randomised controlled trials and is frequently used. The trials were assessed as 0-5 points in the Jadad scale. This scale consists of a total of 5 questions and using this scale, randomisation, the existence of double-blinding, withdrawing from the study and the exclusion from the study are assessed as "0" and "1" points. In addition, the appropriateness of the randomisation scheme and an appropriate explanation of the double-blinding method are scored as "+1" and "-1". Table 1 shows the Jadad scores of the studies in the present review (13).

Results

As a result of the search conducted using the aforementioned keywords, a total of 31 articles were found. Six of the 31 articles found were duplicates and were therefore excluded. The remaining 25 trials were screened according to the inclusion and exclusion criteria, after which 9 randomised controlled trials were retained for the systematic review. The included trials were conducted between 2009-2016 (Figure 1).

In the trials, the patients were classified according to the Rome II and Rome III criteria for constipation developing in cancer, Parkinson, multiple sclerosis, orthopaedics and traumatology patients. The abdominal massage was applied to the patients for constipation management in the supine position and in the direction of the colon, with different types of circular movements (kneading, vibration, effleurage and superficial or deep stroking techniques), for 10-40 minutes and 1 to 2 times a day or week. The abdominal massage was applied by the patients themselves or by healthcare professionals at home, work, or in the clinic

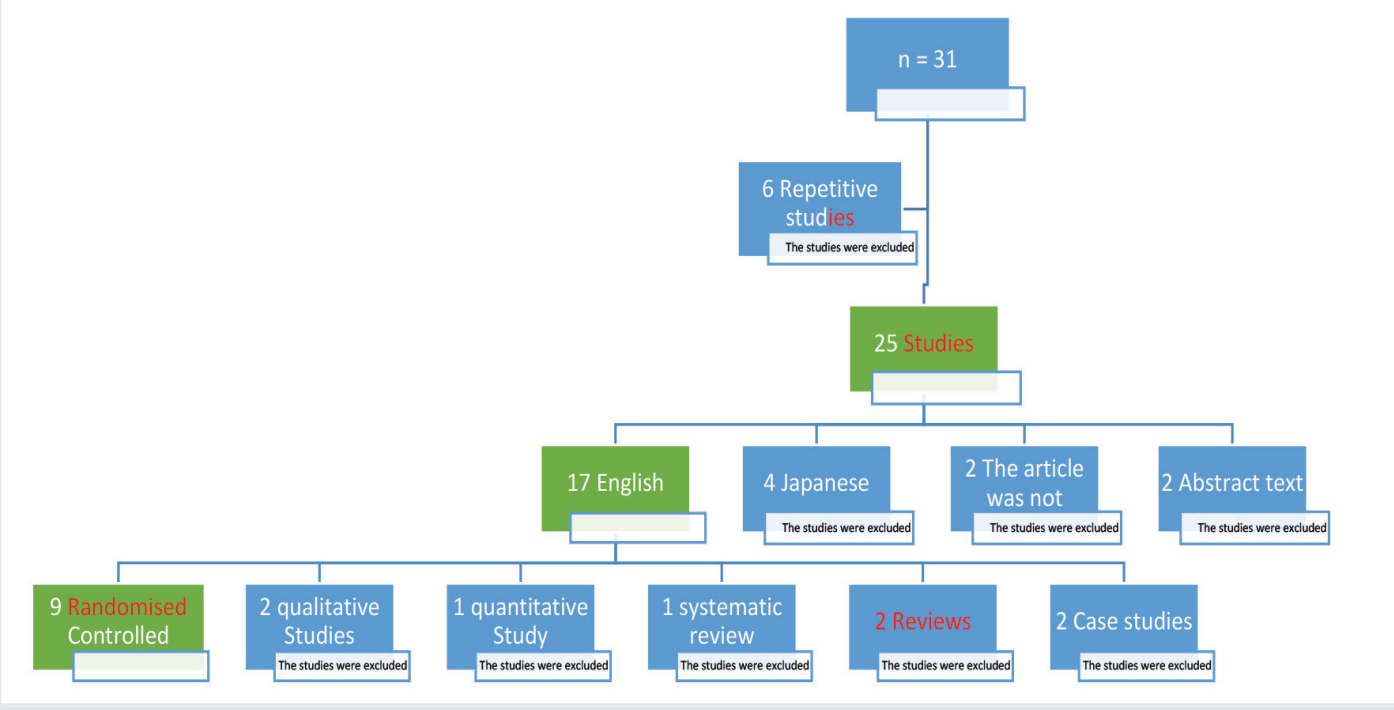

Figure 1. Consort flow chart

Table 1. Jadad Score Assessment-Scoring Criteria

The first author, year	Randomisation	Double-blinding	Was withdrawing from the study explained?	Was randomisation performed reliably?	Is the double-blinding study method appropriate?	Total score
Turan and Aşt (12)	1	0	1	+1	−1	2
Kassolik et al. (19)	1	1	1	+1	+1	5
McClurg et al. (10)	1	0	1	+1	−1	2
Silva and Motta (14)	1	0	1	+1	−1	2
Lai et al. (18)	1	0	1	+1	−1	2
Lämås et al. (15)	1	0	1	+1	−1	2
McClurg et al. (10)	1	0	0	+1	−1	2
Lämås et al. (16)	1	0	1	+1	−1	2
Lämås et al. (15),	1	0	1	+1	−1	2

and the patients watched a video of the massage before the application.

In 6 randomised controlled trials, abdominal massage and laxatives were applied to the experimental groups while the standard clinical protocol [laxatives and/or lifestyle change (diet, activity, fluid intake, etc.)] was applied to the control groups. In one study, the tensegrity-based massage was applied to the control group while the classical abdominal massage was applied to the experimental group. In another study, the classical abdominal massage was applied to a group, aroma massage was applied to another group while only laxatives were applied to the third group. Moreover, in another study, abdominal massage, breathing exercises and isometric abdominal muscle training were administered to the experimental group while only laxatives were applied to the control group (Tables 2, 3).

Table 2. The characteristics of the studies included in the systematic review

Study (first author, year)	Aim of the study	Study group	Applied intervention/ approach	Assessment	Conclusion	Jadad score (0-5)
Turan and Aşt (12)	To determine the effect of abdominal massage on constipation and the quality of life in the orthopaedics and traumatology patients	E=30 C=30	Postop 4th day, 2 times a day for 3 days, 15-minute abdominal massage laxative use and lifestyle change	• Gastrointestinal Symptom Rating scale, • Constipation Severity scale, • Bristol Visual Stool scale • The Patient Assessment of Constipation Quality of Life (PAC-QOL)scale, • European Quality of Life scale (EQ-5D)	It was determined that the abdominal massage applied to the patients diagnosed with postoperative constipation reduced the constipation symptoms, the time intervals between defaecations and enhanced the quality of life	2
Kassolik et al. (19)	To compare the efficacy of tensegrity-based massage and the classical abdominal massage applied to constipated patients	E=15 C=14	Tensegrity massage for 20 minutes, 2 times a week, for 21 days Abdominal massage for 10 minutes, 2 times a week, for 21 days	• Rome III questionnaire • Bowel diary	It was observed that the massage based on the tensegrity principle had a more positive effect on the quality and amount of bowel movements compared to the classical abdominal massage	5
McClurg et al. (10)	To reduce the constipation symptoms in Parkinson patients	E=16 C=16	abdominal massage every day for 6 weeks, Change of lifestyle	• Gastrointestinal Symptom Rating Scale • Constipation Severity Scale • Neurogenic Bowel Dysfunction • Bowel diary	An abdominal massage is an effective approach in Parkinson patients for the treatment of constipation	2
Silva and Motta (14)	To compare the muscle training-abdominal massage-diaphragm breathing and the medical treatment in patients with chronic functional constipation.	E=36 C = 36	Twice a week for 6 weeks, 12-40 min (Abdominal Massage + breathing Exercise + isometric abdominal muscle training) Laxatives	• Frequency of defaecation and faecal incontinence	At the end of 6 weeks, together with the combined use of the isometric training of the abdominal muscles, breathing exercises and the abdominal massage, there was an increase in the defaecation frequency and no change was observed in the faecal incontinence	2
Lai et al. (18)	To examine the effect of aroma massage on constipation in terminal cancer patients	Aroma M:13 Classic M:11 C:8	Aroma M of 15–20 minutes for 5 days Classic Abdominal M of 15-20 minutes for 5 days laxative use and lifestyle change	• Constipation Rating scale • Quality of life scale for Hong Kong (MQoL-HK)	The aroma massage was found to reduce the constipation score in the terminal cancer patients and to enhance the quality of life.	2

D: Experimental group, K: Control group, aromaa M: Aromaa massage, Classic M: Classic massage

In the assessment of constipation, the Gastrointestinal Symptom Rating scale, Constipation Severity index, Bristol Visual Stool scale, Constipation Quality of Life scale, Neurogenic Bowel Dysfunction and bowel diary were used.

It was observed by Turan and Aşt (12) that abdominal massage applied for postoperative constipation in orthopaedics and traumatology patients reduced the constipation symptoms and the time intervals between the defaecations, enhancing the quality of life (12).

Previous studies on constipation among parkinson and multiple sclerosis patients stated that abdominal massage was an effective approach (2,10).

On the other hand, among individuals with chronic functional constipation, the muscle training/abdominal massage/diaphragm breathing combination and medical treatment were compared. With the combined use of isometric training of the abdominal muscles, respiratory exercises and abdominal massage, an increase was observed in the defaecation frequency, whereas no change in faecal incontinence was observed. Of note, the above-mentioned studies were of low quality (14).

In the studies conducted by Lämås et al. (15), it was observed in different years that abdominal massage for constipation management reduced the severity of gastrointestinal symptoms, particularly increased bowel movements and reduced laxative intake. In addition, it was determined that abdominal massage was cost-effective in the long term (15-17).

In the study conducted by Lai et al. (18), to examine the effect of aroma massage on constipation in the terminal cancer patients, aroma massage was applied to a group, the classical massage was applied to another group and laxatives and lifestyle change were applied to the control group. It was shown that aroma massage may be used in terminal cancer patients.

In the study with the highest quality among the studies in the present systematic review, the classical abdominal and tensegrity-

Table 3. The characteristics of the studies included in the systematic review

Study (first author, year)	The aim of the study	The study group	Applied intervention/ approach	Assessment	Conclusion	Jadad score (0-5)
Lämås et al. (16)	To determine the efficacy of abdominal massage on constipation treatment	E=30 C=30	abdominal massage for five days a week, once a day, 15 minutes, 8 weeks laxatives and Lifestyle change	*Bowel diary	The Abdominal massage reduced the use of laxatives and it was asserted that it may be used in the management of constipation.	**2**
McClurg et al. (10)	To assess the effect of abdominal massage on constipation management in MS patients	E=15 C=15	Abdominal massage for 15 min daily and 4 weeks Change of lifestyle	*Constipation scoring system *Neurogenic bowel dysfunction *Bowel diary	The abdominal massage was found to be effective in reducing constipation in MS patients	**2**
Lämås et al. (16)	To examine the effect of abdominal massage applied for constipation on the cost	E=29 C=29	Abdominal massage + laxatives for 15 minutes 5 days a week and 8 weeks Laxatives and lifestyle change	*Gastrointestinal Symptom * Rating scale	In the management of constipation, abdominal massage may be cost-effective in the long term. An important point will be to determine the people who will benefit	**2**
Lämås et al. (15)	The effect of abdominal massage on laxative use and gastrointestinal function in the constipated people.	E=30 C=30	Abdominal Massage for 15 minutes 5 days a week and 8 weeks Laxatives	*Gastrointestinal Symptom * Rating scale	It was found that abdominal massage reduced the severity of gastrointestinal symptoms, especially constipation and abdominal pain,and increased the bowel movements. No significant correlation was found between the massage and laxative use	**2**

E: Experimental group, C: Control Group, aromaa M: Aroma massage, Classic M: Classic massage

based massages were compared. It was observed that tensegrity-based massage had a more positive effect on the quality and amount of the bowel movements compared to the classical abdominal massage (19).

Discussion

Constipation is currently a very important gastrointestinal symptom that is frequently encountered due to several reasons. This systematic review is the first of its kind that focuses on abdominal massage techniques applied for constipation management. All of the randomised controlled trials investigating the efficacy of abdominal massage on constipation management, were included into the present study. The number of relevant studies was limited and the methodological quality of the studies varied

After examining the studies that were included in the systematic review, it was observed that they were heterogeneously distributed in terms of intervention, disease, assessment scales and the study results. All the studies revealed that the use of abdominal massage for constipation management was an effective approach. The studies showed that abdominal massage reduced the severity of gastrointestinal symptoms, increased bowel movements and the frequency of defaecation, reduced constipation symptoms and enhanced the quality of life of the patients (2,10,12,14,15,17,18). They also showed that it was a cost-effective method because it decreased the use of laxatives (16). No side effect was reported in the studies.

In most of the studies included in the review, abdominal massage was performed on the patients in the supine position with circular movements in the direction of the colon (12,14,15,19). There were differences in massage techniques in the studies and the most frequent techniques were kneading, vibration, effleurage and superficial or deep stroking (12,15,19). In the studies, the duration of the massage varied between 10-40 min. Additionally, the frequency of the massage was either daily (2,10,12,15-18) or 1 to 2 times a week (14,19).

The reviewed studies revealed that abdominal massage is usually effective in treating constipation. The study by Turan and Aşt (12) revealed that patients receiving abdominal massage twice a day on post-operative 4, 5 and 6 days for 15 minutes defaecated more frequently in the postoperative period than the control group patients and that there was a statistically significant difference between the groups. In addition, it was found that abdominal massage reduced constipation symptoms, decreased time intervals between defaecations and enhanced the quality of life. Similarly, in the study conducted by McClurg et al. (2); abdominal massage was applied to multiple sclerosis patients for constipation management for 15 min every day for 4 weeks and it was found to be more effective compared to the control group. Also, McClurg et al. (2), applied abdominal massage to Parkinson patients for constipation management every day for 6 weeks and a change of lifestyle was made in the control group. As a result of the study, it was observed that there was a symptomatic recovery in both groups. However, there was no significant difference between the groups (10).

There are 3 different studies by Lämås et al. (15), evaluating the effect of abdominal massage on constipation management. The first study was conducted in 2009 and abdominal massage was applied to patients with constipation for 15 min once a day, for 5 days in a week, for 8 weeks. As a result of the study, it was reported that abdominal massage reduced gastrointestinal symptoms and increased bowel movements; however, it was determined that there was no significant correlation between massage and the use of laxatives (15). In their study which was conducted in 2010, the effect of self-massaging and massage by professionals on cost was evaluated for abdominal massage throughout 16 weeks. It was determined that self-massaging could be cost-effective for constipation management in the long term (16). In their third relevant study conducted in 2011, abdominal massage applied for constipation management reduced the use of laxatives and they stated that it could be an effective approach for constipation management (17).

On the other hand, in the study by Lai et al. (18), aroma massage, classic abdominal massage and laxative-lifestyle change were compared. It was reported that aroma massage reduced the constipation score and increased the quality of life compared to the control and classic abdominal massage (18). Similarly, in the study by Kassolik et al. (19), abdominal massage was compared with tensegrity-based massage and it was shown that tensegrity-based massage was more effective in improving the quality of bowel movements and amount of defaecation compared to the classic abdominal massage.

In the study by Silva et al. (14); the combined use of abdominal massage, isometric abdominal muscle training and diaphragm exercises was compared with the use of laxatives in patients with constipation and it was determined that there was an increase in the frequency of defaecation with the combined treatment; whereas, there was no change in faecal incontinence at the end of 6 weeks (14).

In all the studies, not only abdominal massage, but also laxatives were applied in the experimental group; whereas, laxatives and/or lifestyle change were applied in the control group. For constipation management, abdominal massage was used instead of laxatives and this reduced the number of laxatives used, although it is recommended to use both in combination (2,12,16). When the quality of the randomised controlled trials was assessed in the present review, it was observed that most of them were of low quality.

Study Limitations

The limitation of the study is that it assessed only articles published in English. We did not find any randomised controlled trial published in Turkish that evaluated the effect of abdominal massage on constipation. In addition, all the studies that were found had low quality data and the studies were conducted in different sample groups.

Conclusion

Abdominal massage is a cheap method without any side effects, which can easily be applied by the patients themselves, their relatives or other healthcare professionals in environments such as the home, workplace or hospital. The effect of abdominal massage on constipation was evaluated in different studies and it was found to be effective. In the light of these finding, it can be recommended that abdominal massage be regularly applied to patients with constipation. Particularly, patients who have a risk of constipation in the clinics can be taught on how to perform the abdominal massage, in order to prevent the patients from getting constipated and also to enhance their quality of life. In addition, the use of laxatives can be reduced and thus, cost-effective care can be provided.

When the Jadad scores of the studies were taken into consideration, it was observed that only one of the studies had a high Jadad score; therefore, it is considered that randomised controlled trials performed with a larger sample of patients including those having a similar diagnosis and receiving a similar treatment in order to determine the efficacy of abdominal massage in constipation management are required.

Ethics

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Concept: E.E.K., V.K., F.A., G.C., Design: E.E.K., V.K., F.A., G.C., Data Collection or Processing: E.E.K., V.K., G.C., Analysis or Interpretation: E.E.K., V.K., F.A., G.C., Literature Search: E.E.K., G.C., Writing: E.E.K., V.K., G.C.

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Case Report

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Use of Antipsychotic Long-acting Injection in Ekbom Syndrome: A Case of Delusional Parasitosis

Ekbom Sendromunda Uzun Etkili Antipsikotik Enjeksiyon Kullanımı: Bir Delüzyonel Parazitoz Olgusu

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ABSTRACT

Ekbom syndrome is the clinical term for delusional parasitosis and is characterized by the patient's fixed and false conviction of being infested with parasites without any objective evidence. Patients with Ekbom syndrome often consult dermatologists, however, sometimes they might try to heal themselves by "removing" the parasites, which may lead to a skin-picking disorder or excoriation. The patient's obsessive treatment of such skin lesions ultimately leads to a vicious cycle that further distances them from psychiatry. Patients with poor adherence to psychiatric treatment may become chronic if left untreated. Although the benefit of antipsychotics in Ekbom syndrome is well-known, a chronic patient who has insufficient social support is not expected to comply with oral therapy. Antipsychotic long-acting injection should be considered as an option for such patients. In this case report, we present a male patient with delusional disorder who showed a symptomatic improvement after being treated with antipsychotic long-acting injection.

Keywords: Ekbom syndrome, delusional infestation, delusional parasitosis, delusional disorder, antipsychotic long-acting injection

ÖZ

Klinikte delüzyonel parazitoz olarak adlandırılan Ekbom sendromu, herhangi bir nesnel kanıt olmadan parazitlerle enfekte olduğu sabit ve yanlış öznel inancı ile karakterizedir. Ekbom sendromlu hastalar sıklıkla dermatologlara başvururlar ve bazen ekskoriyasyona neden olabilecek parazitleri "kazıyarak" kendilerini iyileştirmeye çalışırlar. Bu deri lezyonlarının zorunlu tedavisi, nihayetinde hastayı psikiyatriden uzaklaştıran kısır bir döngüye neden olur. Zaten psikiyatrik tedaviye uyumu zayıf olan bu hastalar, tedavi edilmezse hastalık kronik hale gelebilir. Ekbom sendromunda antipsikotiklerin yararı bilinmesine rağmen, kronik olan ve sosyal desteği yetersiz olan bir hastanın oral tedaviye uyum sağlayacağı beklenmemektedir. Antipsikotik uzun etkili enjeksiyon bu hastalarda bir seçenek olarak düşünülmelidir. Bu olgu sunumunda, antipsikotik uzun etkili enjeksiyon tedavisi ile semptomatik iyileşme gösteren delüzyonel bozukluğu olan bir erkek hasta sunuyoruz.

Anahtar Sözcükler: Ekbom sendromu, delüzyonel infestasyon, delüzyonel parazitoz, delüzyonel bozukluk, antipsikotik uzun etkili enjeksiyon

Introduction

Delusional parasitosis, also known as Ekbom syndrome, is a rare psychiatric disorder, generally affecting women and more commonly seen among married individuals. A person with this syndrome has a false and constant belief that their body is infested by parasites or insects, and this delusion continues even when no medical evidence of parasites or insects is found in the patient's body (1,2). The patients often report experiencing an itch-like sensation that binds to their delusion of the presence of parasites under or inside their skin. Some patients even try to heal their

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skin by scraping it off using disinfectants and pesticides (1). This causes a vicious cycle of skin lesions, itching and delusional belief among the patients. The lesions are often found on the trunk and scalp (2) of the patient, and it is because of the lesions that the patients are often referred to dermatologists. When referred to a psychiatrist, most patients are hopeless and convinced that the psychiatrists are incompetent and cannot provide the right treatment. They are usually angry and stressed about it. A large number of patients refuse to see a psychiatrist in any way, and like any paranoid patient, they are meticulous, demanding, disturbing and arrogant. The story often reverts to the physical symptoms and so the patients either refuse to take the treatment or do not comply with it (3). Delusional parasitosis has been classified as "delusional disorder, somatic subtype" in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) (4). It can be classified as primary and secondary etiologically. Although the diagnostic criteria of Ekbom syndrome have been defined, there is no consensus on its treatment. The opinion that treating the disease as a classical delusional disorder and treating it is common (2). In this case report, we discuss the recovery process of antipsychotic long-acting injections in a patient with Ekbom syndrome who developed various skin-related complications but refused oral antipsychotic treatment.

Case Report

A 75-year-old male patient was referred to our psychiatry clinic with the suspicion of psychotic symptoms by a dermatologist accompanied by social workers. The patient had consulted various dermatologists for over a course of approximately 20 years with the complaint of lice, *Pediculus humanus*, in his hair. Although the patient did not have any skin problems, he had used many different lice medications for many years. However, nothing ever worked for him and he eventually decided go bald. Nevertheless, when his hair began to regrow, he assumed them to be lice coming out of his head and started constantly dealing with his scalp. As a result, many lesions appeared on the patient's scalp. He finally consulted dermatologists to treat those lesions. When he started receiving the treatment, he went back to thinking that he has lice in his head and the doctors finally agreed. Every time he was referred to the psychiatrist to break this vicious cycle, he reacted with anger. The patient was and is living alone and is still on clobetasol propionate therapy. The physical examination of the patient showed excoriation and lichenification on the scalp. The neurological examination was unremarkable. Hemogram and biochemistry parameters were within normal limits. Magnetic resonance imaging was normal. The patient's self-care was decreased. Speech content was impoverished. Stereotypes were available. The patient's answers to the questions were irrelevant, his mood was dysphoric, affect was inappropriate and his mind was impoverished. No pathological finding was detected in perception. The patient was diagnosed with delusional disorder and was started on risperidone long-acting injection 37.5 mg, once in 15 days, because it was thought to be incompatible with oral therapy. After a follow-up in consultation with the dermatologist, the patient's complaints were controlled within a month, and subsequent follow-ups and treatment were continued through home care services. At the end of the three-month follow-up, no similar symptoms were reported.

Discussion

The most important step in the treatment is to build confidence in the patient–physician relationship. For adequate treatment of delusional parasitosis, it is necessary to differentiate between the different types (1). While antipsychotic drugs provide significant treatment in primary delusional parasitosis, they are only used symptomatically in cases secondary to somatic diseases and the treatment of the underlying disease is required. Typical antipsychotics, atypical antipsychotics, antidepressants, electroconvulsive therapy and dermatological agents can be used individually or in combination (3). In most cases of delusional parasitosis, once symptoms have settled, response to treatment is generally low. The delusional system settles and becomes chronic in patients who remain untreated for long periods of time. Suicide has also been reported as one of the outcomes (2).

In contrast to the common features of Ekbom syndrome, our case was a male patient living alone. The patient was in a vicious cycle and adherence to treatment was poor. He did not believe that his illness could have a psychiatric aspect. Since he had not been treated for many years, the disease had become chronic and various complications had arisen. Since it was thought that oral treatment would not be appropriate in such a patient, antipsychotic long-acting injection was initiated, and follow-up was provided through home care services. The majority of cases and studies in the literature focus on oral treatments. Traditionally, typical antipsychotic pimozide is considered as the first choice of drug, but it comes with a number of serious side effects (5,6). According to Aït-Ameur et al. (7), pimozide is currently the most effective treatment. However, compliance with oral treatment is not possible in chronic patients with inadequate social support (2,8). Nevertheless, antipsychotic long-acting injection also has some serious side effects-dystonia, oedema and neuroleptic malignant syndrome to name a few. In order to respond quickly to these possible side effects, a follow-up is recommended at short intervals (8-10).

In conclusion, this case report shows that antipsychotic long-acting injection use is an important treatment option in patients with chronic, non-compliant Ekbom syndrome. It is recommended that clinicians keep in mind the use of antipsychotic long-acting injections in this disorder, which is difficult to treat even under normal conditions. Further systematic research should be conducted with respect to antipsychotic long-acting injection use in Ekbom syndrome to provide a greater understanding of both its prevalence and aetiology.

Ethics

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: E.Ç., M.H.Ö., Design: E.Ç., M.H.Ö., Data Collection or Processing: E.Ç., M.H.Ö., Analysis or Interpretation: E.Ç., M.H.Ö., Literature Search: E.Ç., M.H.Ö., Writing: E.Ç., M.H.Ö.

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