



Clinical Practice and Knowledge of Pediatric Surgeons about Eosinophilic Esophagitis in Children with Esophageal Atresia

Çocuk Cerrahlarının Özofagus Atrezili Çocuklarda Eozinofilik Özofajit Konusunda Klinik Uygulamaları ve Bilgi Düzeyleri

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ABSTRACT

Objective: The study examined the clinical practice and knowledge of pediatric surgeons regarding diagnosis and treatment of eosinophilic esophagitis (EoE) in children with esophageal atresia (EA).

Methods: Pediatric surgeons who were involved in diagnosis and treatment of EA from Turkey were included. An online survey, which included 26 questions related to clinical practice and knowledge of pediatric surgeons was administered via Google forms. The survey included questions regarding descriptive information of participants, diagnosis, treatment, and knowledge about EoE in children with EA.

Results: Fifty seven pediatric surgeons responded to the study. Reflux symptoms resistant to treatment and recurrent anastomotic strictures were most commonly reported as symptoms of EoE. Endoscopy with biopsies was the most commonly selected diagnostic method for EoE with nearly half of the surgeons obtaining appropriate biopsies. Diet elimination, proton pump inhibitors and systemic steroids were most commonly reported to be used in the treatment of EoE. Of pediatric surgeons 17.5% (n=10) had low-level knowledge, 45.6% (n=26) had moderate level knowledge, and 36.8% (n=21) had high-level knowledge.

Conclusion: The EoE can be seen in association with EA. This association may cause dysphagia, food impaction, vomiting and decreased quality of life. The study results suggest that pediatric surgeons have some strengths and weaknesses in terms of clinical

ÖZ

Amaç: Çalışmada, çocuk cerrahlarının özofagus atrezili (ÖA) çocuklarda eozinofilik özofajitin (EÖ) tanı ve tedavisi ile ilgili klinik uygulamaları ve bilgileri incelenmiştir.

Yöntemler: Türkiye'de ÖA'nın tanı ve tedavisinde görev alan çocuk cerrahları dahil edildi. Google formları aracılığıyla çocuk cerrahlarının klinik uygulamaları ve bilgileriyle ilgili 26 sorudan oluşan çevrimiçi bir anket uygulandı. Anket; katılımcıların tanımlayıcı bilgileri ve ÖA'lı çocuklarda EÖ'nün tanısı, tedavisi ve bunlarla ilgili bilgilerini içeren sorular içeriyordu.

Bulgular: Çalışmaya 57 çocuk cerrahı yanıt verdi. Tedaviye dirençli reflü semptomları ve tekrarlayan anastomoz darlıkları en yaygın olan EÖ semptomları olarak bildirildi. Biyopsi ile endoskopi, EÖ için en yaygın olarak seçilen tanı yöntemi ve cerrahların yaklaşık yarısı uygun biyopsiler alıyordu. Diyet eliminasyonu, proton pompası inhibitörleri ve sistemik steroidler en yaygın EÖ tedavi yöntemleri olarak bildirildi. Çocuk cerrahlarının %17,5'i (n=10) düşük düzeyde bilgiye sahipti, %45,6'sı (n=26) orta düzeyde bilgiye sahipti ve %36,8'i (n=21) yüksek düzeyde bilgiye sahipti.

Sonuç: EÖ, ÖA ile birlikte görülebilmektedir. Bu ilişki disfaji, gıda sıkışması, kusma ve yaşam kalitesinin düşmesine neden olabilmektedir. Çalışma sonuçları, ÖA'lı çocuklarda EÖ tanısı ve tedavisi ile ilgili klinik uygulama ve bilgi açısından çocuk cerrahlarının bazı güçlü ve zayıf yönlerinin olduklarını göstermektedir. Bu nedenle bu çocukların bakımında iyileşme, çocuk cerrahlarının farkındalığını ve bilgisini artırarak, uygulamaların heterojen

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practice and knowledge regarding diagnosis and treatment of EoE in children with EA. Therefore, improvement in the care of these children could be achieved by increasing awareness and knowledge of pediatric surgeons, decreasing heterogeneous nature of practice patterns and creating a consensus in clinical settings.

Keywords: Esophageal atresia, eosinophilic esophagitis, pediatric surgeon, knowledge

doğasını azaltarak ve klinik ortamlarda bir fikir birliği oluşturarak sağlanabilir.

Anahtar Sözcükler: Özofageal atrezi, eozinofilik özofajit, çocuk cerrahı, bilgi

Introduction

Esophageal atresia (EA) is the most common birth defect of the esophagus and affects 1 in 2,500 live births (1). Children with EA experience a high rate of morbidity, which lasts lifelong. Patients have varying degrees of morbidities like esophageal dysmotility, anastomotic strictures, gastroesophageal reflux disease (GERD), dysphagia and feeding difficulties (2).

Eosinophilic esophagitis (EoE) is a chronic allergic disorder, which is characterized by esophageal eosinophilia and esophageal dysfunction. It causes vomiting, dysphagia, feeding difficulties, food allergy, and decreased quality of life (3). Children with EA are shown to have a significant prevalence of EoE ranging between 3-17% (4-7). There are several contributing and underlying factors including food impaction, treatment-resistant strictures and increased allergen exposure due to motility problems underlying EoE development in children with EA. However, it is difficult to diagnose EoE in patients with EA due to similarities of symptoms with GERD, dysphagia and esophageal dysmotility (3). For instance, the study with the largest number of patients with EA and EoE suggested that in addition to fluoroscopic swallowing studies, endoscopic evaluation with multiple biopsies was important in children who suffered from increasing dysphagia (5). Vomiting, dysphagia or feeding problems were more common in patients with EA and EoE resulting in a higher likelihood of undergoing fundoplication and gastrostomy surgeries in comparison to those who did not have associated EoE (5). Pediatric surgeons not only have an important role in the management of children with EA but they also design their long-term follow-ups (1,2). Therefore, awareness of pediatric surgeons about the symptoms suggestive of EoE, and necessity to perform biopsies and referral of the patients to appropriate disciplines if needed are important. Pediatric surgeons are to be involved in developing standardized consensus and providing improvement in care.

In a recent study, dysphagia as one of the most common complication in these children from the perspective of pediatric surgeons was investigated, and it was suggested that there was a need for a standardized protocol in dysphagia management and their knowledge was found to be high (8). The importance of the awareness and knowledge of pediatric surgeons is also known to handle EoE in children with EA. However, there is no study to evaluate their current clinical practice and knowledge in terms of EoE in children with EA in literature. Determination of the current practice and knowledge may provide better understanding of the pitfalls of management delivered by pediatric surgeons,

reveal good practices, and contribute to create consensus in national and international areas. Therefore, the current study aimed to define clinical practice and knowledge of pediatric surgeons from Turkey regarding diagnosis and treatment of EoE in children with EA.

Methods

The online survey study was carried out at Hacettepe University. The Hacettepe University Non-invasive Clinical Research Ethics Committee approved the study protocol (approval number = GO20/528).

Participants

Pediatric surgeons who currently worked in Turkey and were involved in diagnosis and treatment of EA were included in the study. The invitation was done by using a national e-mail platform already in use for online communication among pediatric surgeons in Turkey. The online survey was administered via Google forms. All volunteering participants were required to provide informed consent prior to reach survey questions by clicking the start button of the survey. All data were collected anonymously.

Procedure

Two pediatric surgeons with more than 20 years of clinical and research experience in the treatment of children with EA developed the draft questions. A pilot study was performed to test clarity of the questions before survey distribution. Two pediatric surgeons and one physical therapist who were university-affiliated experts with a minimum of 10-year work experience and routinely encountered patients with EA in practice discussed each question, and minor changes were made through their feedback. The survey included 26 questions, which was estimated to take 15 minutes to complete.

The survey included (i) 4 questions related to descriptive information of participants, (ii) 8 questions related to diagnosis, (iii) 4 questions related to treatment, and (iv) 10 questions related to knowledge. Descriptive section questioned the type of hospital, occupational experience, the number of children with EA in annual follow-up and the number of children with EA who had EoE. In the diagnosis section, there were questions related to consultations in the long-term follow-up, the endoscopy applications and the diagnosis of EoE. There were two questions related to the treatment of GERD and two questions regarding the treatment of EoE. In the knowledge section, participants were asked to state "yes" or "no" for the statements. Only one

option was the correct answer, which received one point, and the incorrect answer received zero point. Therefore, the total knowledge score ranged between 0 to 10 points. In addition, the total score was assessed based on Bloom's cut off point (9). According to Bloom's cut off point, the level of knowledge was classified into three as "low-level", "moderate-level", and "high-level" knowledge. The total score less than 60% (0-5 scores) referred to low-level knowledge, 60-79% (6-7 scores) indicated moderate-level knowledge, and 80-100% (8-10 scores) referred to high-level knowledge. The statements were related to time of occurrence of esophagitis (Q1), frequency by gender (Q2), risk related to type of atresia (Q3), condition in prematurity (Q4), genetic relationship (Q5), relationship between esophagitis and anti-acid therapy (Q6), relationship between esophagitis and motility impairment (Q7), relationship between esophagitis and atopic diseases and food allergies (Q8), basal analysis (Q9), and cautions before anti-reflux treatment (Q10). Appendix 1 indicates the survey questions in detail.

The survey was started in July 2020. A reminding e-mail message was sent after each four weeks, and the survey was closed twelve weeks after initial posting, and responses were analyzed.

Statistical Analysis

The statistical analysis was performed by using IBM-SPSS for Windows version 20. Descriptive statistics were expressed as number/percent for qualitative data, and mean, standard deviation, minimum and maximum values for quantitative data.

Results

A total of 57 pediatric surgeons were participated in the current study. The descriptive characteristics of participants are shown in Table 1.

Diagnosis: In the long-term follow-up of children who underwent EA operation, 73.7% (n=42) of pediatric surgeons got routine consultation from pediatric gastroenterology, 36.8% (n=21) from pediatric pulmonology and 26.3% (n=15) from pediatric allergy/immunology units. The rate of pediatric surgeons who did not get any support from other disciplines was 22.8% (n=13). The responses related to the endoscopy applications and the diagnoses of EoE are presented in Table 2 and Table 3, respectively.

Treatment: In treatment section, the questions were related to GERD and EoE. The answers are given in Table 4.

Knowledge: The percentage of correct answers for each questions was as follows: Q1: 66.7% (n=38), Q2: 71.9% (n=41), Q3: 70.2% (n=40), Q4: 64.9% (n=37), Q5: 47.4% (n=27), Q6: 56.1% (n=32), Q7: 89.5% (n=51), Q8: 96.5% (n=55), Q9: 21.1% (n=12), Q10: 93% (n=53). The mean knowledge score was 6.64 ± 1.92 (min=1, max=9). The rate of pediatric surgeons with low-level knowledge was 17.5% (n=10), moderate-level knowledge was 45.6% (n=26) and high-level knowledge was 36.8% (n=21).

Discussion

The care of children with EA, which requires multidisciplinary follow-up should be handled systematically from childhood to adulthood (10,11). Therefore, standard management guidelines in terms of gastrointestinal and nutritional complications in

Table 1. The descriptive characteristics of pediatric surgeons and their clinical practice

	N	%
Hospital		
University hospital	39	69.6
Training hospital	14	25.0
Non-training state hospital	1	1.8
Private hospital	2	3.6
Occupational experience		
0-5 years	8	14.0
6-10 years	15	26.3
11-15 years	12	21.1
>16 years	22	38.6
Number of children with EA treated per year		
< 5	18	31.6
5-10	22	38.6
>10	17	29.8
Number of patients who were diagnosed as having EoE while being under follow-up for EA		
None	27	48.2
<2	19	33.9
2-5	9	16.1
>5	1	1.8

EA: Esophageal atresia, EoE: Eosinophilic esophagitis

Table 2. The responses related to the endoscopy applications in children with EA

	N	%
The percentages of indications for endoscopy		
Esophageal dilatation	50	87.7
Suspected GERD	29	50.9
Reflux esophagitis follow-up	42	73.7
After stopping proton pump inhibitors	1	1.8
Suspected EoE	35	61.4
In asymptomatic adolescents	3	5.3
Routine surveillance for esophagitis	3	5.3
Which type of endoscopy		
Does not perform endoscopy	2	3.5
Rigid endoscopy	8	14
Flexible endoscopy	33	57.9
Both rigid and flexible endoscopy	14	24.6

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children with EA are important to improve the quality of care to these patients and guide clinicians (12). In addition to clinical studies' results and what is suggested in the guidelines, defining the clinical practice and knowledge of primary responsible clinicians regarding children with EA is also important to reveal

Table 3. The responses related to the diagnosis of EoE in children with EA

	N	%
Signs and symptoms of EoE in children with EA		
Food impaction	25	43.9
GERD symptoms resistant to treatment	50	87.7
Recurrent anastomotic strictures	44	77.2
Recurrence of GERD findings	23	40.4
Airway aspiration	17	29.8
Diagnostic methods for EoE		
Contrast upper GI studies	3	5.3
pH meter/impedance	2	3.5
Endoscopy and biopsy	51	89.5
Esophageal manometry	0	0
Videofluoroscopic swallowing assessment	1	1.8
Endoscopy findings for EoE		
Red streaks and white exudates	42	73.7
Trachealization or ringing	26	45.6
Crepe paper mucosa, fragile mucosa	32	56.1
Varicose veins in the lower end of the esophagus	4	7
Mucosal bleeding centers	30	52.6
Location of endoscopic biopsies and the number of samples in a patient with suspected EoE		
No need for a biopsy	3	5.3
Two from each quadrant from the lower esophagus	12	21.1
Two from each quadrant from the upper esophagus	3	5.3
Two each from the lower, middle and upper esophagus	24	42.1
Only the areas seen as suspicious	15	26.3
Number of eosinophils/high power field required to diagnose EoE in endoscopic biopsy specimens		
Less than 5	2	3.5
Between 5-14	11	19.3
Less than 15	4	7
Equal to and more than 15	27	47.4
No idea	13	22.8
EA: Esophageal atresia, EoE: Eosinophilic esophagitis		

what is exactly performed. Therefore, we aimed to determine the current practice and knowledge of pediatric surgeons in terms of EoE in children with EA.

In the long-term follow-up of children who were operated on for EA, pediatric surgeons reported that they mostly got help from pediatric gastroenterology unit. However, approximately one quarter of them could not get any collaboration from other disciplines. The percentage of clinicians who did not have any help from other discipline was remarkable. A multidisciplinary approach is necessary to have a favorable long-term outcome and better quality of life (12-14). Therefore, we believe that the awareness of other team members including pediatric gastroenterologists, pediatric pulmonologists, etc. should be increased as well as pediatric surgeons to improve clinical care of these children.

A substantial number of pediatric surgeons (42.1%) favor routine medical therapy for GERD in the first year of life in all patients with EA as recommended in ESPGHAN-NASPGHAN

Table 4. The responses related to the treatment of GERD and EoE in children with EA

Medical treatment approach for GERD in children with EA	N	%
Only to symptomatic patients	18	31.6
All cases with anastomotic strictures	8	14
First 1 year in all EA cases	24	42.1
Treatment after diagnostic testing	7	12.3
First choice for GERD treatment in children with EA		
H ₂ receptor blockers	9	15.8
Proton pump inhibitors (PPI)	20	35.1
Alginate and/or prokinetics and H ₂ receptor blockers together	19	33.3
Alginate and/or prokinetics, PPI	9	15.8
Other disciplines which are involved in the consultation of patients with suspected EoE		
Pediatric gastroenterology	54	94.7
Pediatric hematology	1	1.8
Pediatric allergy	45	78.9
Pediatric immunology	19	33.3
Treatment of EoE		
Diet elimination	42	73.7
Systemic steroids	25	43.9
Proton pump inhibitors	38	66.7
Esophageal dilatation	12	21.1
Intralesional applications (mitomycin -C, etc.)	6	10.5
EA: Esophageal atresia, EoE: Eosinophilic esophagitis		

guidelines (12). One third of responders prescribe anti-reflux medication only in symptomatic patients and 12% of them prescribe after testing for reflux. Proton pump inhibitors (PPI) (35.1%) and alginate and/or prokinetics and H₂ receptor blockers together (33.3%) were the first line of choice for GERD treatment by pediatric surgeons.

The most common indications for endoscopy for pediatric surgeons are esophageal dilatation, follow-up of reflux esophagitis, and suspicion of EoE or GERD in accordance with the literature (12). Only one pediatric surgeon reported that he/she planned endoscopy after stopping proton pump inhibitors. More than half of the pediatric surgeons preferred flexible endoscopy for children with EA, and approximately 25% preferred both rigid and flexible endoscopy. The results show that pediatric surgeons in Turkey follow international consensus regarding endoscopy applications (12).

The responding pediatric surgeons reported that they suspected EoE in patients with GERD symptoms resistant to treatment (87.7%), recurrent anastomotic strictures (77.2%) and food impaction (43.9%). In addition, they also reported that recurrent gastroesophageal reflux and airway aspiration were also signs of EoE in children with EA. These findings suggest that most pediatric surgeons are aware of the considerable overlapping between GERD and EoE symptoms in children with EA. It has been reported that patients with long gap EA and EoE have 1.9 times higher relative risk to develop strictures and surgical treatment of strictures are needed if they become resistant to dilatation treatment (3). The results of survey confirm that majority of pediatric surgeons suspect EoE in case of recurrent strictures.

Endoscopic evaluation with biopsies is crucial for diagnosis of EoE (12,15). EoE can be definitely diagnosed by esophageal biopsy revealing more than 15 eosinophils/HPF (12,15). In our survey, 89.5% of pediatric surgeons reported that they performed endoscopy and took biopsies whenever they suspected from EoE. The finding of "red streaks and white exudates" was the most frequently associated endoscopy finding with EoE (73.7%) by pediatric surgeons followed by crepe paper and fragile mucosa, mucosal bleeding centers and trachealization or ringing, in descending order. Interestingly, half of them consider mucosal bleeding as an endoscopic sign for EoE and 7% of them find varicose veins in the lower end of esophagus suggestive for diagnosis.

Since EoE is described as a patchy disease, it is important to take biopsies from widespread locations (3). In our study, 42.1% of surgeons preferred two biopsies each from the lower, middle and upper esophagus for suspicion of EoE, and 47.4% of them considered more than 15 eosinophils/HPF diagnostic for EoE. These results suggest that nearly half of the surgeons obtain appropriate biopsies and consider the results correctly according to the guidelines. However, 26% of responders obtain biopsies only from the suspected areas and 22.8% of them had no idea about the number of eosinophils in the biopsy specimens for EoE diagnosis. These percentages suggest that

there is a need to increase awareness, knowledge and clinical applications of pediatric surgeons in terms of endoscopic evaluations and interpretations for EoE in children with EA. Pediatric gastroenterology (94.7%), pediatric allergy (78.9%) and pediatric immunology (33.3%) disciplines are the most commonly co-involved disciplines in patients with EA with suspected EoE. This may simply be dependent on the availability of the discipline in the institution at which the pediatric surgeon works or a personal preference depending on the enthusiasm of the other disciplines to collaborate in the care of the patients with EA in a given institution.

Although, pediatric surgeons do not directly dictate the treatment of EoE, they report diet elimination (73.7%), proton pump inhibitors (66.7%) and systemic steroids (43.9%) as most frequent treatment options in EoE. This is compatible with the recommended treatment protocols for children with EA (16). In a study performed in 2016, the authors reported that dilatations could be needed for strictures in patients with coexistent EoE with EA although seldom (17). The role of pediatric surgeons in the treatment of EoE is mainly limited to esophageal dilatations for strictures. About one fifth of pediatric surgeons in our study mentioned that they carried out dilatations for these patients. Interestingly, 10% of pediatric surgeons reported intralesional applications for the treatment for EoE. The use of any intralesional applications has not been reported in EoE before and possibly has no beneficial effect on EoE related esophageal strictures.

Study Limitations

Our study had a limitation because only volunteering pediatric surgeons answered the questions and they might be the ones with a special interest in EA and/or EoE. Bearing this fact in mind, the knowledge of pediatric surgeons was found to be above average in this study. Most participants had moderate (45.6%) to high (36.8%) level of knowledge. Wrong answers were mostly related to basal impedance analysis and genetic relationship. The most correct answers were related to relationship between esophagitis and atopic diseases and food allergies, and cautions before anti-reflux treatment. These results are also very important because determining the lack of knowledge as to the degree or aspect may provide clinicians to organize and participate in educational programs, improve their clinical applications, and increase the success of care regarding EoE in children with EA.

Conclusion

The EoE is a chronic inflammatory disease of the esophagus and can be seen in association with EA. Children with EA and also suffering from EoE have higher incidence of dysphagia, food impaction, vomiting and feeding difficulties, which result in decreased quality of life of both patients and their families. Therefore, the clinical practice and knowledge regarding its diagnosis and treatment are important in addition to clinical studies and management guidelines. The current study results suggest that pediatric surgeons have some strengths and weaknesses in terms of clinical practice and knowledge about this

association. Therefore, their awareness, knowledge and clinical practice should be increased to improve the care of these children.

Ethics

Ethics Committee Approval: The online survey study was carried out at Hacettepe University. The Hacettepe University Non-invasive Clinical Research Ethics Committee approved the study protocol (approval number=GO20/528).

Informed Consent: provided informed consent prior to reach survey questions by clicking the start button of the survey.

Peer-review: Externally peer reviewed.

Authorship Contributions

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

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