ORIJINAL ARAȘTIRMA ORIGINAL RESEARCH

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# **Complementary and Alternative Medicine Use in Pediatric Gastroenterology Outpatient Clinic: Cross-sectional Study**

## Pediatrik Gastroenteroloji Polikliniğinde Tamamlayıcı ve Alternatif Tıp Kullanımı: Kesitsel Çalışma

<sup>©</sup>Burcu GÜVEN<sup>a</sup>, <sup>©</sup>Elif SAĞ<sup>a</sup>, <sup>©</sup>Fatma İSSİ<sup>a</sup>, <sup>©</sup>Fazıl ORHAN<sup>b</sup>, <sup>©</sup>Murat ÇAKIR<sup>a</sup>

<sup>a</sup>Department of Pediatric Gastroenterology, Karadeniz Technical University Faculty of Medicine, Trabzon, TURKEY <sup>b</sup>Department of Pediatric Allergy, Karadeniz Technical University Faculty of Medicine, Trabzon, TURKEY

ABSTRACT Objective: Although there is sufficient data on the use of complementary and alternative medicine (CAM) in adults, the data on children is relatively limited. The present study was designed to investigate the frequency and factors associated with CAM usage in children with chronic liver and gastrointestinal diseases. Material and Methods: The study included patients aged 0-18 years who were followed up for chronic liver disease or gastrointestinal diseases. A questionnaire was administered to their parents, which probed information on the demographic characteristics and CAM use in children and the socioeconomic status and educational level of parents. Results: The study involved a total of 135 patients (60% girls, mean age of 10.45±5.05 years). Of these, 20 patients (14.8%) were found to be using CAM. The duration of CAM users' follow-up period was significantly higher than non-CAM user (5.84±3.71 years vs. 4.06±3.25 years, p=0.030). The frequency of CAM usage was significantly higher in patients with celiac disease (22.9%, p=0.049) and liver transplant recipients (44.4%, p=0.009). The frequency of CAM usage was significantly higher in patients who were not prescribed or were currently not using any conventional medicine compared to patients using conventional medicine (65% vs. 38.3%, odds ratio: 2.997). Conclusion: Although the frequency of CAM usage was low in our patient group, we consider that parents and physicians should be in full cooperation about the use of CAM and the effectiveness, side effects, toxicity, and potential drug interactions of CAM therapies.

Keywords: Complementary therapies; liver diseases; gastrointestinal diseases; child

ÖZET Amaç: Erişkinlerde tamamlayıcı ve alternatif tıp (TAT) kullanımına ilişkin yeterli veri olmasına rağmen cocuklara ilişkin veriler kısıtlıdır. Bu çalışma, kronik karaciğer ve gastrointestinal hastalıkları olan çocuklarda TAT kullanımıyla ilişkili faktörleri ve sıklığını araştırmak için tasarlanmıştır. Gereç ve Yöntemler: Çalışmaya kronik karaciğer hastalığı veya gastrointestinal hastalık nedeniyle takip edilen 0-18 yaş arası hastalar alındı. Ebeveynlere, çocukların demografik özellikleri ve TAT kullanımı, ebeveynlerin sosyoekonomik durumu ve eğitim düzeyi hakkında bilgi veren bir anket uygulandı. Bulgular: Çalışmaya toplam 135 hasta dâhil edildi (%60 kız, ortalama yaş 10,45±5,05 yıl). Bunların 20'sinin (%14,8) TAT kullandığı tespit edildi. TAT kullanan hastaların takip süresi kullanmayan hastalara göre anlamlı olarak yüksekti (5,84±3,71 yıl vs. 4,06±3,25 yıl, p=0,030). TAT kullanım sıklığı çölyak hastalarında (%22,9, p=0,049) ve karaciğer nakli alıcılarında (%44,4, p=0,009) anlamlı olarak daha yüksekti. TAT kullanım sıklığı, konvansiyonel ilaç reçete edilmemiş olan veya hâlen herhangi bir konvansiyonel ilaç kullanmayan hastalarda, kullanan hastalara göre daha yüksekti (%65'e karşı %38,3; göreceli olasılıklar oranı: 2,997). Sonuc: Hasta grubumuzda TAT kullanım sıklığı düşük olmasına rağmen, TAT kullanımı ve TAT tedavilerinin etkinliği, yan etkileri, toksisitesi ve potansiyel ilaç etkileşimleri konusunda ebeveynler ve hekimlerin tam iş birliği içinde olması gerektiğini düşünüyoruz.

Anahtar Kelimeler: Tamamlayıcı tedaviler; karaciğer hastalıkları; gastrointestinal hastalıklar; çocuk

Rapid advancements in the diagnosis and treatment of diseases have brought a remarkable increase in the use of complementary and alternative medicine (CAM) beginning from the mid-twentieth century. Although there is sufficient data on the use of CAM in adults, the available data on children is relatively limited. Researchers investigating the frequency of the use of CAM in children have mostly focused on children with chronic diseases or insufficiency.<sup>1,2</sup>

Correspondence: Burcu GÜVEN Department of Pediatric Gastroenterology, Karadeniz Technical University Faculty of Medicine, Trabzon, TURKEY/TÜRKİYE E-mail: burcuguven55@gmail.com Peer review under responsibility of Turkiye Klinikleri Journal of Pediatrics. Received: 09 Jun 2021 Received in revised form: 27 Jul 2021 Accepted: 10 Aug 2021 Available online: 12 Jul 2021 2146-8990 / Copyright © 2021 by Türkiye Klinikleri. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Parents naturally want to make the best choices for their children. Therefore, parents of children with chronic diseases feel restricted by various factors such as the chronic nature of the disease, lack of treatment, and the complexities and ambiguities of the treatment being administered. In such cases, the parents search for new treatment options on which they could have a better control and about which they could make active decisions more easily.<sup>2</sup> At that point, CAM may seem a viable option for such parents. Moreover, parents mostly prefer CAM to strengthen the immune system and to promote the healing chances, physical stabilization, and relaxation of the patients.3 McCann and Newell showed that children with chronic illnesses are three times more likely to use CAM than a healthy population.<sup>4</sup> The 2007 and 2012 National Health Interview Surveys also indicated that 12% of children in the general population used CAM and revealed that this rate was even higher in children and adolescents with chronic diseases.5

The present study was designed to investigate the frequency of CAM usage in children with chronic liver disease or gastrointestinal diseases. It is important to be aware of CAM usage in these patients because they have increased risk for the side effects and drug interactions of CAM.

## MATERIAL AND METHODS

### STUDY POPULATION

The study included patients aged 0-18 years who were followed up at Karadeniz Technical University Faculty of Medicine, Pediatric Gastroenterology Clinic, which is a tertiary and referral health center, for chronic liver disease or gastrointestinal diseases between October 1, 2019 and December 31, 2019.

### STUDY PROTOCOL

A questionnaire consisting of 14 questions that was previously used in Turkish children was administered to their parents by a physician who had no previous interaction with the patients. The questionnaire probed the demographic characteristics and CAM use in children and the socioeconomic status and educational level of parents.<sup>6</sup> Additionally, the types of CAM therapies (acupuncture, vitamins, fish oil, yoga, quail egg, honey, prayer, amulet, massage, and cupping) used for children were also recorded (Table 1). The parents filled out the questionnaire themselves.

Data about the disease characteristics of the patients were retrieved from the clinical records of the patients.

Economic statuses of the parents were classified into three groups according to their monthly income: <2,000 TL (low), 2,000-5,000 TL (moderate), and >5,000 TL (high).<sup>7</sup>

The study was approved by the local ethics committee (Karadeniz Technical University Ethics Committee, Approval No: 2019/176). Both patients and parents were briefed about the study and each parent provided a signed informed consent form. The study was conducted per the principles of the Helsinki Declaration.

### STATISTICAL ANALYSIS

Data were analyzed using SPSS version 21.0 (IBM Statistics, Armonk, NY). Quantitative variables were expressed as mean, standard deviation, and minimum-maximum values. Categorical variables were expressed as frequencies (n) and percentages (%). Differences between groups (CAM user vs. non-CAM user) were calculated using independent-samples t-test for normally distributed data and using Mann-Whitney U test for non-normally distributed data. The chi-square test or Fisher's exact test was used where applicable. Logistic regression analysis was used for determining the risk factors for CAM therapies and the odds ratios were presented with the confidence interval. A p value of <0.05 was considered significant.

## RESULTS

The study involved a total of 135 patients (60% girls, mean age of  $10.45\pm5.05$  years). The questionnaire was filled out by the mother of 112 (82%) patients and by the father of 23 (17%) patients. Primary diagnosis of the patients was celiac disease in 48 (35.5%), chronic hepatitis in 29 (21.5%) (including autoimmune hepatitis in 27 and chronic hepatitis B

1	TABLE 1: Questionnaire a	dministered to the patients'	parents.		
	Complementary a	nd alternative medicine form			
Name:	Surname:	Age:		Gender:	
Disease:					
Duration of follow-up:					
Regularly used drugs:					
Mother's education level	Father's education le	vel	Monthly income		
Primary school	Primary school		<2,000 TL		
Secondary school	Secondary school			2,000-5,000 TL	
High school	High school	-		>5,000 TL	
University	University				
1- Have you ever used one or more of the non-		sed by the public? (If no, go to au	estion 12)		
Yes No	I don't remember	seu by the public. (If no, go to qu	cstion 12)		
2-If so, for which disease/diseases did you app		fly asthma convulsions favor y	vinamy traat infacti	ong )	
2-ii so, for which disease diseases did you app	iy these methods: (Colds, colds)	nu, asuma, convuisions, rever, u	rmary tract miecu	ons,	
3- If yes, which one(s)?					
4-Which method have you used in the last 12	months?				
5- How many times have you used these methods	ods in the last 12 months?				
<5 times 5-10 tim	nes	>10 times			
6- Who suggested this method to you?					
Doctors Relatives	Friends	Media	Social media		
<ul> <li>7-Can you rate the effects of the method you u</li> <li>8-How did these methods affect the course of</li> </ul>		enerit) to 10 (completely recovere	a) <i>:</i>		
No change Slightly in		y İmproved Worsene	d		
9-Why did you use this treatment method?					
	tion from a trusted person Oth	er treatments weren't enough	I believe in natural i	methods Others (explain)	
10- How do you think doctors generally appro	oach such treatments?				
□ They get angry / they despise □ They as	re not interested 🛛 They	suggest 🛛 They don't make a	a sound even if they	don't suggest	
11-What is your current attitude when you co	mpare the drug treatments reco	ommended by doctors with compl	ementary and alter	rnative medicine?	
□ I only use doctor's medicine □ I only use	complementary and alternative n	nedicine 🛛 I use both together	🗆 I don't u	se any	
12-Which of the following non-drug methods	used among the people do you k	now/heard?			
□ Acupuncture □ Hor	meopathy (giving the disease-caus	ing substance in small doses)	□ Vitamins/	minerals	
Diet applications (No salt, fat, etc.)	h oil		Quail egg	s	
🗆 Yoga 🔅 Hy	pnosis		□ Bioenergy	/	
□ Honey □ Bee	e milk		□ Spa		
	ass sticking		□ Sublingua	al cutting	
	ditional Chinese medicines		□ Mesir pas		
□ Herbal medicines (wild melon, linden, ginger,	medicinal herbs, teas, etc.)		□ Spine mas	ssage	
Cave treatment	nulet-talisman		□ Turkish b	ath	
	tal magnet bracelets			gate, etc. rings, necklaces)	
Prayer Blo				nsidered sacred	
-	ashing with salt water		□ Incense		
	hers (explain)				
13-Can complementary and alternative medic		have side effects?			
Yes No					
14-Would you like to try such a treatment (if	you have used it before) in the f	uture?			
Yes No		5 m			

virus (HBV) infections in 2), inflammatory bowel disease in 20 (14.8%) (Crohn's disease in 14 and ulcerative colitis in 6), liver transplant recipients in 9

(6.7%), cystic fibrosis in 8 (5.9%), metabolic liver disease in 7 (5.2%) (Gaucher disease in 5 and glycogen storage disease in 2) and functional gastroin-

testinal problems in 14 (10.4%) (gastroesophageal reflux in 9 and functional constipation in 5) patients.

Of these, 20 patients (14.8%, 95% CI: 19.2-20.8) were found to be using CAM. The duration of CAM users' follow-up period was significantly higher than non-CAM user (5.84±3.71 years vs. 4.06±3.25 years, p=0.030). The three most commonly used CAM therapies included herbal medicine [linden (Tilia cordata), sage tea (Salvia officinalis), chamomile tea (Matricaria chamomilla), rosehip (Rosa Canina), parsley (Petroselinum Crispum), tumeric (Curcuma longa)], (n=9; 45%, 95% CI: 6.81-11.19), honey (n=7; 35%, 95% CI: 4.81-9.19), and prayer (n=3; 15%, 95% CI: 0.81-5.19). Four patients used herbal medicine and honey together. Moreover, bioenergy was used by 2(10%) patients and quail eggs, amulet, and cupping were used by 1 (5%) patient each (Figure 1). During the use of CAM, only one patient with celiac disease discontinued treatment and the symptoms (abdominal pain and vomiting) worsened. This patient initiated gluten-free diet again.

CAM usage was recommended by relatives (n=10; 50.0%), friends (n=4; 20.0%), media (n=6; 30%) and physicians (n=2; 10%). For 2 patients, CAM was recommended by relatives and media. Most common indications for CAM usage, as revealed by the parents, included celiac disease or concurrent with gluten-free diet (n=9; 45%), chronic hepatitis with chronic HBV infection (n=1; 5%), recurrent infections associated with chronic diseases (n=4; 20%), treatment of allergic asthma in liver

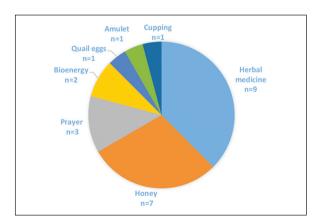


FIGURE 1: Complementary and alternative medicine modalities preferred by the patients/parents.

transplant recipients (n=1; 5%), urinary tract infection with cystic fibrosis (n=1; 5%), and symptomatic treatment of diarrhea (n=1; 5%), anemia (n=1; 5%), abdominal distention (n=1; 5%), and abdominal pain (n=1, 5%) associated with chronic diseases.

Of the 20 patients using CAM, 9 (45%) patients were found to have no change in their disease course, 7 (35%) patients were found to improve slightly, 3 (15%) patients were found to recover completely, and 1 (5%) patient was found to have worsened symptoms after CAM use. Of all participants, 79% of them claimed that CAM could have a side effect and 80.7% of them did not want to try this method again if they experienced any side effect. No significant difference was found between the users and non-users of CAM in terms of "knowledge about CAM side effects" and "trying again after an experience of any side effect" (p=0.053, p=0.187).

Frequency of CAM usage was significantly higher in patients with celiac disease (22.9% vs. 10.3%, p=0.049) and in liver transplant recipients (44.4% vs. 12.7%, p=0.018) compared to patients with other diseases. The frequency of CAM usage was significantly higher in patients who were not prescribed or were not using any conventional medicine (including celiac disease in 11, glycogen storage disease in 1 and functional abdominal pain in 1) compared to other patients (65% vs. 38.3%, p=0.030). On binary logistic regression analysis, celiac disease (OR 2.577, p=0.05, 95% CI: 0.983-6.756), liver transplantation (OR 5.5, p=0.018, 95% CI: 1.335-22.652), and non-medication (OR 2.997, p=0.030, 95% CI: 1.110-8.088) were found to be significant risk factors for CAM usage. No significant difference was established between the users and non-users of CAM with regard to the mother and father's educational level and monthly income (p=0.205, p=0.423, p=2.79, respectively) (Table 2).

## DISCUSSION

In this study, we evaluated the frequency and risk factors for CAM usage in patients admitted to pediatric gastroenterology and hepatology outpatient clinic. We found that (i) the frequency of CAM usage was 14.8% (95% CI 19.2-20.8), (ii) CAM usage was more common in patients with celiac disease (22.9%) and

TABLE 2: Demographic and clinical characteristics of CAM user and non-CAM user patients.					
	CAM user	Non-CAM user	p value		
	n=20 (%)	n=115 (%)			
Gender, female, n (%)	13 (65)	68 (59.1)	0.621		
Age, mean±SD, year	11.65±3.95	10.24±5.20	0.171		
Rural, n (%)	5 (25.0)	19 (16.5)	0.360		
Duration of follow up, mean±SD, year	5.84±3.71	4.06±3.25	0.030		
Concomitant disease, n (%)					
Chronic liver disease					
Chronic hepatitis	1 (5.0)	28 (24.3)	0.052		
Liver transplantation	4 (20.0)	5 (4.3)	0.009		
Cystic fibrosis	2 (10.0)	6 (5.2)	0.104		
Metabolic disease	1(5.0)	6 (5.2)	0.256		
Chronic GIS disease					
Celiac disease	11 (55.0)	37 (32.2)	0.049		
IBD	0	20 (17.4)	0.998		
Functional GIS	1 (5.0)	13 (11.3)	0.648		
Conventional medicines non-users, n (%)	13 (65)	44 (38.3)	0.030		
Mother's education level					
Primary school graduate	14 (70.0)	59 (51.3)	0.194		
Secondary school graduate	2 (10.0)	19 (16.5)			
High school/university graduate	4 (20.0)	37 (32.2)			
Father's education level					
Primary school graduate	10 (50.0)	45 (39.1)	0.416		
Secondary school graduate	3 (15.0)	18 (15.7)			
High school/university graduate	7 (35.0)	52 (45.2)			
Monthly income					
Low	12 (60.0)	47 (40.9)	0.279		
Moderate	7 (35.0)	58 (50.4)			
High	1 (5.0)	10 (8.7)			

Bold numbers indicate a significant finding at p<0.05; CAM: Complementary and alternative medicine; GIS: Gastrointestinal system; IBD: Inflammatory bowel disease; SD: Standard deviation.

liver transplant recipients (44.4%), (iii) CAM usage was more common in patients who were not prescribed or were not currently using any conventional medicine, (iv) the duration of CAM users' follow-up period was significantly higher than non-CAM user (p=0.030).

To date, CAM usage has been analyzed in pediatric patients with gastrointestinal problems in numerous studies.<sup>8-10</sup> Day et al. reported that 35.9% of the patients in pediatric gastroenterology outpatient clinic were using CAM.<sup>8</sup> In later years, a multicentric study by Vlieger et al. found that 37.6% of the patients with functional and organic gastrointestinal diseases were using CAM.<sup>9</sup> Adams et al. reported a higher frequency of CAM use (68.7%) in pediatric gastroenterology clinics in Canada.<sup>10</sup> In contrast to these studies, the usage of CAM in our study was remarkably low (14.8%), which could be related to the difference in the study design, study populations (subgroup of patients), cultural subspecialties on preferences, and the different definitions of CAM in the studies. For example, in Asian countries such as China and India, ayurvedic medicines and traditional dried herbs are preferred, while energy drinks and probiotics are used in European countries.<sup>11,12</sup> Literature indicates that there is limited data on CAM usage in children with liver diseases and the available studies have mostly investigated the hepatotoxic effects of CAM.<sup>11</sup> Erlichman et al. and Liem et al. evaluated children with chronic viral hepatitis and reported the prevalence of CAM usage as 46% and 71%, respectively.<sup>12,13</sup> In contrast, a recent Turkish study found a remarkably lower rate of CAM usage in children with chronic viral hepatitis (27%).<sup>14</sup> Some other studies, however, obtained similar findings to those of our study and reported this rate as 19.1% in children with chronic HBV infection and as 19.8% in children with functional gastrointestinal disorders.<sup>6,14</sup>

Our findings indicated that CAM usage was more common in patients with celiac disease and in liver transplant recipients. Contrariwise, Vlieger reported that CAM usage was lower in patients with celiac disease (7.9%) compared to patients with other gastrointestinal diseases.9 However, Aziz et al. found no significant difference between patients with celiac disease and healthy controls with regard to CAM usage (21.6% vs. 27%, p=0.09).15 Adherence to lifelong gluten-free diet may be difficult for the patients with celiac disease, and these patients may use CAM therapies, particularly bioenergy and herbal medicine, to cure their diseases. In our study, the patient declared that the symptoms (abdominal pain and vomiting) worsened after CAM usage. These symptoms may occur because of a gluten-containing diet or herbal medicine (Nigella seeds). This patient initiated gluten-free diet again. Literature indicates that liver transplant recipients constitute the group with the second highest frequency of CAM usage. A previous adult study indicated the frequency of CAM usage among liver transplant recipients as 34.4%.<sup>16</sup> The study also noted that the parents primarily preferred herbal medicine for simple infections instead of antibiotics and analgesics due to their fear of hepatotoxicity. Nevertheless, it should be recognized that herbal medicine can also lead to hepatotoxicity and the parents should be informed about this fact.

Literature indicates that the frequency of CAM usage is higher in children with functional gastrointestinal diseases and the most common CAM therapies in these children are herbal medicinal products such as peppermint, turmeric, and iberogast.<sup>17</sup> However, to our knowledge, there is little or no data on the effectiveness of CAM therapies in pediatric patients. Interestingly, our findings indicated that the frequency of CAM usage in children with functional gastrointestinal diseases was remarkably low, which could be attributed to the fact that our hospital is a tertiary health center and that patients that have no benefit from or discontinued CAM therapies are usually referred to our clinic. Additionally, it could be associated with the low number of children with functional gastrointestinal diseases in our study and could also be related to the fact that the questionnaire administered in the present study only queried the CAM therapies that were used by the patients within the last one year. As a matter of fact, CAM is mostly used within the first year after the onset of the disease or when the patient shows no response to medical treatment.<sup>18</sup> Interestingly, this is in contradiction with our study. Most patients used CAM had celiac disease. At the beginning of disease, these patients usually adhere to gluten-free diet well. Over time, these patients' adherence to diet decreases, and they prefer CAM instead of gluten-free diet if there isn't any worsening of their disease. On the other hand, the other patients who were currently not using any conventional medicine, had glycogen storage disease and functional abdominal pain. These patients thought that CAM may be beneficial because there wasn't any alternative conventional medicine in their treatment.

Herbal medicine is a CAM therapy that has long been used in many countries and widely trusted by parents. Of note, herbal medicine is the first-choice CAM in numerous countries.<sup>19,20</sup> Among the studies conducted in Turkey, Araz and Bülbül, and Öztürk and Karayağız reported that herbal medicine was the most common CAM therapy preferred by the patients/parents (82.7% and 77%, respectively).<sup>21,22</sup> Similarly, in our study, herbal medicine was also the most common CAM therapy (45%), followed by honey (35%). Honey is known to form a barrier against infections due to its antibacterial properties and is also known to have immunomodulatory properties. Due to these properties, honey is widely consumed in Turkey.<sup>23</sup> The third most common CAM therapy used by our patients was prayer. Akcay and Yıldırımlar also reported that herbal medicine and religious practices were the most common CAM therapies used by their patients.<sup>24</sup> These high rates could be associated with the growing number of practitioners of traditional medicine in Turkish culture.

It is commonly known that CAM therapies are regarded and promoted as safe products since they are natural, and thus the possibility of their side and harmful effects is often overlooked. In the present study, 15% of the patients/parents indicated that they had complete recovery while one patient (5%) indicated experiencing side effects of the therapies. Tasar et al. reported that only 1% of the parents indicated that the CAM therapies administered in their children had harmful effects and 77% of them indicated that the therapies had beneficial outcomes.<sup>25</sup> Heuschkel et al. reported that parental CAM use and the number of side effects of conventional medicines were predictors of CAM usage (OR=1.9 and OR=1.3, respectively).<sup>26</sup> On the other hand, it has been reported that the administration of CAM therapies in children with poor liver function may have harmful effects and may also lead to indirect side effects such as treatment delay or termination.<sup>27</sup> In our study, the patient with side effect had abdominal pain and vomiting. These symptoms may occur because of a gluten-containing diet or herbal medicine. On the other hand, since the number of patients is very small, it does not reflect the frequency of side effects well. Another limitation of this study, there is no question about side effects seen. It was only asked how CAM affected the course of their disease.

In our study, 79% of the patients believed that CAM therapies may have side effects and 80.7% of them stated that they would move away from such therapies if they experienced any side effects. A German study indicated that 77% of the patients considered that their knowledge about CAM was not sufficient.<sup>28</sup> For all these reasons, physicians need to be well aware of the effectiveness, dosages, side effects, toxicity, and potential drug interactions of CAM therapies and should query patients about their CAM usage, reasons for usage, and anticipated outcomes.

The present study also revealed that CAM therapies were mostly recommended by relatives and the friends of the patients. A study conducted in UK reported that 47% and 18% of the CAM therapies were recommended by the friends of patients and doctors, respectively. The study also noted that 86% of the patients suggested that doctors should support CAM use.<sup>29</sup>

The most important limitation of our study was the small number of patients. The other limitation was that the patients/parents might have filled in the questionnaire with a conviction that physicians are generally biased towards CAM. In a similar way, Adams et al. reported that one-quarter of the patients did not disclose their concurrent use of CAM and conventional therapies to their doctors.<sup>10</sup>

## CONCLUSION

In conclusion, although the frequency of CAM usage was low in our patient group, we consider that parents and physicians should be in full cooperation about the use of CAM and the effectiveness, side effects, toxicity, and potential drug interactions of CAM therapies.

### Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

### **Conflict of Interest**

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

#### Authorship Contributions

Idea/Concept: Burcu Güven, Murat Çakır; Design: Fazıl Orhan, Elif Sağ; Control/Supervision: Fatma İssi; Data Collection and/or Processing: Burcu Güven, Elif Sağ; Analysis and/or Interpretation: Fatma İssi; Literature Review: Burcu Güven, Elif Sağ; Writing the Article: Burcu Güven, Murat Çakır; Critical Review: Fazıl Orhan; References and Fundings: Burcu Güven.

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