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Evaluation of pediatricians' awareness about anaphylaxis

N. CAMBAZ KURT[1], N.O. KUTLU[2]

[1]Department of Pediatrics, Istanbul, University of Health Science, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey
[2]Department of Pediatric Intensive Care, University of Health Science, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey

Abstract. – OBJECTIVE: Anaphylaxis is a severe hypersensitivity reaction with a rapid onset and is potentially life-threatening if not treated promptly. This study aimed to determine the level of knowledge of pediatricians in Turkey in recognizing and treating the clinical symptoms of anaphylaxis, compare the previous studies conducted in Turkey chronologically, and show the current trends on awareness of anaphylaxis in developed and developing countries in the world.

SUBJECTS AND METHODS: Pediatric residents and specialists from all over Turkey were included in the study. A questionnaire was prepared by compiling the current literature. Questions were sent to pediatricians via online applications. Statistical tests were used to analyze the data.

RESULTS: A total of 524 pediatricians participated in the study. All participants accepted that anaphylaxis was a life-threatening condition. Almost all suggested epinephrine as the primary drug used in anaphylaxis. The proportion of pediatricians who knew the appropriate dose, route of administration, and place of administration of epinephrine was 82.8%, 88.9%, and 89.7%, respectively. The rate of pediatricians who recognized the clinical features of anaphylaxis was over 90%. The proportion of pediatricians who knew the epinephrine auto-injector and dose was 74.4% and 53.1%, respectively. Pediatricians with less than 10 years of experience and those working in public hospitals had better knowledge about atypical symptoms of anaphylaxis.

CONCLUSIONS: Although there are still inadequacies in identifying atypical symptoms and treating anaphylaxis, our study revealed that the level of awareness of anaphylaxis had shown an increasing trend in Turkey over time. On the other hand, the knowledge on diagnosing and treating anaphylaxis still needs to be improved, especially for physicians working in rural areas of developing countries.

Key Words:
Anaphylaxis, Allergy, Epinephrine, Epinephrine auto-injector, Pediatrician.

Introduction

Anaphylaxis in children is an acute, potentially life-threatening, systemic hypersensitivity reaction. The most common cause in children is a food allergy, followed by drugs and bee venom allergies[1]. The estimated prevalence of anaphylaxis has been reported as 0.65% to 2% in children[2]. There has been an increase in the frequency of anaphylaxis recently, which may be related to the frequency of allergies, as well as the increased awareness of anaphylaxis among pediatricians[1].

The first-line treatment for all patients experiencing anaphylaxis is intramuscular epinephrine (adrenaline), for which there are no absolute contraindications[1,2]. Early administration of epinephrine reduces death rates due to anaphylaxis[1]. Although proper prevention, early diagnosis, emergency intervention, and appropriate approach are vital in managing anaphylaxis, studies[3] have shown that the level of knowledge of healthcare professionals about anaphylaxis is insufficient.

This study aimed to demonstrate the knowledge levels of pediatricians in Turkey regarding the recognition and treatment of anaphylaxis and differences in perception among physicians, and also describe chronologic changes and geographic differences in Turkey in comparison with other countries.

Subjects and Methods

Study Design

Pediatric residents and specialists in Turkey, mainly in Istanbul, were included in this cross-sectional, descriptive study. The study was initiated after approval from the local ethics committee. The patients were anonymized, and no identity information was used. Informed consent was obtained from all participants.

Corresponding Author: N. Cambaz Kurt, MD; e-mail: nevinbinnurkurt@gmail.com

Survey questions were answered online by pediatricians. Twenty-four questions were prepared by compiling current literature[4-7]. This questionnaire was created by reviewing previously published literature because there is no validated questionnaire.

Data Collection

Four clinical scenarios were prepared based on the literature review[4-7]. The questions consisted of three parts. The first was the general demographic characteristics of the pediatricians (sex, occupational age, career information, and their institution), the second part was the evaluation of their knowledge about anaphylaxis (the findings of anaphylaxis in the four systems), and the third part evaluated the treatment of anaphylaxis (epinephrine form, dose, application site, and route of administration). Also, issues of discharge, referral to an allergist, and prescription of auto-injectors were questioned in the survey. Four clinical scenarios with atypical presentations were included to evaluate the knowledge levels of the participants. Participation was voluntary and not subject to any award or benefit. Participants were asked to answer questions within 30 minutes online without revealing their identities. All participants answered the questions thoroughly. Pediatricians working in allergy, emergency, and intensive care units were excluded from the study.

Case Scenarios

Four case scenario questions evaluated the level of diagnostic skills of participants.

Case 1: an 8-year-old female patient reports severe abdominal pain, vomiting, cough, and shortness of breath 15 minutes after penicillin injection. Her skin examination was normal, her heart rate was 106/min, her respiratory rate was 24/min, and her blood pressure was 100/70 mm Hg.

Case 2: a 12-year-old boy with a known hazelnut allergy experienced dizziness and weakness 15 minutes after eating a hazelnut dessert. He was taken to the emergency room, and skin, respiratory, and gastrointestinal system examinations were normal. His pulse rate was 100/min, his respiratory rate was 22/min, and his blood pressure was 70/50 mm Hg.

Case 3: a 6-year-old boy reported skin rash, itching, cough, and shortness of breath 5 minutes after a bee sting. The patient's heart rate was 100/min, his respiratory rate was 24/min, and his blood pressure was 95/60 mm Hg.

Case 4: a 5-year-old girl with a peanut allergy reported severe abdominal pain and vomiting half an hour after eating peanut-containing sweets. The patient's heart rate was 105/min, her respiratory rate was 20/min, and her blood pressure was 70/55 mm Hg.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 23.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The Mann-Whitney U and Kruskal-Wallis tests were used to examine the relationship between pediatricians' descriptive characteristics and case, symptom, and treatment scores. Descriptive statistics, frequencies, percentages, and medians were used to evaluate the data obtained from the pediatricians. *p*-values lower than 0.05 were considered statistically significant.

Results

The questionnaire was sent to 1,224 pediatricians via e-mail and online applications, and 524 (42.8%) responded; the margin of error was 5%, and the confidence interval was determined as 95%.

A total of 48.7% (255) of the participants had worked for less than 10 years, and 51.3% (269) had more than 10 years of experience. A total of 72% (378) were specialist physicians, and 27.9% (146) were residents. A total of 73.5% (385) of the participants worked in a university or training and research hospitals, 17.7% (93) worked in public hospitals, and 26.5% (139) worked in private hospitals or offices (Table I).

In recognizing the systemic findings of anaphylaxis symptoms, the most known was respiratory system findings at 99% (519). A total of 96.4% (505) knew cardiovascular system

Table I. Participant characteristics.

	n	(%)
Gender		
Female	307	58.6
Male	217	41.4
Professional Experience		
Less than 10 years	255	48.7
More than 10 years	269	51.3
Academic Title		
Specialist	378	72.1
Resident	146	27.9
Working Place		
Training and Research/ University/State Hospital	385	73.5
Private/Office	139	26.5

findings, 94.7% (496) knew skin mucosa findings, and 89.9% (471) knew gastrointestinal system findings. The rate of knowing atypical symptoms of anaphylaxis was 76.9% (Figure 1).

The percentages of participants recognizing anaphylaxis in the 4-question case scenario assessment were 85.9% (n=450) in case 1, 79.4% (n=416) in case 2, 91.2% (n=478) in case 3, and 74.4% (n=390) in case 4.

All participating pediatricians (98.9%) thought that anaphylaxis was life-threatening. The rate of pediatricians who recognized that the patients presented with clinical features of anaphylaxis was over 90%. A total of 76.4% (391) of the participants had encountered patients with anaphylaxis, and 71.8% (376) had treated patients with anaphylaxis. The proportion of pediatricians who knew about the epinephrine auto-injector (EAI) and the dose was 74.4% (390) and 53.1% (278), respectively. A total of 72.3% (379) of physicians stated that there were no contraindications to epinephrine.

Ten multiple-choice questions assessed the level of knowledge about treatment; 99.2% of physicians knew that epinephrine was the first drug to be used in treatment, 82.8% knew the appropriate dose, 88.9% knew the route of administration, and 89.7% knew the correct place of administration. Most participants (56.1%) stated they kept patients under observation for 12-24 hours after an anaphylactic attack (Table II).

A total of 378 specialist physicians participated in the study. A total of 82.3% (311) knew the correct dose of epinephrine, and 85.7% (324) knew the route of administration (Table III).

A total of 68.7% (258) of the specialists participating in the study have been practicing for more than 10 years, and 66.1% (250) worked in training and research/university/state hospitals. The symptom scores of specialist physicians with fewer than 10 years of working experience were statistically significantly higher than those with more than 10 years of working experience ($p<0.001$).

The case and symptom scores of specialist physicians working in training and research/university/state hospitals were statistically significantly higher than those working in private hospitals/offices ($p=0.01$ and $p=0.02$, respectively). Case and symptom scores of specialists working in training and research hospitals were statistically significant (Table IV).

When EAIs were evaluated in terms of recognition, specialist pediatricians were better than residents in knowing the name of epinephrine auto-injectors (EAIs), the correct dose of EAIs, and prescribing EAIs at discharge after treatment anaphylaxis ($p<0.001$, $p<0.001$, and $p=0.02$, respectively).

There was no statistically significant difference in specialist pediatricians' EAI definitions according to their working years and institutions ($p=0.61$ and $p=0.07$, respectively).

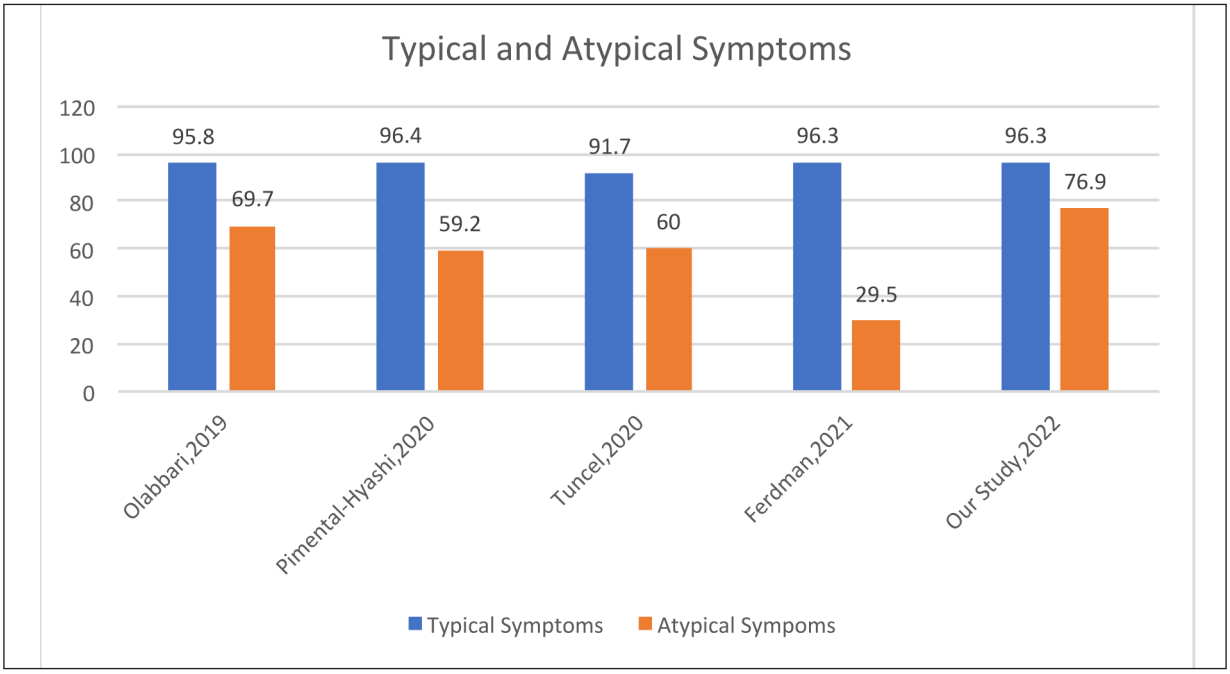

Figure 1. Recognition rates of typical and atypical symptoms of anaphylaxis.

Table II. General knowledge levels of physicians about anaphylaxis treatment.

	n	(%)
What is the first drug to be used in the treatment of anaphylaxis?		
Epinephrine	520	99.2
Cortisol	2	0.4
Salbutamol	2	0.4
Difenhydramine	0	0.0
What is the dose of epinephrine in anaphylaxis?		
0.01 mg/kg	434	82.8
0.1 mg/kg	81	15.5
No opinion	9	1.7
What is the administration route of epinephrine in anaphylaxis?		
IM	466	88.9
SC	49	9.4
IV	9	1.7
Which area is recommended for epinephrine administration in anaphylaxis?		
Vastus Lateralis	470	89.7
Deltoid	39	7.4
Triceps	15	2.9
How many hours do you keep the patient under observation after the attack?		
4-6 hours	75	14.3
12-24 hours	294	56.1
24 hours and above	155	29.6
Would you prescribe EAI at discharge?		
Yes	401	76.5
No	123	27.5
Would you refer the anaphylaxis patient to an allergist after discharge?		
Yes	516	98.5
No	8	1.5

IM: intramuscular, SC: subcutaneous, IV: intravenous, EAI: epinephrine auto-injector.

Table III. Anaphylaxis knowledge levels of specialist physicians.

	(%)
Signs and symptoms of anaphylaxis	
Skin mucosal findings	94.7
Respiratory system findings	98.9
Gastrointestinal system findings	90.7
Hypotension	97.6
General level of knowledge about anaphylaxis treatment	
Anaphylaxis patient encounter	76.7
Treatment for anaphylaxis	75.9
First drug in the treatment of anaphylaxis (epinephrine)	99.5
Epinephrine	
Keeping epinephrine in the department where it works	95.5
Intramuscular administration of epinephrine in anaphylaxis	85.7
Administration dose of 0.01 mg/kg in anaphylaxis	82.3
Vastus Lateralis administration of epinephrine in anaphylaxis	87.3
Absence of specific contraindications for the use of epinephrine	74.9
Epinephrine Auto Injector (EAI)	
Using the EAI	21.4
Knowing the name of the EAI in Turkey	80.2
Dosage of the EAI form in Turkey	57.7
Prescribing EAI to patients at discharge	80.2
Referral to allergist after discharge	98.7
Assessing anaphylaxis with case scenario	
Case 1	87.8
Case 2	81.2
Case 3	92.9
Case 4	74.6

EAI: epinephrine auto-injector.

Table IV. Evaluation of specialist physicians' knowledge of anaphylaxis symptoms and treatment.

Specialist physicians (n=378)		Case	Symptoms	Treatment
		mean±sd	mean±sd	mean±sd std
Gender	Female (n=223)	3.44±0.87	3.82±0.46	7.72±1.56
	Male (n=155)	3.25±0.89	3.82±0.52	7.57±1.75
p		0.01*	0.68	0.52
Working year	Less than 10 years (n=120)	3.45±0.86	3.92±0.26	7.88±1.57
	More than 10 years (n=258)	3.33±0.89	3.77±0.55	7.59±1.67
p		0.14	0.00*	0.23
Institution	Reaching and Training/University (n=250) University/Public (n=250)	3.44±0.83	3.88±0.36	7.68±1.65
	Private/officer (n=128)	3.21±0.95	3.69±0.65	7.62±1.63
p		0.01*	0.00*	0.59

Mann-Whitney U test, $p<0.05$*.

Discussion

According to our study, respiratory system findings were the most common (99%), and gastrointestinal system findings were the least common system findings (89.9%) that defined anaphylaxis symptoms. The rates of pediatricians who knew that the four different case scenarios presented with system involvement were 85.9%, 79.4%, 91.2%, and 74.4%, respectively. Our results were relatively better (82.7%) than previous reports[7-13] from Turkey, even though they were still lower than desired targets.

Recognizing atypical symptoms (gastrointestinal symptoms, hypotension) is important for clinical suspicion of anaphylaxis. Diagnosis of anaphylaxis could be very problematic in patients with atypical symptoms[3,8]. Numerous studies[3,7-9] investigating the knowledge levels of physicians on atypical symptoms demonstrated that the accuracy rates were 54.6% (Figure 1). In our study, the rate of knowing atypical symptoms was 77%. This rate was higher than in the literature.

Specialist physicians with working experience of fewer than 10 years were more successful at symptom scores compared with senior physicians. On the other hand, working experience did not affect therapeutic scores. This result shows current positive progress in medical education and raising awareness of anaphylaxis during the last decades. This finding also indicates the importance of postgraduate education throughout the work-life period.

The pediatricians in our study selected epinephrine as the first-choice medication in anaphylaxis treatment, with an accuracy of 99.2%. In the literature, this ratio ranges between 33-100% (mean: 78.7%)[5,6,8,10,14-26]. These alarming figures are problematic and need to be analyzed for underlying reasons. The diversities of these accuracy rates between the studies could be explained by the differing standards of medical education systems between countries, methodologic biases resulting from the selection of study populations, and the design of questionnaires.

The scores of questionnaires could be affected by the prosperity of countries. Hence, average awareness rates of epinephrine are much higher (81.9%) in developed countries[5,14,15,22,24] than in developing countries (72.9%)[6,8,17,18] (Figure 2). Our study group consisted of physicians who specialized in pediatrics, and the majority (55.7%) worked in universities or training and research hospitals. These factors explain why our diagnostic and therapeutic capabilities are higher than other branch physicians in other countries[6,8,13].

Fortunately, there are improving therapeutic scores in anaphylaxis over time. In the two surveys[15,22] conducted in the United Kingdom in 2007 and 2015, rates increased from 57.9% to 74%. Figure 3 also delineates a similar positive trend in the previous anaphylaxis surveys in Turkey[11-13,25].

Because anaphylaxis requires urgent intervention, calculating epinephrine dosage and medicine preparation is crucial, especially in pediatric age groups. The optimal dose of epinephrine in anaphylaxis is unknown; 0.3 mg devices are effective for treating anaphylaxis in most patients, so the 0.3 mg epinephrine dose is preferred[1]. The European Academy of Allergy and Clinical Immunology (EAACI) suggests prescribing 0.15 mg EAIs for children from 7.5 kg to 25-30 kg and 0.3 mg EAIs for children from 25-30 kg, and at least 0.3 mg EAIs for adolescents and adults at risk of anaphylaxis[1].

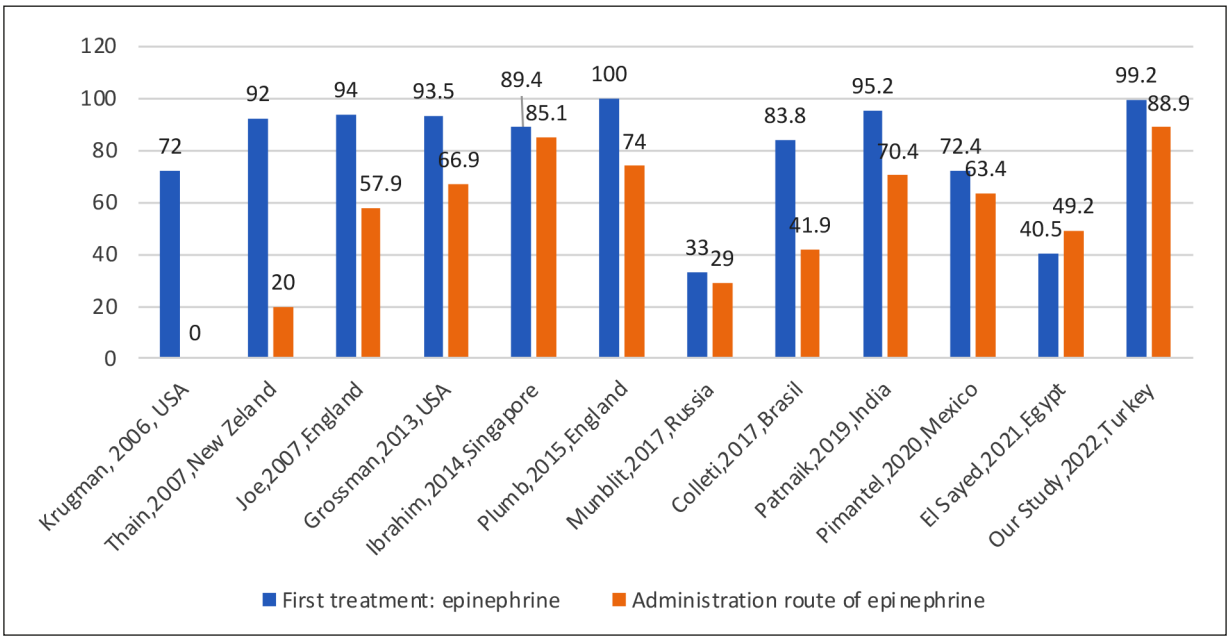

Figure 2. Physicians' opinions on the use and route of administration epinephrine.

A retrospective cohort[27] study of 166 adult patients with anaphylaxis reported a 2.4% incidence of potentially life-threatening complications from inappropriate epinephrine administrations. Previous questionnaire studies[11-13] from Turkey demonstrated that around 65% of physicians could not calculate the epinephrine dose in anaphylaxis. In other countries, these incompetency rates vary between 80% and 44%[8,14,16]. Contrarily, this survey showed that 82.8% of pediatricians could calculate the correct epinephrine dose. However, these optimistic scores might not reflect our national knowledge level on this subject because of the selection method of our study population.

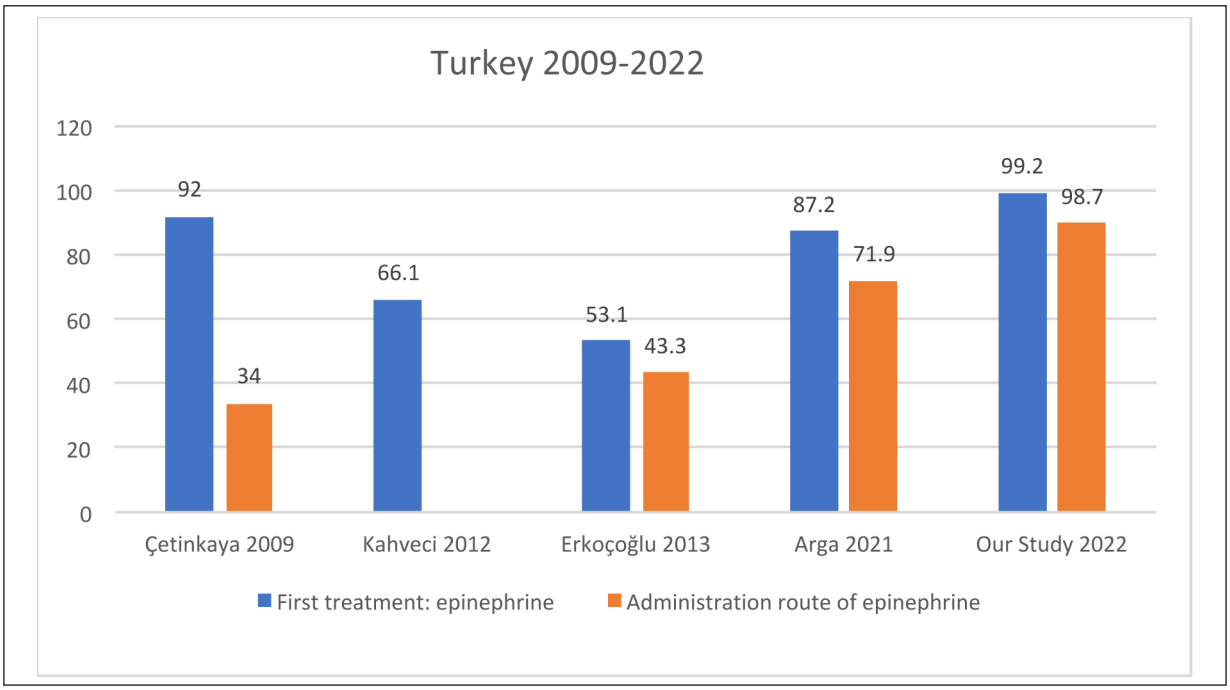

Figure 3. Physicians' knowledge about epinephrine in Turkey.

Epinephrine administration was still known as subcutaneous (SC) by some physicians, as stated in old guidelines8. In the literature, the average rate of physicians who know the correct route of epinephrine administration is 51.7% (20%-85.1%) (Figure 2)[6,8,10,14,18,22,26]. Anaphylaxis, as a state of shock, negatively affects the pharmacokinetics of epinephrine by deteriorating circulation and hindering the possibility of venous access within a short period. Furthermore, the intravenous route may cause lethal complications secondary to iatrogenic overdose or rapid administration of epinephrine[27]. Therefore, epinephrine administration is advised via the intramuscular (IM) route at the outer lateral surface of the leg, in the vastus lateralis muscle[1,4].

In our study, 88.9% of pediatricians specified the route of administration of epinephrine as IM, which is the best result so far. This ratio should be considered a promising result due to our study population's background, because 55.7% were specialist physicians working in university or training and research hospitals.

Anaphylaxis has a high risk of recurrence (estimated as 30%-43%), and long-term preventive measures such as patient education, allergen avoidance, referral to an allergy specialist, and the provision of EAIs are key elements of patient care[28]. Guidelines[28] recommend that patients carry two EAIs at all times.

However, the literature emphasizes that physicians lack knowledge about EAIs[16-21], and less than 40% (mean 32.7%) prescribe EAIs[8,19,21]. This study showed that the proportion of specialists knowing the trade name of EAI, and dosage was 80.2% and 57.7%, respectively. (Table III). The rate of specialist pediatricians who said they would prescribe EAIs to their patients after anaphylaxis was 80.2%, and 21.4% of them had already prescribed an EAI product. The pediatricians' level of knowledge about EAI was higher than in previous studies (Figure 4)[11-13].

The rate of pediatricians who referred patients to an allergist after anaphylaxis was 98.7%. This rate was above (62.2%) of the previous study performed in Turkey[13]. This may be because specialists have easier access to allergy specialists because they work in training and research hospitals.

A biphasic reaction is a potentially life-threatening recurrence of symptoms after the initial resolution of anaphylaxis without re-exposure, which was reported with severe anaphylaxis[29]. The reported frequency of biphasic reactions ranges from 1.4% to 20%, which could be due to the variation in the characteristics of patients, definition of biphasic reaction, and duration of observation[30]. Keeping patients under observation after an attack is important for biphasic anaphylaxis reactions. It is suggested that they are monitored for 6-8 h with respiratory compromise and at least 12-24 h with

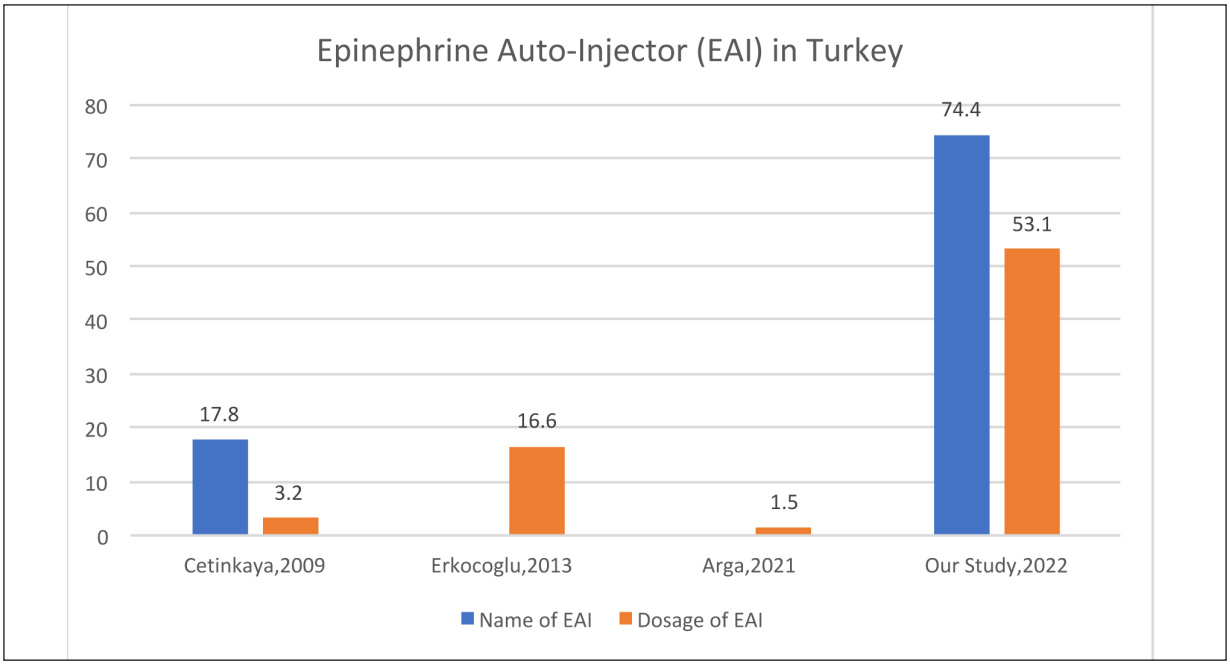

Figure 4. Knowledge levels of physicians about Epinephrine Auto-Injector (EAI) in Turkey.

hypotension[1]. On the other hand, there are scarce studies[23,24] investigating physician attitudes about observation time after anaphylaxis. Our literature search found only two relevant studies[23,24]; one reported that only 37.4% of patients were observed without mentioning observation times, and the other reported an observation rate of 42% of patients for more than 4 hours. In our study, half of the participants (56.1%) recommended 12-24 hours of observation (Table II)[29-31].

Limitations

This study has some limitations. Physicians mainly working in secondary and tertiary hospitals in Istanbul answered the survey questions. The convenience sampling method with the non-random nature of study participants also limits the ability to generalize the survey results to the healthcare workers population with the possibility of under/over-representation. Also, the survey evaluated the theoretical knowledge of physicians and did not reflect their actual skills in clinical practice.

The lack of comparison among different specialties is another limiting factor.

Conclusions

Although there are still inadequacies in the prescription of EAIs, identification of atypical symptoms, and treatment of anaphylaxis, our study reveals that the level of awareness of anaphylaxis has continued to increase in Turkey. The knowledge on diagnosing and treating anaphylaxis still needs to be improved, especially for physicians working in rural areas of developing countries.

ORCID ID

N. Cambaz Kurt: 0000-0003-4066-1834
N.O. Kutlu: 0000-0002-3306-6570

Authors' Contributions

Cambaz Kurt N and Kutlu NO designed the study; Cambaz Kurt N and Kutlu NO collected and analyzed data; Cambaz Kurt N and Kutlu NO wrote the manuscript.
All authors have participated in drafting the manuscript. All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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The authors report no involvement in the research by any sponsor that could have influenced the outcome of this work.

Informed Consent

The patients were anonymized, and the identity information was not included. Informed consent was obtained from the participants.

Ethics Approval

This study was approved by the Basaksehir Cam and Sakura City Hospital Ethics Committee on 14.04.2021, and No.: 54.

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