

Healthcare workers' knowledge level regarding anaphylaxis and usage of epinephrine auto-injectors

Mustafa Arga¹, Erdem Topal², Sila Yılmaz³, Pınar Canızcı Erdemli³,
Kübra Bıçakçı³, Arzu Bakırtaş⁴

Departments of ¹Pediatric Allergy and Immunology, ²Pediatrics, İstanbul Medeniyet University Faculty of Medicine, İstanbul;
²Department of Pediatric Allergy and Immunology, İnönü University Faculty of Medicine, Malatya; ⁴Department of Pediatric Allergy and Asthma, Gazi University Faculty of Medicine, Ankara, Turkey.

ABSTRACT

Background. Inadequate practices in diagnosis and management of anaphylaxis in parallel with an increase in its prevalence may cause serious public health problems today. This is the first study aiming to assess the theoretical knowledge of professional and non-professional healthcare workers from different lines of the healthcare service chain about anaphylaxis management, and their practice approaches for epinephrine auto-injectors (EAI) together.

Methods. The study included 697 participants comprising physicians, dentists, pharmacists, and school staff. In face-to-face interviews, each participant was asked to fill out the questionnaire forms prepared for assessing their demographic characteristics, experience with a case of anaphylaxis and EAI and theoretical knowledge about the diagnosis and treatment of anaphylaxis, and to demonstrate how to use EAI in practice with trainer device.

Results. The rates of 391 physicians, 98 dentists, 102 pharmacists and 105 school staff of knowing the diagnosis criteria of anaphylaxis were 47.6%, 31.6%, 31.1%, 19%, and knowing the first and life-saving treatment of anaphylaxis were 87.2%, 79.6%, 47.6%, 15.2%, respectively. Predictors that affected physicians in knowing the first and life-saving treatment of anaphylaxis were having experience with EAIs [OR:5.5, (%95CI:1.330-23.351, p=0.015)] and a case of anaphylaxis [OR:2.4, (%95CI:1.442-4.020, p=0.001)], and knowing the administration route of epinephrine correctly [OR:1.9, (%95CI:1.191-3.314, p=0.008)]. 31.1% of the participants demonstrated the EAI usage correctly. The EAI usage steps with the most errors were "Place the appropriate injection tip into outer thigh/Press the trigger so it 'clicks'" and "Turn the trigger to arrow direction" (60.3% and 34.9%, respectively).

Conclusions. Healthcare workers' knowledge level regarding anaphylaxis management and ability to use EAIs correctly are not adequate. That most errors were made in the same steps of EAI usage indicates that the industry should continue to strive for developing the ideal life-saving device.

Key words: anaphylaxis, epinephrine auto-injectors, healthcare workers, knowledge, management.

Anaphylaxis is a systemic hypersensitivity reaction that develops suddenly and may threaten life.¹ Therefore, early diagnosis and correct treatment of anaphylaxis is vital.¹ Its first and life-saving treatment is epinephrine.² It may recur despite all preventive measures.¹

Therefore, it is required to prepare an individual emergency written action plan for each patient^{2,3} Epinephrine auto-injector (EAI) is one of the most important components of emergency action plans.² Physicians should provide patients and/or parents with a theoretical and practical training on when and how to use EAIs.² However, physicians worldwide may still perform critically inadequate practices in anaphylaxis management.⁴ In most countries, pharmacies are the places where patients obtain

✉ Mustafa Arga
mustafarga@gmail.com

Received 16th September 2020, revised 24th November 2020,
accepted 6th December 2020.

EAI prescribed by physicians. The fact that pharmacists have adequate level of knowledge regarding anaphylaxis management and EAI usage and give patients and/or parents training on EAI usage may provide an important opportunity for rectifying potential errors in anaphylaxis management.

Most anaphylaxis episodes develop in non-hospital settings such as homes and public spaces. Considering the increase in food allergy prevalence in childhood in recent years, prevalence of anaphylaxis increases day by day in kindergartens and schools.⁵ International and national allergy associations propose suggestions and provide support for reducing this risk and manage anaphylaxis optimally in case it develops in school settings.⁶⁻⁹ It is a requirement that school managers prepare an emergency action plan regarding how to act in cases of anaphylaxis and how to treat it in their institutions, determine professional (e.g. physician, nurse) or non-professional [non-nursing staff (e.g. teacher, school staff)] healthcare workers and ensure they receive related training.⁶⁻⁹ However, studies have shown that schools have considerable inadequacies regarding anaphylaxis management.^{10,11} These inadequacies in the management of anaphylaxis, acknowledged today as a non-rare disease with ever increasing prevalence, can lead to morbidity and mortality for patients, and to serious psychosocial stress for the society and healthcare system.¹²

In this study, our primary aim is to determine the correct EAI usage rates of professional and non-professional healthcare workers from different lines of the healthcare service chain, and our secondary aim is to assess the theoretical knowledge of participants about anaphylaxis management.

Material and Methods

The study included professional and non-professional healthcare workers from two different cities of our country (Istanbul and

Malatya), who participated voluntarily. By statistical analysis, the minimum sample size required to detect a significant difference was determined to be at least 508, considering 6% deviance, type I error (alpha) of 0.05, power (1-beta) of 0.8, effect size of 0.12 and two-tailed alternative hypothesis (H1). The study included emergency medicine specialists, family physicians, pediatricians, internal medicine specialists and dentists who frequently encounter cases of anaphylaxis in health centers; pharmacists; and school staff (nursing and non-nursing staff) responsible for healthcare practices in primary schools who encounter them in public spaces. All participants provided written informed consent for voluntary participation before the study, which was approved by the institutional ethics committee of İnönü University (2020/8-630). Allergists, and healthcare workers who rejected to participate were excluded.

All physicians completed an eleven-item questionnaire, which we had used in our previous study and consisted of questions regarding demographic characteristics (age, gender, and duration as a physician), experience with a case of anaphylaxis and EAIs, theoretical knowledge about the diagnosis and management of anaphylaxis and the indications of EAIs.¹³ The questions related to the diagnosis of anaphylaxis and the indications of EAIs were prepared according to the recommendations of the Second National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network Symposium, and of the European Academy of Allergy and Clinical Immunology.^{14,15}

Pharmacists completed an eight-item questionnaire consisting of questions regarding demographic characteristics (age, gender, duration as a pharmacist), experience with a case of anaphylaxis and EAIs, theoretical knowledge about the diagnosis and treatment of anaphylaxis and about the first and life-saving treatment of anaphylaxis. School staff completed a ten-item questionnaire consisting of questions, in addition to those asked to

pharmacists, regarding their professions and whether they had previously received emergency aid training.

Following the questionnaires, each participant was asked to demonstrate how to use EAIs in one-to-one practice. Participants who responded to the questionnaire that they had previously seen an EAI were given an EAI trainer (Penepin® trainer; Vem Pharmaceuticals, Ankara, Turkey) and asked to demonstrate its usage. Participants who stated that they had never seen an EAI or had seen one but did not know how to use it were given written and visual instruction sheets

that showed the steps of EAI usage, which we had used in our previous study, and asked to demonstrate how to use it on an EAI trainer (Penepin® trainer) (Fig. 1).¹⁶ Those who applied the six steps of EAI usage in the right order were accepted to use the EAI correctly (Fig. 1). Participants' demonstrations and errors in EAI usage steps were recorded on forms prepared beforehand. Meanwhile, participants who made mistakes in usage steps were given training by the responsible researcher on the correct usage of the EAI, which continued until participants demonstrated all steps correctly.



Fig. 1. Instruction sheet for epinephrine auto-injector (Penepin®) usage.

Statistical Analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) 20.0 software (SPSS Inc., Chicago, IL). Normality was evaluated by the Kolmogorov-Smirnov test. Descriptive statistics were expressed as the frequency and percentage for categorical variables, whereas quantitative data were expressed as the median (min-max) for non-normally distributed data. The categorical and quantitative variables were compared using the chi-square test and/or the Mann-Whitney U test. A 2-sided p<0.05 was considered statistically significant.

Results

The study included a total of 697 participants, comprising 391 physicians, 98 dentists, 102 pharmacists and 105 school staff (nurse or non-nursing staff). Demographic characteristics of the participants are shown in Tables I and II.

Of the physicians, 294 (75.2%) had experience with at least one case of anaphylaxis, 186 (47.6%) knew the diagnosis of anaphylaxis, and 341 (87.2%) knew that the first and life-saving treatment of anaphylaxis was epinephrine. 167 (42.7%) and 281 (71.9%) of the physicians correctly knew the epinephrine dose in anaphylaxis treatment and the administration route of epinephrine, respectively (Table I). Family physicians' rates of having experience with a case of anaphylaxis and knowing the first and life-saving treatment of anaphylaxis were lower compared to other physician groups (p<0.001 and p<0.001, respectively) (Table I). Dentists had less experience with a case of anaphylaxis than physician groups (p<0.001). While dentists' rate of knowing the first and life-saving treatment of anaphylaxis was similar to that of physicians, their rates of knowing the epinephrine dose in anaphylaxis treatment and the administration route of epinephrine were found to be significantly low (p=0.078, p<0.001 and p<0.001, respectively) (Table I).

Furthermore, 27 (26.2%) of pharmacists and 16 (15.2%) of school staff had experience with

Table I. Demographic characteristics of physicians and dentists, and their level of knowledge regarding the diagnosis and management of anaphylaxis.

Questionnaire Responses	Family Physician (n:96)	Pediatrician (n:102)	Internal Medicine Specialist (n:95)	Emergency Medicine Specialist (n:98)	All Physicians (n:391)	Dentist (n:98)	p	p
Female [†]	50 (52.1)	43 (42.2)	47 (49.5)	43 (43.9)	183 (46.8)	49 (50)	0.463	0.571
Age, year [median (min-max)]	46 (26-55)*	37 (25-59)	39 (26-56)	34 (25-54)	38 (25-59)	32 (25-54)	<0.001	<0.001
Duration as a physician or dentist, year [median (min-max)]	21 (3-31)*	14 (2-36)	14 (1-33)	10 (2-30)	14 (1-36)	9 (2-31)	<0.001	<0.001
Have experience with a case of anaphylaxis [†]	50 (52.1)*	80 (78.4)	66 (69.5)	98 (100)*	294 (75.2)	31 (31.6)	<0.001	<0.001
Know the diagnostic criteria of anaphylaxis [†]	39 (40.6)	47 (46.1)	34 (35.8)	66 (67.3)*	186 (47.6)	31 (31.6)	<0.001	0.005
Know the first and life-saving treatment of anaphylaxis [†]	64 (66.7)*	94 (92.2)	89 (93.7)	94 (95.9)	341 (87.2)	78 (79.6)	<0.001	0.078
Know the epinephrine dose in anaphylaxis treatment correctly [†]	30 (31.3)	40 (39.2)	40 (42.1)	57 (58.2)*	167 (42.7)	14 (14.3)	0.002	<0.001
Know the administration route of epinephrine correctly [†]	55 (57.3)	81 (79.4)*	61 (64.2)	84 (85.7)*	281 (71.9)	39 (39.8)	<0.001	<0.001
Know the indications of EAI [†]	38 (39.6)	46(45.1)	38 (40.0)	53 (54.1)	175 (44.8)	26 (26.5)	0.147	<0.001
Have experience with EAI [†]	7 (7.3)	9 (8.8)	17 (17.9)	26 (26.5)*	59 (15.1)	4 (4.1)	<0.001	<0.001
Know the epinephrine dose in EAI [†]	-	-	2 (2.1)	4 (4.1)	6 (1.5)	-	NC	NC

[†], n (%); [‡], p value in comparisons between physician groups; [¶], p value in comparisons between physicians and dentists; *, statistically significant group; EAI: epinephrine auto-injector, NC: non-calculated

Table II. Level of knowledge of pharmacists and school staff regarding management of anaphylaxis and epinephrine auto-injectors.

Questionnaire Responses	Pharmacist	School Staff
Female [†]	60 (58.3)	82 (78.1)
Age, year [median (min-max)]	37 (25-55)	38 (25-60)
Duration as a pharmacist or school staff, year [median (min-max)]	14 (1-28)	10 (1-34)
*Career position [†]		
Nursing staff		18 (17.1)
Non-nursing staff (teacher)		87 (82.9)
Have experience with a case of anaphylaxis [†]	27 (26.2)	16 (15.2)
Know the diagnostic criteria of anaphylaxis [†]	32 (31.1)	20 (19.0)
Know the first and life-saving treatment of anaphylaxis [†]	81 (78.6)	30 (28.6)
What should be used as the first and life-saving treatment of anaphylaxis? [†]		
Corticosteroid (e.g. prednol [®] , decort [®])	28 (27.2)	2 (1.9)
Antihistamine (e.g. atarax [®] , avil [®] , zyrtec [®] , deloday [®])	4 (3.9)	10 (9.5)
Epinephrine	49 (47.6)	16 (15.2)
Antibiotics (e.g. penicillin)	-	2 (1.9)
Have experience with EAI [†]	31 (30.1)	5 (4.8)
*Have received emergency aid training [†]		42 (38)

[†], n (%); EAI: epinephrine auto-injector; *This question was used only for school staff.

a case of anaphylaxis. Even though 81 (78.6%) of pharmacists and 30 (28.2%) of school staff responded "yes" to the question of "Do you know the first and life-saving treatment in anaphylaxis treatment?", only 49 (47.6%) of pharmacists and 16 (15.2%) of school staff preferred epinephrine as the first and life-saving treatment (Table II).

Predictor factors that affected knowing the first and life-saving treatment of anaphylaxis were having experience with EAIs [OR:5.5, (%95CI:1.330-23.351, p=0.015)], having experience with a case of anaphylaxis [OR:2.4, (%95CI:1.442-4.020, p=0.001)] and knowing the administration route of epinephrine correctly [OR:1.9, (%95CI:1.191-3.314, p=0.008)] for physicians; whereas having experience with EAIs [OR:6.1, (%95 CI:1.887-20.322, p=0.003)] for pharmacists. There were no significant factors that affected dentists and school staff in knowing the first and life-saving treatment of anaphylaxis.

217 (31.1%) of the participants demonstrated EAI usage correctly in the first attempt, only

32 (4.6%) of whom demonstrated EAI usage correctly without needing the instruction sheet (Table III). Rates of correct demonstration of EAI usage were found similar across physician groups (p=0.584) (Table III). On the other hand, pharmacists' rate of correct demonstration of EAI usage was higher than physicians, dentists and school staff (for each parameter, p<0.001) (Table III). The EAI usage steps with the most frequent errors in all participant groups were "Place the appropriate injection tip into outer thigh/Press the trigger so it 'clicks'" and "Turn the trigger to arrow direction". While the error rates in these steps were not significantly different across physician groups (p=0.938 and p=0.977, respectively), pharmacists were found to make fewer errors in these steps compared to physicians, dentists and school staff (for each parameter, p<0.001) (Table III). 480 (68.8%) participants could not demonstrate the EAI usage steps correctly. However, 273 (56.8%), 165 (34.3%), and 46 (9.5%) of them managed to demonstrate all usage steps correctly after they were demonstrated by the responsible researcher once, twice, and thrice, respectively.

Table III. Participants' rates of correctly demonstrating the usage steps of the epinephrine auto-injector (Penepin®).

Usage steps of the EAI	Physician Groups				All Participant Groups				p	p
	Family Physician (n:96)	Pediatrician (n:102)	Internal Medicine (n:95)	Emergency Medicine (n:98)	Physician (n:391)	Dentist (n:98)	Pharmacist (n:103)	School Staff (n:105)		
Remove the safety cap [†]	81 (84.4)	92 (90.2)	79 (83.2)	88 (89.8)	340 (87)	82 (83.7)	*98 (95.1)	87 (82.9)	<0.001	<0.001
Turn the trigger to arrow direction [†]	59 (61.5)	63 (61.8)	59 (62.1)	57 (58.2)	238 (60.9)	66 (67.3)	*85 (82.6)	65 (61.9)	<0.001	<0.001
Select outer thigh as body part [†]	96 (100)	102 (100)	95 (100)	98 (100)	391 (100)	95 (96.9)	103 (100)	101 (96.2)	NC	NC
Place the appropriate injection tip into outer thigh/Press the trigger so it 'clicks' [†]	31 (32.3)	35 (34.3)	32 (33.7)	31 (31.6)	129 (33)	40 (40.8)	*68 (66.1)	40 (38.1)	<0.001	<0.001
Hold the pen for 10 seconds [†]	76 (79.2)	84 (82.4)	70 (73.7)	80 (81.6)	310 (79.3)	76 (77.6)	*90 (87.4)	80 (76.2)	<0.001	<0.001
Massage the injection area for 10 seconds [†]	79 (82.3)	90 (88.2)	80 (84.2)	88 (89.8)	337 (86.2)	86 (87.8)	*99 (96.1)	87 (82.9)	<0.001	<0.001
Correct demonstration of the EAI in all assessment steps [†]	22 (22.9)	29 (28.4)	20 (21.1)	21 (21.4)	92 (23.5)	32 (32.7)	*60 (58.3)	33 (31.4)	<0.001	<0.001
Correct demonstration of the EAI in all assessment steps without needing the instruction sheet [†]	(1)	3 (2.9)	5 (5.2)	7 (7.1)	16 (4.1)	4 (4)	12 (11.6)	0	NC	NC

[†], n (%), [‡], p value for comparisons between physician groups; [¶], p value for comparisons between physicians, dentists, pharmacists and school staff; *, statistically significant group; EAI: epinephrine auto-injectors, NC: non-calculated

Discussion

Our study showed that healthcare workers from different lines of the healthcare service chain had critical inadequacies in the management of anaphylaxis. This inadequacy is more obvious in pharmacists and school staff. Only one-seventh of the participants stated to have experience with EAIs, only one-third of whom could demonstrate the EAI usage correctly even though instruction sheets were given. The fact that the two most frequent errors were made in the same steps during the demonstration of EAI usage in all participant groups support the view that EAI design can have an important effect on correct usage.

87.2% of our physicians knew that the first and life-saving treatment of anaphylaxis is epinephrine. Altman et al.'s¹⁷ national follow-up study, which included 266 physicians from different specialties similarly to our study, found that this rate was between 81-98%, the lowest rate being in family physicians. In our study, this rate was lowest in family physicians and highest in emergency medicine specialists, as well. Two different studies ascertained that frequent experience with cases of anaphylaxis and knowledge of the diagnosis criteria of anaphylaxis were predictive factors in determining the first treatment correctly.^{19,20} Similarly, our study found that having experience with a case of anaphylaxis (OR:2.4) and additionally having experience with EAIs (OR:5.5) and knowing the administration route of epinephrine correctly (OR:1.9) were significant factors in knowing the first and life-saving treatment of anaphylaxis correctly.

The epinephrine dose in anaphylaxis treatment and the administration route of epinephrine were determined correctly by 42.7% and 71.9% of our physicians, respectively. Studies showed that 23.8-92.6% of physicians chose the administration route of epinephrine and 26.8-81.6% chose the epinephrine dose correctly, depending on their branches.^{20,21} In our country, various studies carried out in the last decade showed that 46% of pediatricians,

43.3% of family physicians and 20% of internal medicine specialists chose the administration route of epinephrine correctly, which may support the increase of physicians' knowledge levels with regard to correctly determining the administration route of epinephrine.²²⁻²⁴ Nevertheless, the rate of pediatricians in our country choosing the epinephrine dose correctly has not changed significantly in the last seven years, in fact it has even decreased.^{13,25} However, it is absolutely necessary to apply all steps in the management of a case of anaphylaxis immediately and correctly for preventing irrecoverable outcomes for the patient.^{1,2} In this regard, in another study in which we assessed pediatricians' competence in anaphylaxis management through case scenarios, we ascertained that only 11.3% of the physicians were able to correctly apply all management steps from diagnosis to discharge recommendations.²⁶

It is required that physicians prepare an individual emergency action plan for each patient before discharge, prescribe EAI to them and train them about when and how to use it.^{9,15} In our study, less than half of the physicians knew the indications of EAIs correctly; and again, the highest rate belonged to emergency medicine specialists. In addition, 15% of our physicians had experience with EAIs, while only one-fourth of them could demonstrate the use of EAI correctly without needing the instruction sheet. Previous studies revealed that more than half of the trainer physicians did not have adequate knowledge about EAI usage.^{13,15} Even though it was shown that giving theoretical and practical trainings to physicians increased their knowledge level about EAI usage, these studies suggest barriers to EAI usage that are not solely practical but incorporate complex psychological features.²⁷ On the other hand, Mahoney et al.²⁸ found in their recent study that "training physicians in psychologically informed strategies produce sustained improvements in their confidence and knowledge around patient auto-injector education, and their likelihood of using strategies in clinical practice". According

to all these results, it is necessary that theoretical and practical training to be given to physicians contain all steps of anaphylaxis management, provide psychological information and be repeated regularly in order to achieve improvement in anaphylaxis management at the required level. These comprehensive training programs to be given to physicians will also ensure correct self-management of patients and/or parents during anaphylaxis.

Concerning anaphylaxis, which is increasingly becoming a public health problem today, it is crucial that pharmacists take part as professional healthcare workers in the preparation of anaphylaxis emergency action plan and provision of trainings on EAI usage for patients. In our study, however, even though nearly three-fourths of the pharmacists stated that they knew the life-saving treatment of anaphylaxis, less than half of them preferred epinephrine as the first treatment. In the questionnaire study carried out by Wormet al.²⁹ in Germany, in which the knowledge levels of 213 pharmacists regarding anaphylaxis management were assessed, 53.9% preferred epinephrine as the first treatment. Although EAIs are sold only in pharmacies in our country, only one-third of the pharmacists in our study stated that they had experience with EAIs, only one-third of whom could demonstrate the practical usage of the EAI correctly without needing the instruction sheet. Nevertheless, other studies on this topic also ascertained that 24.4% and 17% of pharmacists could demonstrate EAI usage correctly.^{29,30} While Salter et al.³¹ found that physicians' rate of correct EAI usage increased to 88% after reading the instruction sheet, this rate increased to 58% in our study. This may be primarily associated with study designs. Regular allergist follow-up, repetition of training at regular intervals and encouraging patients and/or parents about EAI usage enhance their frequency of use.³² However, it may not be easy for patients to continue regular follow-ups or contact the allergist if they want to ask something on this topic during follow-up. Therefore, in-time training of patients on EAI usage is

crucial for enhancing their awareness of and competence with EAIs. Hence, pharmacists are an important link between the patient and the physician. Indeed, Salter et al.³¹ determined that pharmacists who asked patients if they had an anaphylaxis emergency action plan, told them to go to the emergency department after using the EAI and inform them about epinephrine's side effects demonstrated EAI usage 16, 4.5 and 4 times more correctly. These results indicate that when pharmacists have detailed and extensive knowledge about anaphylaxis, they can act willingly about and contribute greatly to this issue. A study from Australia revealed that giving pharmacists e-learning or lecture programs including the national anaphylaxis emergency action plan nearly doubled their related minimum standard knowledge levels (45% pretest, 87% posttest), and this could continue for seven months.³³ Therefore, giving pharmacists detailed trainings on anaphylaxis beginning from their education years will render them a crucial link of the anaphylaxis management chain within the healthcare system.

Schools are places where development of anaphylaxis is observed most frequently in non-domestic social life.⁵⁻⁸ Schools have legal liabilities for the protection of students' health; therefore, it is important for schools to establish policies and give school staff training about anaphylaxis management in order to take preventive measures for children with anaphylaxis, make early diagnosis when its symptoms develop, and perform the correct treatment.⁵ However, results of studies from around the world demonstrate the inadequacies in prevention and management of anaphylaxis in schools that might lead to serious outcomes. Mohammed Elhassan et al.³⁴ found that school managements prohibited performing injection in 16% of schools that had students with anaphylaxis history; while Korematsu et al.³⁵ ascertained that in 79% of students who developed anaphylaxis at school, school staff did not administer epinephrine with EAI but wait for parents to come. In our

study, although one-fourth of the school staff said that they knew the first and life-saving treatment of anaphylaxis, only 15% preferred epinephrine. Additionally, there were no professional healthcare workers (nursing staff) in 82.9% of schools, and teachers (non-nursing staff) were the responsible ones in case students need emergency medical aid. In two studies that assessed the applications of preschools and primary schools in our country regarding anaphylaxis management in the last eight years, availability rates of professional healthcare workers in schools were similar.^{11,36} One of these studies found teachers' rate of preferring epinephrine as the first and life-saving treatment as 0%, and the other as 3%.^{11,36} However, in order to successfully implement scientific suggestions in countries, it is crucial that legislators and official authorities become more aware of this issue and legal infrastructures be established. None of the healthcare practitioners in schools in our study knew how to use EAIs, while Ercan et al.¹¹ found this rate as 4%. Studies showed that training given to non-nursing staff about prevention and management of anaphylaxis and EAI usage were effective in anaphylaxis management and EAI usage.³⁷ Furthermore, Devetak et al.³⁸ demonstrated that specific training on this topic provided to future teachers in their first year at university considerably improved their attitudes and knowledge levels about anaphylaxis in their last year. In our country, the Ministries of National Education and Health manage the policies on healthcare practices. The fact that these institutions cooperatively develop policies for prevention and management of anaphylaxis in schools and trainings on anaphylaxis management are added to the college curriculum of future teachers considering they play a crucial role as healthcare practitioners in schools will be the main determinants in resolving these problems and improving anaphylaxis outcomes.

Only around one-third of the participants given the written and visual instruction sheet were able to demonstrate the EAI usage correctly in practice. The two EAI usage steps with the most

frequent errors in all participant groups were "Place the appropriate injection tip into outer thigh/Press the trigger so it 'clicks'" and "Turn the trigger to arrow direction". Various studies carried out with Penepin[®] and other commercial EAIs showed that the steps in which errors were made could be the same for each EAI regardless of the applicator's identity. This supports the fact that the errors made in EAI application might be associated with EAI design.^{13,16} It was shown that the reduction of the number of steps in EAI usage in recent years, keeping the needle within a protective shield after application and adding audio instructions were effective in increasing the rates of correct usage and reducing problems related to erroneous applications.³⁹ However, despite the industry's intensive efforts in the improvement of EAI design, unfortunately current commercial auto-injectors do not possess all of the ideal features required for a life-saving treatment.⁴⁰ For Penepin[®], making modifications that eliminate the need for the application step of "Turn the trigger to arrow direction" can be effective in enhancing correct usage rates.

Our study found that pharmacists' rate of correct EAI usage was significantly high compared to all other participant groups; while the rates of school staff and dentists were high compared to physicians, though not significantly. This may have two reasons. The first one may be that these groups were more willing to learn and considered the study process an educational opportunity; and the second one is that physicians may have felt highly stressed during one-to-one demonstrations due to the study design, which may have reduced correct usage rates. Though this was the case for each participant, physicians may have felt more stressed than other participants, as they knew they were being assessed by their colleagues. This is one of the restrictive aspects of our study. Secondly, investigators were not the same person for the two study centers located in different parts of Turkey; therefore, each investigator's judgment may have led to bias. Thirdly, although the total

number of participants was high, the number of participants in each individual group was low. Fourthly, our study did not include the responsible people in certain public spaces (e.g. shopping malls, playgrounds and camps) where anaphylaxis develops. And the fifth restrictive factor is that the primary design of the study did not include other professional healthcare practitioners (e.g. nurses and paramedics) in addition to physicians and dentists.

In conclusion, healthcare workers' knowledge about anaphylaxis management and capability to use EAIs correctly are not at the required level. Adequate improvement could not be achieved on this topic despite the effort spent in the last ten years. Therefore, in order for current guidelines to be implemented, there is a necessity for regular, sustainable and extensive training for all healthcare workers constituting the healthcare chain, which include all steps of anaphylaxis management, cover its psychological aspects, and are supported by healthcare authorities through legal policies. The fact that the most frequent errors in EAI usage were made in the same steps indicates that the industry should continue to strive to develop the ideal life-saving device.

Authors contribution

The authors confirm contribution to the paper as follows: study conception and design: Mustafa Arga, Arzu Bakırtaş; data collection: Erdem Topal, Sıla Yılmaz, Pınar Canızıcı Erdemli, Kübra Bıçakçı; analysis and interpretation of results: Mustafa Arga, Erdem Topal, Sıla Yılmaz, draft manuscript preparation: Mustafa Arga, Erdem Topal, Arzu Bakırtaş. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

This study was approved by the institutional ethics committee of İnönü University (2020/8-630).

Source of funding

The sponsor had no involvement in this clinical study's design, the collection of data, analysis, and interpretation of data, the writing of the report and the decision to submit the paper for publication. An honorarium, grant, or other form of payment was not given to anyone to produce the manuscript.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Brown GA, Kemp SF, Lieberman PL. Anaphylaxis. In: Adkinson NF Jr, Bochner BS, Burks WW, (eds). Middleton's Allergy: Principles and Practice. (8th ed). Philadelphia: Saunders Inc, 2014: 1237-1260.
2. Sicherer SH, Simons FER, Section on Allergy and Immunology. Epinephrine for first-aid management of anaphylaxis. Pediatrics 2017; 139: e20164006.
3. Wang J, Sicherer SH, Section on Allergy and Immunology. Guidance on completing a written allergy and anaphylaxis emergency plan. Pediatrics 2017; 139: e20164005.
4. Ribeiro MLKK, Chong Neto HJ, Rosario Filho NA. Diagnosis and treatment of anaphylaxis: there is an urgent needs to implement the use of guidelines. Einstein (Sao Paulo) 2017; 15: 500-506.
5. Muraro A, Clark A, Beyer K, et al. The management of the allergic child at school: EAACI/GA2LEN task force on the allergic child at school. Allergy 2010; 65: 681-689.
6. Muraro A, Agache I, Clark A, et al; European Academy of Allergy and Clinical Immunology. EAACI food allergy and anaphylaxis guidelines: managing patients with food allergy in the community. Allergy 2014; 69: 1046-1057.
7. Vale S, Smith J, Said M, Mullins RJ, Loh R. ASCIA guidelines for prevention of anaphylaxis in schools, pre-schools and childcare: 2015 update. J Paediatr Child Health 2015; 51: 949-954.
8. Sicherer SH, Mahr T, American Academy of Pediatrics Section on Allergy and Immunology. Management of food allergy in the school setting. Pediatrics 2010; 126: 1232-1239.
9. Orhan F, Civelek E, Sahiner UM, et al. Anafilaksi: Türk Ulusal Rehberi 2018. Astım Alerji İmmünoloji Dergisi 2018; 16(Ek sayı 1): 1-62.

10. Hogue SL, Muniz R, Herrem C, Silvia S, White MV. Barriers to the administration of epinephrine in schools. *J Sch Health* 2018; 88: 396-404.
11. Ercan H, Ozen A, Karatepe H, Berber M, Cengizlier R. Primary school teachers' knowledge about and attitudes toward anaphylaxis. *Pediatr Allergy Immunol* 2012; 23: 428-432.
12. Tanno LK, Demoly P, Joint Allergy Academies. How can the World Health Organization's International Classification of Diseases (ICD)-11 change the clinical management of anaphylaxis? *Expert Rev Clin Immunol* 2018; 14: 783-786.
13. Arga M, Bakirtas A, Catal F, et al. Training of trainers on epinephrine autoinjector use. *Pediatr Allergy Immunol* 2011; 22: 590-593.
14. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006; 117: 391-397.
15. Muraro A, Roberts G, Worm M, et al; EAACI Food Allergy and Anaphylaxis Guidelines Group. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy* 2014; 69: 1026-1045.
16. Topal E, Karagöl HİE, Yılmaz Ö, et al. Comparison of practical application steps of the previously used adrenaline auto injector in Turkey (EpiPen) and the currently available adrenaline auto injector (Penepin): a multi-center study. *Turk Pediatr Ars* 2018; 53: 149-154.
17. Altman AM, Camargo CA Jr, Simons FE, et al. Anaphylaxis in America: a national physician survey. *J Allergy Clin Immunol* 2015; 135: 830-833.
18. Munblit D, Treneva M, Korsunskiy I, Asmanov A, Pampura A, Warner JO. A national survey of Russian physicians' knowledge of diagnosis and management of food-induced anaphylaxis. *BMJ Open* 2017; 7: e015901.
19. Grossman SL, Baumann BM, Garcia Peña BM, Linares MY, Greenberg B, Hernandez-Trujillo VP. Anaphylaxis knowledge and practice preferences of pediatric emergency medicine physicians: a national survey. *J Pediatr* 2013; 163: 841-846.
20. Olabbari M, Gonzalez-Peris S, Vázquez P, et al. Management of anaphylaxis in Spain: pediatric emergency care providers' knowledge. *Eur J Emerg Med* 2019; 26: 163-167.
21. Solé D, Ivancevich JC, Cardona V. Knowledge of anaphylaxis among iber-American physicians: results of the Ibero-American Online Survey for Physicians on the management and treatment of anaphylaxis (IOSPTA) -Latin American Society of Allergy, Asthma & Immunology (LASAAI). *J Investig Allergol Clin Immunol* 2013; 23: 441-443.
22. Arga M, Bakirtas A, Turktas I, Demirsoy MS. Pediatri asistan ve uzmanları adrenalin otoenjektör kullanımını biliyor mu? *Astım Alerji İmmünoloji Dergisi* 2009; 7: 26-31.
23. Erkoçoğlu M, Civelek E, Azkur D, et al. Knowledge and attitudes of primary care physicians regarding food allergy and anaphylaxis in Turkey. *Allergol Immunopathol (Madr)* 2013; 41: 292-297.
24. Baççoğlu A, Yılmazel Uçar E. Level of knowledge about anaphylaxis among health care providers. *Tuberk Toraks* 2013; 61: 140-146.
25. Tuncel T, Sancakli O, Bag O, Cetin HS, Özdoğru EE. Physicians' approach to anaphylaxis in childhood. *Pediatr Emerg Care* 2020. doi: 10.1097/PEC.0000000000002064.
26. Derinoz O, Bakirtas A, Arga M, et al. Pediatricians manage anaphylaxis poorly regardless of episode severity. *Pediatr Int* 2014; 56: 323-327.
27. Cohen MB, Saunders SS, Wise SK, Nassif S, Platt MP. Pitfalls in the use of epinephrine for anaphylaxis: patient and provider opportunities for improvement. *Int Forum Allergy Rhinol* 2017; 7: 276-286.
28. Mahoney B, Walklet E, Bradley E, O'Hickey S. Improving adrenaline autoinjector adherence: a psychologically informed training for healthcare professionals. *Immun Inflamm Dis* 2019; 7: 214-228.
29. Worm M, Molaie N, Dölle S. Level of knowledge among pharmacists regarding anaphylaxis and the use of epinephrine autoinjectors. *J Dtsch Dermatol Ges* 2018; 16: 1315-1321.
30. Pitsios C, Vasiliadis A, Karakatsanis KP, et al. Availability of epinephrine auto-injectors and knowledge of community pharmacists about their use. *Eur Ann Allergy Clin Immunol* 2019; 51: 234-236.
31. Salter SM, Loh R, Sanfilippo FM, Clifford RM. Demonstration of epinephrine autoinjectors (EpiPen and Anapen) by pharmacists in a randomised, simulated patient assessment: acceptable, but room for improvement. *Allergy Asthma Clin Immunol* 2014; 10: 49.
32. Kapoor S, Roberts G, Bynoe Y, Gaughan M, Habibi P, Lack G. Influence of a multidisciplinary paediatric allergy clinic on parental knowledge and rate of subsequent allergic reactions. *Allergy* 2004; 59: 185-191.

33. Salter SM, Vale S, Sanfilippo FM, Loh R, Clifford RM. Long-term effectiveness of online anaphylaxis education for pharmacists. *Am J Pharm Educ* 2014; 78: 136.
34. Mohammed Elhassan S, Charlson M, Jama H, et al. Management of anaphylaxis in children: a survey of parents and school personnel in Qatar. *BMJ Paediatr Open* 2017; 1: e000077.
35. Korematsu S, Fujitaka M, Ogata M, et al. Administration of the adrenaline auto-injector at the nursery/kindergarten/school in Western Japan. *Asia Pac Allergy* 2017; 7: 37-41.
36. Özen A, Boran P, Torlak F, et al. School board policies on prevention and management of anaphylaxis in İstanbul: where do we stand? *Balkan Med J* 2016; 33: 539-542.
37. Tsuang A, Demain H, Patrick K, Pistiner M, Wang J. Epinephrine use and training in schools for food-induced anaphylaxis among non-nursing staff. *J Allergy Clin Immunol Pract* 2017; 5: 1418-1420.e3.
38. Devetak I, Devetak SP, Vesel T. Future teachers' attitudes and knowledge regarding the management of the potential students' life-threatening allergic reactions in Slovenian schools. *Zdr Varst* 2018; 57: 124-132.
39. Bakirtas A, Arga M, Catal F, Derinoz O, Demirsoy MS, Turktas I. Make-up of the epinephrine autoinjector: the effect on its use by untrained users. *Pediatr Allergy Immunol* 2011; 22: 729-733.
40. Waserman S, Avilla E, Ben-Shoshan M, Rosenfield L, Adcock AB, Greenhawt M. Epinephrine autoinjectors: new data, new problems. *J Allergy Clin Immunol Pract* 2017; 5: 1180-1191.