

The Ability to Use Epinephrine Autoinjector in Patients Who Receive Prescription Immediately after Anaphylaxis

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Keywords

Anaphylaxis · Correct use · Emergency center · Epinephrin autoinjector · Instruction · Training device

Abstract

Background: Epinephrine autoinjector (EAI) is prescribed to prevent a fatal outcome in the case of a repeated anaphylactic reactions. We wanted to determine how adult patients who received their first prescription as part of an urgent treatment of an anaphylactic reaction or at their family physician were instructed on the use of EAI. **Methods:** Nurses assessing patients' knowledge asked the patient to demonstrate how to use the EAI training device. Patients who performed the critical steps correctly in 1 min were labelled as competent. **Results:** Forty-one patients (24% women, 46 ± 5 years) came for the allergy examination 116 ± 145 days after receiving a prescription for EAI. When prescribing, the doctor or nurse explained the instructions for the use of EAI to 63.4% patients, and 31.7 patients practiced the use of EAI using a training device. At the pharmacy, 22% received explanation and 7% also practiced using a training device. Fifty-four percent of patients were able to effectively administer EAI adrenaline within 1 min. Higher education level was

associated with sufficient knowledge about the use of EAI ($p = 0.026$). At the time of the visit to the allergy specialist clinic, 61% of patients had EAI with them. The shelf life of EAI was known to 63% of patients. **Conclusions:** The activities to increase the prescription rate of EAI immediately after treatment of anaphylactic episode are not sufficient to prevent severe outcome after the repeated episodes of anaphylaxis as nearly a half of patients are not able to use EAI correctly.

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Introduction

Anaphylaxis is a life-threatening systemic allergic reaction. Epinephrine autoinjector (EAI) is prescribed to a patient with a history of anaphylactic reaction and the risk of recurrence of anaphylaxis upon contact with the allergen [1, 2]. Early and proper epinephrine use improves clinical outcomes [1, 3–5]. Awareness that patients have EAI with them at all times is the most important step in the use of EAI in the case of anaphylaxis.

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There are 2 other obstacles in the EAI injection process, namely, the correct use of EAI and the use of EAI at the right time [5].

EAI used in first aid in the event of an anaphylaxis is known to pose a risk of adverse events. Proper use is relatively safe although in 2007 there were over 2,500 reports of unfortunate outcomes in the United States. Seventy-five percent of these were injection into the finger, which can result in finger gangrene [6].

Following discharge from ED [7], it is advised that all patients with anaphylaxis are issued a prescription for EAI and trained with the use of the device. Patients should be taught how to avoid the allergy triggers and an initial emergency action plan should be explained.

In the study we wanted to determine how adult patients who received their first prescription as part of an urgent treatment of an anaphylactic reaction or at their family physician were instructed on the use of EAI. We wanted to identify the factors that influence the proper use of EAI and determine in which steps they most often make a mistake.

Materials and Methods

The study was approved by the National Ethics Committee (214/09/13). The study was performed in the outpatient clinic of a tertiary allergy institution. Patients with a history of anaphylaxis who were referred for the first allergy examination and had already been prescribed EAI in an emergency center or by a family physician were asked to demonstrate the use of an EIA using a training device. The correct use of EAI was monitored step by step:

1. Open the yellow lid of the protective box.
2. Take the EAI out of the protective box.
3. Remove the blue safety cap.
4. Select the upper lateral thigh for application.
5. Place the orange part of the autoinjector on your thigh.
6. Activate EAI so that a click is heard.
7. Hold EAI for at least 3 s.
8. After removing the EAI, gently massage the application site for 3 s.
9. Call emergency medical services on 112.
10. Rest, avoiding physical activity.
11. Know the instructions for deciding when to use adrenaline during an allergic reaction: shortness of breath, wheezing in the throat or chest, weakness, and feeling of losing consciousness.

The steps 1, 2, 3, 6, 7 were regarded as critical steps as omitting any of these steps would prevent the patient from receiving epinephrine [3]. Nurses assessing patients' knowledge gave the training device to the patient and asked them to demonstrate how to use the EAI. Patients were observed for 1 min. Their performance was assessed using a checklist. Patients who performed the critical steps correctly were labelled as competent in using EAI. Patients

were divided into 2 groups: group with sufficient knowledge and group with insufficient knowledge about the use of EAI. Patients were also asked about the explanation and training in how to use the EAI at the time of prescription and when dispensed at the pharmacy.

Statistical Analysis

Statistical analysis was performed using Microsoft Excel 2013. First, we made descriptive statistics to determine frequencies and percentages. Differences between groups were calculated by *t* test (difference between averages) and by χ^2 test (difference between frequencies). The value of $p < 0.05$ was regarded as statistically significant.

Results

We included 41 patients (24% women) who came for the allergy examination 116 $\pm$ 145 days after receiving a prescription for EAI (Table 1). Their ages were 46 $\pm$ 5 years. In 3 patients the cause of anaphylaxis was food, in 1 it was drug related, 33 were from insect stings, and in 4 the cause was unknown. Twenty-seven patients were prescribed EAI in the emergency center, 10 by the family physician, and in 4 cases by a specialist in the hospital. When prescribing, the doctor or nurse explained the instructions for the use of EAI to 26 patients (63.4%), and 13 patients (31.7%) practiced the use of EAI using a training device. At the pharmacy, 9 patients (22.0%) received explanation about the use of EAI, 3 of whom also practiced using a training device.

Based on the demonstration of the use of the EpiPen training device, 22 (54%) patients were able to effectively administer EAI adrenaline within 1 min (Table 2). We found no difference between the time elapsed from the anaphylactic event and the ability to use the EAI correctly. The most common critical mistake was not removing the blue safety cover. Other common mistakes were problems with activation of autoinjector and holding the needle in place for at least 3 s. We found statistically significant higher education level in the group with sufficient knowledge about the use of EAI ($p = 0.02564$).

At the time of the visit to the allergy specialist clinic, 25 patients (61%) had EAI with them. Reasons given by most patients for not having EAI with them were that they do not need it at this time of year because there are no insects, that they have it in the car, or that there is no need for it in the allergy office. EAI are carried by 29 patients (71%) at their workplace, and 4 do not carry the EAI at work. The rest of the patients were not employed or were retired. The shelf life of EAI was known to 26 (63%) of patients.

Table 1. Characteristics of patients who were able or unable to use EAI

	Group 1 (N = 22) N (%)	Group 2 (N = 19) N (%)	p value
Gender			
Male	16 (72.7)	15 (78.9)	ns
Female	6 (27.3)	4 (21.1)	
Age (average±SD), years	43.3±13.6	48.7±17.3	ns
Education			
Primary school	0	1 (5.3)	<0.05
High school	15 (68.2)	17 (89.4)	
College	1 (4.5)	0	
Faculty	5 (22.8)	1 (5.3)	
Postgraduate	1 (4.5)	0	
Etiology of anaphylaxis			
Food	1 (4.5)	2 (10.5)	ns
Insect sting	18 (81.9)	15 (78.9)	
Drugs	0 (0)	1 (5.3)	
Unknown	3 (13.6)	1 (5.3)	
EAI prescribed at			
Emergency department	15 (68.2)	12 (63.2)	ns
Family physician	5 (22.7)	5 (26.3)	
Other	2 (9.1)	2 (10.5)	
Education on the use of EAI by physician/nurse			
Only prescription without education	4 (18.2)	11 (57.9)	<0.05
Explanation only on the use of EAI	7 (31.8)	6 (31.6)	ns
Explanation and training using a training device	11 (50)	2 (10.5)	<0.05
Education on the use of EAI by a pharmacist			
Only dispensing without education	14 (63.7)	18 (94.7)	ns
Explanation only on the use of EAI	5 (22.7)	1 (5.3)	ns
Explanation and training using a training device	3 (13.6)	0 (0)	ns
Patient carried EAI during the visit at our outpatient office	17 (77.3)	8 (42.1)	<0.05
The patient has an EpiPen with them at work	18 (81.8)	11 (57.9)	ns
The patient knows the shelf life of EAI	19 (86.4)	7 (36.8)	<0.05

EAI, epinephrine autoinjector.

Table 2. Knowledge of individual phases of EpiPen use: group 1: sufficient knowledge about the use of EAI; group 2: insufficient knowledge about the use of EAI

	Group 1 N = 22	%	Group 2 N = 19	%	p value
1. Removes the protective box by lifting the yellow cover	22	100	16	84	0.08
2. Takes the injector out of the protective box	22	100	16	84	0.08
3. Removes the blue safety cover	22	100	6	32	0.00002
4. Place of application: upper lateral part of the thigh	21	95	14	74	0.061
5. Places the orange part of the autoinjector on your thigh	19	86	10	53	0.038
6. Activates: presses hard against the thigh until a click was heard	21	95	6	32	0.000045
7. Holds for at least 3 s	19	86	5	26	0.0001
8. Removes the EpiPen and gently massages the application site for 3 s	10	45	2	10	0.0138
9. Calls emergency medical services on 112	21	95	11	58	0.012
10. Avoids physical activity	19	86	8	42	0.0024

EAI, epinephrine autoinjector.

Discussion

EAI is available as a reimbursed medical device in Slovenia since 2009. According to anaphylaxis guidelines, patients with anaphylaxis should be issued EAI as soon as possible, preferably immediately after treatment of the acute episode in the emergency center [8]. However, only prescription does not guarantee that the patient is able to use the drug. Patients are well adherent to EAI treatment if they have EAI prescribed, carry it with them all the time, and are able to use it properly in the event of anaphylaxis. The main finding of our study is that despite the patients receiving the first prescription of EAI in the emergency center or by their family doctor, a large proportion did not receive instruction regarding its use and were not able to use it efficiently. Only a half (54%) of patients effectively performed the critical steps of EAI use when visiting a specialist allergology clinic.

In a Japanese cohort of patients, 28.8% were prescribed EAIs within 30 days after their initial severe anaphylactic episode. One-third of these patients were prescribed EAIs from the same facility in which initial treatment was administered for severe anaphylaxis [9]. Data from Anaphylaxis Registry similarly showed that only 37% of patients with anaphylaxis were prescribed EAI before referral to specialized allergy centers [10]. The EIA prescription rate is higher in allergy providers compared to family and emergency doctors which emphasize the need for referral to a specialist.

Cohen analyzed the published literature about the pitfalls in the use of epinephrine in allergic reactions. They addressed the pitfalls as lack of EAI availability, inadequate training of patients on use of an EAI, uncertainty about when or how to administer epinephrine, concern for systemic effects of epinephrine, failure to administer, and accidental injury. They found 9 reports evaluated patients or providers on their ability to use an EAI. The conclusion of those reports was that training is effective, but the benefits of training dissipate quickly with time [11].

In a study performed by Quercia and colleagues the training program, which includes a clear explanation of the injection technique and the use of EAI, a practical demonstration of the training device in polyclinic activity showed 80% correct use of EAI in those who received training compared to 10% success in those who did not receive training [4].

Consecutive adult patients, who came to the follow-up visit required for the renewal of the EAI prescription, were checked for their ability to use the device. Ninety-three percent of patients believed they knew the correct

use of the autoinjector. However, 22% of patients failed to pull off the safety cap, 26% did not handle the injector correctly, and in 37% the site of the injection was wrong [12].

Even in patients who were trained in the use of the EpiPen, the ability to use the device was insufficient: 38% of patients even did not remove the cap before trying to apply the EAI [13]. Fifteen percent of untrained subjects injected into their finger [14].

We showed a correlation between higher education level and the ability to correctly use the EAI, which is similar to the results of Ridolo [12]; however, not all studies confirmed that result [15]. The less educated population cares less about their health, which means there is a need to focus on that group with even more active health education.

When the trainer is an allergist, the ability of patients to use the adrenaline autoinjector increases 17-fold compared to when the trainer is a general practitioner [16].

Our study showed that only a few patients received education and training about EAI during dispensing of the device in the pharmacy. In the Netherlands, pharmacists showed considerable gaps in knowledge about anaphylaxis and its management. Only 8% of respondents gave correct answers concerning the proper EAI demonstration, and 1 demonstrated the EAI use correctly [17].

Better results were found in Australia, where 65.2% of community pharmacists accurately demonstrated the steps required to inject epinephrine [18]. These data suggest that opportunities exist to improve the quality of care provided by pharmacies to high-risk allergic patients.

The ability to use EAI decreased [15] with the longer time from the last visit and the first instruction. The study of Sirin [3] recommends that training be repeated every 6 months. Several studies have shown that less than 60% of patients carry their EAI with them regularly [19].

In the study of Segal, only 46% of patients brought the device with them to the follow-up visit [13]. Sancez showed that among 120 patients, 58% had EAI with them in the office or at home and 28% had a consultation within 6 months of prescribing EAI [5].

More than a half of patients reported feeling that they did not need EAI [15]. In our study, 61% of patients had EAI with them when they came to the clinic for an examination. However, many patients stated that they do not need to carry EAI during winter season because there is no possibility of insect stings in that period.

With the analysis of a large database of filled prescriptions, Kaplan found that less than 50% of patients refilled their EAI even once and only 11% refilled at all expected

refill times [20]. In Japan, among patients who were prescribed EAI for anaphylaxis, 55.4% refilled their EAI prescriptions at least once after their initial prescription. Younger patients were more likely to refill EAI prescriptions [9].

Sixty-three percent of patients in our study knew the shelf life of their EAI. The study of Quercia [4] showed that 75% of patients who received an education program and only 32% of those who did not receive an EAI program did pay attention to the EAI duration date.

The importance of the proper use of EAI was recognized also by the European Medicines Agency which recommended several measures, including the introduction of more effective educational material, to ensure that patients and carers use adrenaline autoinjectors successfully. The European Medicines Agency's Committee for Medicinal Products for Human Use concluded that training of the user is of paramount importance. The companies that market adrenaline autoinjectors are asked to ensure provision of educational material for patients including a training device with which patients can practice [21].

Conclusion

The initiatives to prescribe EAI immediately after episodes of anaphylaxis are appropriate as the referral time to allergy specialist is considerable (in our study: 116 ± 145 days). However, in our real-life study, we showed that the activities to increase the prescription rate of EAI immediately after treatment of anaphylactic episode are not sufficient to prevent severe outcome after the repeated episodes of anaphylaxis as nearly a half of patients are not

able to use EAI correctly. Early and continuous health education of a patient with anaphylaxis is key to preventing adverse outcomes in anaphylactic reactions. This requires better involvement of nurses and family and emergency doctors; however, we see the most opportunities for improvement in the issuance of EAI in the pharmacy.

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Statement of Ethics

The study was approved by the National Ethics Committee (214/09/13). Subjects have given their written informed consent

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.K. and M.K. designed the study and analyzed and interpreted data. They equally wrote the main manuscript text and reviewed and approved the manuscript.

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