



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

Erdem Topal¹, Hacer İlbilge Ertoý Karagöl², Özlem Yılmaz³, Mustafa Arga⁴, Burcu Köksal⁵, Özlem Özbek Yılmaz⁵, Hülya Anıl⁶, Koray Harmancı⁶, Şeyhan Kutluğ⁷, Fadıl Öztürk⁷, Hasan Cem Razi⁸, İpek Türkteş⁹, Mehmet Sadık Demirsoy⁹, Arzu Bakırtaş⁹

¹Department of Pediatrics, Division of Pediatric Allergy and Asthma, İnönü University School of Medicine, Malatya Turkey

²Department of Pediatrics, Division of Pediatric Allergy and Asthma, Yıldırım Beyazıt University School of Medicine, Ankara, Turkey

³Department of Pediatric Allergy and Asthma, Mersin City Hospital, Mersin, Turkey

⁴Department of Pediatrics, Division of Pediatric Allergy and Asthma, Medeniyet University School of Medicine, İstanbul, Turkey

⁵Department of Pediatrics, Division of Pediatric Allergy and Asthma, Başkent University School of Medicine, Ankara, Turkey

⁶Department of Pediatrics, Division of Pediatric Allergy and Asthma, Eskişehir Osmangazi University School of Medicine, Eskişehir, Turkey

⁷Department of Pediatrics, Division of Pediatric Allergy and Asthma, Ondokuz Mayıs University School of Medicine, Samsun, Turkey

⁸Department of Pediatric Allergy and Asthma, Acıbadem Hospital, Ankara, Turkey

⁹Department of Pediatrics, Division of Pediatric Allergy and Asthma, Gazi University School of Medicine, Ankara, Turkey

Cite this article as: Topal E, Ertoý Karagöl Hİ, 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 Pediatri Ars* 2018; 53(3): 149-54.

Abstract

Aim: It has been shown by a great number of studies that the correct use of adrenaline auto injectors prescribed to patients with anaphylaxis is associated with the design of the auto injector, in addition to training. The aim of this study was to compare the skills of adults in using two different auto injectors prescribed to patients with anaphylaxis.

Material and Methods: Parents of patients aged between 1 and 18 years who referred to allergy outpatients were included in the study.

Results: A total of 630 volunteers from nine centers were included in the study. Four hundred fifty-seven (72.5%) of the participants were females and 235 (37.3%) were undergraduates. The rate of showing all the steps of auto injector trainers correctly

by the participants was found as (60.2%) (n=379) for EpiPen and 42.9% (n=270) for Penepin (p<0.001). The most frequent mistake with both auto injector trainers was the step of "place appropriate injection tip into outer thigh/press the trigger so it clicks." When the preferences of the volunteers were asked after training and application, 527 (83.7%) chose EpiPen, stating that it was easier and simpler to use.

Conclusions: Our study showed that the correct usage rates of both adrenaline auto injectors were much lower than expected and there could be mistakes in the application of both. It could be appropriate to make improvements in the design of Penepin, which is still the only available adrenaline auto injector in Turkey, such that its application steps will be simpler and quicker.

Keywords: Adrenaline auto injector, anaphylaxis, EpiPen, Penepin

Introduction

Anaphylaxis is a serious allergic reaction; it can start suddenly and result with death (1). In anaphylaxis that develops in society, adrenaline auto injectors may be lifesaving (2). Thus, it is important for patients and/

or their relatives to know how to use adrenaline auto injectors when faced with an anaphylaxis attack. Today, there are a few kinds of adrenaline auto injectors used in European countries. The first of these was EpiPen, which began to be used in 1994, and Anapen and Auvi-Q, which began use later, respectively.

Corresponding Author: Erdem Topal E-mail: erdemtopal44@gmail.com

Received: 01.03.2018

Accepted: 18.07.2018

©Copyright 2018 by Turkish Pediatric Association - Available online at www.turkpediatriarsivi.com

DOI: 10.5152/TurkPediatriArs.2018.6734

Studies have shown that patients make mistakes in the use of EpiPen auto injectors (3-5). Thus, in order to decrease the rate of errors, EpiPen was redesigned in 2011. In Turkey, EpiPen adrenaline auto injectors were prescribed mostly by physicians until one year ago, and the drug was provided through pharmacist associations from abroad. However, the Penepin adrenaline auto injector, which is designed and manufactured in Turkey, has been used since May 2016. When the newly manufactured and currently used Penepin adrenaline auto injector is compared with EpiPen, some differences could be seen in terms of application. In particular, the safety step includes a second step when compared with the EpiPen adrenaline auto injector.

The aim of this study was to compare the practice steps of the Penepin adrenaline auto injector with the EpiPen adrenaline auto injector.

Material and Methods

Study centers

Nine centers located in different parts of Turkey were included in the study. The centers of the study were as follows: Gazi University (Ankara), Inonu University (Malatya), Basket University (Ankara), Yıldırım Beyazıt University (Ankara), Eskişehir Osmangazi University (Eskişehir), Ondokuz Mayıs University (Samsun), Medeniyet University (İstanbul), Mersin City Hospital (Mersin) Acıbadem Ankara Hospital (Ankara).

Study design

Parents of patients aged between 1 and 18 years who referred to Pediatric Immunology and Allergy were included in the study. The parents were given written and visual brochures that showed the steps of use of EpiPen and Penepin auto injectors (Figure 1, 2). Later, adrenaline auto injector trainers that did not include drug (adrenaline) and needle (EpiPen® trainers and Penepin®) were given and the parents were asked to demonstrate how to use them. The errors in the steps of use were recorded. In addition, the time was recorded for the demonstration steps. The parents who made errors in demonstration steps were shown how to use the auto injector again by the responsible researcher and the training was continued until the participant demonstrated the steps correctly. It was randomly determined as to which auto injector trainer to give first.

Exclusion criteria

Volunteers who were prescribed or whose children and/or relatives were prescribed adrenaline auto injectors previously, healthy patients, volunteers who had and/or those whose relatives had diabetes and who knew how to use insulin auto injectors, and illiterate volunteers were excluded from the study.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 15.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics are expressed as frequency and percentage for categorical variables, and quantitative data are expressed as mean and standard deviation. McNemar's test and the paired t-test were used to compare two groups (Penepin group and EpiPen group). A two-sided $p < 0.05$ was considered as statistically significant. The research protocol was approved by the ethics committee of Inonu University School of Medicine (Number: 2017/2-3, Date: 01.17.2017), and all participants gave informed consent.

Results

A total of 630 volunteers from nine centers were included in the study. Four hundred fifty-seven (72.5%) of the participants were females and 235 (37.3%) were undergraduates. The mean age of the participants was 34.13 ± 7.93 years. For the first try, 379 (60.2%) of the participants demonstrated all the steps of using the EpiPen auto injector trainer correctly, and 270 (42.9%) demonstrated all the steps of the use of the Penepin auto injector trainer correctly ($p < 0.001$). When the demonstration times were compared, it was found as 57.2 ± 23.9 seconds with the EpiPen auto injector and 89.8 ± 42.4 seconds with the Penepin auto injector ($p < 0.001$) (Table 1). The most frequent error with both auto injector trainers was the step of "Placed appropriate injection tip into the outer thigh/press the trigger so it clicks" (Figure 3). In addition, 10% of the volunteers stirred with tip point after pulling down the orange cap (Table 2). The rates of participants who required ≥ 2 training demonstrations to perform injections correctly were 8.8% and 20.6% for the EpiPen group and Penepin group, respectively ($p < 0.001$). When the preferences of the volunteers were asked after training and application, 527 (83.7%) chose EpiPen stating that it was easier and simpler to use.

DEMONSTRATION OF EPIPEN APPLICATION STEPS



Figure 1. Written and visual brochures for steps of EpiPen auto injector usage

DEMONSTRATION OF PENEPIEN APPLICATION STEPS



Figure 2. Written and visual brochures for steps of Penepin auto injector usage

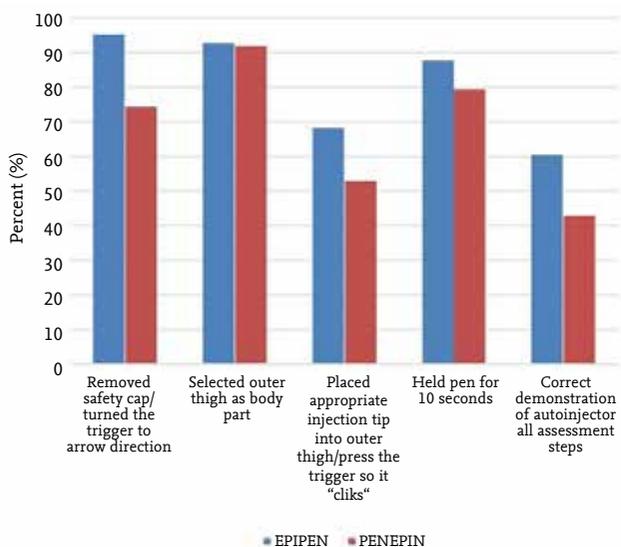


Figure 3. The comparison of study parameters between EpiPen and Penepin groups (critical steps)

Discussion

In this study, the use of two adrenaline auto injectors was compared for the first time among parents of pediatric patients as demonstrated in practice. Our most significant result was that in the use of both auto injectors, more than one-third of the parents made errors at least in one step. This shows that both auto injectors have aspects that should be developed technically to decrease errors made by users. In addition, our study showed that the volunteers applied all the critical application steps of EpiPen auto injector correctly more frequently when compared with Penepin. In terms of demonstration times, EpiPen was demonstrated in a shorter time than Penepin. The most frequent error with both auto injector trainers was the step of "Place appropriate injection tip into outer thigh/press the trigger so it clicks."

Table 1. Comparison of study parameters between EpiPen and Penepin groups (critical steps)

Assessment steps	EPIPEN	PENEPIN	p ^a
Removed safety cap/ turned the trigger to arrow direction, n (%)	600 (95.2)	468 (74.3)	<0.001
Selected outer thigh as body part, n (%)	586 (93)	580 (92.1)	0.55
Placed appropriate injection tip into outer thigh /press the trigger so it 'clicks', n (%)	430 (68.3)	334 (53)	<0.001
Correct demonstration of auto-injector all assessment steps, n (%)	379 (60.2)	270 (42.9)	<0.001
Time (s) to administer ^b , second	57.2±23.9	89.8±42.4	<0.001

^aMcNemar's test and paired t test were used to compare two groups. A two-sided p<0.05 was considered as statistically significant

^bMean±standard deviation

Table 2. Other mistakes of assessment steps of adrenaline auto-injectors

Other mistakes of assessment steps of Penepin auto-injector	
	n (%)
After pull down orange cap stir with tip point	63 (10)
Turned middle of auto-injector pen	8 (1.2)
Turned button of trigger back and forth a few times	6 (0.9)
Before the injection, pressed the trigger	4 (0.6)
Other mistakes of assessment step of EpiPen auto-injector	
	n (%)
Inject the hand	11 (1.7)
Jab auto-injector successively 3 times	1 (0.1)

The first critical application step of the EpiPen adrenaline auto injector is to take off the blue safety tip. With Penepin, the first critical application step is to pull down the orange tip, from which the needle comes out, and to turn the trigger button on the other tip of the auto injector without pressing it. Almost all of the volunteers demonstrated this step correctly with EpiPen, but three out of four volunteers demonstrated it correctly in Penepin. Studies that assessed the use skills of adrenaline auto injectors used in European countries (EpiPen, Anapen, Auvi-Q) showed that almost all patients applied this step correctly (6, 7). We think that the reason why more errors were made with Penepin results from the fact that this step actually has two steps in Penepin. Thus, it would be appropriate to redesign this step for Penepin.

Our study showed that errors were made in another critical step of adrenaline auto injectors, which was "Place appropriate injection tip into outer thigh/press the trigger so it clicks." In both auto injectors, the volunteers made errors in this step most frequently. Two-thirds of the volunteers demonstrated this step correctly in EpiPen, but only half of the volunteers in

Penepin demonstrated this step correctly. Similarly, studies that assessed the usage skills of adrenaline auto injectors showed that of the critical steps, errors were made most frequently in this critical step (3, 6, 8). Our study showed that more errors were made in Penepin for this step. We think that the reason for this error results from the fact that this step includes two phases by hitting the application area fast first, and then pulling the trigger. In addition, the fact that a small number of volunteers pulled the trigger before hitting the application area increased the rate of errors. Thus, we think that redesigning this step in Penepin as a simpler one-step application would decrease the rate of errors.

The design of our study was in the form of giving the user guide of the auto injector and demonstrating the application to volunteers who had never seen how to use an auto injector before. While assessing the application time, the timing started from the moment the participant started to read the guide. In this assessment, the time for applying Penepin was almost two times longer than that of EpiPen. In a study that assessed the user skills of two different adrenaline auto injectors currently used in Europe (EpiPen, Auvi-Q), the demonstration time of both auto injectors was found as almost one-third of the demonstration time of Penepin (7). We believe that this results from the fact that the application steps of Penepin are higher in number and more complicated. Considering that it is very important to make the first intervention without losing time when anaphylaxis develops, we believe that the user steps and user guide should be made simpler and clearer for Penepin.

When the rates of demonstrating all the critical steps of both auto injectors were assessed, it was found that almost two-thirds of the EpiPen group

were demonstrated correctly, whereas this rate was almost one-third for the Penepin group. We think that this result was due to the simpler and easier use of EpiPen. In parallel with this thought, when the volunteers were asked which auto injector they preferred, the great majority stated that they preferred EpiPen. They also stated that the reason was because it was easier to use and simpler to apply the EpiPen auto injector.

Our study showed that errors were also made except for the practical steps of Penepin application. In particular, after the first critical step of pulling down the orange tip on the side of the needle, 10% of the volunteers played with the tip. This could cause undesired injections because the needle comes out of this tip. A similar problem was previously reported in studies conducted with EpiPen (8, 9) and the manufacturer redesigned the auto injector in 2011. Thus, we believe that it would be more appropriate to redesign the Penepin in this respect.

The limitation of our study is that the volunteers were not real patients experiencing anaphylaxis, they may not have concentrated like patients with anaphylaxis would when their skills were being assessed. This result could have caused negative effects on the correct usage rates. In addition, if the participants were invited for a second time for auto injector demonstrations after a certain period, the contribution would be better for evaluation. However, we believe that because the study was multi-centered and included volunteers from different parts of Turkey, it has a positive effect in terms of generalizing the results of the study.

As a conclusion, our study showed errors in the use of both auto injectors. In addition, it was shown that the majority of volunteers preferred using the EpiPen auto injector and that they used this auto injector faster and made fewer errors. Thus, it would be appropriate to make developments in the design of Penepin, which is still the only available adrenaline auto injector in Turkey, such that its application will be simpler and quicker.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of İnönü University School of Medicine (2017/2-3;01.17.2017).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.T., A.B.; Design - E.T., A.B.; Supervision - E.T., A.B.; Data Collection and/or Processing - H.İ.E.K., Ö.Y., M.A., B.K., Ö.Ö.Y., H.A., K.H., Ş.K., F.Ö., H.C.R., İ.T., M.S.D.; Analysis and/or Interpretation - E.T., A.B.; Literature Review - E.T., A.B.; Writing - E.T., A.B.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary reports Second National Institute of Allergy and Infectious Disease / Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol* 2006; 117: 391-7. [\[CrossRef\]](#)
2. Simons FER. Anaphylaxis, killer allergy: long-term management in the community. *J Allergy Clin Immunol* 2006; 117: 367-77. [\[CrossRef\]](#)
3. Topal E, Bakirtas A, Yilmaz O, et al. A real-life study on acquired skills from using an adrenaline auto injector. *Int Arch Allergy Immunol* 2013; 160: 301-6. [\[CrossRef\]](#)
4. Sicherer SH, Forman JA, Noone SA. Use assessment of self-administered epinephrine among food-allergic children and pediatricians. *Pediatrics* 2000; 105: 359-62. [\[CrossRef\]](#)
5. Kim JS, Sinacore JM, Pongracic JA. Parental use of EpiPen for children with food allergies. *J Allergy Clin Immunol* 2005; 116: 164-8. [\[CrossRef\]](#)
6. 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. [\[CrossRef\]](#)
7. Camargo CA Jr, Guana A, Wang S, Simons FE. Auvi-Q versus EpiPen: preferences of adults, caregivers, and children. *J Allergy Clin Immunol Pract* 2013; 1: 266-72. [\[CrossRef\]](#)

8. Arga M, Bakirtas A, Topal E, et al. Effect of epinephrine auto injector design on unintentional injection injury. *Allergy Asthma Proc* 2012; 33: 488-92. [\[CrossRef\]](#)
9. Bakirtas A, Arga M, Catal F, Derinoz O, Demirsoy MS, Turktas I. Make-up of the epinephrine auto injector: the effect on its use by untrained users. *Pediatr Allergy Immunol* 2011; 22: 729-33. [\[CrossRef\]](#)