

ORIGINAL ARTICLE

Make-up of the epinephrine autoinjector: the effect on its use by untrained users

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Abstract

Background: Part of the problems related to proper use of the epinephrine autoinjector may be related to the design of the autoinjector itself.

Aim: We investigated whether minor modifications in the design of the currently available epinephrine autoinjector ease its use and abrogate common use errors.

Methods: All interns other than those who had previously worked in allergy department in a medical school were invited to the study. Two identical epinephrine autoinjector trainers (Epipen trainer®) were used, one of which was modified by changing the gray safety cap to red and placing a yellow arrow pointing to the black injection tip. A written and visual instruction sheet for each trainer was provided. Participants were asked to demonstrate the use of the Epipen trainer either with the original or with the modified one. They were scored and timed for their demonstration.

Results: Out of the 224 interns who were invited to participate, one hundred and sixty-four interns (73.2%) participated in the study. The number of participants correctly demonstrating the use of epinephrine autoinjectors was 22.6% and 65% in unmodified and modified trainer groups, respectively ($p < 0.001$). The mean time to administer trainers was 26.78 ± 10.6 and 15.88 ± 2.55 s; total median scores were 3.08 ± 1.48 and 4.47 ± 0.84 in unmodified and modified groups, respectively ($p < 0.001$ for both). Significantly fewer participants had presumptive unintentional injection injury while using modified (5%) compared with unmodified trainer (45.2%) ($p < 0.001$).

Conclusion: Few and simple modifications in the design of epinephrine autoinjector were found effective in increasing its correct use and decreasing common use errors by untrained users. (Clinical trials identifier: NCT01217138).

Epinephrine autoinjectors are often prescribed to patients for pre-hospital management of anaphylaxis (1). Their proper and timely use is very important to prevent mortality from anaphylaxis (2). However, it is still underprescribed in the high-risk group of food-allergic adolescents (3). Although most parents of children with food allergies are aware of the importance of carrying epinephrine autoinjector at school (4), the decision to manage an allergic reaction with epinephrine autoinjector among teenagers with food hypersensitivity depends upon individual tolerance of risk (5). Also, lack of understanding and training on how to use autoinjectors by patients and parents was reported as a factor to underuse them (6–8). Worse still, most of the physicians do not know

how to use epinephrine autoinjectors, either (9–12). Very recently, the key impediments to the use of epinephrine autoinjectors were discussed in a review (13). One of the impediments is inadequate education and training of users and health care providers (13, 14). Training for health care professionals (15), patients, and caregivers (9) was shown to improve the correct use of adrenalin autoinjector. Nevertheless, another impediment in the use of epinephrine autoinjector may be related to its design (11–17). One of the justifications to think about a probable suboptimal device design is mistakes in epinephrine autoinjector's use in real life. Unintentional self-injection injury is among the most reported mistakes (14, 16). Another justification is repeated

mistakes during autoinjector use even by physicians despite one-to-one training (15). This study therefore aimed to investigate the hypothesis whether minor modifications in the design of the epinephrine autoinjector improve its correct use and abrogate common use errors.

Methods

At the end of a theoretic lecture on anaphylaxis, we invited all interns of 2009–2010 terms in our faculty to participate in our study. Theoretic lecture included practical issues of anaphylaxis such as diagnosis, management, and avoidance as well as indications of epinephrine autoinjector prescription but did not cover how to use it. The only inclusion criterion of the interns to participate in the study was to give an informed consent. Exclusion criteria were a previous experience of working in an allergy department, previous training on the use of epinephrine autoinjector, and having an epinephrine autoinjector for self or a family member use currently or previously. We used two trainers (Epipen trainer®; Meridian Medical Technologies Inc., Columbia, MD, USA) in the study exactly identical to the original epinephrine autoinjector except medication and needle. In order for both trainers to look alike, we wrapped them in gray adhesive paper. This way, the instruction sheet on the trainer, which was written in English, was also covered as it could have distracted participants and might have affected their performance. After that, we modified one of the trainers by both changing gray safety cap to red with spray paint and placing a yellow arrow pointing to the black injection tip (Fig. 1). We provided three-step written and visual instruction sheet to demonstrate the use of epinephrine autoinjector in Turkish exactly as it was given on the original trainer. We changed the instructions of the second trainer according to the modifications we made. We used a system originally devised by Sicherer et al. (8) to score the use of epinephrine autoinjector and modified it by excluding the first step that is recognition of device because epinephrine autoinjector is not available in pharmacies in Turkey (Table 1). In this way, a maximum score of five points was possible (one point for each step). We randomly allocated participants into one of the two intervention groups (group 1 = unmodified epinephrine autoinjector; group 2 = modified epinephrine autoinjector). All participants were unaware of the type of intervention. We asked them to demonstrate the use of epinephrine autoinjector trainer on themselves after reading the three-step written and visual instruction sheet that we provided. No attempts were made to increase their stress during assessment. Each participant was scored and timed separately by one of the authors (MA, FC, OD).

The primary study parameter was the rate of participants' correct demonstration of the use of the epinephrine autoinjector, which was defined as participants' successive achievement of the five steps of the scoring system (i.e., taking a maximum score of 5) originally devised to assess the use of epinephrine autoinjector. Secondary study parameters were the mean total score, mean time required to administer autoinjector, and presumptive unintentional self-injection of

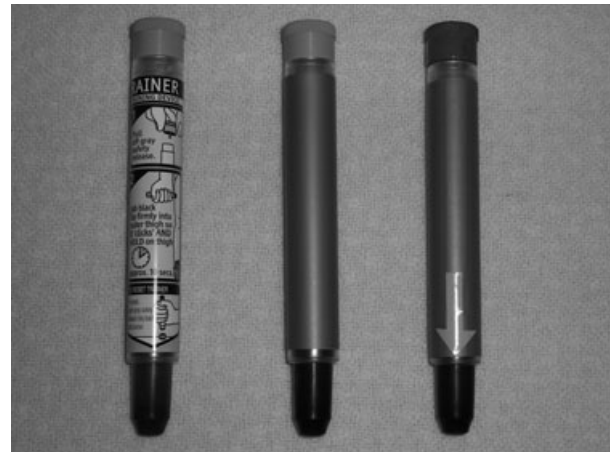


Figure 1 From left to right: Original Epipen trainer; Epipen trainers used in the study: wrapped with a gray sticky paper (unmodified) and wrapped with a gray sticky paper and modified by marking the injection end with a yellow arrow and changing the color of safety cap from gray to red (modified).

Table 1 Scoring system*

1. Removed gray cap
2. Select outer thigh as body part
3. Placed black end into outer thigh
4. Pressed to activate
5. Held pen for >5 s

*Modified from Sicherer et al. (8).

autoinjector into thumb (defined as tackling with black tip of autoinjector trainer in order to eject needle after removing safety cap). The research protocol was approved by ethics committee of Gazi University Faculty of Medicine (Number-Date: 232-05/25/2009), and all participants gave informed consent (Clinical trials identifier: NCT01217138).

Statistical analysis

Statistical analysis was performed by Statistical Package for Social Sciences (spss) 11.5 software (SPSS Inc., Chicago, IL, USA). Whether or not the metric discrete variables were shown as mean $\pm$ s.d., the number of cases and percentages were used for nominal data. The mean differences between groups were compared using Student's t-test. Nominal data were evaluated by Pearson Chi-square or Fisher's Exact test, where applicable. A p value of <0.05 was considered as statistically significant.

Results

We screened 224 interns for eligibility and enrolled 168 for the study (Fig. 2). There were no interns who were trained on the use of epinephrine autoinjector previously or have

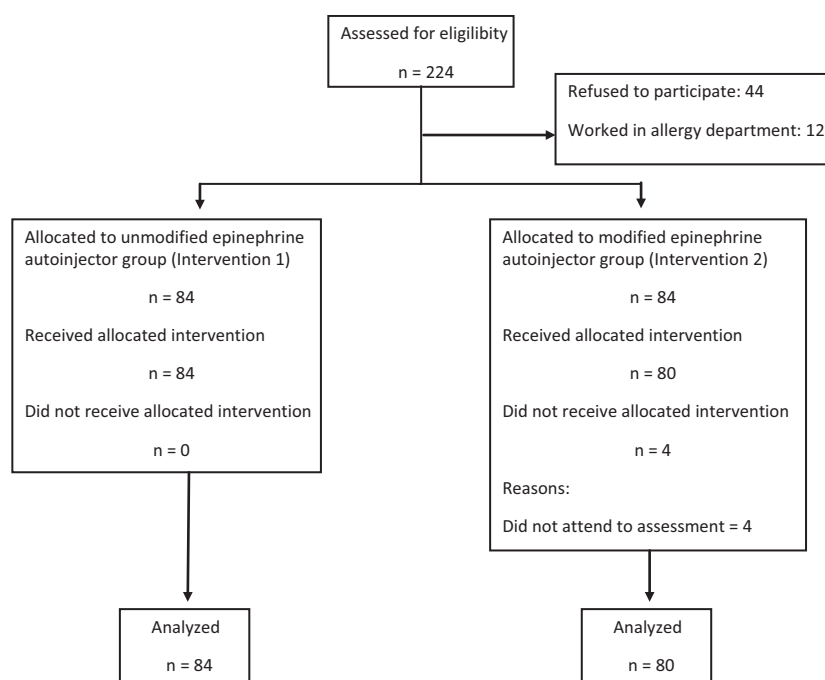


Figure 2 Study flowchart.

epinephrine autoinjector for self or family use. They were randomized to either unmodified (n:84) or modified (n:84) epinephrine autoinjector groups. Although accepted, four interns randomized to modified epinephrine autoinjector group did not attend the study, so the study was completed with 164 interns (73.2%). Eighty-three of the participants were men (50.6%), and the mean age was 24.4 ± 1.19 yr. The study groups were similar in both age and sex ($p = 0.123$ and $p = 0.276$, respectively) and experience of treating allergic reactions ($p = 0.466$). All participants needed to read instruction sheet before they demonstrated the use of trainers. The group using the modified epinephrine autoinjector trainer did significantly better than the group using the unmodified epinephrine autoinjector trainer for primary and secondary outcome parameters of the study ($p < 0.001$ for all) (Table 2). The modified epinephrine autoinjector group was also better than the unmodified epinephrine autoinjector group in removing security cap ($p = 0.003$), placing black injection tip into outer thigh ($p < 0.001$), pressing to activate ($p < 0.001$), and holding autoinjector for > 5 s ($p < 0.001$) except selecting outer thigh as body part for injection ($p = 0.115$) (Table 2).

Discussion

This is the first study that investigated the effect of changes in the design of previously available epinephrine autoinjector (EpiPen) on its proper use. The modifications in the design were few, simple, and inexpensive. We demonstrated that minor modifications in the design of epinephrine autoinjector improved its correct use, decreased common use errors, and

shortened the time required to administer it by untrained users.

Unintentional self-injection is the most common mistake reported in real life during epinephrine autoinjector use (14, 16). Simons and colleagues (14) observed that the number of unintentional injections is increasing in parallel with the increased rate of anaphylaxis and high and increasing dispensing rate of epinephrine autoinjectors. Attempt to inject with the wrong end of the epinephrine autoinjector after removing safety cap leads to unintentional self-injection injury. Actually, it was reported that some users thought gray safety cap as a protective cover over the needle orifice (18, 19). In our view, gray is an indistinct color for a safety cap and may not attract attention at the first glance. Also, it is a transition color to black and can easily be mistaken as the injection tip by the users. However, changing the color of safety cap from gray to red and placing a yellow arrow pointing toward black injection tip decreased unintentional needle stick injury 9-folds (45.2% in unmodified vs. 5% modified device). These simple modifications not only decreased probable self-injection injury during demonstration but also shortened the time of the application of the autoinjector by almost 12 s by untrained users.

Frew (13) defined an ideal epinephrine autoinjector as delivering correct dose of adrenaline to the correct tissue compartment within correct time frame as well as being easy, convenient, robust, safe, and reliable to withstand real-life use. Among these five features, simplicity and safety of use increases patients' compliance and correct use by increasing comprehension and decreasing anxiety and fear to use adrenalin autoinjector. In this regard, the changes in our study

Table 2 Comparison of study parameters between modified and unmodified epinephrine autoinjector groups

	Unmodified epinephrine autoinjector group n = 84	Modified epinephrine autoinjector group n = 80
Primary study parameter		
Correct demonstration of autoinjector use, n (%)	19 (22.6)	52 (65.0)*
Secondary study parameters		
Time (s) to administer (mean $\pm$ s.d.)	26.78 $\pm$ 10.6	15.88 $\pm$ 2.55*
Total score (mean $\pm$ s.d.)	3.08 $\pm$ 1.48	4.47 $\pm$ 0.84*
Presumptive self-injection into thumb, n (%)	38 (45.2)	4 (5.0)*
Assessment steps		
Removed security cap, n (%)	71 (84.5)	79 (98.8)†
Select outer thigh as body part, n (%)	62 (73.8)	68 (85.0)
Placed black end into outer thigh, n (%)	56 (66.7)	77 (96.3)*
Pressed to activate, n (%)	32 (38.1)	72 (90.0)*
Held pen for >5 s, n (%)	38 (45.2)	62 (77.5)*

*p < 0.001 and †p < 0.05 compared with unmodified epinephrine autoinjector group.

decreased confusion about the injection tip and safety cap of the device by the users and attenuated the need to interrupt the demonstration to check the instructions again. These changes improved almost all steps of demonstration except selecting outer thigh as body part. This result was not unexpected because the modifications in our study did not focus on improving the selection of injection area. Also, selecting outer thigh as the injection site was probably not difficult for interns as participants of our study.

At the time we were conducting our study (study start date: June 2009 and completion date: May 2010), previous generation Epipen autoinjector was available. New generation Epipen has become available since April 2010 (20). The new device has five modifications. Our modifications to ease identification of injection tip by yellow arrow and changing color of safety cap from gray to red to prevent confounding of safety cap with injection tip are similar to two of new generation Epipen autoinjector's but lack modifications to facilitate the grip, carry case, or built-in needle protection all of which certainly require a high capital and technology in hand. Even these two modifications in our study resulted in much easier and safer use of epinephrine autoinjector. To our knowledge, there is no published study comparing new generation Epipen to previous generation Epipen. In this respect, our study gives a hint that new generation Epipen will probably be much more robust, convenient, and safer to use by patients than the previous generation Epipen.

The problems with the existing epinephrine autoinjectors also led other researches to work on developing new epinephrine delivery systems (21). Gosbee et al. (19) commented that human limitations and capabilities were important design issues. Thus, two novel epinephrine autoinjector prototypes (INT01 and INT02) designed according to human factors engineering methods were tested by 7- to 55-yr-old

participants (21) and practicing nurses with experience using epinephrine autoinjectors (22). In both the studies, novel epinephrine autoinjector prototypes were preferred as a safer alternative to previous generation Epipen and Twinject by the study participants.

Although this is the first study documenting the effect of changes in design of previous generation Epipen on its proper use, it has also some limitations. First, the study participants are interns and not patients or their caregivers. Second, we did not train the participants prior to assessment, which limits its generalization to a real setting where the person should be trained before given an autoinjector. Third, the investigation could not be conducted under simulated conditions. Fourth, the scoring system that we used to determine the changes in correct use of epinephrine autoinjector may be inadequate to assess functional performance of these devices, which probably requires development of better, validated tests as Frew (13) stated. Nevertheless, this study showed that few and simple modifications in the design of epinephrine autoinjector were found effective in increasing its correct use and decreasing common use errors by untrained users. Still, future repeat studies with the new generation of Epipens available would be interesting in order to add further value for the practicing allergist. Certainly, real-life experiences in a stressful condition like anaphylaxis could be different, and even the best designed epinephrine device may fail without training patients on its proper use.

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