

Effect of epinephrine autoinjector design on unintentional injection injury

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ABSTRACT

Epinephrine is an essential medication for the treatment of anaphylaxis. Factors associated with autoinjector design may have a role in its correct use. We compared a new and old epinephrine autoinjector with respect to correct autoinjector use. We invited all interns of the 2011–2012 training period in our medical school. The participants were randomly assigned into two groups. After all participants were given a three-step written and visual instruction sheet about epinephrine autoinjector use, they were asked to show its use either with the old or the new epinephrine autoinjector trainer. The old and new trainers, which were exactly identical to the original epinephrine autoinjectors except for the medication and needle, were used. The performance of each participant was assessed with a standardized scoring system. Among 220 invited interns, 180 (81.8%) were enrolled. The number of participants correctly showing the use of epinephrine autoinjectors and the mean total score did not differ significantly between the two groups ($p = 0.639$ and $p = 0.233$, respectively). Significantly fewer participants had unintentional injections in the new compared with the old epinephrine autoinjector group ($p < 0.001$). When all assessment steps are considered, only the rate of placing a wrong tip into the outer thigh was significantly lower in the new compared with the old epinephrine autoinjector group ($p < 0.05$). The new epinephrine autoinjector is more effective in unintentional injection injuries than the old one; however, it still does not fulfill the criteria of an ideal epinephrine autoinjector.

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Epinephrine is the single life-saving drug known for the treatment of anaphylaxis.¹ Therefore, all guidelines recommend prescription of epinephrine autoinjectors for patients who have a risk of recurrence of anaphylaxis.^{1–3} This leads not only to an increase in the frequency of epinephrine autoinjector prescription but also errors in its use.^{4,5} The most important factors associated with incorrect epinephrine autoinjector use are lack of physician, patient, and/or caregiver training in autoinjector application and deficiency of autoinjector design.^{6,7} Most studies and reports of real-life experiences show that common mistakes are repeatedly encountered in similar steps of epinephrine autoinjector use.^{8–13} Thus, it may be inferred that currently available epinephrine autoinjectors do not possess the features of a life-saving device. A recently published report indicated that simple modifications to the design of epinephrine autoinjectors significantly improve accurate administration rates.¹⁴

To attenuate the design-associated errors in autoinjector use, drug companies have been working to develop new devices. EpiPen (Dey Pharm LP, Napa, CA)

is the most commonly used form of epinephrine autoinjectors throughout the world. A new EpiPen was marketed in April 2010.¹⁵ However, the new EpiPen is still not available in some countries such as Turkey. To our knowledge, no research has been conducted to investigate whether the new EpiPen improves autoinjector use compared with the old EpiPen. Therefore, in this study we aimed to compare the new and old EpiPen with respect to correct autoinjector use.

METHODS

We informed all interns of 2010–2011 in our faculty about the study and enrolled the those who gave informed consent. Exclusion criteria were a previous experience of working in an allergy department, previous training on the use of the epinephrine autoinjector, and having an epinephrine autoinjector for self or a family member currently or previously. We used old and new trainers (EpiPen trainer; Meridian Medical Technologies, Inc., Columbia, MD) that were exactly identical to the original epinephrine autoinjectors except for the medication and needle (Fig. 1). We provided a three-step written and visual instruction sheet about epinephrine autoinjector use. The instruction sheet was translated from the original trainer package insert. We used a scoring system that was used in previous studies.^{10–12,14,16} In this scoring system a maximum score of 5 points was possible (1 point for each step). Participants successively doing 5 steps were accepted to show autoinjector use correctly. We randomly allocated par-

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Figure 1. New (left) and old EpiPen trainers (right).

ticipants into one of the two groups (old EpiPen and new EpiPen). We asked them to show the use of the epinephrine autoinjector trainer on themselves after reading the 3-step written and visual instruction sheet that we provided. All participants were unaware of the type of epinephrine autoinjector trainer. Each participant was scored and timed separately by one of the authors. The research protocol was approved by Ethics Committee of Gazi University Faculty of Medicine (Number/Date: 365/December 14, 2011).

The primary study parameter was the rate of participants showing correct epinephrine autoinjector use. Secondary study parameters were the mean total score, mean time to administer epinephrine autoinjector, and presumptive unintentional injection injury rate, which is defined as touching or playing with the injection tip of the autoinjector trainer to eject the needle after removing the safety cap.

Statistical Analysis

Statistical analysis was performed by Statistical Package for Social Sciences (SPSS) 11.5 software (SPSS, Inc., Chicago, IL). Whether the metric discrete variables were shown as mean $\pm$ SD, number of cases and percentages were used for nominal data. The Kolmogorov-Smirnov test was preferred as the test of normality, which was used to determine whether continuous variables were distributed normally or nonnormally. Groups with categorical variables were compared using Mann-Whitney U

test. Nominal data were evaluated by Pearson chi-square or Fisher's exact test, where applicable. The level of statistical significance was set at $p < 0.05$.

RESULTS

Among 220 invited interns, 32 (14.5%) who did not give consent and 8 (3.7%) who worked previously in the Allergy Department were excluded. The remaining 180 (81.8%) participants were randomized to either the old ($n = 90$) or the new EpiPen ($n = 90$) groups. One hundred seven of the participants were men (59%) and the mean age was 23.7 ± 1.64 years. The mean age and sex were similar between two groups ($p = 0.175$ and $p = 0.129$, respectively). The number of participants correctly showing the use of the epinephrine autoinjector and the total score did not differ significantly between the two groups ($p = 0.639$ and $p = 0.233$, respectively; Table 1).

Mean time to administer the epinephrine autoinjector was significantly shorter in the new EpiPen compared with the old EpiPen (16.8 ± 2.9 seconds and 15.5 ± 2.8 seconds, respectively; $p = 0.001$). The number of participants performing presumptive unintentional injection injury differed significantly between the two groups (old EpiPen, 18; new EpiPen, 2 participants; $p < 0.001$). None of the assessment steps, except placing the wrong injection tip into the outer thigh, differed significantly between groups ($p > 0.05$; Table 1).

DISCUSSION

This is the first study comparing the effects of the new and old EpiPen on correct epinephrine autoinjector use. The new EpiPen was not found to be superior to the old EpiPen considering the primary study parameter that is the number of participants showing its use correctly. Supporting this finding, the mean total score of both new and old EpiPens were similar. However, presumptive unintentional injection injury rate was nine times less with the new EpiPen compared with the old one. Mean time to administer the epinephrine autoinjector was also 1.5 seconds shorter with the new device, which may not have a clinical importance but was statistically significant.

The main innovation with the new EpiPen seems to be related to colored tips of the autoinjector. The change in colors of the injection and safety tips compared with the old EpiPen enabled users to abstain from unintentional injection injury. Significant decrease in placement of the wrong end of the autoinjector in the new EpiPen is also related to this finding. Surprisingly, the new EpiPen showed no superiority in the percent of correct demonstrations or in the other assessment steps. This was an unexpected result for us because we used the same parameters in our previous

Table 1 Comparison of study parameters between old and new EpiPen groups

	Old EpiPen Group (<i>n</i> = 90)	New EpiPen Group (<i>n</i> = 90)
Primary study parameter		
Correct demonstration of autoinjector use, <i>n</i> (%)	57 (63.3)	60 (66.7)
Secondary study parameters		
Unintentional injection, <i>n</i> (%)	18 (20)	2 (2.2)*
Time (s) to administer (mean $\pm$ SD)	16.83 $\pm$ 2.94	15.51 $\pm$ 2.81†
Total score (mean $\pm$ SD)	4.34 $\pm$ 0.97	4.59 $\pm$ 0.65
Assessment steps		
Removed safety cap, <i>n</i> (%)	84 (93.3)	89 (98.9)
Selected outer thigh as body part, <i>n</i> (%)	89 (98.9)	89 (98.9)
Placed appropriate injection tip into outer thigh, <i>n</i> (%)	74 (82.2)	87 (96.7)†
Pressed to activate, <i>n</i> (%)	78 (86.7)	75 (83.3)
Held pen for >5 s, <i>n</i> (%)	65 (72.2)	73 (81.1)

**p* < 0.001 and †*p* < 0.05 compared with the old EpiPen group.

study and found that the modified-design EpiPen was significantly superior to the old EpiPen in all parameters.¹⁴ Certainly, the modified-design EpiPen that we used in our previous study was different from the new EpiPen but the aim of such modifications was similar. We looked back at our data and realized that the conflicting results between the two studies were emanating from the old EpiPen group. The only difference between the methodologies of our previous study and this one was the content of instruction sheets given to the participants. The written parts of the instruction sheets were exactly the same because they were given in the original package inserts translated into Turkish for both old and new EpiPens. However, the visual parts of the written explanations were in the form of colored photographs that differed from our previous study where we used the drawings provided on the original EpiPen inserts. We did not perform this modification (change from colored drawings to colored photographs) on purpose (Fig. 2). Therefore, we did not know that the visual demonstration in the form of colored photographs would lead to such an improvement in correct use of old EpiPens. As a result, this coincidental finding indirectly points to the importance of instruction sheets for correct autoinjector use.

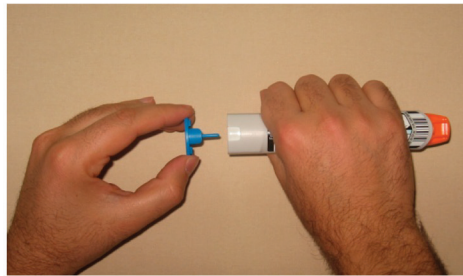
Attempts to inject with the wrong end of the epinephrine autoinjector result in unintentional injection injury that is the most common mistake reported in real life^{5,13} and in studies.^{10–12,14} In a comprehensive study, authors documented a total number of 15,190 unintentional injections, 60% of which were between years 2003 and 2007, which tended to increase annually. This was attributed to increased prevalence of anaphylaxis and increased dispensing rates for the epinephrine autoinjector.¹³ Several factors related to epinephrine autoinjector design deficiency leading to un-

intentional injection injuries are identified: *e.g.*, autoinjectors have a pen-like appearance but do not function like a pen, exposure to the needle after administration of epinephrine, and confusion of the safety cap as a cover over the needle orifice.^{5,7,13,17,18}

Other important factors related to unintentional injection injuries with EpiPen autoinjectors are contrast failure between the gray safety cap and the black tip with the needle.^{11,14} To overcome these design-related challenges, the new EpiPen includes a needle shield that conceals the needle after the administration of epinephrine, thus hindering postinjection needle-stick injuries. Additionally, the colors of the ends with the safety cap and needle are rendered more conspicuous such as blue and orange. We found that the unintentional injection rate was nine times, number of participants who omitted to remove the safety cap and placed the wrong end into the outer thigh were both six times less with the new EpiPen than the old EpiPen. Our results indicate that modifications in the design of epinephrine autoinjectors make them safer and more handy. However, the use of training equipment and not the active autoinjector may not directly reflect information on unintentional release of the needle in real life. Therefore, we can only talk about presumptive unintentional injection injury in our study.

Inadequate pressure to activate and inadequate time to hold the autoinjector in place were the other common application mistakes documented by us and others, which ranged between 21–63.3% and 50–72%, respectively.^{8,10–12,14,16,19} In this study the rates of these two application errors did not differ significantly between the groups. This might be because of the fact that participants were aware that this was a study and not a real-life experience or it might be attributed to the fact that improvements attained by new design auto-

A.

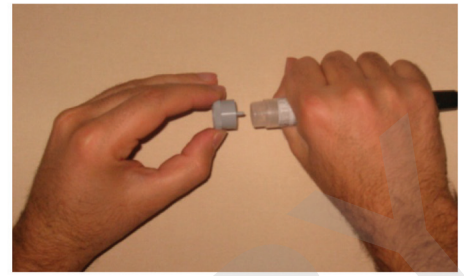


Pull off blue safety release



Swing and firmly push orange tip against outer thigh so it 'clicks'. Hold on thigh 10 seconds to simulate drug delivery.

B.



Pull off gray safety release



Jab black tip firmly into outer thigh so it 'clicks' and hold on thigh approximately 10 seconds.

Figure 2. Instruction sheets of the (A) new and (B) old EpiPens.

injectors do not influence these application steps. To overcome these application errors, the width of the needle bore may be increased to decrease the time needed to inject epinephrine to the tissue compartment. Also, a novel epinephrine autoinjector (Intelliject Inc., Richmond, VA) with a verbal instruction system is underdevelopment to surmount these application errors.²⁰ However, the etiology of inadvertent epinephrine autoinjector use is so complicated that it can not be explained only by design-related factors.¹ Education and training of physicians, patients, and/or caregivers^{6,16,21,22} as well as development of a standardized assessment criteria for a more prudent investigation of efficacy of the epinephrine autoinjectors⁷ are the other important factors that can not be negligible.

There are some limitations of our study. All participants were interns but not patients and/or their care-

givers. Also, interns were tested with written and visual instructions but not with individual training by oral instructions and demonstration by a doctor or nurse. However, in practice, this ideal education by hands-on training is not given in most ambulatory and emergency clinics except allergy departments. In addition, results of this study may not reflect the advantages and disadvantages of the new EpiPen over the old version in real-life applications because an episode of anaphylaxis is a genuine life-or-death issue producing extreme anxiety for both the patient and the caregiver that may result in unintentional injection injuries.

The new EpiPen was more effective in preventing application errors such as removing the safety cap, placing the wrong tip into the outer thigh, and unintentional injection injuries than the old EpiPen. However, it still does not fulfill the criteria of an ideal

epinephrine autoinjector. In addition, this study pointed to the importance of the visual demonstration of the instruction sheets for correct application of the autoinjector.

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