

COMPARISON OF ADRENALINE AUTO-INJECTOR DEVICES: EASE OF USE AND ABILITY TO RECALL USE

Marnie N Robinson¹, Shyamali C Dharmage², Mimi LK Tang^{1 3 4}

1. Department of Allergy and Immunology, Royal Children's Hospital, Melbourne Australia
2. Unit of Allergy and Lung Health, Centre for Epidemiology and Biostatistics, School of Population and Global Health, University of Melbourne, Australia
3. Department of Paediatrics, The University of Melbourne, Australia
4. Allergy and Immune Disorders, Murdoch Children's Research Institute, Melbourne Australia

Corresponding author:

Mimi Tang

Department of Allergy and Immunology

Royal Children's Hospital

Flemington Road

Parkville 3052

Australia

+61 03 9345 5733

mimi.tang@rch.org.au

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Abstract

Background: A limited number of adrenaline auto-injectors are currently available. EpiPen and Anapen are available in Australia, New Zealand, UK, and parts of Europe and Asia. Few studies have compared the performance of these devices

Objective : to compare the intuitiveness of use of these devices. A secondary aim was to compare the ability to recall use of each device after a period of 3 months.

Method: A random sample of 100 subjects naïve to both the EpiPen and Anapen were recruited from staff and families attending Royal Children's Hospital, Melbourne Australia

Subjects were randomized to Anapen (n=53) or EpiPen (n=47) and asked to demonstrate use of a "trainer" device (i) prior to and (ii) after receiving training in its correct use. A subset (n=32) participated in a follow up study to evaluate (iii) the ability to recall correct use of each device. **Results:** Most subjects correctly demonstrated all steps in use of the EpiPen and Anapen both prior to (89% vs 79%, $p=0.17$) and after training on use (100% vs 100%). However, after 3 months, significantly more participants correctly demonstrated use of EpiPen (87%) compared to Anapen (35%) ($p=0.003$) and critical errors that would likely result in failure to administer adrenaline were more common with Anapen (59% vs 13%, $p=0.01$).

Conclusion: Most study participants correctly demonstrated the use of both devices without prior training. There was greater attrition in correct use of Anapen compared to EpiPen over time. Critical errors in administration were more likely with Anapen than EpiPen.

Highlights box

- previous studies have documented errors with use of adrenaline auto injector devices by patients, parents and medical professionals.
- Anapen and the re designed EpiPen are easy and intuitive to use, with or without prior instruction. A marked decline in the ability to correctly demonstrate use of the Anapen (but not the EpiPen) after a 3 month period was observed. Critical errors that would result in failure to deliver adrenaline were more common with the Anapen device.
- patients prescribed adrenaline auto injectors should review and practice use of their device at least at 3 monthly intervals

Keywords

Adrenaline auto injector, Epipen , Anapen, anaphylaxis

INTRODUCTION

Adrenaline auto-injectors deliver a pre-measured dose of adrenaline and are prescribed for the management of anaphylactic reactions occurring outside a health care setting. The pre-measured design allows use by people without medical training. In recent decades, there has been a significant increase in the prevalence of documented food allergy¹ and anaphylaxis² in industrialised^{1 2} and developing countries³. This coincides with a significant increase in the number of adrenaline auto-injector devices prescribed^{4 5i}

Several studies have documented difficulties with use of adrenaline auto-injectors^{6 7} and inability of parents⁶ and medical practitioners⁸⁻¹⁰ to correctly administer the Epipen auto-injector. Alarming high rates of mistaken self injection with Epipen auto-injectors have also been reported^{8 9}. These findings highlight the importance of patient/carer education on when and how to use these devices.

Epipen and Anapen are the predominant devices used in Australasia, United Kingdom and parts of Europe. The Epipen and Anapen have a different appearance and method of administration. Based upon aforementioned difficulties associated with Epipen use, the device was redesigned and a 'new look' Epipen was introduced into Australia and the UK in 2011 and 2012 respectively. Anapen was listed for use in Australia in 2010 but has been licensed in the UK and Europe since 2003¹¹.

Both devices require a multistep technique for administration with instructions printed on the side of the device. An important difference, is that Anapen has two caps that require activation for use - a needle protection cap (that covers the needle) and a safety cap (that prevents accidental firing); whereas the Epipen has a single safety cap (that prevents accidental firing). Anapen therefore requires an extra operational step. Once activated by release of the safety cap, the method of delivery of adrenaline also differs between the devices with a syringe mechanism in the Anapen and a cartridge mechanism in the Epipen.

Few studies have compared the functionality or usability of adrenaline auto-injector devices. One study compared the functionality of the Anapen with the original design Epipen¹² and concluded that Epipen was significantly more capable of consistently and rapidly delivering a dose of adrenaline than the Anapen device under standardized conditions. In another study, Brown compared the ability of mothers to use the original Epipen or Anapen after a 30 minute individualized demonstration on use of the respective device

and concluded that the Anapen was easier to use than the EpiPen¹³. There are no studies comparing the Anapen device with the redesigned EpiPen.

In this study, we compared the redesigned EpiPen and Anapen, and assessed whether one of these devices was more intuitive to use than the other and whether the use of one device was more easily recalled after a period of elapsed time.

METHOD

Study Setting and Sample

This study was conducted at the Royal Children's Hospital in Melbourne, Australia. Participants were recruited from visitors, parents and hospital staff over a 3 month period. We aimed to compare the use of the redesigned EpiPen and Anapen by individuals who had not received prior training in their use. Exclusion criteria were: attendance at allergy/ immunology outpatient clinics, personal history or having a child with food allergy or insect anaphylaxis/anaphylaxis from any cause, previous prescription/education in use of an adrenaline auto injector, and staff members working in allergy/ immunology, respiratory or emergency departments.

Data Collection

Participants were recruited and randomized using a computer generated random number sequence to the Anapen or the EpiPen group. Demographic data was collected including age, education level and occupation. Participants were assessed by a single investigator (i) prior to, (ii) immediately after and (iii) 3 months after receiving training in use of their assigned "trainer" device. Participant's ability to use the adrenaline auto-injector was assessed using a 5 step scoring system for the EpiPen (adapted from Sicherer et al) and a 6 step scoring system for the Anapen (devised for study) (supplementary table 1).

Assessment 1: Participants were allowed 2 minutes to familiarize themselves with the trainer device (Anapen or EpiPen – see figure 1). During this time, participants were able to review instructions printed on the side of the device and practice its use; no instruction on use was provided. Participants were then asked to demonstrate use of the device. This assessed the "intuitiveness" of use for each device in the absence of specific training.

Assessment 2: Participants were instructed on how to correctly use the trainer device by an Allergist and asked to demonstrate the use of the trainer device immediately afterwards. This assessed the participant's ability to use the device following appropriate instruction.

Assessment 3: A subset of participants participated in a second phase of the study.: 40 participants agreed to take part ; 32 were able to be contacted 3 months after initial recruitment and all participated in phase 2 of the study. Prior to reassessment, it was confirmed that the participant hadn't been exposed to the respective adrenalin auto-injector/trainer device during the intervening period. Participants were given the trainer device and asked to immediately demonstrate its use (without opportunity to read instructions). This part of the study assessed "recall" of the use of the respective device.

This study was approved by the Royal Children's Hospital ethics committee and all participants gave informed consent prior to commencing this study.

Statistical Analysis

Data was analysed using STATA version 12. Socio demographic characteristics were compared to ensure comparability between the two groups (both in the first and second phases of the study). The proportion of subjects for each outcome assessment was compared between the 2 groups at each of the time points, using Pearson's chi squared statistic. The conventional cut off of $p < 0.05$ was used to determine statistical significance.

RESULTS

Study Population

140 people were approached to be involved in the study. 40 were excluded due to: child with food allergy (20) personal prescription/use of adrenaline auto injector (2) and because of previous education in the use of an adrenaline auto-injector (18). 100 subjects were recruited and randomized : Anapen (n=53) or Epipen (n=47) group. Table 1a shows demographic data for study participants.

Ability to correctly use a device prior to and after instruction on use

Overall, 84 participants (84%) correctly demonstrated the use of their assigned adrenaline auto-injector trainer device without prior training - 42 of 53 (79.25%) correctly demonstrated all 6 steps involved in

Anapen use, 42 of 47 (89.36%) correctly demonstrated all 5 steps involved in Epipen use (table 2). There was no significant difference between groups in the ability of the naïve participants to use each device ($p=0.17$).

Following specific instruction in use of individual trainer device, all participants (100%) in both the Anapen and Epipen group correctly demonstrated use of their assigned adrenaline auto-injector device.

Ability to recall correct use of a device

32 participants were reassessed at 3 months (Anapen $n=17$; Epipen $n=15$). There were no significant differences between groups for age or educational level (Table 1b). There were no significant differences between participants and non participants in the follow-up study (data not shown). After 3 months, the ability to recall all steps in the use of the assigned auto-injector device was significantly lower in the Anapen group compared to Epipen group (Anapen 6 of 17 (35%) vs Epipen 13 of 15 (87%), $p=0.003$) (Table 2).

Comparison of the specific errors made with each device

There are “critical steps” for each device that if performed incorrectly result in failure to deliver adrenaline to the recipient. There are 3 critical steps in Epipen use : (1) removal of blue safety cap, (2) placement of orange needle end on upper thigh, (3) exerting downward pressure to activate . There are 4 critical steps for Anapen: (1) removal of grey safety cap, (2) removal of black cap covering needle end, (3) placement of black needle end on thigh (4) pushing red button to activate. We compared critical errors made by participants for each device (Table 3).

The proportion of subjects who would have failed deliver adrenaline as a result of incorrectly performing one or more of these “critical steps” was compared (table 4). At initial assessment, 6% of subjects administering the Epipen failed to deliver adrenaline compared to 17% of subjects using the Anapen ($p = 0.13$). After 3 months, 13% of subjects demonstrating the Epipen compared to 59% of subjects demonstrating the Anapen ($p=0.01$) would have failed to deliver adrenaline.

Table 1a: Demographic characteristics of all participants

Age of participants	Anapen group (n=53)	Epipen group (n=47)	Total (n=100)
<30 years	18 (18%)	17 (17%)	(35) 35%
30-40 years	17(17%)	10 (10%)	(27) 27%
40-50 years	4 (4%)	11 (11%)	(15) 15%
50-60 years	10 (10%)	6 (6%)	(16) 16%
>60 years	4 (4%)	3(3%)	7 (7%)
Highest educational level achieved by participants			
Year 10	11 (11%)	8 (8%)	19(19%)
Year 12	11(11%)	10 (10%)	21(21%)
Technical institute	1 (1%)	0	1 (1%)
University	28 (28%)	25 (25%)	53 (53%)
Post graduate	2(2%)	4(4%)	6 (6%)

Table 1b: Demographic data for participants of 3 month follow up study

Age of participants	Anapen group (n=17)	Epipen Group (n=15)	Total (n=32)
<30 years	3 (9%)	3(9%)	6 (19%)
30-40 years	8 (25%)	3 (9%)	11 (34%)

40-50 years	2 (6%)	5 (16%)	7 (22%)
50-60 years	4 (12%)	3(9%)	7(21%)
>60 years	0	1 (3%)	1 (3%)
Highest education level achieved			
Year 10	3 (9%)	3 (9%)	6 (19%)
Year 12	5 (16%)	4 (12%)	9 (28%)
University	8 (25%)	6 (19%)	14 (44%)
postgraduate	1(3%)	2 (6%)	3 (9%)

Table 2: Ability to completely correctly use the Anapen or Epipen adrenaline auto-injector device

Score	Anapen group	Epipen group	P value
Completely correct use at baseline without prior instruction	42/53 (79%)	42/47 (89%)	0.17
Completely correct use after instruction	53/53 (100%)	47/47(100%)	NA
Completely correct use at 3 months	6/17 (35%)	13/15 (87%)	0.003

Table 3: Errors made in the use of Anapen and Epipen devices

<i>Anapen score</i>	Initial assessment (n=53)	Immediately after instruction (n=53)	At 3 months (n=17)
Failure to remove black needle protector*	2 (4%)	0 (0%)	3 (18%)
Failure to remove grey safety cap*	3 (6%)	0(0%)	3(18%)
Failure to Select upper outer thigh	0(0%)	0(0%)	0 (0%)
Failure to Place black end on thigh*	4 (8%)	0(0%)	5 (29%)
Failure to push red button to activate*	7 (13%)	0(0%)	10(59%)
Failure to hold >10 seconds	5(9%)	0(0%)	5(29%)
<i>Epipen score</i>	Initial assessment (n=47)	Immediately after instruction (n=47)	At 3 months (n=15)
Failure to remove blue safety cap*	0 (0%)	0 (0%)	1 (7%)
Failure to select upper outer thigh	0(0%)	0 (0%)	0 (0%)
Failure to place orange end	3 (6%)	0 (0%)	1 (7%)

on thigh*			
Failure to push down to activate*	0 (0%)	0(0%)	0(0%)
Failure to hold for >10 seconds	4 (9%)	0 (0%)	1 (7%)

* Critical errors marked in bold text

Table 4: Proportion of subjects who made one or more critical errors in administration of Epipen and Anapen

	Anapen Group	Epipen Group	P value
Number of participants making one or more critical error at baseline	9/53 (17%)	3/47 (6%)	0.13
Number of participants making one or more critical error immediately after training	0/53 (0%)	0/47 (0%)	NA
Number of participants making one or more critical error at 3 month follow up	10/17 (59%)	2/15(13%)	0.01

Figure 1 : picture of Anapen and EpiPen “trainer” device (instructions are printed on casing)



DISCUSSION

A number of studies have previously documented difficulties with use of the original EpiPen by patients, care givers and medical practitioners⁸⁻¹⁰ however there is a paucity of such studies for the Anapen adrenaline auto injector device and only one study has compared the usability of these devices¹³. This is the first study comparing adrenaline auto-injector devices in terms of ease and intuitiveness of use prior to training, and the ability to recall correct use after a period of elapsed time. Additionally, it is the first study to assess the re-designed EpiPen. We found both devices were easy and intuitive to use, with or without prior instruction. There was however, a marked decline in ability to correctly use Anapen (but not EpiPen) after a 3 month period. Critical errors that would result in failure to deliver adrenaline to a recipient were more common with Anapen compared to EpiPen both without instruction and when assessed 3 months after instruction.

Most participants were able to correctly demonstrate the use of both devices without prior education when allowed to read the instructions on the device: slightly more participants were able to demonstrate correct use of the EpiPen compared to the Anapen (89% and 79% respectively) however this was not statistically significant. Furthermore, all participants were able to correctly use both the Anapen and EpiPen after instruction. These findings differ from previous studies⁸⁻⁹ of the original EpiPen that reported very high rates of failed EpiPen use. Our findings suggest that design changes in the new EpiPen (that is, clear distinction between colour of safety cap (blue) and colour of needle end (orange), diameter of injection end being clearly narrower than barrel and the addition of a large arrow pointing towards injection end) have made the device

easier and more intuitive to use. Such simple design changes were suggested by Bakirtas who reported that similar design modifications increased the correct use of the original Epipen device¹⁴.

Brown recently compared use of the original Epipen and Anapen in a cohort of mothers who received a 30 minute individual demonstration on anaphylaxis and use of the adrenaline injector device and found that Anapen was significantly easier to use than the older design Epipen¹³. In contrast, all participants in our study correctly used both devices following instruction on use. Our study suggests that the redesign of the Epipen resulted in improved ease and intuitiveness of use.

Despite high rates of correct use for both devices at first encounter and following training, we identified a marked attrition in the proportion of participants who correctly used Anapen when assessed at 3 months that was not observed for Epipen. Only 35% of participants correctly demonstrated all steps in Anapen use at 3 months compared with 87% for Epipen. The most plausible reason for the greater attrition in the Anapen group is that the Anapen requires an extra operational step which is likely to make it more difficult to remember the correct operational sequence.

Critical errors that would result in failure to deliver adrenaline were also more common for Anapen than Epipen. This was the case when subjects were assessed without prior instruction and also when asked to recall use at 3 months after instruction. Of concern, there was a much greater likelihood of failure to deliver adrenaline to a recipient with the Anapen when subjects were asked to recall its use 3 months after formal training in its use than when they used the device for the first time with only 2 minutes to read the instructions (59%vs 17%). This suggests that the Anapen is difficult to use when relying upon recall and also that reading of instructions can greatly assist with correct use. In contrast, the likelihood of failed delivery of adrenaline with the redesigned Epipen was low, whether subjects were using the device without prior instruction or 3 months after instruction (6% and 13% respectively). These findings suggest that the Epipen is easier to use than the Anapen where a subject is unfamiliar with the device and has to rely on reading instructions as well as when relying upon recall of how to use the device following previous instruction.

Interestingly, while there are 3 critical steps in the use of the Epipen, errors were made in only 2 of these steps (placement of orange end of device on thigh and failure to remove blue safety cap). In contrast, errors were made in all 4 critical steps in use of the Anapen. The most common critical error in the use of the Anapen, both initially (without training) and at 3 months, was failure to press the red button to activate the device. Failure to place the needle end of the Epipen onto the thigh was a very common error in previous studies of the original

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design EpiPen^{9 13}, however only 6% of subjects made a similar error with the redesigned EpiPen in this study. Hence, redesign of the EpiPen apparently addressed this concern. One could postulate that similar design changes in the Anapen may also reduce user error.

The opportunity to read instructions (visible on each trainer device and “real life” device) appears to be an important factor supporting correct use, particularly for the Anapen, since the proportion of subjects who correctly used the Anapen at 3 months, when they were not allowed time to study the instructions on the device prior to demonstration, was markedly lower than the proportion of subjects who successfully demonstrated correct use at initial evaluation. In real life situation of anaphylaxis, failure of use may be minimized by prior education/training in the use of such devices and taking time to read instructions before use.

While both devices seem intuitive to use in this study setting, this is only one aspect of ensuring correct use. It is imperative that “would be” users (parents/ care givers) are also able to recognize when the advice should be used. Previous studies have confirmed that appropriate education is a key factor in ensuring appropriate use⁶. Indeed, training parents in the use of the adrenaline auto-injector device has been shown to be a significant factor in improving parental comfort with future use¹⁵. It therefore remains important to provide appropriate education when prescribing an adrenaline auto-injector to increase the likelihood of correct use. Provision of a “replica”/trainer device may also increase familiarity and comfort with use of the devices.

There are several caveats to consider; this study includes a relatively small sample size and a larger population based study to determine whether these findings can be replicated is warranted. Additionally, participants in this study had a reasonably high level of education which may not be reflective of the community at large, however ability to correctly use the devices was not related to educational level in this study. It would also be important to reassess the use of both devices over longer periods of elapsed time to ascertain whether there is further attrition in ability to use the auto-injectors over time. Finally, the assessments did not occur in the acute setting of anaphylaxis and therefore findings may not be directly transferable to the real life situation where levels of stress are likely to be higher and risk of error greater.

CONCLUSION

Both the Anapen and redesigned EpiPen devices were able to be administered correctly by most subjects without prior education in their use under controlled study conditions when allowed to read instructions on

the device. There was however, significant attrition in the ability to use the Anapen over a relatively short period of time and critical errors that would result in failure to deliver adrenaline to a recipient were more common with Anapen than EpiPen. It is therefore imperative that regular reinforcement of the correct use of adrenaline auto injector devices occurs. Further, it remains essential that there is adequate education in recognition of symptoms and signs of anaphylaxis and timing of use of the adrenaline auto injector.

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Supplementary Table 1. Scoring System for EpiPen and Anapen

Score	Anapen	EpiPen
1	Remove black needle protector	Remove blue safety cap
2	Remove grey safety cap	Select upper outer thigh
3	Select upper outer thigh	Place orange end on thigh
4	Place black end on thigh	Pushed down to activate
5	Push red button to activate	Hold for >10 seconds
6	Hold for >10 seconds	NA