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Intelliject's novel epinephrine autoinjector: sharps injury prevention validation and comparable analysis with EpiPen and Twinject

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Abstract

Background—Currently marketed epinephrine autoinjectors (EAs) are prone to misuse that may lead to injury or a missed dose. A novel EA (NEA) (Intelliject Inc) was created to reduce such injuries by including features such as a unidirectional perceived injection end and a retractable needle.

Objectives—To validate the sharps injury prevention features of the NEA and to obtain feedback on, and preference for, features of the NEA compared with Twinject and EpiPen.

Methods—Twenty-eight health care professionals experienced with using the EpiPen or Twinject each injected 18 NEAs into an orange and provided confirmation of needle injection and retraction. Half of the injections were conducted using wet hands to replicate diaphoretic hands or wet environmental conditions. Participants provided feedback via a post-test questionnaire and gave ordinal preference rankings for the NEA, EpiPen, and Twinject based on shape, size, ease of use, ease of training, and overall preference. Participants also described known cases in which the Twinject or EpiPen was not correctly administered.

Results—For all 505 tested NEAs, the needle injected and retracted as intended. For overall preference, 100% of the experienced health care practitioners ranked the NEA first. Half of the participants recalled incidents in which the EpiPen or Twinject did not work as intended or caused an injury.

Conclusions—The sharps injury prevention feature was verified for the NEA, and health care professionals experienced in the use of EpiPen and Twinject for allergic emergencies perceived the NEA to be a safer and preferred alternative.

INTRODUCTION

For patients at risk for anaphylaxis, an epinephrine autoinjector (EA) can be a lifesaving device. However, there have been reported cases in which injuries have occurred with currently marketed EAs (EpiPen [Dey Pharma LP, Napa, California] and Twinject [Shionogi Pharma Inc, Atlanta, Georgia]),^{1–9} such as injecting into one's hand or digit instead of the patient's thigh as intended.² This injury is presumably due to the symmetrical design of the devices that makes it difficult to determine which end contains the needle. Also, after injection, for all Twinject devices and those EpiPen devices manufactured before April 2010

(the latest version of the EpiPen has a plastic needle sheath that is released after the device has been actuated), the needle remains exposed as a sharps hazard until properly disposed of in a special container. The Needlestick Safety and Prevention Act of 2000 outlines the need for “safer medical devices” with engineered sharps injury protections.^{10,11}

Other reported concerns with current EAs include lack of knowledge of how to correctly use the devices^{1,3} and the size and shape of the devices (the newest version of the EpiPen is >6 in long, with a 1-in diameter, and the Twinject is slightly longer but narrower), which make them difficult to carry at all times as needed. Improving device usability and safety requires awareness and adoption of a new approach from medical device manufacturers.^{12–14} Having more intuitive and usable devices could abrogate many of the common use errors that lead to hazards. An alternative, the novel EA (NEA) (Intelliject Inc, Richmond, Virginia), was designed to minimize the risk of such hazards. The NEA is a credit card-sized (3.25×2 in) EA (with a thickness similar to a small cell phone) that includes an “interactive system” with voice instructions and flashing diode lights located near the injection end to help guide the user through the injection process. The system detects when certain user actions occur and provides voice instructions that repeat until a task is completed successfully; eg, as soon as the safety guard is removed, it proceeds to the instruction, “to inject, press black end firmly against outer thigh while holding in place for 5 seconds.” The device also has a unidirectional perceived injection end (that blinks with a flashing diode as the previous instruction is being read aloud) and a retractable needle feature after injection (Fig 1). The needle autoinjects when the device is placed against the outer thigh and then pushed firmly, rather than the “swing and jab” motion required for EpiPen.¹⁵ In addition, the needle retraction mechanism minimizes the amount of time a needle resides in the patient, which may lessen the potential for injection site reactions (pain, bruising, or bleeding). Finally, users need to hold the device in place for only 5 seconds rather than the 10 seconds for EpiPen and Twinject. The user is guided in the amount of time to hold the device because as soon as the user presses firmly and the injection takes place, the device counts down, “5, 4, 3, 2, 1. Injection complete. Call 911.”

A previous study¹ compared first-time use of 2 earlier versions of the NEA, 1 without the interactive prompt system and 1 with the interactive prompt system, with EpiPen and Twinject. In that study, children (aged 7–10 and 11–15 years) and adults (aged 16–55 years) performed simulated use scenarios with models of the devices containing no needle or drug. Results confirmed the benefit of the interactive voice-prompting system, and participants were significantly more likely to use the NEA prototype with the interactive voice system correctly compared with the NEA prototype without the interactive system, EpiPen, and Twinject. Preference was also for the NEA with the interactive prompt system.

The purpose of the present study was to validate the sharps injury prevention features (autoinjection and retractable needle) of the production model NEAs and to solicit preferences from health care workers among the NEA, EpiPen, and Twinject. Because the devices were being injected into oranges, the interactive system was disabled for the needle retraction test phase of the study to avoid participant confusion (because the voice instructions instruct the user to “inject into the outer thigh”). Only after completing injection of the devices into oranges were nurses shown the NEA with the interactive voice system.

METHODS

Study Design

This study was approved by the institutional review board at the University of Virginia. It used a within-participants protocol with 28 participants aged 18 to 65 years recruited via flyers and e-mails sent to hospitals, clinics, and schools throughout Charlottesville, Virginia,

and surrounding communities. This cohort size ($n = 28$) was considered logistically possible and sufficiently varied to meet the primary end point goal of verifying needle injection and retraction while also being able to assess usability opinions from a variety of potential users. All the participants were practicing nurses who had used or trained patients in the use of either the EpiPen or Twinject in the previous 12 months. The study was conducted between February 12 and February 28, 2009, in the Human Computer Interaction Laboratory at the University of Virginia School of Engineering and Applied Science. Participants read and signed a consent form that informed them of the study risks and benefits, and they were provided with a parking pass if needed, were paid \$100 for participation, and were reimbursed for mileage if traveling more than 30 miles round-trip. The study lasted approximately 60 minutes per participant, and each trial was videotaped. Participants were not given sponsor information until after completing the study.

Procedures

The study was conducted in 3 phases (training, testing, and comparative evaluation). In the training phase, participants were first read an introduction describing the study and then trained on the correct use of the NEA system using a device that did not contain a needle, drug, or interactive system. To continue with the study, the participant had to demonstrate successful use of the NEA without needle or drug 3 times in a row (all the participants did so within 4 tries). The facilitator then demonstrated how to inject an NEA that included the needle and drug (but with the interactive system disabled) into an orange.

In the testing phase, each participant injected 18 NEAs (including needle and drug but no interactive system), except 1 who tested 19 devices (due to not following the protocol for 1 device), for a total of 505 devices tested. Injections were made into an orange through a piece of paper taped on top of the orange with a circle on it to help the participants target the injection site. After each injection, the participant and facilitator determined whether the needle injected and retracted by checking for a puncture through the paper placed on the orange (needle injection success) and by inspecting the device to see if the needle was no longer visible (needle retraction success). A fresh piece of paper, a different orange, and a new EA were used for each injection. For half of the devices tested, participants first dipped their hands into a bucket of water to simulate sweaty palms or rainy conditions. The other half of the devices was tested using dry hands. The order in which participants tested using dry or wet hands first was counterbalanced.

After the testing phase, participants were asked to rate the NEA on a scale from 1 (strongly disagree) to 5 (strongly agree) on several usability and learnability categories and to write down their favorite and least favorite NEA features. During the last (comparative evaluation) phase of the study, the interviewer demonstrated how the EpiPen and Twinject autoinjectors are used based on each device's labeling. Then participants demonstrated their use of trainer versions of EpiPen and Twinject, again using an orange as an instructional model. The facilitator also showed the participants the NEA with the interactive system and showed the NEA, EpiPen, and Twinject after injection (the latter 2 have a needle exposed). After completing all the demonstrations, the participants were asked to fill out a questionnaire that included ranking the 3 products on the following criteria: size preference, shape preference, ease of use, ease of training patients in use, perceived safety, and overall preference. They were also asked to write down (1) advantages or disadvantages of the NEA compared with existing products, (2) any instances that they knew of where someone used an EA incorrectly, and (3) any final comments or feedback.

Statistical Analysis

To demonstrate that the true failure rate of the NEA needle retraction feature is less than 1% per FDA guidance,¹⁶ the number of devices, rather than the number of participants, was used to determine sample size. Table 1 lists the upper bounds of 95% confidence intervals (CIs) based on the binomial distribution for an observed failure of 0, 1, 2, or 3 devices in a test sample of 100, 200, 500, and 1,000 devices.¹⁶ The selection of a sample size greater than 500 devices was based on having a sufficient number of devices needed to demonstrate a failure rate with a 95% CI that has an upper limit of less than 1%, using the Clopper-Pearson method for calculating the CI.¹⁷ Because the number of participants was predetermined to be 28, each participant was scheduled to test 18 unique devices, for a total of 504 devices, exceeding the required 500 suggested through the previously mentioned analysis.

RESULTS

Participants' demographic and baseline characteristics are summarized in Table 2. All 28 participants had previously heard of the EpiPen compared with 11 (39%) who had heard of the Twinject. Twenty-four participants (86%) had access to an EpiPen placebo trainer to facilitate training patients and caregivers on the proper use of the EpiPen device, and 7 (25%) had access to a Twinject placebo trainer. Most participants (n = 25, 89%) reported having 1 to 5 encounters (either using or training patients on how to use the EpiPen or Twinject) in the past year. Three participants (11%) had more than 20 encounters in that time frame.

Correctly Following Protocol and Injection Time

A previous study¹ tabulated errors during use (participants for that study were untrained). In this study, participants were trained, and none of them made any errors when injecting except 1 participant who removed the device before holding it in place for 5 seconds. For completeness, we had this participant inject 1 more device than originally planned. Data from all 505 injections are included in the following analyses.

The mean (SD) injection time (the time from picking up the device from the table to injecting it into the orange, including removal of the outer case and safety cover) was 6.7 (3.06) seconds. There was no statistically significant difference in injection times for participants with wet vs dry hands. The mean (SD) hold time (the time between injection and removal from the orange) was 6.1 (1.19) seconds.

NEA Autoinjection and Needle Retraction

In terms of the proper functioning of the NEA needle (ie, successfully injecting into the orange and completely retracting back into the device), there were no device failures (95% CI for failure rate, 0.00%–0.73%) and, therefore, the study met the primary objective that the upper limit of the failure rate is less than 1.0%. For the 1 participant who removed the device from the orange after approximately 1 second, the needle was already fully retracted into the housing of the device, and the injection had already been completed successfully.

Subjective Evaluation Results – Testing Phase

Most participants provided positive responses for the NEA (either “agree” or “strongly agree”) for each of the 6 post-test satisfaction statements (Table 3). The participants' favorite and least favorite features were independently classified into categories by the authors, and discrepancies were then resolved through consensus (Table 4).

Subjective Evaluation Results – Comparative Evaluation Phase

All 28 participants ranked the NEA first in overall preference to the EpiPen and Twinject. Most participants ranked the NEA first in terms of perceived safety (n = 27, 96%), ease of use (n = 26, 93%), ease of training patients in use (n = 26, 93%), preferred size (n = 22, 79%), and preferred shape (n = 19, 68%).

Written comments (all listed advantages and disadvantages of the NEA compared with existing products and final comments made by participants at the end of the study) were independently classified into categories by each author (comments by the same participant that would be classified the same were counted only once). Discrepancies were then resolved through consensus. The categories that emerged and the number of negative vs positive comments for each category are given in Table 5.

Personal Experience With Existing Products

Fourteen of the participants (50%) described instances where an existing EA was used incorrectly. Seven participants (25%) described 1 or more instances where a patient or caregiver injected upside down, eg, causing injection into the hand or finger of the administrator of the injection (who may or may not have been the patient). In 1 of these cases, it was the Twinject rather than the EpiPen that was injected upside down. In this case, the administrator was unable to determine how to administer the second dose that comes with the Twinject. Five participants (18%) described instances when the EpiPen either injected before going through the patient's clothing (described by 2 participants [7%]) or did not inject at all (described by 4 participants [14%]). Four participants (14%) described instances where the EpiPen was not held in place long enough for the injection to complete, causing leakage at the injection site and incomplete dose administration. Two participants (7%) described instances where the person administering the device forgot to remove the gray safety cap of the EpiPen, causing a delay in administration. Finally, 1 participant (4%) described 2 instances where exposed needles stuck people after injection.

DISCUSSION

For this study, practicing nurses with current experience using EAs were recruited to each inject 18 production model NEAs into an orange and to provide preference rankings for the NEA compared with EpiPen and Twinject. All 505 tested NEA devices successfully injected and had full needle retraction, the primary end point of the study. When asked to list benefits of the NEA design, many cited the quickness of the injection, ease of use, portability, the voice instructions (including the countdown feature that helps administrators judge how long to hold the device in place), the retractable needle, and the fact that so little force is required for administration compared with existing EAs. In several instances, participants demonstrating the EpiPen during the study actually broke through the skin of the orange owing to the force with which they swung and jabbed the device. Less force and less time required for correct administration may lead to fewer misfires and less pain at the injection site.

Several nurses periodically had difficulty pulling the NEA out of its protective case or removing the red safety cap, particularly with wet hands, and some cited this as their least favorite feature. There is always a tradeoff for how best to design safety covers. They should be neither too easy nor too difficult to remove. If the safety guard is too easy to remove, it may come off with the outer case, as happened a few times in a previous study¹ with an earlier model of the device. In addition, it is important that the safety guard can be removed by trained individuals but not by untrained small children who may find a device lying around the house.

Several nurses also felt that the rectangular shape was awkward to hold, but others cited it to be “hand friendly” and their favorite feature. Some were specifically concerned that the size might be difficult for smaller hands. However, the previous study¹ showed that participants as young as 7 years old had no problems holding the device, and most participants in the previous study¹ and in the present study preferred the shape and size of the NEA over that of the EpiPen or Twinject. For overall design, 100% of the participants in this study ranked the NEA first over EpiPen and Twinject.

In conclusion, the results of this study, together with those of the previous study,¹ demonstrate that the NEA has several effective safety features: (1) a unidirectional perceived injection end, significantly reducing the likelihood of a digital injection and subsequent missed dose; (2) voice instructions to assist in guiding the user through the injection process; (3) a compact form factor, which should increase the likelihood of the device being carried with the patient at all times; (4) a simple “press and hold” autoinjection mechanism that reduces the amount of force required by the user to ensure a successful injection; and (5) an immediate needle retraction mechanism that eliminates any sharps hazard potential. Potential users (previous study¹) and nurses familiar with EAs (present study) prefer the NEA, with the previously mentioned features cited as improvements over current products.

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Figure 1.
Novel epinephrine autoinjector.

Table 1Upper 95% Confidence Limits Based on the Binomial Distribution for an Observed Failure Rate^a

No. of failures	No. of devices tested			
	100	200	500	1,000
0	3.6	1.8	0.7	0.3
1	5.4	2.7	1.1	0.6
2	6.9	3.5	1.4	0.7
3	8.3	4.3	1.7	0.9

^aData are given as percentages.

Table 2

Demographic and Baseline Characteristics of the 28 Study Participants

Characteristic	Value
Age, y	
Mean (SD)	45.6 (11.45)
Range	26–65
Sex, No. (%)	
Male	3 (11)
Female	25 (89)
Handedness, No. (%)	
Left	1 (4)
Right	24 (86)
Ambidextrous	3 (11)
Current occupation, No. (%) ^a	
Emergency department nurse	9 (32)
Pediatric nurse	7 (25)
School nurse	4 (14)
Allergy and asthma clinic nurse	4 (14)
Other ^b	8 (29)
Highest level of education, No. (%)	
Nursing technical school	6 (21)
Associate's degree	10 (36)
Bachelor's degree	9 (32)
Master's degree	2 (7)
Doctorate degree	1 (4)

^aCategories are not mutually exclusive. Participants were allowed to choose more than 1 category.

^bNurse in acute care, radiology, labor and delivery, family practice, clinic, or public health.

Table 3Mean Satisfaction Ratings of the Participants for the Novel Epinephrine Autoinjector^a

Product characteristic	Mean rating
It is easy to use when wet	3.71
It works well with hand size	4.11
The user does not need extensive training for correct operation	4.32
The design makes it easy to use	4.36
It is not easy to skip a crucial step to properly use	4.50
It did not require multiple uses to learn how to use correctly	4.57

^aThe ratings use a scale from 1 (strongly disagree) to 5 (strongly agree).

Table 4

Classification and Number of Least Favorite and Favorite Features of the Participants About the Novel Epinephrine Autoinjector Before Seeing the Version With the Interactive Voice System

Comment category	Favorite feature, No.	Least favorite feature, No.
Ease of use	9	0
Not having to “jab” into patient for a successful injection	6	0
Portable	6	0
Ease of gripping/holding	5	2
Quickness of the injection	3	0
Retractable needle	3	0
Written directions easy to read	2	0
Hearing the hiss of the injection	2	2
Looks less like a “needle”	1	0
Overall design	1	0
Safety cover on same end as needle	1	0
Shape	1	1
Ease of removing outer case	1	5
“None” or “N/A”	0	8
Ease of removing red safety cap	0	6
No. of steps before injection	0	2
Slippery when wet	0	2
Aiming the injection	0	1
Size	0	1

Table 5

Classification and Number of Negative and Positive Open-Ended Comments (of 28 possible) Made by Participants About the Novel Epinephrine Autoinjector at the End of the Study

Comment category	Positive comments, No.	Negative comments, No.
Interactive voice system	20	0
Quickness of the injection	12	0
Ease of use	11	0
Retractable needle	8	0
Portable	6	0
Appearance (looks less like a “needle”)	5	0
Safety	4	0
Not having to “jab” into patient for a successful injection	3	0
Hearing the hiss of the injection	3	0
No. of steps before injection	3	0
Enclosed system	1	0
Ease of removing outer case	1	0
Shape for gripping/holding	1	6
Slippery when wet	0	2
Confirmation that medication injected	0	1
Aiming the injection	0	1
Ease of removing red safety cap	0	1