

Human factors engineering validation study for a novel 0.1-mg epinephrine auto-injector

Evan Edwards, M.S.,¹ Catherine Kessler, Ph.D.,¹ Naomi Cherne, Ph.D.,² Emily Dissinger, M.S.,² and Adam Shames, M.B.A.²

ABSTRACT

Background: Anaphylaxis in infants and young children is increasing. Historically, epinephrine auto-injectors (EAI) were not available in a dose or platform designed for patients who weighed <15 kg, and, therefore, 0.15-mg EAI were prescribed for these patients. Results of ultrasound studies indicate that currently marketed 0.15-mg EAI have needle lengths that may strike bone in ~29 to 43% of patients who weigh <15 kg and result in possible intraosseous injection. An EAI with a more weight-appropriate 0.1-mg dose and shorter needle length has been developed to potentially help minimize the risk of striking bone during epinephrine injection in patients who weigh 7.5–15 kg.

Objective: A human factors usability study was completed to validate the 0.1-mg EAI user interface.

Methods: This study was conducted with parents of children who were severely allergic so to evaluate simulated use of the 0.1-mg EAI by the intended user group. Fifteen participants were enrolled and received training on using the 0.1-mg EAI. Approximately 24 hours later, the participants completed a simulated emergency-use scenario by using the 0.1-mg EAI with an infant manikin. The primary end point was successful simulated administration of a meaningful epinephrine dose.

Results: All the participants simulated administration of a meaningful epinephrine dose. Fourteen participants successfully used the 0.1-mg EAI per the instructions for use in the simulated emergency-use scenario. One participant did not press the EAI against the thigh for the length of time defined for this critical task; however, the EAI was pressed long enough for complete delivery of the 0.1-mg dose.

Conclusion: This study validated the user interface of the 0.1-mg EAI for the intended users, uses, and use environments.

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The prevalence of food allergies and anaphylaxis has been increasing in children, including infants and toddlers.^{1,2} Between 2005 and 2014, emergency department visits for anaphylaxis increased by approximately 130% in children ages 0–4 years.³ Hospitalizations for food-induced anaphylaxis also increased from 2000 to 2009 in children <2 years of age.⁴ These data trends, combined with studies that indicated the need for early introduction of potential food allergens,^{5,6} helped lead to recent changes in National Institute of Allergy and Infectious Diseases guidelines.⁷ Current recommendations include the introduction of appropriate peanut-containing foods in certain infants as

young as 4–6 months old, which may paradoxically result in more children being exposed to potential allergens. An increasing prevalence as well as difficulty in recognizing atypical symptoms⁸ of anaphylaxis are confounding factors for caregivers of young children. Timely administration of epinephrine in the prehospital setting is vital to minimizing the severity of a life-threatening allergic reaction where delay in administration has been identified as a significant factor in anaphylaxis fatalities.^{9,10} Therefore, there are compelling reasons to provide an appropriate epinephrine auto-injector (EAI) to caregivers of infants and toddlers who have a history of or who are at risk of anaphylaxis.

Historically, EAI were available in two doses: 0.15 mg and 0.3 mg for patients 15–30 kg and ≥30 kg, respectively. Multiple publications recommend prescribing a 0.15-mg EAI to patients < 15 kg, despite the dose being higher than standard weight-based dosing of 0.01 mg/kg.^{11,12} The rationale is that the benefit of timely administration of epinephrine outweighs the risk. Another option is to train caregivers to draw up a weight-based epinephrine dose by using a vial and a syringe. However, this may take several minutes and the epinephrine dose may be inaccurate.^{2,13} For children < 15 kg, the appropriate needle length is also important. Ultrasound studies have shown that the needle length of currently available 0.15-mg EAI

From ¹Departments of Innovation, Development & Industrialization and Clinical Development kaleo, Inc., Richmond, Virginia, and ²Core Human Factors, Inc., Bala Cynwyd, Pennsylvania

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Address correspondence to Evan Edwards, M.S., kaleo, Inc., 111 Virginia St, Suite 300, Richmond, VA 23219

E-mail address: Evan.Edwards@kaleo.com

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could result in possible intraosseous injections in ~29 to 43% of patients who weigh 7.5–15 kg.^{14,15} According to Kim *et al.*,¹⁵ the recommended optimal needle length for this patient population is between 7 and 8 mm, much shorter than the ~12.7 mm exposed needle length in currently marketed 0.15-mg EAI.

The objective of this usability study was to determine the ability of caregivers of infants and toddlers to use an EAI specifically designed for patients who weigh 7.5–15 kg. Method(s) of instruction, ease of use, and user's confidence in properly and safely using the EAI were assessed. The 0.1-mg EAI is identical to the currently marketed AUVI-Q (epinephrine injection, USP [kaleo, Inc., Richmond, VA]) 0.15 mg and 0.3 mg but delivers 0.1 mg of epinephrine, has a nominal exposed needle length of 7.5 mm, and has unique labeling specific for the intended population. The 0.1-mg EAI has a needle that automatically retracts and that features voice instructions to guide the user through the injection process, including instructing the user to hold the EAI against the patient's thigh for 2 seconds and to seek emergency medical attention. This study validated the user interface of the 0.1-mg EAI for the intended users, uses, and use environments.

METHODS

Participants

Adult caregivers of infants and toddlers (ages 0–5 years) with severe allergies were eligible to participate in the study. Inclusion criteria required the participants to be ages ≥ 18 years and English-language proficient, with no severe visual, hearing, or dexterity impairments. Approximately 50% were to have previous experience with using or being trained on the use of an EAI within the year before enrollment. Individuals who worked in a profession that could potentially introduce bias to the study (*e.g.*, health care professionals, human factors engineers, medical device developers) or who have participated in an auto-injector device usability study in the previous 6 months were excluded.

Study Design

The protocol was reviewed and approved by the Allendale Investigational Review Board (IRB) and was determined to be a nonsignificant risk study. The participants were informed that the study purpose was to evaluate a drug-delivery device used to administer epinephrine during anaphylaxis. The study device was the same as the actual 0.1-mg EAI, including the voice instructions, visual cues, and proposed device labeling but without a needle or the force mechanism to activate an injection. The study involved a one-on-one training session on the 0.1-mg EAI. Approximately 24 hours later, the participants completed an anaphylaxis simu-

lated emergency-use scenario in which they used the EAI on an infant manikin. A new 0.1-mg EAI was used with each participant. After the simulated-use experience, the participants answered questions about their experience.

Procedures

The participants were recruited by using a recruitment agency and the IRB-approved screener. Eligible participants completed the test session at Core Human Factors, Inc., Bala Cynwyd, Pennsylvania. At the test session, the IRB-approved informed consent was reviewed and signed. Eligible participants completed a 30-minute one-on-one training session with a nurse educator in which a trainer device that performed exactly like the actual 0.1-mg EAI (without a needle or medication) was used to demonstrate correct use. The Patient Information and Instructions for Use (IFU) leaflets were provided to the participants for review. The participants practiced with the trainer device by using a skin pad until they demonstrated correct use.

The participants were scheduled to return ~24 hours later for the simulated-use test, which was completed in a replicated living room with a movie playing in the background and an infant manikin (a simulated patient with severe allergies) propped up on the sofa. The participants were read background information on severe allergic reactions and the use of epinephrine for the treatment of anaphylaxis until definitive emergency medical care is obtained. The participants were then given a task card that stated, "Imagine that you have just entered a room and see that your infant is having a severe allergic reaction and they are crying and having trouble breathing. You need to deliver epinephrine using the device found in this bag to prevent the reaction from becoming fatal." The participants were asked if they understood the task and were ready to start. The participants' actions were video recorded and observed by the test moderator (NC, ED) and the data analyst (NC, ED). Use errors were recorded on the case report form. When the participants indicated that they were finished with all the tasks, the test moderator asked questions about the participants' experience and perceived root cause(s) of each use error.

End Points

EAI administration tasks were defined based on the IFU for the 0.1-mg EAI. Tasks considered essential for successful administration of epinephrine were defined as critical (Table 1). The primary end point of the study was successful administration of what would be a meaningful dose of epinephrine by using the 0.1-mg EAI (*i.e.*, completion of all critical tasks). The secondary end points of the study were evaluation of the critical

Table 1 Critical tasks and Instructions for Use tasks for administering epinephrine when using the 0.1-mg epinephrine auto-injector

Critical tasks
Remove auto-injector from the outer case
Pull off the red safety guard
Place black end of auto-injector against any muscle (e.g., thigh, arm, or buttocks)
Press firmly to activate
Hold for at least 1 s
Instructions for Use tasks
Remove auto-injector from outer case
Pull off the red safety guard
Hold (or show knowledge to hold) infant's leg in place during injection
Place black end of auto-injector against thigh
Press firmly to activate
Hold for 2 s
Seek emergency medical assistance

and IFU task errors committed during the simulated-use scenario and participants' responses to post-simulated-use questions about their experience with using the 0.1-mg EAI.

RESULTS

Participants

Fifteen participants (12 women, 3 men) were enrolled (mean age, 34.1 years). The highest level of education completed was a master's degree (1), bachelor's degree (9), associate's degree (1), and a high school diploma (4). Nine participants (60%) had either been trained on or had experience with using an EAI within the past year (8 had experience or training with using an EpiPen or EpiPen Jr [Mylan Specialty L.P., Morgantown, W.V.; epinephrine injection, USP] and 1 participant could not remember the name of the EAI that was used). Seven participants (47%) had children who were severely allergic and who weighed ≤15 kg, and 8 (53%) had children who were severely allergic and who weighed >15 kg. The caregivers of the children who weighed > 15 kg were considered appropriate for inclusion in the study because they had recently cared for a child in the 7.5–15-kg weight range.

Usability Test Scenario

All 15 participants successfully completed a 30-minute training session with the same nurse educator. Approximately 24 hours later, all the participants returned to the study site and completed the simulated emergency-use scenario. Fourteen participants (93%) completed all the critical tasks as defined in Table 1. One participant had one critical task error of not hold-

ing the EAI against the infant manikin's leg for at least 1 second after activation. This same participant also did not complete the use scenario in accordance with the IFU tasks because she did not hold the EAI in place for 2 seconds after activation. The other 14 participants (93%) completed simulated use of the 0.1-mg EAI in accordance with the IFU tasks.

Two participants (13%) experienced difficulties during the simulated emergency-use scenario but self-corrected. One participant struggled to remove the EAI's outer case and originally held the device with the back facing her and tried to pull the case from the bottom instead of pulling the auto-injector up from the case. One participant initially placed the EAI against the infant manikin's leg without first removing the red safety guard. There were no device malfunctions during the usability testing. Instructions were not given to the participants on how to position the infant manikin for the injection. Three different positions were used: 6 participants placed the manikin supine on the couch, 5 held the manikin on their lap while seated, and 4 left the manikin propped up on the couch. The main reasons that the participants chose these specific manikin positions included: to keep the leg from moving, to have access to the thigh, and to comfort or keep the infant calm.

Post-Simulated-Use Questions

All the participants answered open-ended questions about the ease of use, confidence with using, shape, size, safety, and training on the 0.1-mg EAI. Overall, the participants found the 0.1-mg EAI easy to use and reported that they would feel confident using the device (93%). Voice prompts and/or step-by-step instructions, minimal steps, easy access, training and/or practicing, easy to hold and/or handle, and have a firm grip were reasons why the participants stated that the EAI was easy to use and why they would be confident with using the device. One participant stated that the EAI was neither easy nor difficult to use. In addition, she said that she would not be confident with using the device in a real-life emergency because she felt only health care professionals would feel comfortable in such a situation.

All the participants used positive descriptors for the size and shape of the 0.1-mg EAI, including great, perfect, compact, not bulky, a good size for the hand, and convenient to store and carry. Two participants (13%) thought it may be harder to find in the bottom of a bag than a larger device. Twelve participants (80%) thought that the EAI was safe and attributed this to a never-visible needle, tightly fitted case and safety guard, short hold time, and/or voice prompts. Three participants (20%) said the device was neither safe nor unsafe. The participants were asked about the IFU and

the trainer device used during the 0.1-mg EAI training. Many of the participants (73%) felt that the IFU was helpful, contained clear instructions, and/or would be a good resource. A few did not remember the IFU (2) or thought it was unnecessary if receiving training (1). One participant stated that the IFU had too many words and not enough pictures. No participants reported any difficulties or negative impressions of the trainer device and overall found the trainer to be “helpful” and/or “like using a real device.”

DISCUSSION

Applying human factors engineering in developing drug-device combination products is imperative in optimizing the user interface as well as identifying, reducing, or eliminating use-related hazards (*e.g.*, needle-stick injuries, unintentional epinephrine injection into a digit, and failure to carry EAI consistently due in part to a lack of portability). Failure of correct use or delay in use is potentially associated with poor user-interface design.

EAI is used during life-threatening emergency situations. It is critical that the EAI be used correctly every time for prompt administration of epinephrine. Therefore, a root cause and/or risk assessment of the single critical task failure (not holding the EAI in place for at least 1 second) and the IFU task failure (not holding for at least 2 seconds) was completed. The participant heard the click when the EAI was activated and assumed that the injection was complete. On lifting the device from the manikin's leg, she realized that she was supposed to have waited 2 seconds. Frame-by-frame video review of the testing session showed that the total time that the 0.1-mg EAI was held against the manikin's leg was ~0.3 seconds. Actual drug delivery time for the 0.1-mg EAI is <0.1 second; therefore, the entire dose of epinephrine would have been delivered.

Nervousness and confusion about which way to remove the outer case by one participant caused a delay (~19 seconds) but did not prevent administration of the epinephrine dose, which still occurred in <60 seconds. The ~3-second delay observed when one participant forgot to remove the red safety guard was minor compared with what would happen if there were not a safety guard to protect against unintentional activation. As a redundant feedback mechanism, voice prompts seemed to aid in self-correction, and the participant was able to administer a timely dose.

Because infants and toddlers are unable to self-administer epinephrine, the 0.1-mg EAI includes graphics on the device label specifically focused on caregiver administration. This differs from labeling on other EAI for which the focus is on self-administration. The IFU states to hold an infant or young child's leg firmly in place and limit movement during injection to help

minimize the risk of injection-related injury. Although all the participants held the infant's leg, the infant's body positioning varied. Of note, a potential risk factor in fatal anaphylaxis is having the patient in a seated or upright position.¹⁶ Instructions that include positioning the infant in a supine position (while holding the infant's leg firmly in place) may be appropriate.^{16,17} Most participants considered the 0.1-mg EAI labeling, including the patient instructions, IFU, voice instructions, and the trainer device, useful. All the participants considered the size and shape as positive. Most felt that the product was safe and easy to use and that they would be confident in using it during an allergic emergency.

Study Limitations

This study was conducted under simulated conditions and may not be representative of an actual anaphylaxis emergency. Similarly, how a parent or caregiver may respond during an actual emergency with his or her infant or toddler may be different than responses noted during this simulated-use scenario. The 0.1-mg EAI used did not contain a needle or force mechanism to activate the injection so that the participants could simulate administration of epinephrine to a manikin without the risk of exposure to the drug or needle. These modifications resulted in some of the injection activation sounds being absent. However, the impact of this modification on the results seemed to be nominal because the participants who experienced use errors and/or difficulties did not attribute them to the lack of injection activation sounds.

CONCLUSION

This usability study validated the 0.1-mg EAI for the intended users, uses, and use environment. One participant did not keep the EAI positioned on the thigh for the entire hold time, and two participants completed, with difficulty, removing the outer case or red safety guard; but all the participants simulated administering a meaningful dose of epinephrine. AUVI-Q 0.1 mg meets a previously unmet medical need as the first EAI designed specifically for patients with life-threatening allergies who weigh 7.5–15 kg by providing an appropriate dose and nominal exposed 7.5-mm needle length. This may mitigate bone strikes as well as possible intraosseous injection of epinephrine.

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