

IN-DEPTH REVIEWS

A Review of Auto-Injector Pen Safety and Preventative Strategies

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ABSTRACT

Reports of auto-injector pen injuries have increased over the past decade. However, the true incidence of these injuries is unknown. We present the case of an accidental digital self-injection by a dermatologist whilst he was trying to administer the medication to a patient presenting with anaphylaxis as an example of a typical auto-injector injury. Additionally, we discuss safety issues, commonly reported injuries of accidental self-injection, and review the safety guidelines for use of a common auto-injector pen. Finally, we explore common barriers to proper auto-injector handling and suggested preventative strategies in order to decrease injuries caused by auto-injectors.

INTRODUCTION

Auto-injectors, in this case defined as autoinjector pens, have recently seen a rise in reports of injuries caused by accidental or improper self-injection. There has been 15,190 incidents from unintentional epinephrine auto-injectors alone reported from 1994 to 2007 to US Poison Control Centers. Sixty percent of these were reported from 2003 to 2007.¹

More recently, from 2013 to 2014, there were a total of 6,806 reported cases of unintentional epinephrine auto-injector injuries.² However, auto-injectors are not only limited to epinephrine as they can contain a variety of drugs and biological products such as Adalimumab (Humira), Etanercept (Enbrel), and Secukinumab (Cosentyx) to name a few. Despite an increase in reporting, the true incidence of auto-injector injuries is

unknown. The goal of this article is to provide the reader with an overview of auto-injector pen handling guidelines, commonly encountered injuries, common barriers to proper handling, as well as possible preventative strategies. This article endeavors to increase awareness of possible consequences of mishandling auto-injectors and what steps can be taken to reduce injuries for both patients, caregivers, and health professionals in the future.

CASE REPORT

After a patient had presented to clinic with features consistent with anaphylaxis, a 55-year-old dermatologist tried to administer a dose of epinephrine using an auto-injector pen before transferring the patient to the emergency department. Whilst trying to administer the medication, he suffered from an accidental auto-injection into the volar

September 2018 Volume 2 Issue 5

aspect of his right thumb. The dermatologist then experienced severe pain, tachycardia, diaphoresis, and subsequent blanching of his right thumb. He immediately pulled out the needle from his thumb and found the tip to be bent after hitting the bone. This prevented the entire dose of epinephrine from being injected.

A few minutes later his thumb became pale, cool, and numb from the tip down to the base. Subsequent radiograph showed no bone abnormalities. After a literature search, he decided to wait for symptoms to resolve on their own. Six hours after the initial injury, his thumb began to re-perfuse and regained some of its color as well as sensation. Eight hours after the initial injury, he returned to baseline without any lasting pain, numbness, or blanching.

AUTO INJECTOR SAFETY GUIDELINES & FEATURES

The current EpiPen epinephrine auto-injector package insert emphasizes safe use guidelines to avoid lacerations, embedded needles, and accidental injections. First, it stresses the importance of never pressing or placing any digit over the orange tip of the injector, which is the end that dispenses the injection needle; instead, the hand should encircle the injector circumferentially during injection, with the thumb overlapping the index finger.^{3,4} This prevents the user from accidental auto-injection should they unknowingly hold the auto-injector upside-down.

It also warns against removing the blue safety cap before the user is ready to inject; this cap should be pulled straight off rather than bent or twisted off. To prevent lacerations and embedded needles, the insert now advises caregivers to firmly hold

the leg of young children during injection administration. Finally, the insert warns anyone who experiences accidental self-injection to visit their nearest emergency department immediately for evaluation and treatment.⁴

Epinephrine auto-injector devices now have several safety features to prevent injuries to patients and caregivers. The blue safety cap is designed to prevent the injection needle from deploying prematurely and must be removed for injection to proceed. The orange tip contains the injection needle and exists to cover the needle once the needle is removed from the patient's thigh. Moreover, patients are strongly encouraged to carry epinephrine auto-injectors in sets of two, in case one dose proves to be sub-therapeutic or the administrator of the first dose accidentally self-injects.⁴

SAFETY ISSUES

Despite the potentially life-saving effects of epinephrine auto-injector use, certain safety hazards have been shown to affect users. Perhaps the most studied safety concern in the literature is accidental injection. Despite an increasing number of reports of accidental digital auto-injection, a retrospective cohort study of 6 Texas Poison Control Centers over six years showed that only four cases of ischemic sequelae resulted from the 365 calls regarding accidental epinephrine injection. In all four cases, the patient responded to vasodilatory therapy and symptoms resolved without serious complications.^{1,5} Of the 127 cases of digital auto-injection examined in the study in which the patients had follow-up, the most common of these temporary symptoms were pain (68%), blanching (42%), discoloration (17%), and numbness (16%); a small minority experienced ecchymosis (3.1%), ischemia (3.1%), and decreased capillary refill (1.6%).⁵

Long term sequelae of accidental auto-injector pen injections are rare but do occur. A 2007 literature review of 59 case reports of accidental epinephrine auto-injection found four instances of prolonged neuropraxia following the injury, one of which took 10 weeks to resolve. This same patient experienced documented ischemia reperfusion pain. Interestingly, the same study showed no cases of digital necrosis or improved outcomes in cases where vasodilators such as terbutaline or phentolamine were administered.⁶

Other safety hazards of auto-injector use include laceration (usually occurring when a caregiver attempts to inject a squirming child), embedded needles, and perforation of bone with the needle.^{3,4,7} These incidents are reported relatively infrequently, mostly occur in children, and require further study to determine potential prevention techniques and specific treatment guidelines.

BARRIERS & PREVENTATIVE STRATEGIES

Despite manufacturer's guidelines being available for the use of pen auto-injectors, injuries continue to occur. Therefore, research has focused on finding preventable contributing factors to auto-injector injuries as well as suggesting additional strategies to minimize injuries. One of the primary barriers to the safe use of auto-injectors is the lack of knowledge and proper training on part of the prescribing physicians, patients, and caregivers on the correct handling and use of auto-injector pens.⁸⁻¹¹ With a provider being unable to demonstrate the proper use of an auto-injector, successfully educating both patients and caregivers becomes unlikely.

In fact, in one study looking at 100 physicians consisting of both residents and

fellows/consultants, only 2 of them were able to demonstrate all steps of an auto-injector pen administration correctly. 57% of them did not hold the pen in place for >5 seconds, 21% failed to apply enough pressure to activate, and 16% had a self-injection into the thumb.

Of these same physicians, 45 had previously prescribed epinephrine auto-injectors with just 3 of them having demonstrated its use to parents and children.⁸ Furthermore, when studies have looked at parents and children who have been prescribed an epinephrine auto-injector they have also consistently shown a lack of knowledge on proper use.^{9,10} In a study with 49 enrolled parents, only 24% were able to recall all the steps to correctly administer their child's medication. Half of the enrollees did not remember to remove the cap before using the device and to hold the device in place for several seconds.⁹

Low rates of physicians providing their patients with written materials and availability of placebo trainers can further contribute to the patient's inability to properly use auto-injectors.^{10,11} Proper training can help diminish both injuries and improper use of auto-injector pens. When physicians were given both hands-on training along with a lecture on anaphylaxis with re-demonstration of an epinephrine auto-injector, the correct use of auto-injectors increased from 23.3% before training to 74.2% after it. The rate at which the most common mistakes occurred significantly decreased after training, although the ranking did not change. Of note, holding the auto-injector in place for >5 seconds increased from 48.3% to 82.1% after training while accidental self-injection into thumb decreased from 36.4% to 7.3%.¹²

Another possible barrier to minimizing injuries is a lack of an intuitive design of auto-injectors. However, making small modifications to the design of auto-injector

pens can greatly decrease the rate at which injuries occur when using auto-injectors.^{13,14}

For instance, in a particular study where researchers modified an epinephrine auto-injector by placing a yellow arrow pointing to the black injection tip as well as changing the gray safety cap to red; the rate at which injuries occurred was lower in the group with the modified auto-injector when compared to the group with an unmodified version. With a total of 164 interns participating in the study split into two groups, 22.6% of those in the unmodified group demonstrated correct administration of the epinephrine auto-injector compared to 65% in the modified group. Additionally, 45.2% of the participants in the unmodified group had presumptive unintentional injection injuries while only 5% of participants in the modified group did.¹³ Therefore, further efforts should be made by manufacturers to provide both clinicians and patients with safer and more intuitive designs.

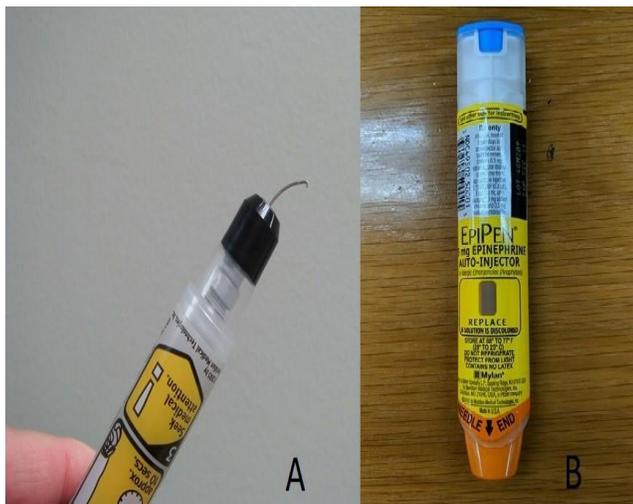


Figure 1. (A) Older epinephrine auto-injector model showing a black needle-end and a bent needle after accidental self-injection by a dermatologist. **(B)** Newer color-coded epinephrine auto-injector model showing a blue safety cap and an orange needle-end.

Some have even suggested that by having a more intuitive design, correct use of auto-injectors can be improved even when used by individuals with minimal training.¹⁵ Another suggestion that has been made is to change the order of steps for administration by placing the needle's end to the outer mid thigh first, before removing the safety cap.¹⁶ These could help reduce the contribution of a lack of proper training in the occurrence of auto-injector injuries, although this is yet to be further investigated.

DISCUSSION

After reviewing the types of injuries caused by auto-injectors, common contributing factors, and preventative strategies, we believe further emphasis should be placed on early thorough resident training and auto-injector design modifications. With a combination of proper training and design modifications, achieving a decrease in the rate of auto-injector injuries and improper handling appears possible. This has the potential to not only prevent mishandling injuries, but to also improve medication compliance for diseases managed with prescribed auto-injectors and outcomes of patients presenting with anaphylaxis by performing prompt medication administration.

In an effort to reduce improper handling, design changes made to the EpiPen since its first introduction to the market included color-coding both ends of the auto-injector by having a blue safety cap and an orange needle-end (Figure 1). Other auto-injectors types like Auvi-Q, an epinephrine auto-injector, features electronic voice instructions that guides users through the process of epinephrine injection administration.¹⁷ Despite the recent design changes seen in epinephrine auto-injectors, further

improvements to aid in the intuitive use of auto-injectors can still be made.

We encourage the reader to take time to familiarize themselves with the variety of auto-injectors used in their respective practice by reading the manufacturer's guidelines and by practicing with placebo trainers if available. Furthermore, properly demonstrating the correct administration steps of auto-injectors to patients when prescribing, and subsequently reinforcing these steps during follow-up visits, should remain a vital component of patient education to aid in medication compliance and reduction of injuries.

Conflict of Interest Disclosures: None.

Funding: None.

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References:

1. Simons, F. E., Edwards, E. S., Read, E. J., Jr., Clark, S., & Liebelt, E. L. (2010). Voluntarily reported unintentional injections from epinephrine auto-injectors. *The Journal of Allergy and Clinical Immunology*, 125(2), 419-423. doi: 10.1016/j.jaci.2009.10.056.
2. Anshien, M., Rose, S. R., & Wills, B. K. (2016). Unintentional Epinephrine Auto-injector Injuries. *American Journal of Therapeutics*. doi:10.1097/mjt.0000000000000541
3. Posner, L. S., & Camargo, C. A. (2017). Update on the usage and safety of epinephrine auto-injectors, 2017. *Drug, Healthcare and Patient Safety*, 9, 9-18. doi:10.2147/dhps.s121733
4. EpiPen (epinephrine injection, USP) Auto-Injector and its Authorized Generic. <https://www.epipen.com/en/>. Accessed February 20, 2018.
5. Muck, A., Bebart, V., Borys, D., & Morgan, D. (2007). Six Years of Acute Unintentional Epinephrine Digital Injections: Lack of Ischemia or Significant Systemic Effects. *Academic Emergency Medicine*, 14(5 Supplement 1). doi:10.1197/j.aem.2007.03.1267
6. Fitzcharles-Bowe, C., Denkler, K., & Lalonde, D. (2006). Finger Injection with High-Dose (1:1,000) Epinephrine: Does it Cause Finger Necrosis and should it be Treated? *Hand*, 2(1), 5-11. doi:10.1007/s11552-006-9012-4
7. Schintler, M. V., Arbab, E., Aberer, W., Spindel, S., & Scharnagl, E. (2005). Accidental perforating bone injury using the EpiPen autoinjection device. *Allergy*, 60(2), 259-260. doi:10.1111/j.1398-9995.2004.00620.x
8. Mehr, S., Robinson, M. and Tang, M. (2007), Doctor – How do I use my EpiPen?. *Pediatric Allergy and Immunology*, 18: 448–452. doi:10.1111/j.1399-3038.2007.00529.x
9. Gold, M. S., & Sainsbury, R. (2000). First aid anaphylaxis management in children who were prescribed an epinephrine autoinjector device (EpiPen). *Journal of Allergy and Clinical Immunology*, 106(1), 171-176. doi:10.1067/mai.2000.106041
10. Sicherer, S. H., Forman, J. A., & Noone, S. A. (2000). Use Assessment of Self-Administered Epinephrine Among Food-Allergic Children and Pediatricians. *Pediatrics*, 105(2), 359-362. doi:10.1542/peds.105.2.359
11. Grouhi, M., Alshehri, M., Hummel, D., & Roifman, C. M. (1999). Anaphylaxis and

- epinephrine auto-injector training: Who will teach the teachers?. *Journal of Allergy and Clinical Immunology*, 104(1), 190-193. doi:10.1016/s0091-6749(99)70134-x
12. Arga, M., Bakirtas, A., Catal, F., Derinoz, O., Harmanci, K., Razi, C. H., Turktas, I. (2011). Training of trainers on epinephrine autoinjector use. *Pediatric Allergy and Immunology*, 22(6), 590-593. doi:10.1111/j.1399-3038.2011.01143.x
 13. Bakirtas, A., Arga, M., Catal, F., Derinoz, O., Demirsoy, M. S., & Turktas, I. (2011). Make-up of the epinephrine autoinjector: the effect on its use by untrained users. *Pediatric Allergy and Immunology*, 22(7), 729-733. doi:10.1111/j.1399-3038.2011.01195.x
 14. Arga, M., Bakirtas, A., Topal, E., Yilmaz, O., Karagol, I. H., Demirsoy, M. S., & Turktas, I. (2012). Effect of epinephrine autoinjector design on unintentional injection injury. *Allergy and Asthma Proceedings*, 33(6), 488-492. doi:10.2500/aap.2012.33.3609
 15. Gosbee, L. L. (2004). Nuts! I Can't Figure Out How to Use My Life-Saving Epinephrine Auto-Injector! *The Joint Commission Journal on Quality and Safety*, 30(4), 220-223. doi:10.1016/s1549-3741(04)30024-9
 16. Kränke, B., Reiter, H., Kainz, J. T., & Arbab, E. (2011). How to improve the safety of adrenaline (epinephrine) autoinjectors. *Journal of Allergy and Clinical Immunology*, 127(6), 1645. doi:10.1016/j.jaci.2011.02.009
 17. AUVI-Q | Home. About AUVI-Q | AUVI-Q. <https://www.auvi-q.com/about-auvi-q/>. Accessed February 20, 2018.