

Digital Ischemia From Accidental Epinephrine Injection

Salman Ibn Mujtaba, MD; Aljoharah Alameel, MD; Bashayer Hamad, MD; Taimur Salar Butt, MD

A 28-year-old woman presented to the ED after accidentally injecting the entire contents of an epinephrine autoinjector into her right thumb.

Patients presenting to the ED with injuries due to accidental self-injection with an epinephrine pen typically receive treatment to alleviate symptoms and reduce the potential of digital ischemia leading to gangrene and loss of tissue and function. Although there is no consensus or set guidelines in the literature regarding the management protocol of such cases, many reports support pharmacological intervention. There are, however, other reports that advocate conservative, nonpharmaceutical management (eg, immersing the affected digit in warm water) or an observation-only approach.

We present the first case report in Saudi Arabia of digital ischemia due to accidental injection of an epinephrine autoinjector, along with a review of the literature and management recommendations.

Case

A 28-year-old woman presented to the ED in significant pain and discomfort 20 minutes after she accidentally injected the entire contents of her aunt's epinephrine autoinjector (0.3 mg of 1:1000) into her right



Figure 1. EpiPen needle embedded in the patient's thumb.

thumb. The patient, who was in significant pain and discomfort, stated that she was unable to remove the injector needle, which was firmly embedded in the bone of the palmar aspect of the distal phalanx in a manner similar to that of an intraosseous

Dr Ibn Mujtaba is an emergency physician, department of emergency medicine, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia. **Dr Alameel** is an intern, College of Medicine, Al Faisal University, Riyadh, Saudi Arabia. **Dr Hamad** is an intern, College of Medicine, Al Faisal University, Riyadh, Saudi Arabia. **Dr Butt** is an emergency physician, department of emergency medicine, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.

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Figure 2. After removal of Epipen from the right thumb.

injection (Figure 1).

The patient's vital signs and oxygen saturation on presentation were within normal limits. The emergency physician successfully removed the embedded needle through moderate countertraction. On examination, the patient's right thumb was pale and cold, and had poor capillary refill (Figure 2). Due to concerns of the potential for digital tissue ischemia leading to tissue loss and gangrene, warm, moist compresses were applied to the affected thumb, followed by 2% topical nitroglycerin paste, after which the thumb was covered with an occlusive dressing. Since there was no improvement in circulation after 20 minutes, an infiltrate of 5 mg (0.5 mL of 10 mg/mL) of phentolamine (α -agonist) mixed with 2.5 mL of 2% lidocaine was injected at the puncture site and base of the right thumb.¹ Hyperemia developed immediately at both injection sites, and the patient's right thumb returned to a normal color and sensation 1 hour later, with a return to normal capillary refill. She remained in stable condition and was discharged home. Prior to discharge, the patient was educated on the proper handling and administration of an epinephrine autoinjector.

Discussion

Epinephrine is an α - and β -adrenergic agonist that binds to the α -adrenergic receptors of blood vessels, causing an increase in vascular resistance and vasoconstriction. Although the plasma half-life of epinephrine is approximately 2 to 3 minutes, subcutaneous or intramuscular injection resulting in local vasoconstriction may delay absorption; therefore, the effects of epinephrine may last much longer than its half-life.

The incidence of accidental injection from an epinephrine autoinjector is estimated to be 1 per 50,000 units dispensed.² To date, there are no established treatment guidelines on managing cases of digital injection. An online PubMed and Google Scholar search of the literature found one systematic review,³ four observational studies,⁴⁻⁷ seven case series,⁸⁻¹⁴ and several case reports^{1,15-33} on the subject. Most of the patients in the published retrospective studies (71%) were treated conservatively with warming of the affected hand and observation, and the majority of patients in the case reports (87%) were treated pharmacologically, most commonly with topical nitroglycerin and phentolamine.^{1,3-34} All of the patients in both the retrospective studies and case reports had restoration of perfusion without necrosis, irrespective of treatment modality. However, patients who were managed conservatively or who were treated with topical nitroglycerin required a longer duration of stay in the ED, suffered from severe reperfusion pain, and in some cases, had a longer time to complete recovery (≥ 10 weeks).⁸

Pharmaceutical and Nonpharmaceutical Management

Phentolamine. Phentolamine is a nonselective α -adrenergic antagonist that binds to $\alpha 1$ and $\alpha 2$ receptors of blood vessels, resulting in a decrease in peripheral vascular resistance and vasodilation. Phentolamine directly antagonizes the effect of epinephrine by blocking the α -adrenergic recep-

tors, which in our patient resulted in immediate return of digital circulation and full resolution of symptoms.

Topical Nitroglycerin. Nitroglycerin is a nitrate vasodilator that when metabolically converted to nitric oxide, results in smooth muscle relaxation, venodilation, and arteriodilation. Patients suffering from digital ischemia and vasoconstriction may be treated with topical nitroglycerin paste to reverse ischemia by causing smooth muscle relaxation of digital blood vessels.

Conservative Management. As previously noted, not all cases of digital epinephrine injection are treated pharmacologically. Some patients are not treated, but kept in observation until the ischemic effects of epinephrine have resolved. Likewise, some patients are treated conservatively with warm water compresses or by fully immersing the affected digit in warm water to facilitate reversal of vasoconstriction and ischemia.^{3,8}

Treatment Efficacy

In 2007, Fitzcharles-Bowe et al⁸ published a review of 59 cases of digital injection with high-dose epinephrine from 1989 to 2005. In this review, 32 of the 59 patients received no treatment, 25 patients received pharmacological treatment and in two patients, the treatment was unknown. Phentolamine was the most commonly used pharmacological agent (15 of 25 cases or 60%). Although none of the patients experienced digital necrosis, those treated with a local infiltration of phentolamine experienced a faster resolution of symptoms and normalization of perfusion. In 2004, Turner¹ reported a case of a 10-year-old boy who was treated with phentolamine following an accidental injection of epinephrine into his left hand. While circulation returned to the affected digit within 5 minutes of receiving the phentolamine injection, the patient continued to experience reduced sensation in the digit 6 weeks later.⁸

Interestingly, one of the coauthors of the Fitzcharles-Bowe et al⁸ report inten-

tionally injected three of the digits of his left hand (middle, ring, and small fingers) at the same time with high-dose epinephrine to carefully observe and document the outcomes. All three of the digits became very pale and cool, with decreased sensation. The author treated himself conservatively (observation-only). He experienced spontaneous return of circulation in two of the digits within 6 to 10 hours. Although there was some spontaneous return of circulation to the third digit after 13 hours, the author noted prolonged, intense reperfusion pain 4 hours after return of circulation. He also suffered from neuropraxia in the third digit, which did not fully resolve until 10 weeks after the injury.⁸

A review of the literature shows phentolamine to be a safe and effective treatment for patients presenting with digital ischemia, with no long-term adverse effects or complications. Moreover, phentolamine appears to be safe and effective for use in both adult and pediatric patients.^{3,8,35-38}

Accidental Injection Prevention

Some of the cases of accidental epinephrine injection are due to user error. For example, a novice user may be holding the incorrect end of the injector in his or her hand when attempting to administer/ deploy the device, resulting in premature dislodgement of the needle.³⁹

Although, most of the autoinjector devices available today are user-friendly, we believe the addition of a safety feature such as a trigger or safety-lock may further help to reduce accidents. The European Medicines Agency recommends that all patients and caregivers receive training on the proper handling and administration of epinephrine autoinjectors, citing this as the most important factor to ensure successful use of an epinephrine autoinjector and reduce accidental injury.⁴⁰ The patient in this case had not received any formal education or training regarding autoinjector use prior to this incident.

Safety of Lidocaine-Containing Epinephrine in Digital Anesthesia

Aside from cases of accidental digital epinephrine injection, clinicians have traditionally been taught to avoid using lidocaine with epinephrine for digital anesthesia. However, since the introduction of commercial lidocaine with epinephrine in 1948, there are no case reports of digital gangrene from commercially available lidocaine-epinephrine formulations.^{41,42} In a multicenter prospective study by Lalonde et al⁴³ of 3,110 consecutive cases of elective injection of low-dose epinephrine in the hand, the authors concluded the likelihood of finger infarction is remote, particularly with possible phentolamine rescue therapy. Moreover, lidocaine-containing epinephrine (1%-2%) has a much lower concentration of epinephrine per mL of solution (5-10 mcg/mL) and appears to be safe for digital use.

Conclusion

This case describes the presentation and treatment of accidental digital injection of epinephrine, highlighting and supporting the benefits of local infiltration with phentolamine and observation until full recovery of perfusion. Local treatment with phentolamine not only facilitates recovery and return of capillary refill, but also shortens the duration of symptoms and alleviates vasoconstriction. In less severe cases, watchful waiting and observation may be appropriate and effective.

This case also underscores the importance of patient and caregiver education on the proper handling and administration of epinephrine autoinjectors to decrease the incidence of accidental injection.

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