

Evaluation and treatment of accidental autoinjection of epinephrine

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Epinephrine is a direct-acting sympathomimetic agent that promotes vasoconstriction, decreases mucosal edema, and increases bronchodilation. It is used in the treatment of bronchospasm, asthma, anaphylaxis, and cardiac arrest and is manufactured for intravenous, intramuscular, subcutaneous, oral inhalation, and intratracheal administration.¹ Epinephrine is available for self-administration in the emergency treatment of allergic reactions leading to anaphylaxis.² This self-administered form of epinephrine is available as an autoinjector in a dose of 0.3 mg (EpiPen, Mylan Specialty L.P.) or 0.15 mg (EpiPen Jr.). The EpiPen autoinjector is formulated as a 1:1000 dilution of epinephrine and the EpiPen Jr. autoinjector as a 1:2000 dilution, with the 0.3-mg dose used for patients weighing more than 30 kg and the 0.15-mg dose for patients weighing 15–30 kg.²

The advantage of this intramuscular mode of delivery is enhanced bioavailability to the site of action. This route is preferred over intra-

Purpose. A case of accidental autoinjection of epinephrine is described.

Summary. A 47-year-old man arrived at the emergency department after accidental injection of epinephrine with an autoinjector into his left thumb. His vital signs were stable at admission. The patient was allergic to nuts and thought he may have eaten something containing a pine nut. The patient reported feeling itching in his throat but had no shortness of breath or swollen tongue. He tried to self-administer an epinephrine injection, but it did not inject. While he was checking the device, it accidentally injected into his left thumb pad. A review of systems revealed throat discomfort, a tingling sensation of the tongue, and a left-thumb puncture with pain. Physical examination of the left thumb pad revealed a pale, cool thumb with diminished capillary refill and punctuate black discoloration at the site of

injection. Topical nitroglycerin paste was applied but had no effect, so terbutaline was ordered. The terbutaline injection was prepared as a 1:1 preparation of terbutaline sulfate 1 mg/mL and 0.9% sodium chloride injection. The immediate effects were the return of color from pale white to red and observable perfusion to the area within seconds. After 20 minutes, the red color remained, with observable perfusion and warmth, in addition to complete neurosensory function. Sixty minutes after terbutaline administration, the patient was discharged home.

Conclusion. A 47-year-old man who accidentally injected himself in the thumb with an epinephrine autoinjector was successfully treated with subcutaneous terbutaline. The treatment had an immediate effect, including revascularization and resolution of pain.

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venous administration because epinephrine is a local vasoconstrictor. If given intravenously in emergencies, epinephrine may restrict blood flow to the area of the injection site, causing subsequent damage to extremities. Furthermore, epinephrine

may cause ventricular tachycardia. The autoinjector allows immediate absorption of epinephrine into muscle and subsequent diffusion into the bloodstream. The device itself is used in addition to supportive care for the patient, who should seek

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medical attention immediately after administration.³

While this device has been designed to prevent life-threatening anaphylactic shock, it is not without risk.⁴ Although it is designed to be used by individuals without medical training, the incidence of accidental self-injection is estimated at 1 per 50,000 EpiPen units.⁵ A systematic review of published reports of unintentional injection of epinephrine from an autoinjector over the past 20 years found that greater than two thirds of accidental self-injections occurred in the last 6.3 years.⁶

Due to epinephrine's potent α -agonist activity, ramifications of an accidental dislodgement of the epinephrine autoinjector needle into a digit may include reduced blood flow to the area due to local vasoconstriction, tissue ischemia, and subsequent necrosis.⁷ These patients' symptoms often include pain, blanching, decreased surface temperature, pallor, and edema. Rapid reversal would seem an obvious and necessary component to salvage the affected digit. Reversal agents used have included phentolamine, terbutaline, and topical nitroglycerin.

Phentolamine is an α -adrenergic receptor antagonist that has been commonly used to treat accidental epinephrine injection.⁸ However, since May 2011, phentolamine injection has been in short supply.⁹ Because of this shortage, alternatives such as topical nitroglycerin and terbutaline, both with vasodilatory effects, have been suggested. Published reports of success with terbutaline are dated, brief, and nondescriptive, and they offer little-to-no visual evidence of outcomes associated with the use of this agent.

We present a case of autoinjector dislodgement into the pollex, more commonly known as the thumb, due to misuse.

Case report

A 47-year-old man arrived at the

emergency department after accidental injection of epinephrine with an autoinjector into his left thumb. His vital signs were stable at admission (temperature of 36.6 °C [97.8 °F], heart rate of 64 beats/min, respiratory rate of 18 breaths/min, blood pressure of 130/74 mm Hg, oxygen saturation at 100%). The patient was allergic to nuts and thought he may have eaten something containing a pine nut. The patient reported feeling itching in his throat but had no shortness of breath or swollen tongue. The patient self-administered 50 mg of diphenhydramine but continued to have discomfort in his throat. He then tried to self-administer an epinephrine injection, but it did not inject. While he was checking the device, it accidentally injected into his left thumb pad. A review of systems revealed throat discomfort, a tingling sensation of the tongue, and a left-thumb puncture with pain. The patient was in no apparent distress. However, physical examination of the left thumb pad revealed a pale, cool thumb with diminished capillary refill and punctuate black discoloration at the site of injection (Figure 1).

One-half inch of topical nitroglycerin was applied to the left thumb, and the thumb was wrapped in gauze. After 30 minutes, the nitroglycerin paste did not produce an observably significant improvement in perfusion, so terbutaline was ordered. The terbutaline injection was prepared as a 1:1 preparation of terbutaline sulfate 1 mg/mL and 0.9% sodium chloride injection, with 1 mL terbutaline sulfate and 1 mL 0.9% sodium chloride injection based on the efficacy observed with previous use of this preparation.¹⁰ The preparation was injected in two parts directly into the site of the epinephrine injection. The immediate effects were the return of color from pale white to red and observable perfusion to the area within seconds.

After 20 minutes, the red color remained, with observable perfusion

and warmth, in addition to complete neurosensory function (Figure 2). Sixty minutes after terbutaline administration, the patient was discharged home. During telephone follow-up, two weeks after the incident, the patient reported no issues and full recovery with regard to his thumb in relation to the self-injection.

Discussion

The need to treat an accidental injection of epinephrine in a digit remains controversial and comes from the established dogma in medical education that accidental injection of epinephrine can lead to devastating necrosis and possible amputation of the digit. This idea can be traced back in the literature to 21 cases published before 1950 in which epinephrine was implicated, perhaps erroneously, as the cause of digital gangrene.¹¹ These cases involved patients who developed digital necrosis after receiving injections of procaine or cocaine in combination with epinephrine in their fingers for local anesthesia. It is now suspected that the acidity of procaine was more likely the cause of tissue necrosis than the use of epinephrine.¹¹

To date, no cases of tissue necrosis associated with commercially available epinephrine have been reported,¹² which raises the issue of whether watchful waiting in combination with nonpharmacologic treatments should be the medical strategy of choice. Although published case reports and case series support some pharmacologic approach to treatment, Singer¹² and Muck et al.¹³ recently debunked the myth that epinephrine injection in the digits is associated with devastating necrosis and possible amputation. Muck et al. conducted a review of all cases of accidental epinephrine injections reported to six Texas poison control centers from 2000 to 2005. Of the 365 reports identified, 213 involved a digit; of these reports, 127 contained complete follow-up informa-

Figure 1. Left thumb before administration of terbutaline.

Figure 2. Left thumb 20 minutes after terbutaline administration.


tion. Of the 127 cases reviewed, all patients had complete resolution of their symptoms. Sixty-eight patients (54%) were not seen in a health care facility. No local or systemic effects were reported in 10% of patients; the most common effects were minor in nature (77% of patients), followed by moderate (13%), and major (1 patient, who was discharged home with no systemic effects). There were no reported hand surgery consultations, systemic effects, or vascular-related complications. Interventions were documented for 29 (23%) of the 127 reported cases and included 19 patients who received topical nitroglycerin, 7 who received local phentolamine injection, 2 who received both nitroglycerin and local

phentolamine injection, and 1 who received terbutaline. Forty patients had only warm soaks of the affected digit as their treatment. This study is limited by its design as a retrospective analysis and by the use of only one state's database. Furthermore, there was no follow-up for the patients included in the study. Based on these data, Muck et al. suggested that watchful waiting was a reasonable approach for these patients but stated that medical intervention should be considered for patients who experience persistent or worsening pain or decreased capillary refill lasting more than two hours.

Phentolamine is an α -adrenergic receptor antagonist that competitive-ly antagonizes the vasoconstrictive

effects of epinephrine.¹⁴ Several case reports have demonstrated the utility of phentolamine in the reversal of tissue ischemia after accidental subcutaneous injection of epinephrine.⁸ These studies showed tissue reperfusion within minutes after subcutaneous injection of phentolamine, with no tissue necrosis or long-term sequelae. A systematic literature review analyzed cases of digital epinephrine injection between 1900 and 2005 and found that phentolamine 0.5–4.5 mg was used as the treatment in 14 cases, with no patients developing digital necrosis.⁸ Ease of use, quick and effective reversal of ischemia, and no reported adverse effects are cited as reasons for using phentolamine as the initial option for accidental digital injection of epinephrine.¹⁵

Alternatives to phentolamine for accidental digital epinephrine injection are controversial, and the current medical literature lacks specific guidance. Agents such as topical nitroglycerin and subcutaneous terbutaline have been used to treat accidental digital injection of epinephrine, with no patients developing tissue necrosis.⁸ Topical nitroglycerin promotes vasodilation, and various case reports reviewed by Fitzcharles-Bowe et al.⁸ reported the use of topical nitroglycerin with varying degrees of success, all with no long-term sequelae. In six of the reviewed case reports, topical nitroglycerin was applied as part of the therapy. Four of these cases involved topical nitroglycerin without any other vasodilatory agent, leading to reperfusion in 6, 12, and 13.5 hours. One case provided no timeline for reperfusion. None of the reports indicated that topical nitroglycerin had immediate effects. In our patient, the effect of topical nitroglycerin was not shown to be substantial, with no change in perfusion in the thumb from initial presentation.

Terbutaline is a selective β -2-receptor agonist, which, like phentolamine, directly antagonizes the

effects of epinephrine through vasodilation to promote revascularization of the affected area.¹⁰ The recommendation to use this agent as an alternative stems from a series of three case reports.¹⁵ In each of the three cases, epinephrine self-injection occurred by discharge of an autoinjector into the pad of the thumb. The first case involved a pediatric patient who received a 3-mL injection of subcutaneous terbutaline sulfate (1 mg of terbutaline sulfate/10 mL 0.9% sodium chloride injection) followed by nitroglycerin ointment, which led to symptom resolution in 30 minutes. The second case involved an adult patient who received 0.5 mg of terbutaline sulfate subcutaneously, which led to immediate symptom resolution. The patient received a second dose of 0.5 mg terbutaline sulfate plus nitroglycerin paste and was observed for one hour and then discharged. In the final case, an adult patient received two doses of 0.5 mg terbutaline sulfate administered subcutaneously and given 15 minutes apart. While there were no signs of ischemic progression after terbutaline administration, a hand surgeon was contacted; phentolamine was administered, leading to immediate tissue reperfusion. Our patient was treated with 1 mg of terbutaline

sulfate administered subcutaneously. The treatment had an effect within seconds, including revascularization and resolution of pain, which remained until the patient was discharged more than one hour after terbutaline administration, with no adverse effects.

Conclusion

A 47-year-old man who accidentally injected himself in the thumb with an epinephrine autoinjector was successfully treated with subcutaneous terbutaline. The treatment had an immediate effect, including revascularization and resolution of pain.

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