

Epi-Curious

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A 66-year-old man unintentionally injects his thumb with an epinephrine auto-injector.

Case

A 66-year-old man with a history of atrial fibrillation and hypertension, for which he takes warfarin and metoprolol, respectively, was “experimenting” with his wife’s epinephrine auto-injector when he unintentionally discharged the medication into his right thumb. He presented to the ED within 1 hour of the incident, complaining of numbness and paleness in the affected digit (Figure 1). Vital signs were: blood pressure, 137/88 mm Hg; heart rate, 87 beats/min; respiratory rate, 14 breaths/min; temperature, afebrile. Oxygen saturation was 100% on room air. On physical examination, the patient was in no acute distress, and cardiac, pulmonary, and abdominal examinations were normal.

What are auto-injectors and why are they so useful?

Auto-injectors contain an enclosed needle that is released by means of a spring mechanism when the injector unit is activated. Although intravenous route is the most efficacious for rapid drug delivery, establishment of access by a layperson is not feasible. Intramuscular and subcutaneous auto-injectors, therefore, are an effective alternate option and provide a safe route for medications in which oral administration is contraindicated due to a high hepatic first-pass effect.

The availability of preloaded epinephrine auto-injectors has proved life-saving for patients suffering from anaphylaxis, as rapid administration can limit progression of this potentially fatal disorder. An adult-strength auto-injector delivers a single dose of 0.3 mg of epinephrine, USP, (1:1000) (0.3 mL) in a sterile solution and is indicated for patients weighing 30 kg (66 lb) or more; a pediatric strength auto-injector delivers a single dose of 0.15 mg epinephrine, USP, (1:2000) (0.3 mL) in a sterile solution, and is indicated for patients weighing between 15 and 30 kg (33 to 66 lb).¹ (In both strengths, approximately 1.7 mL of solution remains in the injector postdeployment.)¹

What are the concerns of epinephrine injection in a distal appendage?

Epinephrine is a catecholamine that acts primarily on β -adrenergic receptors and, at high concentrations (eg, after local injection), causes α -adrenergic-mediated vasoconstriction.² Historically, based on concerns of tissue ischemia and digital necrosis, its use as a digital-block anesthetic was generally not recommended. Despite this long-standing belief, recent reviews of the literature and case studies support its safety,³⁻⁶ and local epinephrine blocks for digital lacerations are now common, providing both extended pain relief and a bloodless field. Although pallor and pain at the injection site have been reported,

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review data show no incidence of tissue necrosis.

In one recent study, 9 healthy participants received a single subcutaneous digital block of 3.0 mL of 1% lidocaine to the right middle finger and 3.0 mL of 1% lidocaine with epinephrine (1:100,000) to the left middle finger.⁷ There was little difference in digital circulation between the groups (as determined by pulse oximetry) and no cases of tissue necrosis. Of note, anesthetic effect was achieved sooner, with a markedly prolonged duration, in the lidocaine plus epinephrine group versus lidocaine alone.⁷

In addition, a literature review published in 2007 also failed to demonstrate any adverse outcomes in prospective, randomized clinical trials evaluating epinephrine as a digital-block anesthetic.⁸ As ischemic time of an entire extremity is well tolerated for several hours in many surgical procedures, this review suggested that prior reports of tissue necrosis likely resulted from one or more of the following: poor technique; nonstandard concentrations of epinephrine; usage of expired, acidic procaine; and improper tourniquet use.⁸



FIGURE 1 Pallor of right thumb prior to treatment

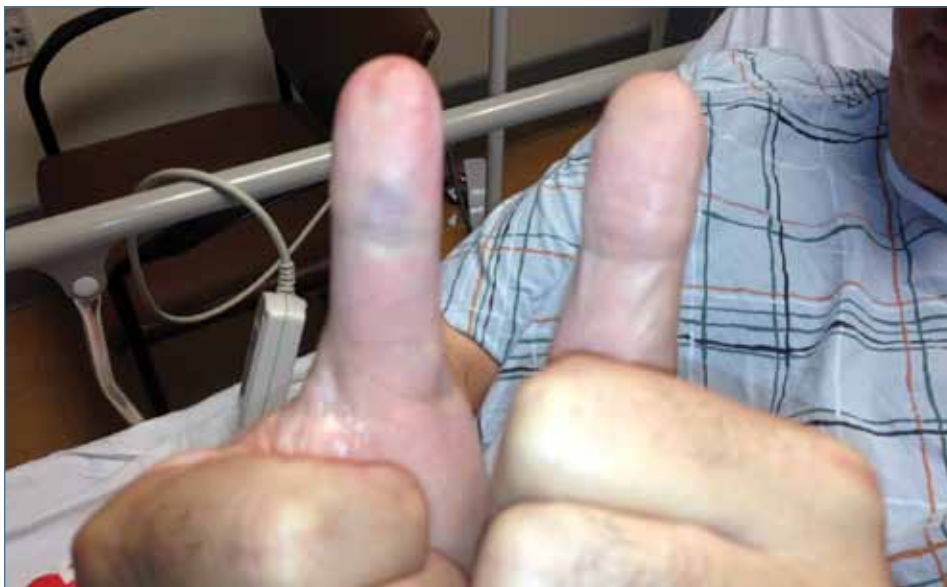


FIGURE 2 Right thumb after application of nitroglycerin paste and 30-minute immersion in warm water

What are other auto-injectors to which patients may be exposed?

Other commonly prescribed auto-injectable medications include insulin, etanercept, enoxaparin, sumatriptan, atropine, and pralidoxime (2-PAM).

Insulin. The type of insulin in an auto-injector (commonly referred to as an “insulin pen”) determines the

duration of patient observation for development of hypoglycemia.

Etanercept is a tumor necrosis factor inhibitor for the treatment of rheumatoid arthritis. Although it is an immunosuppressant, a single, acute injection is unlikely to produce serious pathology.

Enoxaparin is a low-molecular-weight heparin that inhibits factor Xa and is used by patients with venous thromboembolic disease. Single acute injections are unlikely to significantly increase the risk of bleeding, and there is rarely a reason to measure factor Xa activity.⁹

Sumatriptan is a 5-hydroxytryptamine (serotonin) 1B and 1D receptor agonist used to treat migraines and cluster headaches. Because triptans induce vasoconstriction, inadvertent injections can be managed with nitroprusside, nitroglycerin, or phentolamine.¹⁰ Most of the available data on triptan-induced vasoconstriction, though, are limited to cases of oral overdose.

Atropine and 2-PAM. Atropine, an anticholinergic, and 2-PAM, a cholinesterase reactivator, are available as auto-injectors in a combined package commonly known as a “Mark I Nerve Agent Antidote Kit” (NAAK). NAAKs are specifically for use by first responders and military personnel to treat nerve-agent exposures (eg, sarin).¹¹ A 1990s survey from Israel reported several pediatric cases of unintentional self-injection with

atropine auto-injectors.¹² Almost half of the children in this survey experienced systemic effects of atropinization (eg, dry mouth, disorientation, drowsiness, dilated pupils, mydriasis, dysphagia, tachycardia, unsteady gait, dry, flushed skin); however, there were minimal serious adverse events and no reports of mortality. There are limited data regarding the adverse effects of 2-PAM; however, available data suggest its relative safety in children.¹³

Aside from adverse effects of the drug injected, mechanical damage from pressure of the auto-injector itself can cause vascular compression and resulting ischemia. This is particularly a concern with high-pressure injectors such as epinephrine and 2-PAM because needle length for each is typically 1 to 1.25 inches, and the needle can lodge in the trabecular bone of the finger, making removal difficult.¹⁴

How are digital epinephrine injections managed?

Initial management includes application of nitroglycerin paste directly to the affected area (eg, to the exposed segment of the injected digit).¹⁵ The entire hand may then be gloved and immersed in warm water to enhance skin permeation of the nitroglycerin and promote vasodilation.¹⁵ Without treatment, symptoms typically resolve within 1 to 2 hours due to the rapid elimination half-life and short duration of epinephrine.¹⁶

If symptoms do not resolve promptly with the above noninvasive management, digital block of the affected digit with 1% lidocaine solution (without epinephrine!) might relieve discomfort. In cases that still fail to improve, local injection of phentolamine (approximately 1 mg) directly through the puncture site can be considered.^{15,17} Phentolamine is a short-acting α -adrenergic antagonist that can reverse the vasoconstrictive effects of epinephrine and provides nearly immediate relief.^{15,17-19}

Case conclusion

Nitroglycerin paste was applied to patient's right thumb; the hand was gloved and immersed in warm water. After approximately 30 minutes, pallor resolved and patient regained sensation in his thumb, with no reperfusion pain (Figure 2). He did not, therefore, require either lidocaine or phentolamine for symptom resolution and was discharged without report of sequelae.

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