

# Accidental digital epinephrine injection

## *To treat or not to treat?*

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Epinephrine autoinjectors are widely prescribed for the self-treatment of anaphylaxis. Accidental digital injection of epinephrine is an increasingly common occurrence and can be associated with profound ischemia of the affected digit. Several case reports of such injuries exist; however, it is unclear what the appropriate treatment of accidental digital epinephrine injection should be. We will present a case of accidental digital epinephrine injection, review the available literature, and suggest treatment options.

### Case

A 68-year-old man presented to the emergency department (ED) with a cold and pale thumb after accidentally injecting himself with his wife's epinephrine autoinjector device. The injury had occurred 20 minutes before he arrived at the ED and he had injected most of the epinephrine autoinjector into the pulp of his thumb. He reported initial pain in the thumb, but at presentation his complaints were of a cold and numb digit. On examination, a puncture wound was visible on the thumb pulp, distal to the interphalangeal joint. The digit was cold and pale, and there was no capillary refill distally. The patient was insensible to an area extending proximal past the interphalangeal joint.

The thumb was soaked in warm water for 30 minutes with no change. Nitroglycerin paste was then applied. Sensation slowly began to return to the digit 45 minutes later; within 2 hours capillary refill had improved but sensation remained diminished compared with the other digits. After 4 to 5 hours, the capillary refill had substantially improved; however, sensation still had not fully returned to normal.

### Discussion

Epinephrine's actions, including increased peripheral vascular resistance and blood pressure, as well as bronchodilation, make it a mainstay of treatment of anaphylaxis.<sup>1,2</sup> Epinephrine use in local anesthesia has been widely discouraged when treating end-artery structures because of the risk of vascular insufficiency or necrosis. However, several reports of use of a commercial lidocaine-epinephrine mixture under these circumstances exist, with no adverse outcomes.<sup>3,4</sup> In a literature review, Denkler found 48 cases of digital necrosis following anesthetic blocks.<sup>5</sup> Less published data exist about epinephrine autoinjectors, which contain 5 to 10 times the amount of epinephrine used with local anesthetic agents.

Accidental epinephrine injection into a digit was first reported in 1989.<sup>6</sup> Various treatment methods have been described, including watchful waiting and subsequent spontaneous resolution.<sup>6</sup> One of the challenges

### EDITOR'S KEY POINTS

- Accidental digital injection of epinephrine is an increasingly common occurrence and can be associated with profound ischemia of the affected digit. Choosing an appropriate management plan can be challenging because it is often difficult to assess the amount of epinephrine that has been injected into the digit.
- Treatment methods range from conservative management to local infiltration with  $\alpha$ -antagonists.
- A protocol for treatment of epinephrine-induced digital ischemia should be available in emergency departments and other primary care sites. Although there is currently no clear treatment protocol for accidental digital epinephrine injection, conservative measures (eg, warming, nitropaste) can safely be tried initially. If the digital ischemia does not respond, injection with phentolamine is advisable.

### POINTS DE REPÈRE DU RÉDACTEUR

- L'injection accidentelle d'épinéphrine dans un doigt se produit de plus en plus souvent et peut être associée à une ischémie profonde du doigt affecté. Il peut être difficile de choisir la prise en charge appropriée car il est souvent impossible d'évaluer exactement la quantité d'épinéphrine qui a été injectée dans le doigt.
- Les modes de traitement varient d'une prise en charge conservatrice jusqu'à l'infiltration locale d' $\alpha$ -bloquants.
- Il faudrait établir, dans les urgences et les autres établissements de soins primaires, un protocole de traitement d'une ischémie digitale induite par l'épinéphrine. Même s'il n'existe actuellement pas de protocole précis de traitement pour les injections accidentelles d'épinéphrine dans un doigt, on peut d'abord essayer sans risque des mesures conservatrices (p. ex. réchauffement, nitrate en pâte). Si l'ischémie digitale n'y répond pas, on conseille une injection avec de la phentolamine.

in deciding on an appropriate management plan is that it is often difficult to assess the amount of epinephrine that has been injected into the digit. It has been suggested that because onset of digital ischemia occurs within 1 hour of injection, no treatment is required if the patient has no symptoms upon presentation and the physical examination findings are normal.<sup>7</sup> When selecting a management strategy, one should consider that no reports of digital necrosis following digital epinephrine injection exist, irrespective of treatment. Here we present several management strategies.

**Spontaneous resolution.** Spontaneous return of circulation following accidental autoinjection of epinephrine has been reported<sup>8,9</sup>; however, this approach is associated with more severe reperfusion pain, as well as a delayed return of sensation, of up to 10 weeks.<sup>10</sup> In a study by Fitzcharles-Bowe et al, the authors injected their own digits with high-dose epinephrine to document the outcome.<sup>11</sup> In one case, blood flow spontaneously returned to the digits in 6 to 14 hours; however, sensation took up to 33 hours to resolve, and the author experienced a further 10 weeks of partial neurapraxia in the finger that was injected with the highest dose of epinephrine. Mrvos et al studied 28 cases of accidental injection of epinephrine, 23 of which involved digital injection. Overall, 86% required minimal, if any, treatment, and all experienced return of normal circulation. This study raises the possibility that most cases do not need invasive treatment.<sup>12</sup> However, most case reports of accidental injection of epinephrine document some form of treatment.

**Conservative and less well studied treatments.** Conservative treatments include warm water soaks, nitroglycerin paste, and massage. Reports of other, less well studied treatments include amyl nitrite inhalation, iloprost infusion, and stellate ganglion block.<sup>13</sup>

**Topical nitroglycerin.** Topical nitroglycerin is often reported as an initial treatment. Lee and Thomas<sup>14</sup> described 2 cases of accidental injection with an autoinjector device that were treated with topical nitroglycerin. One patient was treated with a 10-mg nitroglycerin patch, which was applied for 48 hours; the other was treated with gauze that was spray soaked in 400 µg of nitroglycerin. In both cases, return of digital circulation was achieved within 1 hour.<sup>14</sup> However, there are several reports in which topical nitroglycerin was used without effect, leading to eventual reversal of epinephrine with other conservative measures<sup>9</sup> or an  $\alpha$ -antagonist.<sup>14,15</sup>

**Digital blocks and other reported options.** Digital blocks are another possible treatment option. Digital sympathetic nerves travel within the neurovascular bundle, in

close proximity to the digital arteries.<sup>16</sup> Theoretically, one could blunt the sympathetic response to epinephrine by using a nerve block. Maguire and colleagues successfully treated a patient following accidental digital injection with an epinephrine autoinjector device with a digital block, using 1 mL of 2% lidocaine mixed with 0.5 mg of phentolamine.<sup>10</sup> Two other reported treatments of accidental epinephrine injection are calcium channel blockers and terbutaline, but the results for calcium channel blockers have been disappointing<sup>8,17-19</sup> and those for terbutaline have been equivocal.<sup>17</sup>

**Phentolamine.** Phentolamine has been used following accidental digital injection with epinephrine autoinjector devices, as it is an  $\alpha$ -antagonist that competitively inhibits the effects of epinephrine.<sup>1,20-22</sup> The concentration and volume of phentolamine used for such treatment varies widely in the literature, but several reports have used 2 to 3.5 mg in volumes of 1 to 2 mL. It can be injected at the puncture site, administered intra-arterially, or used as a digital block.<sup>7,10,13,23</sup> It is prudent to use small volumes to prevent worsening any ischemia. Also, owing to its short half-life, more than 1 injection might be necessary.<sup>8</sup> Phentolamine has a rapid onset of action, and several studies report return of circulation within minutes after injection.<sup>11,13,23</sup> In one study, phentolamine reversed epinephrine injection after 1 hour 25 minutes in human subjects, compared with the controls that took 5 hours 19 minutes.<sup>24</sup>

Phentolamine is the most frequently cited treatment in cases of accidental injection with epinephrine autoinjector devices. It is successful even in cases where a considerable period of time has passed between autoinjection and treatment.<sup>6,25</sup> There have been no reported adverse reactions following phentolamine use<sup>10,16</sup>; however, given the potential side effects of hypotension and arrhythmia, it has been suggested that blood pressure and external cardiac monitoring would be prudent after injection.<sup>26</sup> In one study that looked at the effects of epinephrine in local anesthesia of digits, patients with a history of ischemic digits and vasospastic conditions were excluded.<sup>4</sup> This raises the issue of whether a lower threshold for  $\alpha$ -antagonist use should be considered when treating patients with known peripheral vascular conditions.

Most of the articles in the literature on accidental epinephrine injection are case reports, making it difficult to adequately compare the various treatment options. However, in a study comparing the effectiveness of nitroglycerin, phentolamine, and sodium nitroprusside following intra-arterial norepinephrine injection, phentolamine was more effective at vasodilation than either nitroglycerin or sodium nitroprusside.<sup>27</sup> In 1989, Aycock et al used epinephrine injection in a rat foot model to test the effect of phentolamine or labetalol reversal. One

hundred percent of rats in the control group and 70% of rats in the labetalol group demonstrated evidence of tissue necrosis, whereas none of the phentolamine-treated animals developed necrosis.<sup>28</sup>

## Proposed management plan

Epinephrine autoinjector devices are increasingly prescribed for the treatment of anaphylaxis. Unfortunately, accidental digital epinephrine injection is not an uncommon occurrence. Several case reports describe different methods of treatment, ranging from conservative management to local infiltration with  $\alpha$ -antagonists. Given the incidence of accidental injection with epinephrine autoinjectors, a protocol for treatment of epinephrine-induced digital ischemia should be available in EDs and other primary care sites. Although there is currently no clear treatment protocol for accidental digital epinephrine injection, our review suggests that conservative measures (eg, warming, nitropaste) can safely be tried initially. If the digital ischemia does not respond, injection with phentolamine is advisable. A lower threshold for use of phentolamine might be advisable if the patient suffers from peripheral vascular disease.



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### Competing interests

None declared

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### References

- Westfall TC, Westfall DP. Adrenergic agonists and antagonists. In: Brunton LL, Lazo JS, Parker KL, editors. *Goodman and Gilman's the pharmacological basis of therapeutics*. 11th ed. New York, NY: McGraw-Hill Companies Inc; 2006. p. 237-97.
- Biaggioni I, Robertson D. Adrenoceptor agonists and sympathomimetic drugs. In: Katzung BG, Masters SB, Trevor AJ, editors. *Basic and clinical pharmacology*. 11th ed. New York, NY: McGraw-Hill Companies Inc; 2009. p. 127-48.
- Johnson HA. Infiltration with epinephrine and local anesthetic mixture in the hand. *JAMA* 1967;200(11):990-1.
- Waterbrook AL, Germann CA, Southall JC. Is epinephrine harmful when used with anesthetics for digital nerve blocks? *Ann Emerg Med* 2007;50(4):472-5.
- Denkler K. A comprehensive review of epinephrine in the finger: to do or not to do. *Plast Reconstr Surg* 2001;108(1):114-24.
- Deshmukh N, Tolland JT. Treatment of accidental epinephrine injection in a finger. *J Emerg Med* 1989;7(4):408.
- Sherman SC. Digital EpiPen® injection: a case of conservative management. *J Emerg Med* 2011;41(6):672-4. Epub 2009 Sep 17.
- ElMaraghy MW, ElMaraghy AW, Evans HB. Digital adrenaline injection injuries: a case series and review. *Can J Plast Surg* 1998;6(4):196-200.
- Skorpinski EW, McGeady SJ, Yousef E. Two cases of accidental epinephrine injection into a finger. *J Allergy Clin Immunol* 2006;117(2):463-4. Epub 2005 Nov 28.
- Maguire WM, Reisdorff EJ, Smith D, Wiegstein JG. Epinephrine-induced vasospasm reversed by phentolamine digital block. *Am J Emerg Med* 1990;8(1):46-7.
- Fitzcharles-Bowe C, Denkler K, Lalonde D. Finger injection with high-dose (1:1,000) epinephrine: does it cause finger necrosis and should it be treated? *Hand (N Y)* 2007;2(1):5-11.
- Mrvos R, Anderson BD, Krenzelo EP. Accidental injection of epinephrine from an autoinjector: invasive treatment not always required. *South Med J* 2002;95(3):318-20.
- Hinterberger JW, Kintzi HE. Phentolamine reversal of epinephrine-induced digital vasospasm. How to save an ischemic finger. *Arch Fam Med* 1994;3(2):193-5.
- Lee G, Thomas PC. Accidental digital injection of adrenaline from an autoinjector device. *J Accid Emerg Med* 1998;15(4):287.
- Molony D. Adrenaline-induced digital ischaemia reversed with phentolamine. *ANZ J Surg* 2006;76(12):1125-6.
- McCauley WA, Gerace RV, Scilley C. Treatment of accidental digital injection of epinephrine. *Ann Emerg Med* 1991;20(6):665-8.
- Stier PA, Bogner MP, Webster K, Leikin JB, Burda A. Use of subcutaneous terbutaline to reverse peripheral ischemia. *Am J Emerg Med* 1999;17(1):91-4.
- Khairalla E. Epinephrine-induced digital ischemia relieved by phentolamine. *Plast Reconstr Surg* 2001;108(6):1831-2.
- Mol CJ, Gaver J. A 39-year-old nurse with accidental discharge of an epinephrine autoinjector into the left index finger. *J Emerg Nurs* 1992;18(4):306-7.
- Velissariou I, Cottrell S, Berry K, Wilson B. Management of adrenaline (epinephrine) induced digital ischaemia in children after accidental injection from an EpiPen. *Emerg Med J* 2004;21(3):387-8.
- Zucker G. Use of phentolamine to prevent necrosis due to levarterenol. *J Am Med Assoc* 1957;163(16):1477-9.
- Jordan LK. An unusual case of digital ischemia. *N C Med J* 1969;30(10):418-9.
- Hardy SJ, Agostini DE. Accidental epinephrine auto-injector-induced digital ischemia reversed by phentolamine digital block. *J Am Osteopath Assoc* 1995;95(6):377-8.
- Nodwell T, Lalonde D. How long does it take phentolamine to reverse adrenaline-induced vasoconstriction in the finger and hand? A prospective, randomized, blinded study: the Dalhousie project experimental phase. *Can J Plast Surg* 2003;11(4):187-90.
- Burkhart KK. The reversal of the ischemic effects of epinephrine on a finger with local injections of phentolamine. *J Emerg Med* 1992;10(4):496.
- McGovern SJ. Treatment of accidental digital injection of adrenaline from an auto-injector device. *J Accid Emerg Med* 1997;14(6):379-80.
- Coffman JD, Cohen RA. Intra-arterial vasodilator agents to reverse human finger vasoconstriction. *Clin Pharmacol Ther* 1987;41(5):574-9.
- Aycock BG, Hawtof DB, Moody SB. Treatment of peripheral ischemia secondary to lidocaine containing epinephrine. *Ann Plast Surg* 1989;23(1):27-30.

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