BRIEF REPORT

Phentolamine Reversal of Epinephrine-Induced Digital Vasospasm

How to Save an Ischemic Finger

Joseph W. Hinterberger, MD, Harry E. Kintzi, MD, FACEP

A 17-year-old girl accidently injected her thumb with an adult autoinjector epinephrine syringe, resulting in rapid digital ischemia. Local infiltration of 0.5% phentolamine mesylate injected at the puncture site immediately resolved the ischemia and resulted in no long-term sequelae. Similar cases of epinephrine-induced digital ischemia are reviewed herein, revealing phentolamine to be the drug of choice for reversal of this type of ischemia. Alternative attempts to restore blood flow included warm water immersion, amyl nitrite inhalations, metacarpal nerve block, and application of topical nitroglycerine paste; each was found to be ineffective. We conclude that digital ischemia secondary to accidental injection of epinephrine can be quickly and safely reversed with the use of 0.5% phentolamine locally infiltrated in the region of accidental injection. *(Arch Fam Med. 1994;3:193-195)*

The use of lidocaine hydrochloride with epinephrine as a local anesthetic, combined with the widespread use of automatic epinephrine injectors in the treatment of allergic reactions, has resulted in the inadvertent injection of epinephrine into the digits. The result is often ischemia resistant to traditional reperfusion attempts. Below is a review of case reports, including one from our own experience, describing the use of phentolamine mesylate in the reversal of epinephrine-induced ischemia. From these reports, as well as from other supporting basic science data, we recommend the use of local phentolamine in the treatment of epinephrine-induced vasospasm.

REPORT OF A CASE

A 17-year-old black girl presented to the Lancaster (Pa) General Hospital emergency department approximately 30 minutes after accidentally discharging an adult autoinjector anaphylaxis syringe (Epipen, Center Laboratories, Port Washington, NY) into the pad of her left thumb. The thumb was cold, white, and insensible to a well-defined demarcation just proximal to the interphalangeal joint. Both of us were familiar with the use of phentolamine in the reversal of norepinephrine bitartrate–induced intravenous-site ischemia in the critical care unit setting; therefore, the decision was made to administer phentolamine.

Two milliliters of a 0.5% phentolamine solution was injected both at the initial puncture site and along the line of ischemic demarcation bilaterally. The thumb pad became progressively pink during injection and began to regain sensation and warmth within 5 minutes. In 1 hour, the thumb had returned to completely normal color, sensation, and warmth, with only minimal residual tenderness at the injection sites. The patient was discharged in excellent condition, and telephone follow-up 1 month later revealed no adverse long-term sequelae.

HISTORICAL REVIEW

Early studies by Zucker[1] revealed phentolamine to be the drug of choice in re-

From the Department of Family and Community Medicine (Dr Hinterberger) and Lancaster (Pa) Emergency Associates (Dr Kintzi), Lancaster General Hospital.

versal of soft-tissue ischemia due to accidental norepinephrine extravasation. The use of phentolamine in reversal of epinephrine-induced vasospasm, however, was first reported by Jordan[2] in 1969. A 19-year-old dental assistant cut a digital artery and, without knowing the possible untoward effects, used a 1:1000 epinephrine solution to stop the bleeding. Two hours later, her then blanched, cold digit was immersed in warm water without effect. Subsequent amyl nitrite inhalations were likewise ineffectual. Eventually, 5 mL of 0.1% phentolamine was injected circumferentially around the finger with instant return of spurting arterial blood.

In 1989, Deshmukh and Tolland[3] also reported using phentolamine for this purpose. A 39-year-old school nurse accidentally injected her right index finger at the palmar aspect of her distal crease with an anaphylaxis syringe (Epi-pen). She was seen 6 hours after the injection, at which time the distal one half of her finger was cold, numb, and pale. One milliliter of 1% phentolamine was infiltrated into the puncture area, and the finger became warm and pink within 30 minutes.

Pharmacologic and physiologic research continued to confirm the benefit of phentolamine in the reversal of ischemia. In 1987, Coffman and Cohen[4] studied fingertip blood flow and capillary flow in subjects with fingers that were vasoconstricted by intra-arterial norepinephrine or body cooling. Sodium nitroprusside, nitroglycerine, and phentolamine were compared, and although each showed evidence of increased fingertip blood flow, only phentolamine increased both fingertip blood flow and capillary flow.

Further support came from Aycock et al[5] in 1989. A rat foot model was used to determine the effectiveness of phentolamine vs labetalol hydrochloride vs control in the reversal of ischemia after injection of lidocaine with epinephrine. None of the rats in the phentolamine-reversal group developed necrosis, while 70% of the animals in the labetalol group and 100% of the animals in the control group did develop local necrosis.

Maguire and Reisdorff[6] described an accidental injection of a pediatric automatic injector (Epi-pen Jr) into the distal right index finger of a 17-year-old boy. In this case, 1 mL of 0.5% phentolamine was mixed with 1 mL of 2% lidocaine and was injected at the proximal finger in a digital block technique. There was partial restoration of circulation 15 minutes later, at which time an identical digital block was performed. Neurovascular integrity was complete 15 minutes after the second block procedure.

In June 1991, McCauley et al[7] described an adult autoinjector accident to the right index fingertip. The resultant ischemia was resistant to a metacarpal nerve block, as well as to the application of topical nitroglycerine paste to the entire finger. Approximately 3 hours after the injury, 1.5 mg (concentration unspecified) of phentolamine mesylate was injected into the original puncture site subcutaneously. The entire finger was warm and pink within 20 minutes.

Of note, none of the reported cases describe any adverse effects of phentolamine at the doses used. The two case reports that provide information regarding vital signs before, during, and after phentolamine use report stable vital signs, with no significant deviations in blood pressure.[6,7]

COMMENT

Epinephrine causes vasoconstriction of the arterioles by its action at the α_1 and α_2 postsynaptic receptors of the perivascular smooth muscle.[8] As an α-adrenergic blocking agent, phentolamine binds selectively to the α class of adrenergic receptors and thereby competitively blocks the vasoconstrictive effects of epinephrine. Traditional indications for use of phentolamine include hypertension (specifically when associated with monoamine oxidase inhibitors, pheochromocytoma, or cocaine intoxication), shock, autonomic hyperreflexia, Raynaud's phenomenon, and peripheral vascular disease.[9,10] Although clearly of value in treating the ischemia of accidental epinephrine injection, the use of phentolamine in this setting is relatively new.

The use of epinephrine in anesthetic agents for the digits, tip of the nose, and penis is generally discouraged. Nevertheless, local anesthetics containing epinephrine have been used in the hand without untoward effects.[11] The common theme in the case reports reviewed herein is the accidental self-injection of anaphylaxis syringe units by patients and health care workers. The phrase "Epi-pen thumb" has been coined to describe this event, and its annual incidence has been estimated as one accidental injection per 50 000 Epi-pen units.[6]

In each case presented, phentolamine, in varying concentrations and administration techniques, was successfully used to reverse the ischemic effects of epinephrine. Alternative attempts at restoring blood flow, including warm water immersion, amyl nitrite inhalations, metacarpal nerve block, and use of topical nitroglycerine paste, were universally ineffective. In comparing the various methods of phentolamine dilution and administration, it is our opinion that a 0.5% solution administered by direct local infiltration to the ini-

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tial puncture region is most prudent. The 0.5% concentration provides sufficient phentolamine for effectual reversal of ischemia, while not presenting an inordinate amount of fluid to the pulp spaces of the finger. The local infiltration allows phentolamine direct access to the affected α receptors, whereas the digital block technique may inappropriately allow phentolamine to diffuse proximal to the affected region before its maximum effect.

In our patient, we chose to use local infiltration at the site of accidental injection as well as at the line of ischemic demarcation. Although successful, the choice to infiltrate along the ischemic line was arbitrary and probably unnecessary. This is especially true in light of the immediate color return to the thumb pad even during infusion of phentolamine to the puncture site. In addition, lidocaine should not be added to the mixture since it may interfere with the clinical assessment of sensation once blood flow has returned.

In the cases presented above, accidental autoinjection of epinephrine into the digits of the hand caused severe ischemia, which was rapidly reversed with phentolamine. No systemic ill effects were reported. We recommend the use of 0.5% phentolamine infiltrated locally into the region of accidental injection as the primary means of reversing epinephrine-induced digital ischemia.

Accepted for publication November 3, 1993.

Reprint requests to the Department of Family and Community Medicine (Dr Hinterberger) or Lancaster Emergency Associates (Dr Kintzi), Lancaster General Hospital, 555 N Duke St, Lancaster, PA 17604-3555.

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