FPIN's Help Desk Answers

Reducing Amputation Rates After Severe Frostbite

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Clinical Question

Is tissue plasminogen activator (tPA) effective in reducing digital amputation rates in patients with severe frostbite?

Evidence-Based Answer

In patients with severe frostbite, tPA plus a prostacyclin may be used to decrease the risk of digital amputation. (Strength of Recommendation [SOR]: B, based on a single randomized controlled trial [RCT].) tPA can be used alone and is associated with lower amputation rates compared with local wound care. (SOR: C, based on lower-quality cohort studies.)

A 2011, open-label RCT (n = 47) compared tPA plus iloprost (Ventavis), iloprost alone, and buflomedil (not available in the United States) in patients with frostbite extending just past the proximal phalanx or injury proximal to the metacarpal or metatarsal joint.[1] Digital perfusion was not assessed before treatment. All patients underwent rapid tissue rewarming and received 250 mg of aspirin and 400 mg of intravenous (IV) buflomedil. Patients then received 100 mg of IV tPA plus an IV infusion of iloprost (0.5 to 2 ng per kg per minute) for six hours per day, iloprost alone, or 400 mg of IV buflomedil per day. After eight days, a technetium-99m scan was used to identify digits at risk of amputation. In the buflo-medil group, nine of 15 patients were at risk of amputation compared with zero of 16 in the iloprost group ($P < .001$) and three of 16 in the tPA plus iloprost group ($P < .03$). After three months, four patients in the iloprost group had amputations compared with three in the tPA plus iloprost group. Statistical testing between the tPA plus iloprost and the iloprost alone groups was not reported, and comparisons between groups were complicated by unbalanced randomization; there were 25 digits in the tPA plus iloprost group with severe disease and only three and nine digits in the other treatment arms. Thus, no conclusions can be reached about the effect of tPA plus iloprost compared with iloprost alone.

A 2007 retrospective cohort trial evaluated the use of tPA in six patients with severe frostbite.[2] After rapid rewarming, patients underwent digital angiography, and those with significant perfusion defects received intraarterial tPA (0.5 to 1 mg per hour IV infusion) and heparin (500 units per hour IV infusion) for up to 48 hours. Patients who presented after 24 hours and had normal or uninterpretable angiography results (n = 26) received local wound care. The tPA group had a lower amputation rate (10% vs. 41%; $P < .05$), but patients in the control group were not matched for injury severity.

A 2005 prospective cohort trial evaluated the use of tPA in 19 patients with severe frostbite (no perfusion on technetium-99m bone scan).[3] In patients who received intraarterial or IV tPA, 33 of 174 affected digits (19%) were amputated. In eight historical control patients who had undergone local wound care alone, at least 60 of 65 affected digits (92%) were amputated.

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