Stiff fingers as an unwanted side effect of intravascular tadalafil gel abuse

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ABSTRACT
The internet provides the public with unregulated access to a wide range of medications. We present the case of a 43-year-old man who purchased oral tadalafil gel on the internet and injected it into his left radial artery. He presented 48 hours after injection with signs of ischaemia distal to the injection site requiring a combination of medical and surgical treatment. This unique case highlights the potential dangers of unregulated access to medication and the consequences of intravascular injection of oral gels.

KEYWORDS
Ischaemic limb – Intra-arterial drug abuse

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In 1998 the US Food and Drug Administration approved the drug sildenafil (Viagra©; Pfizer, New York, US), a phosphodiesterase 5 (PDE5) inhibitor for the treatment of erectile dysfunction. Along with similar analogues such as tadalafil (Cialis©; Lilly, Indianapolis, IN, US) and vardenafil (Levitra©; Bayer, Wayne, NJ, US), these drugs are now first-line treatment for erectile dysfunction worldwide. In addition to their therapeutic use, PDE5 inhibitors are popular recreational drugs owing to their perceived ability to enhance sexual performance.

In recent years, there has been an exponential increase in the availability of prescription-only medication via websites. While many legitimate sites have enhanced patient care, there has been an alarming growth of unregulated sites linked to an increase in prescription drug abuse, including PDE5 inhibitors, with potentially disastrous consequences.

We present the case of a 45-year-old man who purchased oral tadalafil gel without prescription from an internet site and injected it into the radial artery of his left wrist. Twenty-four hours following injection, he developed acute ischaemia of his hand and digits. We believe this to be the first reported instance of this type of drug being abused in this manner.

Case History
A 45-year-old, right-hand dominant man presented to the accident and emergency department 48 hours after intra-arterial injection of oral tadalafil gel into the radial artery of his left wrist. His intention was to inject the gel intravenously, hoping that this would enhance and expedite the effect. Immediately after the injection, he experienced severe pain in his hand distal to the site of injection but claims this subsided. Twenty-four hours thereafter, he noticed mottling of the skin with reduced sensation to the digits. He waited a full 48 hours to seek medical attention, by which time his left hand was discoloured with widespread dusky mottling.

On examination, the patient’s hand was mildly oedematous but soft, with a normal range of non-tender movement at all joints. The capillary refill time in his digits was 12–15 seconds (Fig 1). There was a large ischaemic area on the dorsum of the hand with a small central necrotic area (Fig 2). Doppler ultrasonography revealed audible, pulsatile arterial flow in the ulnar and radial arteries, the palmar arch, the digital vessels in the little and ring fingers to the level of the distal palmar crease, and in the middle and index fingers to the level of the middle of the proximal phalanx. On account of these findings, it was decided that the injury was limited to the microvasculature of the skin and distal digits, and surgical intervention was not immediately indicated.

Medical treatment was initiated involving intravenous heparin infusion aiming for an activated partial thromboplastin time ratio of 1.5 to 2.5 to prevent further thrombosis and intravenous iloprost (Ventavis©; Bayer) (100µg, diluted to 500ml using normal saline, infused over six hours, once daily) to encourage vasodilation and reperfusion via collateral vessels. The patient showed immediate signs of improved perfusion with the commencement of iloprost, which coincided with subjective feelings of increased warmth and decreased pain to the digits.
After 36 hours of medical treatment, the patient’s hand had become more oedematous and painful, with capillary staining in the tips of his index finger and thumb. Digital perfusion was not detected by pulse oximetry. In light of these developments, prophylactic carpal tunnel decompression and a thenar eminence fasciotomy was performed. He received an eight-day course of iloprost and was discharged with daily subcutaneous low molecular weight heparin injections (dalteparin, 15,000 units, once daily). The patient attended weekly outpatient plastic surgery dressing clinics and physiotherapy sessions twice a week. The tip of his thumb and index finger subsequently autoamputated without further surgical intervention.

Discussion

Limb ischaemia is a recognised complication of inadvertent and deliberate intra-arterial injection. Case reports document pain and ischaemia immediately following injection of oral preparations of drugs due to embolisation of the drug in distal vessels resulting in devastating tissue loss.4

In the case described, there was immediate pain distal to the injection site that rapidly subsided and the clinical signs of ischaemia did not develop for 24 hours. We suggest this time delay may be due to the inflammation of the microvessels by the gel, leading to gradual swelling, subsequent occlusion and the resultant ischaemia. Tadalafil, the active ingredient of the gel, is a potent vasodilator that has been used to treat vasospasm. We therefore believe the ischaemia seen in this case was due to the action of the gel causing gradual swelling and occlusion, and not the drug contained in it. Similar observations were made in cases of intra-arterial oral temazepam gel injection resulting in catastrophic tissue loss.5 However, on histological examination, there was no identifiable embolism of the gel. Instead, the histological study showed significant endothelial cell swelling, vasculitis, capillary thrombosis and interstitial oedema.

Conclusions

Iloprost is a synthetic prostacyclin analogue that is used routinely to treat pulmonary artery hypertension but it has also been used in scleroderma, Raynaud’s disease and limb ischaemia owing to its vasodilatory effect. In this case, the injury to the vasculature was thought to be confined to microvessels where no surgical or radiological intervention was possible.

As a result, we hypothesise that in these instances, the use of iloprost may limit the extent of the injury to the most distal tissues where there is no potential for collateral flow and, when used in conjunction with an anticoagulant, it may help to prevent retrograde thrombosis and limit further tissue loss. This is supported by findings from other reports.4 Our advice to others who may face similar cases would therefore be to make prompt assessment of the level of the vascular occlusion to establish whether surgical or medical treatment is most appropriate. Attention should be paid to the swelling resulting from reperfusion after medical treatment and early surgical decompression is advised in these instances.

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