Combination treprostinil with sympathectomy and vascular reconstruction to treat recurrent digital ulcer disease

Sir,

Digital ulceration is an obliterator vascularity associated with substantial morbidity (1). We present two patients with critical digital ischaemia treated with intravenous (IV) treprostinil and surgery, followed by maintenance therapy with oral treprostinil to prevent recurrence.

Case 1. A 50-year-old female with limited systemic sclerosis (anti-nuclear antibody (ANA) 1:640 with centromere pattern) presented with acute digit-threatening necrotic ulcers of her right third finger. Six months prior, she had required partial amputations of her 2nd and 5th right digits and had sympathectomy of the right ulnar artery. Ucercation recurred despite aspirin, clopidogrel, amlopidine, pentoxifylline, and bosentan. She was admitted for IV treprostinil with right snuff box, palmar arch, and common digital sympathectomy. She was discharged on oral treprostinil (Table I) without further amputations or hospitalisation.

Case 2. A 21-year-old female with diffuse systemic sclerosis (ANA 1:640 and antitopoisomerase I - 4.5) presented with left thumb and right third digit-threatening ulcer disease. She was admitted for IV treprostinil and continued cilostazol and tadalafil. Due to progressive digital ulceration after an injury and required IV treprostinil to salvage the digits before transitioning back to oral treprostinil. Due to progressive gangrenous ulcerations on her bilateral first, third, and fourth digits she was admitted for IV treprostinil (Table I). Arteriogram showed thrombosis of the ulnar arteries bilaterally. She underwent left ulnar arteriogram showed thrombosis of the ulnar artery, presumably due to the anatomy, as it is more likely to be compressed by thickened forearm fascia in its course through Guyon’s canal.

Digital ulcerations are common (~50%) in systemic sclerosis. Despite anti-platelet and oral vasodilators, 4.8% require amputation (1); prostanooids are reserved for recurrent or refractory ulceration (2). Digital sympathectomy is an efficacious option, which improves wound healing (3). Resolution of ulcers were seen more commonly after treatment with sympathectomy and bypass when compared to sympathectomy alone (4). Despite this data, sympathectomy (5) and vascular reconstruction are rarely performed.

Treprostinil (6) and iloprost (7) are prostacyclin analogs that have been used to salvage digits, but the IV format limits their use. Treprostinil has an oral form and despite it improving digital perfusion (8), it did not prevent recurrent ulceration compared to placebo (9). However, discontinuing oral treprostinil was associated with an increase in digital ulcer recurrence (10). This suggests that oral maintenance therapy may be valuable once ulcers heal. No previous study evaluated combination treprostinil and sympathectomy/reconstruction to prevent future ulcer disease.

Given the pain, disability, and health care utilization associated with digital ulceration, better treatment strategies are needed to improve and maintain perfusion. After conservative therapy fails, we recommend a multidisciplinary approach using prostanooids and vascular reconstruction. We found utilising treprostinil (parenteral followed by oral) in combination with extensive sympathectomy (with or without arterial reconstruction) leads to improved and sustained perfusion. Further studies are needed to evaluate this strategy in reducing recurrent ulcerative disease.

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References

Table I. Treprostinil therapy used to treat digital ulcer disease.

<table>
<thead>
<tr>
<th>Hospital Day</th>
<th>Patient 1</th>
<th>Patient 2</th>
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<tbody>
<tr>
<td></td>
<td>Hospitalisation - 1</td>
<td>Hospitalisation - 2</td>
</tr>
<tr>
<td>0</td>
<td>IV treprostinil initiated at 4 ng/kg/min</td>
<td>IV treprostinil initiated at 2 ng/kg/min</td>
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<tr>
<td>2-4</td>
<td>Treprostinil was titrated up to 10 ng/kg/min with improvement in pain and perfusion.</td>
<td>Treprostinil was titrated up to 10 ng/kg/min with improvement in finger pain and perfusion.</td>
</tr>
<tr>
<td>8-12</td>
<td>Treprostinil was transitioned to oral 1.25 mg every 8 hours.</td>
<td>Treprostinil was transitioned to oral 6 mg every 8 hours.</td>
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<tr>
<td>14-16</td>
<td>IV treprostinil was increased to 12 ng/kg/min with improved pain and perfusion. It was transitioned to 2 mg every 8 hours.</td>
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</tbody>
</table>

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