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Increase in skin perfusion pressure after maggot debridement therapy for critical limb ischaemia

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Summary

Skin perfusion pressure (SPP) is the perfusion pressure at the skin level, and it can serve as an index of peripheral circulation in the skin and subcutaneous tissue. We report a 78-year-old man with critical limb ischaemia who, despite having undergone several catheter interventions, still had severe ulcers with exposed bone on his right foot. We performed transmetatarsal amputation. The tissue around the surgical site became necrotic several days later, and did not respond to conservative therapy. Therefore, we opted for maggot debridement therapy (MDT), given that maggots favour necrotic tissue. After the therapy, SPP around the ulcer increased from 12 to 54 mmHg on the dorsal aspect, and from 17 to 44 mmHg on the plantar aspect. Wound healing was successfully activated by MDT, leading to complete healing within 2.5 months after MDT. We believe that MDT probably contributed to increase the blood supply to the ischaemic wound.

The number of patients with critical limb ischaemia (CLI) is increasing worldwide. Maggot debridement therapy (MDT) is one of a number of treatments currently available for CLI. While it is known that necrotic tissue is selectively eliminated through the action of proteolytic enzymes in maggot saliva, most of the mechanisms involved in MDT have not been fully elucidated. We report a case of CLI successfully treated with MDT in which skin perfusion pressure (SPP) was found to have increased after MDT.

Report

A 78-year-old man presented with severe ulcers, with exposed bone on his right foot, including the first and second toes, and the lateral aspect of the foot (Fig. 1). He had no diabetes mellitus, but accompanying diseases included hypertension, kidney failure, and atrial fibrillation. He had already undergone several catheter interventions. On admission to our hospital, his ankle–brachial pressure index was 0.57 on the right side and 0.5 on the left side, and SPP of the right foot was 42 mmHg dorsally and 42 mmHg on the plantar aspect as measured by a skin perfusion pressure system (SensiLase PAD 3000; Kaneka Medix Corp. Osaka, Japan). We performed conservative therapies such as hyperbaric oxygenation and basic fibroblast growth factor administration. However, no granulation of the exposed bone occurred, and the total size of the ulcerated area did not change. His pain gradually worsened, indicating worsening ischaemia. SPP of the right foot was 12 mmHg dorsally and 17 mmHg on the plantar aspect. Therefore, we scheduled a modified trans-metatarsal amputation, which was performed 1.5 months after admission. The amputation level was decided according to SPP, but the tissue around the surgical site became necrotic several days later, and the wound did not respond to other conservative therapy (Fig. 2a). Given that maggots favour necrotic tissue, we performed two rounds of MDT (Fig. 2b,c). For 2 days, 5–10 larvae/cm^2 (Japan Maggot Company, Okayama City, Japan) were applied to the necrotic

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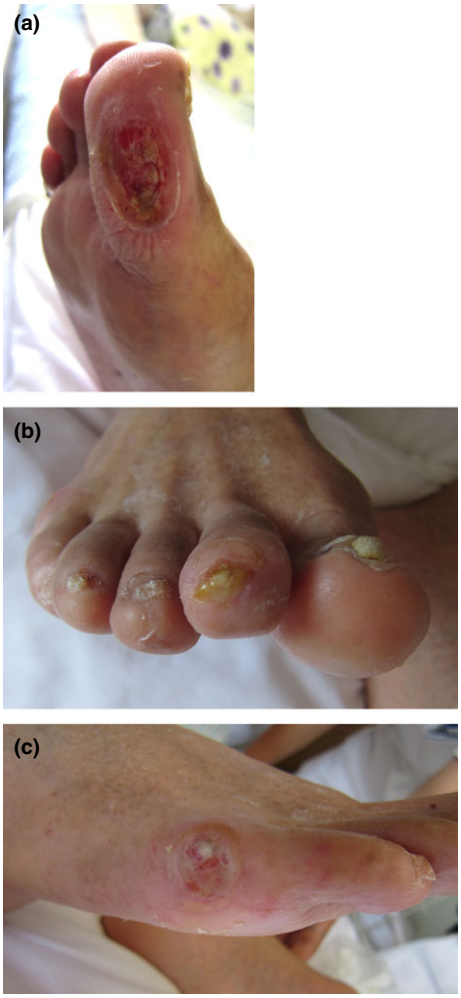

Figure 1 Photographs at initial presentation: (a) right first toe, (b) right second toe, and (c) lateral foot.

ulcers. Around 200 larvae were used in total. After the first of round MDT, SPP increased from 12 to 42 mmHg on the dorsal aspect of the foot and from 17 to 33 mmHg on the plantar aspect. After the second round of MDT, SPP rose to 54 mmHg on the dorsal and 44 mmHg on the plantar aspect (Fig. 3). During these two rounds of MDT, no other treatments such as hyperbaric oxygenation or basic fibroblast growth factor administration were given. The wound healing was successfully activated by MDT, as the wound was completely healed by 2.5 months after MDT (Fig. 2d), and walking ability was preserved.

MDT has a long history of use. In 1931, Baer reported its effectiveness for chronic osteomyelitis. With the invention of antibiotics, various other treatments to promote wound healing were developed, and clinicians ceased using MDT. However, because of the

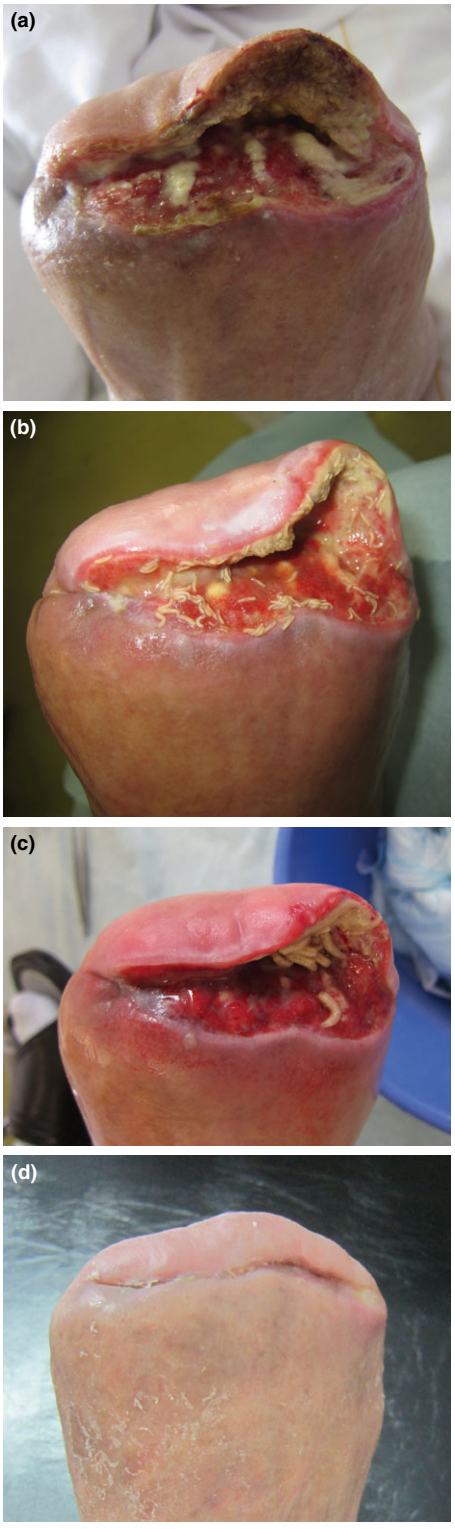

Figure 2 (a) Two months after modified transmetatarsal amputation; (b) maggots placed on the ischaemic wound; (c) 2 days after initial maggot placement; (d) 6 months after maggot debridement therapy.

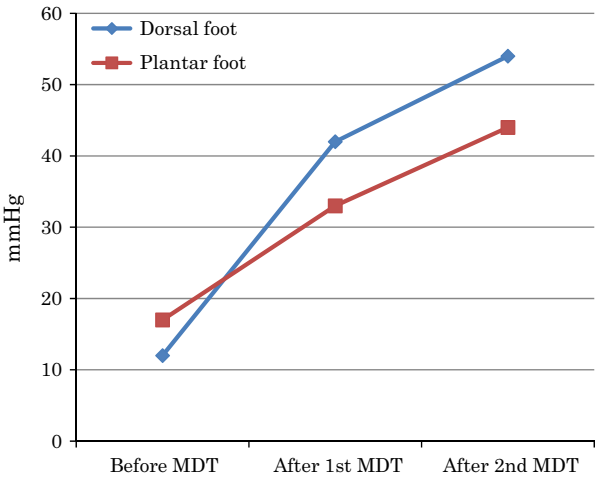

Figure 3 Change in skin perfusion pressure before and after maggot debridement therapy.

rise in antibiotic resistance and failure of modern wound care to heal many chronic infected wounds, use of medicinal larvae was re-introduced as a treatment in the late 1980s.[1] Although the mechanism of MDT is not completely understood, what is apparent is that necrotic tissue is selectively eliminated through the action of proteolytic enzymes in maggot saliva, and bacteria in the wound are destroyed by maggot secretions, including an antimicrobial peptide.[2,3] The efficacy of MDT for debridement has been proven in randomized clinical trials,[4] but evidence for any antimicrobial activity with the use of maggots comes mainly from laboratory studies. In 2010, Bexfield *et al.*[5] demonstrated for the first time that the amino acid-like compounds present in maggot excretions/secretions may mediate wound healing by stimulating angiogenesis.

MDT is used for the debridement of chronic wounds that are necrotic and infected. In general, MDT is suited to the treatment of distal ulcers with sufficient blood supply, such as infected diabetic gangrene. It had been thought that an ischaemic ulcer is a contraindication for MDT, but an increasing number of recent reports have documented its effectiveness for such ulcers.[6,7] Our patient had severe CLI, which had not responded to conservative treatment. Fortunately, the necrotic tissue was replaced by good granulation on the surface of the wound after the second round of MDT. This enabled conservative therapy to continue, and led to complete healing within 2.5 months. During MDT, SPP elevation was observed in the tissue around the ischaemic wound, and in particular, was increased almost into the normal range after the first round of MDT. To our knowledge, this is the first reported case of successful treatment by maggot debridement to indicate that MDT contributes to improving local perfusion, based on the observation of increased SPP.

SPP is the perfusion pressure at the level of the skin, and it serves as an index of peripheral circulation in the skin and subcutaneous tissue, while laser Doppler measures the blood pressure at the level of the capillary.[8] In our case, we think it likely that the blood supply at the skin level was increased and the peripheral circulation improved by the increase in SPP observed in the tissue around the ischaemic wound. It has been shown that amino acid derivatives contained in larval secretions exhibit significant proangiogenic effects *in vitro* on a human endothelial cell line, acting to promote the growth of blood cells.[5] Zhang *et al.*[9] showed a significant increase in the upregulation of vascular endothelial growth factor expression after MDT. The laboratory findings and clinically elevated SPP observed after MDT in the present case supports the notion that MDT can improve local perfusion in patients with CLI.

Learning points

- To our knowledge, this is the first reported case of MDT in which observation of elevated SPP suggests that the treatment is successful by contributing to improvement in local perfusion.
- Ischaemic ulcer is a good candidate for MDT.
- This case supports the hypothesis that MDT can improve local perfusion in patients with CLI.

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