CASE REPORT

The use of an extract of *Hypericum perforatum* and *Azadirachta indica* in a neuropathic patient with advanced diabetic foot

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SUMMARY

The successful use of an extract of *Hypericum* flowers (*Hypericum perforatum*) and nimh oil (*Azadirachta indica*; Hyperoil) in foot wounds with exposed bone in a patient with bilateral advanced diabetic ulcers, has been reported previously. It was hypothesised that this amelioration was linked with the improved glycaemic control and peripheral microvascular circulation. In this case report, the surprisingly successful outcome of another patient using Hyperoil for infection damaged diabetic foot, without prior use of surgical procedure, is described. The patient had no macrovascular pattern impairment. Diabetic foot healing paralleled with controlled local infection and enhanced glycaemic control. The outcome of this patient suggests that the effectiveness of this inexpensive therapy using Hyperoil for diabetic foot is not only linked with the presence of severe microvascular disorder, but also with the appropriate local treatment for ulcer being a must for its recovery.

BACKGROUND

Diabetes and its complications are becoming one of the major concerns for healthcare systems.¹ Patients with diabetes affected by leg/foot ulcers are difficult to manage.² The enhancement of diabetic ulcer home care may show significant improvement in the management of these diabetic complications with a consequent reduction of healthcare resources currently needed.^{1 2}

Hyperoil is a mixture of *Hypericum* flowers extract (*Hypericum perforatum*) and nimh oil (*Azadirachta indica*) produced by RIMOS S.r.L. Mirandola (MO)—Italy (Medical Device Class IIB CE0476). The successful use of Hyperoil in advanced diabetic ulcers has already been described.³ Previous experiences encouraged us to apply the use of Hyperoil to patients with foot ulcers not yet needing surgical procedures.

CASE PRESENTATION

A 67-year-old woman, 159 cm tall and weighing 81 kg (body mass index 32), affected by type 2 diabetes for 25 years, was hospitalised on 25 June 2012 presenting fever and diabetic ulcers at the third and fourth toes of the left foot, probably caused by shoe microtrauma. The patient experienced painful diabetic neuropathy for 8 years. An oedematous inflammation, linked to the presence of local infection, was observed as a symptom of cutaneous microvascular damage due to diabetic disease.

The eco-colour Doppler assessment did not show clinically significant venous or arterial anomalies. The laser Doppler fluximetry showed a big toe maximal perfusion of 241 PU (normal range 230–250 PU, Perfusion Unit, at 44°C) and foot dorsal supine/dependent transcutaneous partial pressure oxygen of 62 mm Hg/70 mm Hg (supine/dependent normal range: 60–65 mm Hg/70–75 mm Hg) did not reveal limb ischaemia.⁴

A significant lower –40% reduction of venuloarteriolar reflex (VAR, normal range ≥60%) was measured with laser Doppler,⁵ highlighting diabetic neuropathy.⁶

Complete clinical assessment included RX foot examination in two projections, which showed osteolysis and osteonecrosis with diffused microbubbles on the external side of the left foot.

The patient had very poor glycaemic control (fasting blood glucose 271 mg/dL; glycated hemoglobin (HbA1c) 14.2%), high blood pressure (130/80 mm Hg) treated with telmisartan 80 mg/day, while her other haematochemical examinations did not show any clinically relevant abnormality or renal function impairment (creatinine 0.7 mg/dL; blood urea nitrogen 19 mg/dL).

Therapy for diabetes was revised to 10 IU of fast acting insulin in the morning, 16 IU fast acting insulin at lunch and dinner plus 24 IU of basal insulin overnight.

Exudate culture revealed the presence of *Corynebacterium striatum*. Because of this, the patient was treated with ciprofloxacin 400 mg/day intravenous and teicoplanin 200 mg/day intravenous.

Physicians suggested amputation of the leg to avoid the risk of septicemia.

Even though the patient was unable to stand-up or walk, she refused amputation and remained hospitalised, requesting a supplementary consult.

On 2 July the patient, despite a debridement, presented adhesive fibrine on all exposed surface of the subcutaneous tissues, a vast dorsal necrosis area and undermined edges (figure 1A). Dressing treatment began by applying a few drops of Hyperoil on gauze used for cleaning the ulcer (figure 1B).

Subsequently, a little Hyperoil was dropped into the ulcer. Gauze dressing with a few drops of Hyperoil added to it was then applied over the ulcer to keep it sterile until the next day, when a new medication was applied in the same manner.

The day after, the area to be debrided was clearly visible: the edges showed a reduction of inflammation; the process of fibrinolysis had begun, cleaning

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Figure 1 Left foot at the beginning of Hyperoil treatment on 2 July 2012 (A), with further administration of Hyperoil treatment (B) and after 24 h (C).

the bed of the ulcer and displaying a clear demarcation between the necrosis and the granulation tissue (figure 1C).

The ulcer gradually improved in the next few days (figure 2A), the adhesive fibrine progressively detached from the bottom of the wound (figure 2B), the tendons became clean, the granulation tissue increased on the proximal dorsum area of the foot (figure 2C) and no undermined edges were seen, except in the basal area of the third and fourth toes (figure 2D).

The patient was discharged on 11 July 2012 to be admitted to a hospice for the elderly; clivarine 4200 U/day was prescribed.

Therapy with Hyperoil, applied once a day on the ulcer, was continued to maintain debridement. The ulcer improved further (figure 2E) while an abnormality of the cutaneous tropism appeared on the foot plantar area, containing some exudates from the basis of the third and fourth necrotic toes (figure 2F).

As the patient had no significant improvement in fever, a deep debridement below the third and fourth toes (figure 2G) and an incision behind the plantar area was performed to strip them down to a cavity, producing exudates and blood, on 16 July 2012 (figure 2H).

On 24 July 2012 the fever continued; there was *Corynebacterium* growth in the urine culture (performed on 16 July) showing concomitant urinary infection. Specific antibiotic therapy was started.

On 28 July 2012 another surgical cleansing was performed to remove the third and fourth finger (figure 3A, B) and the incision behind the plantar was stuffed using gauze with a few drops of Hyperoil (figure 3C, D).

An improvement of glycaemic control was observed (HbA1c 10%) even though urinary culture remained positive; thus antibiotic therapy was maintained.

On 14 August 2012 the fever abated, hypertension was well under control and glycaemic control continued to improve (fasting blood glucose 130 mg/dL; HbA1c 8%).

In the following months the therapy remained unchanged; the plantar incision slowly healed.

The dorsum and plantar ulcers (figure 3E, F) reduced in size due to proper granulation tissue.

On 18 October 2012 HbA1c fell to 6%; the diabetic ulcers continued to improve resulting in complete recovery on 20 December 2012 (figure 3G, H). Finally, her neuropathic pain disappeared and the patient was able to walk autonomously.

INVESTIGATIONS

Eco-colour Doppler, Laser Doppler Fluximetry, Transcutaneous Partial Pressure Oxygen (TcPO₂).

DIFFERENTIAL DIAGNOSIS

Critical limb ischaemia, large vessels atherosclerotic disease, microvascular thrombosis.

TREATMENT

Surgical debridement, minor amputation.

OUTCOME AND FOLLOW-UP

The patient did not have any new ulcers or recurrence in the old lesions at 18 months follow-up.

Figure 2 Left foot during Hyperoil therapy.

Figure 3 Left foot from surgical cleansing (A–E) to wound recovery.

DISCUSSION

Preparations of *Hypericum perforatum*⁷ and nimh⁸ have been used for centuries in traditional medicine. Hyperoil is a mixture of *Hypericum* and nimh extracts.³ Its original formulation could explain the observed clinical effects on fibrin reduction and the improvement of granulation and cutaneous tissue.^{3,9}

This is the first case where the positive use of Hyperoil, together with improved diabetes control, has clearly reversed the worsening of diabetic foot ulcers in a patient affected by severe diabetes without adjunctive cardiovascular disease of large vessels. The use of Hyperoil was started before the patient had significantly improved her glycaemic control, showing effectiveness per se, avoiding invasive debridement procedures and possible leg amputation, and leading to soft foot ulcer recovery.

As in a case previously described,³ the use of Hyperoil could have reduced the possibility of local reinfection, supporting the maintenance of diabetes control and furthermore, it did not worsen local microcirculation.

Further properly designed, controlled clinical trials are needed to establish the effectiveness of Hyperoil in the treatment of diabetic ulcers in a wider population.

Learning points

- The use of Hyperoil improved diabetic foot in a patient with diabetic neuropathy and no clinically relevant peripheral vascular disease.
- Patients with diabetic foot ulcer might significantly improve their diabetes control while recovering from ulcers, thus avoiding major amputations.

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Contributors MLI coordinated the management of the case; CC followed the patient and collected clinical data; and ML provided surgical expertise. All authors contributed to the collection of data, revised the article critically, gave their approval to this version and take full responsibility for the content.

Competing interests MLI occasionally acts as consultant for RIMOS.

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