Efficacy of honey gel in the treatment of chronic lower leg ulcers: A prospective study

ABSTRACT
Chronic leg ulcers are a common medical problem among elderly patients and have a dramatic impact on quality of life as a result of pain, disability, and social isolation. Regardless of their cause, chronic leg ulcers remain difficult to treat. In recent years, there has been increasing interest in the use of honey as a therapeutic agent.

Objective: To evaluate the efficacy of honey-based dressings in the treatment of chronic leg ulcers.

Methods: Ten patients with chronic (mean duration 3.3 years) leg ulcers who had received non-honey based treatments with no improvement were included in this study. A honey gel dressing was applied twice a week as the only treatment.

Results: Seven patients experienced complete healing of their leg ulcers. The remaining three patients showed a significant reduction in wound size, which was achieved in a mean time of 101 days (range 28-174 days).

Conclusion: Honey-based dressings appear to be an efficient and easy to use treatment for leg ulcers.

Key words: Chronic lower leg ulcer, venous leg ulcer, dressings, honey gel

INTRODUCTION
Lower leg ulcers affect 15-18 out of 10,000 adults in developed countries, with venous leg ulcers (VLUs) representing up to 84% of all leg ulcer cases (Watson, 2011). These ulcers have an important impact on the quality of life and health of patients (Callum, 2000). Treatment of VLU patients also has a significant economic impact; the annual cost of treatment of VLUs in the UK and Sweden is estimated to be between 1,300-2,500 Euros per patient. Costs increase for lesions with long healing times or for larger ulcerations, as well as for ulcers that are defined as “difficult to treat” (Ragnarson Tennvall, 2005). Difficult to treat cases can cause significant morbidity (Faria, 2011), seriously impact the patient’s quality of life (González-Consuegra, 2011), and consequently increase treatment costs.

Evidence-based treatment options for VLUs include leg elevation, compression therapy, topical (active) dressings, pentoxifylline, and aspirin therapy. Surgical management can be considered for ulcers that are large, of prolonged duration, or refractory to conservative measures (Collins, 2010).

In clinical practice surgery is rarely an option due to the nature of the pathology in the lower limb.

Instead, common treatment options include compression therapy as standard care in combination with a variety of dressings, although meta-analyses have not yet identified the ideal dressing type (Palfreyman, 2006; O’Meara, 2009). The recent resurgence of the use of honey in wound management (Al-Waili, 2011) triggered our prospective study of the efficacy of honey-based treatment in the management of venous leg ulcers.

STUDY DESIGN
In this prospective study we evaluated the efficacy of a honey gel dressing in a group of patients with difficult to treat VLUs. Patients with lower leg ulcers who presented at the University Hospital between February and October 2010 were recruited for this study. All patients with chronic lower leg ulcers, regardless of ulcer depth, area, or presence of infection, were included. Patients were randomly selected for treatment as outpatients with consultation or for inpatient treatment. Exclusion criteria were
unlikelihood of wound improvement due to cutaneous necrotizing vasculitis, lower limb cellulitis, or severe lower limb arterial insufficiency.

**PATIENTS**
The study included ten patients: six females and four males with an average age of 73 years (age range 57-83). Underlying pathologies included diabetes mellitus (n=3), hypertension (n=4), and a range of other factors that influence wound healing (Table 1). Seven patients had venous ulcers, one had a mixed venous and arterial ulcer, one had a post-trauma ulcer, and one had an ulcer related to diabetes mellitus (Table 1). Standard criteria for the diagnosis of leg ulceration were used.

Leg ulcers had been present in these patients for an average of 3.3 years (range: 2 months-5 years). During that period, patients were treated with a range of products and techniques in primary care centres without improvement (Tables 2 & 3). For our study, the patients themselves before initiation of the honey gel treatment were used as controls. To ensure that application of honey gel was the only variable, the same wound management regimen that was followed in the pre-study treatment period was applied during our study, except that honey gel was now used as a topical dressing (Moghazy, 2010). Patients consented to the honey gel regimen prior to the start of the study. During the treatment period no compression therapy was performed in any patient.

**MATERIALS**
The honey gel (L-Mesitran Soft, Triticum, NL) used in this study contains 40% medical-grade honey, ultra-purified hypoallergenic medical grade lanolin (Medilan), polyethylene glycol, and Vitamins C and E. All of these ingredients have individual beneficial effects on wound management and healing (Cutting, 2005) and the honey product as a whole has proven antibacterial efficacy (Stephen-Haynes, 2011).

**METHODS**
Patients were treated only with honey gel. The honey gel was applied twice weekly directly over the wound and covered with a sterile cotton dressing. Compression was not used during the period of treatment with the honey gel.

During the observation period the patients were seen for consultation at weeks 2, 4, and on a monthly basis thereafter. Ulcer size was measured using the Opsite Flexi-grid® system.
Dermocorticoids (betametasone valerate cream) and emollients were applied to the peri-wound area when necessary. No topical or systemic antibiotics were used.

Adverse reactions, including subjective unfavourable symptoms, were registered when present.

RESULTS

A reduction in wound size was observed in all patients in a mean time of 101 days (range: 28-174 days) (Table 4). Seven patients showed complete healing of the wound and the mean degree of reduction of ulcer extension was 90%, ranging from less than 10% to 100% (Table 4). Patient 7, who showed the smallest reduction in wound size, complained of pain after application of the honey gel and abandoned the study.

DISCUSSION

A primary factor contributing to the chronic nature of VLUs is poly-microbial biofilm infection, where several bacterial species colonize the wound. The most common organisms found in VLU biofilms include various anaerobes, Staphylococcus (Wolcott, 2009), and Pseudomonas aeruginosa (Jacobsen, 2011). The honey-based product used in our study has a known broad-spectrum antibacterial effect, which could have contributed to the accelerated healing. In vitro research using antibiotic-resistant clinical isolates and extended spectrum b-lactamase (ESBL)-producing strains of bacteria showed that this honey gel is highly effective and has stronger antibacterial activity than other honey products (Manuka) (Stobberingh, 2010; Stephen-Haynes, 2011). The efficacy of honey in wound healing is further attributed to its low pH, its ability to produce hydrogen peroxide, and its osmotic action (Molan, 2006; Stephen-Haynes, 2011). It is particularly important that the honey used for wound care is free from residues and sterilized, because honey can contain clostridial spores in addition to non-pathogenic Bacillus spp. Only gamma irradiation effectively sterilizes honey without reducing its efficacy (Postmes, 1993; Molan, 1996) and the use of non-sterilized honey samples cannot be justified (Cooper, 2009).

The honey gel used in this study may also have a direct positive effect on wound healing. Du Toit (2009) examined the cell morphological effects of honey- and silver-impregnated dressings on two key cellular components of wound healing, keratinocytes and fibroblasts, using an
the complexity of VLU management. Studies (Jull, 2008), the study design (Firth, 2010), and healing. This might reflect the type of honey used in these comparative methods, honey has not been shown to support that honey-based wound management has positive effects on wound healing, ulcer size, and patient comfort. Several previous studies (Table 5, 601 patients) have reported that honey-based wound management has positive effects on wound healing, ulcer size, and patient comfort. However, when compared to standard methods or other comparative methods, honey has not been shown to superior to these methods significant difference in wound healing. This might reflect the type of honey used in these studies (Jull, 2008), the study design (Firth, 2010), and the complexity of VLU management.

However, we did see a significant improvement in wound healing in our study. The patients’ previous treatments were less effective (Table 2) than honey treatment (Table 4), with an observed shortening of healing time from an average of 3.3 years to 101 days. The honey gel was used in monotherapy. Only emollients and, when indicated, topical corticosteroids were allowed as complementary treatment on the peri-ulcerous skin, and in no circumstance were antibiotics or antiseptics used.

Similar results were obtained in a recent retrospective study in which 22 patients with lower extremity ulcers had delayed healing, in part attributed to application of povidone iodine or fusidic acid, and 50% of the wounds were infected. After treatment with honey-based products, all cases progressed to healing (Kegels, 2011). The use of honey may therefore have a place in VLU treatment (Jull, 2013). Antibiotics are not recommended because there is no evidence that the routine use of systemic antibiotics promotes VLU healing. In addition, in light of the increasing problem of bacterial resistance to antibiotics, current prescribing guidelines recommend that antibacterial preparations should only be used in cases of clinical infection and not for bacterial colonisation (O’Meara, 2010).

Honey gel treatment may also be superior to traditional treatments because it is easier for patients to administer. The patients in our study showed low compliance with compression bandage treatment during the pre-study treatment period because a lack of local health facilities, advanced patient age, and the low economic status of the patients often precluded maintenance of correct compression treatment. In contrast, application of honey gel to the wound surface was easy and could be accomplished by the patients themselves or by a relative without specialised skills, as previously reported (Smaropoulos, 2011). Patients were therefore able to follow the treatment protocol provided no adverse effects occurred.

Another advantage of honey-based treatment is that it requires fewer materials and the procedure is less time

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**Table 5: Previous studies on the efficacy of honey in VLU treatment**

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Number of patients</th>
<th>Study period</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olabanji (2000)</td>
<td>Comparative study</td>
<td>50</td>
<td>4 weeks</td>
<td>Reduction in wound size was significantly different.</td>
</tr>
<tr>
<td>Natarajan (2001)</td>
<td>Case report</td>
<td>1</td>
<td>until healing</td>
<td>MRSA was eradicated from the ulcer and rapid healing was successfully achieved.</td>
</tr>
<tr>
<td>Alcaraz (2002)</td>
<td>Case report</td>
<td>1</td>
<td>until healing</td>
<td>The patient’s wounds improved with the honey-based dressing.</td>
</tr>
<tr>
<td>Dunford (2004)</td>
<td>Four-centre feasibility</td>
<td>40</td>
<td>12 weeks</td>
<td>Overall, ulcer pain and size decreased significantly, and odorous wounds were deodorised promptly.</td>
</tr>
<tr>
<td>Schumacher (2004)</td>
<td>Case report</td>
<td>6</td>
<td>until healing</td>
<td>No significant difference from conventional methods recorded.</td>
</tr>
<tr>
<td>van der Weyden (2005)</td>
<td>Case report</td>
<td>1</td>
<td>until healing</td>
<td>Honey was found to be an effective antibacterial, anti-inflammatory, and deodorizing dressing, with total healing of the ulcer achieved.</td>
</tr>
<tr>
<td>Timmons (2008)</td>
<td>Case report</td>
<td>1</td>
<td>until healing</td>
<td>Honey promoted the removal of slough, encouraging the formation of granulation tissue and epithelial tissue growth.</td>
</tr>
<tr>
<td>Jull (2008)</td>
<td>Community-based, open-label randomised trial</td>
<td>368</td>
<td>12 weeks</td>
<td>Honey-impregnated dressings promoted healing, however, not significantly more than usual care.</td>
</tr>
<tr>
<td>Sare (2008)</td>
<td>Case report</td>
<td>3</td>
<td>until healing</td>
<td>Promotion of healing occurred in all instances with a reduction in the incidence of infection, reduction in pain, and the provision of comfort.</td>
</tr>
<tr>
<td>Gethin (2009)</td>
<td>Prospective, multicentre, open label randomised controlled trial</td>
<td>108</td>
<td>12 weeks</td>
<td>Increased incidence of healing, effective desloughing, and a lower incidence of infection than the control.</td>
</tr>
<tr>
<td>Kegels (2011)</td>
<td>Retrospective study</td>
<td>22</td>
<td>until healing</td>
<td>Infected wounds were controlled within a few days. All the wounds progressed to healing without any adverse effects.</td>
</tr>
</tbody>
</table>

**in vitro** tissue explant culture model and found that the honey-impregnated dressings promoted new tissue regeneration. A second study comparing silver-sulphadiazine with the honey gel used in our study reported similar findings; the honey gel significantly stimulated re-epithelialisation, whereas silver sulphadiazine significantly reduced it (Boekema, 2013). In support of these findings, Rossiter et al. (2010) showed that honey products stimulated angiogenesis **in vitro** in an investigation of the influence of honey on growth of the tubular length of rat aorta.
Limitations
The small number of patients and the use of the patients themselves as the treatment controls are limitations of this study.

CONCLUSION
We believe that honey gel treatment may provide a practical and well-tolerated treatment for the management of lower leg venous ulcers, particularly when patient compliance with compression therapy is poor.

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References

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References


