Acceptability to patients of a honey dressing for non-healing venous leg ulcers

- **Objectives:** This four-centre feasibility study was undertaken to determine whether Medihoney, a proprietary blend of honeys, is an acceptable treatment for patients with leg ulcers in terms of pain relief, odour control and overall patient satisfaction.
- **Method:** Forty patients whose leg ulcers had not responded to 12 weeks of compression therapy were recruited. Medihoney dressings were applied on their ulcers for the 12-week study period. All other aspects of their care, including the use of compression bandaging, remained unchanged. Their leg ulcers were assessed every two weeks. This included the use of a patient questionnaire.
- **Results:** Overall, ulcer pain and size decreased significantly and odorous wounds were deodorised promptly. These aspects had a positive impact on patient satisfaction with the Medihoney treatment.
- **Conclusion:** The results support the previously reported positive effects of honey and revealed a high patient acceptance for honey treatment. Following these results, comparative clinical trials, which should also consider pain issues, are now recommended.
- **Declaration of interest:** This study was supported by Paul Hartmann AG, Germany.

venous leg ulcers; pain; malodour; Medihoney

Not all ulcers respond to traditional treatments, and this has led to a search for alternatives.[1] Evidence has accumulated on the efficacy of certain honeys in achieving rapid wound healing. Leptospermum honey from Australia and New Zealand has aroused interest due to its ability to promote wound healing.[2-7] Unfortunately, there are few relevant randomised controlled studies. Existing ones are of poor quality, and often use comparative treatments that are uncommon in the West.[7]

Honey achieves its positive healing effects by:

- Reducing inflammation and the bacterial burden
- Debriding necrotic tissue
- Enhancing angiogenesis, granulation and epithelialisation.[3,8-17]

Other attributes are that it:

- Reduces oedema and pain due to its high osmolarity
- Is antibacterial due to the production of enzymatically generated hydrogen peroxide at a very low but continuous level
- Causes cell stimulation
- Deodorises malodorous wounds[6,18]
- It is non-adherent.[19]

In a review of over 500 ulcers treated with honey, harmful effects were noted in only two cases, where the honey induced pain,[19] possibly due to its acidity or high osmotic potential.

This study investigates whether honey is an acceptable treatment for patients with recalcitrant venous leg ulcers. Pain was a primary outcome measure, but odour and healing were also assessed.

Method

This was a multicentre (four), prospective, descriptive, non-randomised feasibility study conducted between November 2001 and August 2002. Forty patients were recruited, each of whom had non-healing ulcers despite having received compression therapy for at least 12 weeks. Inclusion and exclusion criteria are listed in Table 1.

Full ethical approval was received from each study centre and written consent from each patient and their GP or hospital consultant.

At the start of the study, the wounds were assessed using Doppler ultrasound and measured via digital imaging. Information was obtained on the patients' general and disease-related medical history, and on the duration and aetiology of their ulceration. All patients completed a baseline questionnaire asking them to grade their perceived level of pain, odour and satisfaction with their current dressing regimen, and to state if there was any leakage from the dressing between dressing changes and if the dressings had caused skin problems.

Aspects of the patients' existing treatment, such as method of cleansing, dressing-change frequency and type of compression bandaging/hosiery used, were left unaltered. The only intervention was the application of a honey dressing in place of the previously prescribed primary dressing.

Medihoney Antibacterial Honey (Medihoney, Australia), which is listed on the Australian Register of Therapeutic Goods for treatment of acute and chronic wounds, was used. This is a proprietary

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Table 1. Inclusion and exclusion criteria

Inclusion criteria
Active ulceration (venous, mixed, arterial)
Failure to respond to a minimum of 12 weeks of appropriate treatment
Assessed and managed according to locally and nationally accepted guidelines
Aged over 40 years
Adherence with treatment methods
Exclusion criteria
Known product intolerance
Ulcers larger than 18 x 8cm
Ulceration in existence for more than two years, unless it was a re-occurrence
Health carers were unable to change dressings between allocated assessment times
Known or suspected malignancy, diabetes and immunosuppression
Diagnosed clinical infection in or around wound requiring systemic antibiotics
Exposed tendon or bone
Had received antibiotics within the previous two weeks or are using steroids
Had been in clinical trial in the previous four weeks

Only one ulcer per limb and one limb per person was utilised in this study

Table 2. Patient characteristics

Age (years)	Mean	71
	Range	54–96
Gender	Male	14 (35%)
	Female	26 (65%)
Ulcer aetiology	Venous*	35 (87.5%)
	Arterial§	2 (7.5%)
	Mixed‡	3 (5%)
Recurrent ulcers		29 (72.5%)
Ulcer size (cm^2)	Mean	9.68
	Range	0.19–61.26

* APBI: 0.8–1.3; § APBI: 0.5–0.6; ‡ APBI: 0.6–0.8

blend of honeys, including selected honeys from Australia and New Zealand Leptospermum spp., to ensure a broad spectrum of antibacterial activity.

Medihoney dressings were prepared by applying the honey to a low-adherent, sterile, contact layer placed on top of a sterile dressing pad. The honey was applied to a depth of approximately 3mm (roughly 20g of honey to a 10 x 10cm dressing). The leg ulcer nurse or community nurse applied the compression bandages.

The following were assessed every two weeks:

- Level of pain experienced (assessed using the McGill score, where 0=no pain; 1=mild pain; 2=discomfort; 3=distressing pain; 4=horrible pain; 5=excruiating pain)[20]
- Reduction in odour (0=no odour; 1=mild; 2=moderate; 3=severe)
- General satisfaction with the honey dressing (1=very satisfied; 2=satisfied; 3=neither satisfied or dissatisfied; 4=dissatisfied; 5=very dissatisfied)
- Reduction in leg ulcer size or deterioration in the ulcer's condition. Wound area and perimeter were calculated using Verge Videometer Software (Vista Medical, Canada) and deterioration was determined by wound assessment
- Drop-out rates were monitored and any adverse events recorded.

Different tests were used for the analysis: Student's t-test for differences between results, linear regression for correlation of data and one-way ANOVA for variances between data groups.

Results

Patient characteristics are given in Table 2. Due to the small numbers, the relationship between aetiology and outcome criteria was not analysed.

Six patients required oral antibiotics. Although antibiotics can affect wound conditions, we assumed that tolerance to the Medihoney dressings would not be influenced as these infections were not related to the study ulcer. All of these patients completed the 12-week study.

Drop-out rate

Thirteen patients (32.5%) withdrew from the study for reasons given in Table 3. Two withdrew because of a deterioration in their ulcer. This was thought to be related to the patients' condition, so was not recorded as adverse events.

Table 3. Patient drop-out rate

Reason	No.	%
Increasing ulcer pain	6	15
Deterioration in general health	3	7.5
Deterioration in ulcer condition	2	5
Mistreatment of protocol	1	2.5
Death of patient	1	2.5
Adverse events	0	0

Pain

Fifty per cent of patients experienced a decrease in reported pain levels. The total average pain scores for all 40 subjects decreased significantly from 1.6 ▶

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Table 4. Summary of pain scores and percentage wound reduction and rate of wound reduction

Pain group	No.	Pain score at recruitment	Pain score at study end	Wound size at recruitment (cm^2)	Wound size at study end (cm^2)	% wound reduction	% wound reduction/ week (healing rate)
No pain	4	0	0	2.97 ±2.87[7]	2.42 ±3.03	20.46 ±78.84	12.02 ±25.92
Pain decreased	20	1.7 ±0.8[2]	0.15 ±0.37	7.86 ±7.62	3.98 ±7.73	57.42 ±46.67	10.31 ±14.98
Pain remained the same	5	3.0 ±1.58[5]	3.0 ±1.58[6]	17.35 ±24.82	15.07 ±21.23	24.76 ±52.45	1.82 ±5.61
Pain increased (incl. dropouts)[1]	11	1.36 ±1.21[3]	2.27 ±1.56	11.94 ±13.39	12.94 ±15.39	-6.42 ±75.22	0.08 ±9.88
Pain dropouts	6	2.17 ±0.98[4]	3.33 ±1.21	20.71 ±20.27	23.46 ±21.5	-19.23 ±86.14	-2.16 ±27.55

1 includes two patients with same pain level between recruitment and study end, but with higher levels in between
2 Significant difference in pain score between recruitment and study end ($p=3.54 \times 10^{-9}$; paired Student t-test)
3 Significant difference in pain score between recruitment and study end ($p=2.31 \times 10^{-4}$; paired Student t-test)
4 Significant difference in pain score between recruitment and study end ($p=9.17 \times 10^{-4}$; paired Student t-test)
5 Significant difference in pain score at recruitment between patients whose pain level remained the same and patients whose pain decreased or increased pain (p=0.014 and 1.87×10^{-4}, respectively; unpaired Student t-test)
6 Significant difference in pain score at study end between patients with the same pain and those whose pain decreased ($p=7.92 \times 10^{-8}$; unpaired Student t-test)
7 Significant difference in wound size between recruitment and study end (p=0.0028; paired student t-test)

±1.22 to 1.08 ±1.54 ($p<0.02$; paired Student's t-test) between baseline and the subjects' individual endpoints. Total average pain of all 40 patients decreased with time ($p<0.001$; linear regression).

Table 4 summarises the results for the 40 patients when segregrated into different pain groups. Interestingly, at baseline average pain level for patients whose pain either decreased or increased during the study (including those who dropped out because of pain) was similar and relatively low (Table 4). In contrast, patients who experienced the same level of pain throughout the study had a significantly higher pain level at baseline.

Patients who dropped out because of pain had a higher average pain score at baseline than those whose pain increased during the study, although this was not statistically significant.

Overall, six patients complained about a transient stinging pain after the honey was applied. Eight patients experienced continuous pain after the honey was applied, but not after every treatment. Overall, eight of the 11 patients whose pain increased during the study felt this was due to the honey dressing. However, this could have been partly due to intrinsic factors. Also, pain scores fluctuated in some patients, further obscuring this issue. Importantly, none of the patients described dressing removal as painful, no matter how high the perceived baseline pain level.

On average, healing appeared to be directly associated with pain (Table 4). Pain-free patients had the highest healing rates. Only patients who experienced no or decreasing pain showed a substantial reduction in wound size. Patients who dropped out because of pain had the lowest healing rate.

However, an increase in pain appears to be associated with wound size at recruitment. On average, the larger the wound at baseline, the higher the tendency to experience an increase in or sustained elevation of pain. Wound size at baseline did not vary between patients in the different pain groups ($p>0.05$; one-way ANOVA).

A decrease in pain correlated with the percentage of wound reduction and healing rates ($p<0.05$ for both; linear regression).

Average pain levels per patient were not related to the number of dressing changes ($p>0.05$; linear regression).

Odour reduction

Twenty-four patients had odorous wounds at baseline and two others thought a mild odour developed during the study. At the first assessment the total average odour of these 26 patients had dropped significantly from 1.58 ±0.90 to 0.69 ±0.79 ($p<0.001$; paired Student t-test), with 11 patients saying there was no remaining odour.

Twenty out of 21 patients who experienced a decrease in odour thought this was due to the honey dressing. The other patient did not comment.

Only three patients perceived an increase in odour. Another two said there had been no change.

Odour in the six patients who received oral antibiotics and completed the study had been reduced or eliminated before their administration.

There was no correlation between average odour levels perceived by a patient and the number of dressing changes each week.

Healing

During the course of treatment the average total wound area decreased steadily ($p<0.002$; linear

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regression). Furthermore, the average wound area of all patients decreased significantly. Seven ulcers healed completely.

There was a significant reduction in wound size in the 20 ulcers of patients who did not heal by the end of the study. In contrast, average wound sizes of those who dropped out remained static. At recruitment, their average wound size was significantly larger than those of patients who completed the study but whose ulcers did not heal 'the continuers' and patients whose ulcers healed 'the healers'. There was no statistical difference between wound areas of the latter two groups.

At enrolment wound sizes of healers, continuers and drop-outs varied significantly ($p<0.05$; one-way ANOVA). Healing rates between the three groups varied significantly ($p<0.001$; one-way ANOVA).

There was no correlation between the average number of dressing changes per week and average rate of wound healing ($p>0.05$; linear regression).

Patient satisfaction

Patient satisfaction with the honey dressing was high: most patients were either more or just as satisfied with it as with their previous treatment.

At each two-week assessment average satisfaction scores correlated with those for pain and odour ($p=0.006$ for each; linear regression). There was also a significant correlation between average total satisfaction for each patient and average pain and odour values ($p<0.005$ for both; linear regression).

To pursue this further, general satisfaction scores (which were divided into three groups: an increase in satisfaction with the honey dressing; no change in satisfaction; reduced satisfaction) were examined in relation to pain and odour. For this purpose, numbers were allocated to pain and odour (0=none; 1=improving; 2=unchanged; 3=worse) and then appropriate average values for each satisfaction category were compared.

On average, odour values varied between 'improving' and 'none', but there was no significant difference between the three satisfaction groups ($p>0.05$; 1-way ANOVA).

Pain values suggested a tendency towards decreasing pain in patients whose satisfaction with the honey dressing increased or remained unchanged. There was a tendency to increased pain among those who expressed dissatisfaction.

At recruitment wound size between the three satisfaction groups did not vary significantly ($p>0.05$; one-way ANOVA). A significant average wound reduction was only achieved in patients whose satisfaction with the dressing increased.

Percentage wound reduction between the three groups varied significantly ($p<0.05$; one-way ANOVA), with a significant difference between those who reported increased and reduced satisfaction (Table 5). The healing rate, however, did not vary significantly between these two groups ($p>0.05$; 1-way ANOVA). Six of the seven patients whose satisfaction levels decreased dropped out.

Dressing changes

The frequency of dressing changes was the same as for the former dressing regimen. The average frequency for each patient varied widely from 0.83 to 10.5 changes within each assessment period.

Skin problems

Two patients entered the study with macerated wound edges. In one this improved with use of the honey dressings. The other patient withdrew after two weeks.

Another two patients developed maceration and excoriation of the wound margin after entering the study due to increased exudate level. One withdrew due to an overall increase in pain and a deterioration in the ulcer.

Management of exudate

Ten patients had reported wound leakage between dressing changes before entering the study. Four were using support hosiery, where lack of absorbent layers enhances leakage. Of the 10 patients, two reported no further leakage after using the honey dressing. Five reported leakage up to week 2, while the remaining three reported leakage up to weeks 4, 6 and 8 respectively. It is not clear what influence the honey or change of dressing materials had on this.

Discussion and limitations

To date no studies appear to have investigated the role of honey in the treatment of leg ulceration when used with compression therapy. To ensure healing was not mainly due to compression, wounds were selected that had not responded to at least 12 weeks of compression therapy. Even though this was not a comparative trial, valuable data were still generated.

Though largely ignored in wound studies to date, the major focus of this study was pain. This is a major issue that dominates the lives of many people with leg ulceration. The recent European Wound Management Association (EWMA) position statement on pain at wound dressing changes,[21] stated that 'leg ulcer patients experience greater pain than the normal population, which is not merely a consequence of an elderly population, but rather a feature of the wound and underlying abnormal pain mechanisms'.

Our findings demonstrate that treatment with Medihoney reduced pain levels in half of the patients studied. Health-related quality-of-life studies have shown that pain improves significantly when treatment promotes healing.[21] Accordingly, a ▶

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decrease in wound size was associated with a reduction in pain. It cannot be confirmed whether treatment with honey had a direct effect on pain or if it acted indirectly by stimulating wound healing. Use of honey does, however, lead to a reduction in oedema, which could have a direct effect on pain.

When patients were divided into groups based on their pain status there was a clear association between reduced pain and healing. Patients with no pain had the highest average healing rate. Those whose pain increased, on average, showed hardly any healing. Healing rates in patients whose pain levels improved increased by a factor of seven when compared with those whose pain remained unchanged.

However, individual pain levels at any time point were not a predictor of full healing. Patient tolerance of pain appears to be related to previous experiences of pain. Patients accepted high pain levels if their previous experiences of pain were not exceeded. An increase in perceived pain after the application of honey often resulted in the patient dropping out, even if their pain levels were low. This suggests that patients may be reluctant to consent to new dressings if there is an increase in pain, irrespective of the perceived level of pain.

Six patients withdrew because of pain, and another two because their ulcer deteriorated. It is difficult to determine whether or not these findings can be attributed to Medihoney as there are no comparable data for other wound dressings. But it should be noted that only patients with recalcitrant ulcers were included in the study.

It is still unclear why honey causes pain in some patients. It is might be a result of its low pH. Also, honey's high osmolarity may result in a pulling sensation after application. There is anecdotal evidence that mixing honey with cream can reduce pain but there is no clinical evidence to support this.

None of the patients described Medihoney dressing removal as painful, no matter how high their perceived baseline pain level.

Although this study did not attempt to analyse the clinical effectiveness of Medihoney as a wound-healing agent (no control dressings were included), a significant decrease in the average wound size of the patient population was noted. Ulcers in seven of the 40 patients healed within the 12-week study period. These results strongly indicate that Medihoney had some therapeutic effect.

Honey's reputation as an efficient deodoriser was verified by this study. More than 80% of patients with malodorous wounds reported a positive effect, usually after the first application. An increase in the frequency of dressing changes did not appear to have an appreciable effect on odour. As all wounds have some associated odour, usually related to the presence of bacteria, this may at least be partly be due to Medihoney's antibacterial effect.

During the study, average satisfaction with the Medihoney dressings increased significantly. At first sight, average satisfaction correlated with corresponding values of pain and odour. However, since average values for all three parameters improved simultaneously, a causal relationship between them is not necessarily implied. A differentiated analysis revealed that, on average, odour reduction did not appear to have a significant impact on patient satisfaction, when compared with the previous treatment regimen. In contrast, a reduction in wound size appear to be a crucial influence on satisfaction. Similarly, an increase in pain seemed to have a strong negative effect on patient satisfaction.

However, it cannot be determined to what extent reduced pain and improved healing affect patient satisfaction. Most likely, additional parameters, such as the patient's psychological state, also are influential. Furthermore, all parameters affecting patient satisfaction are perceived differently by each individual patient. A more intricate study design is needed to reach more precise answers.

As this was an initial feasibility study, it was limited by its sample size. The emphasis was on parameters associated with primary acceptance of the dressing. Findings were also reliant on a simple patient questionnaire which used only a visual analogue scale to assess pain. Non-verbal signs of pain, such as facial expressions and specific words, might have generated more specific data.[22]

A more in-depth examination of the overall quality-of-life experience associated with the use of a new dressing could have been achieved by using a disease-specific quality-of-life measure.[23]

Conclusion and recommendations

Evidence from this study suggests that Medihoney Antibacterial Honey is a promising agent in the management of leg ulceration. Most patients' pain scores improved and in many cases healing was achieved. Furthermore, malodorous wounds were promptly and efficiently deodorised. Dressing removal was easy and was never reported as painful.

Accordingly, patient satisfaction with the Medihoney dressings was high. On the basis of the data presented here, we recommend that pain should constitute one of the foci of clinical trials of wound dressings as it appears to have a major impact on patient acceptance of treatment regimens.

An appropriate next step would be a comparative clinical trial to compare the healing effects of Medihoney with commonly used dressings. Studies of Medihoney on other wound types could yield information on the most appropriate wounds for its use. Furthermore, an appropriate study design could help identify optimal intervals for dressing changes. With careful monitoring, the cost-effectiveness of Medihoney treatment could be also evaluated. ■

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