Evidence Table

Clinical Area: Medihoney Primary dressing with Active Manuka Honey for wound management.


Study Type: Randomized controlled trial.

Study Aim: To evaluate the safety and effectiveness of honey as a dressing for venous leg ulcers.

Outcomes

- **Primary:** The proportion of participants with a completely healed reference ulcer at 12 weeks, as determined by the research nurse.
- **Secondary:** Time to healing, change in ulcer area from baseline, incidence of infection, adverse events, health related QoL (HRQoL), and cost effectiveness.

Design

- **Number of subjects:** N= 368 (N=187 in the honey dressing group, and 181 controls).
- **Description of study population:** These were patients enrolled from 4 sites in New Zealand. Their mean age was around 67.5 years, the wound duration was 20 weeks in the honey treatment group and 16 weeks in the controls, mean ulcer area 2.65 cm², around 98% had an ABPI \( \geq 0.8 \), and 19% were smokers.
- **Inclusion criteria:** Men and women >18 years of age, with a venous ulcer with ankle brachial pressure index \( >0.8 \), or a mixed venous and arterial ulceration with ankle brachial pressure \( >0.7 \), able to tolerate compression, and to provide a written informed consent.
- **Exclusion criteria:** History of diabetes, rheumatoid arthritis, history of a peripheral artery disease, allergy to calcium alginate or Manuka honey, or were already using honey for treatment of the leg ulcer.
- **Intervention:** **Honey therapy group:** received Manuka honey dressings that were changed every time the compression bandage was changed (frequency determined by clinical need). The honey was impregnated into calcium alginate dressings. **Controls (usual care group):** received dressing that the nurse judged to be appropriate. The choices included alginate, hydrogel, hydro fiber, hydrocolloid foam, non-adherent, iodine, or silver dressings. All participants received compression bandage as a standard background therapy.
- **Source of outcome data:** Wounds were assessed at baseline and then at weekly intervals. Healing was assessed at 12 weeks by comparing digital photographs to those taken at baseline. Wound swabs were obtained to determine infection, and the short form 36 health survey (SF-36) was used to assess the HRQoL at 12 weeks. As well as the CXVUQ and EuroQoL 5D questionnaires.
- **Length of follow-up:** 12 weeks.

Validity:

- **Blinding?** No.
- **Appropriate randomization procedures?** Yes.
• Appropriate comparison intervention (placebo or adequate dose of accepted intervention)? Yes.
• Treatment/control groups comparable at baseline? Yes.
• Other than intervention, was care/follow-up similar in each group? Yes.
• Adequate compliance with intervention? 31 (16.5%) patients randomized to honey dressing discontinued it during the study mainly due to deterioration of the ulcer or surrounding skin, pain bleeding infection, or based on the health profession advice.
• Sufficient statistical power? Yes.
• Intention to treat analysis? Yes.
• Completeness of follow-up: 98% complete.
• Industry funding? Yes.

• Conclusions regarding validity of methods:

The study was randomized and controlled, however it was the patients and providers were not blinded which is a potential source of bias especially with the subjective outcomes. Moreover, and a variety of therapies were used by the control group.

Results:

Ulcer healing* and change in size at 12 weeks

<table>
<thead>
<tr>
<th></th>
<th>Honey treated</th>
<th>Usual care</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=187</td>
<td>N=181</td>
<td></td>
</tr>
<tr>
<td>Complete healing (no, %)</td>
<td>104 (55.6%)</td>
<td>90 (49.7%)</td>
<td>0.258</td>
</tr>
<tr>
<td>Time to healing (mean days)</td>
<td>63.5</td>
<td>65.3</td>
<td>0.553</td>
</tr>
<tr>
<td>% change in ulcer area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean reduction from baseline</td>
<td>74.1%</td>
<td>65.5%</td>
<td>0.186</td>
</tr>
</tbody>
</table>

*Defined as complete epithelialization of the ulcer with no scab.

Clinically determined infection**

<table>
<thead>
<tr>
<th></th>
<th>N=187</th>
<th>N=181</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (%)</td>
<td>32 (17.1%).</td>
<td>40 (22.1%)</td>
<td>0.228</td>
</tr>
</tbody>
</table>

** Defined as presence of signs and symptoms of infection or a wound swab being obtained, and treatment with antibiotics.

Adverse events***:

<table>
<thead>
<tr>
<th></th>
<th>N=187</th>
<th>N=181</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With at least one event</td>
<td>111 (59.4%)</td>
<td>84 (46.4%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Ulcer pain</td>
<td>47 (25.13%)</td>
<td>18 (9.94%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Deterioration of the ulcer</td>
<td>19 (10.2%)</td>
<td>9 (5.0%)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*** Honey was associated with other higher rates of adverse events but with statistically insignificant difference vs. usual care in local erythema, edema, increased exudates and deterioration of surrounding skin.

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Health related quality of life
There were no statistically significant differences between the two study groups in any of the three HRQoL tools used.

Authors’ Conclusions

The authors concluded that the results of the study showed that using honey-impregnated dressings did not significantly improve venous ulcer healing at 12 weeks when compared to usual care.

Reviewer’s Conclusions

The study had the advantage of comparing the use honey dressings to usual care. It was randomized, controlled and multicenter, and analysis was based on intention to treat. However, the trial was open-label, which may be a potential source of bias especially with the subjective outcomes.

Overall the results of the trial showed no statistically significant differences between the honey dressing and the usual care in rate or time to complete healing. On the other hand, honey dressing was associated with significantly higher rates of overall adverse events, ulcer pain (NNH=7), and deterioration of the ulcer (NNH=10).