**Evidence Table**

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

**References:** Gethin G, Cowman S. Manuka honey vs. hydrogel - a prospective, open label, multicenter, randomized controlled trial to compare desloughing efficacy and healing outcomes in venous ulcers. *J Clin Nurs* 2008; August 23

Gethin G, Cowman S. Bacteriological changes in sloughing venous leg ulcers treated with Manuka honey or hydrogel: an RCT. *J wound Care* 2008;17:241-247

**Study Type:** Randomized controlled trial.

**Study Aim:**
- To compare desloughing efficacy of Manuka honey vs. hydrogel in treating venous leg ulcers after 4 weeks of treatment.
- To determine the qualitative bacteriological changes occurring in a 4-week treatment period with either Manuka honey or hydrogel.

**Outcomes**
- **Primary:** Desloughing over 4 weeks, healing rates after 12 weeks.
- **Secondary:** Change in the qualitative bacteriological analysis of culture swabs taken from the sloughy venous ulcers over the 4-week treatment period.

**Design**
- **Number of subjects:** N= 108
- **Description of study population:** These were patients enrolled from 10 sites in Ireland. Their mean age was 68.5 years, the wound duration was 39.5 weeks in the honey treatment group and 29.9 weeks in the controls, mean wound size around 10 cm. 85.5% and 78% of the wound bed was covered in slough in the honey treatment and hydrogel groups respectively. 30% of the participants had hypertension, 16.5% were smokers, 8% had a history of deep vein thrombosis in the affected leg, and 54% had a recurrent ulcer.
- **Inclusion criteria:** Men and women >18 years of age, with a venous ulcer, ≥50% of wound bed covered in slough, ulcer size <100 cm², ankle brachial pressure index (ABPI) ≥0.8 and able to provide a written informed consent.
- **Exclusion criteria:** Ulcer diagnosed as malignant, having a cavity wound, clinical diagnosis of wound infection, taking antibiotics at randomization for any reason, taking oral immunosuppressant, having poorly controlled diabetes, was previously enrolled in the trial, pregnant or lactating women.
- **Intervention:** The patients underwent cleaning of the wounds with warm tap water at each visit before assessment and treatment. *Honey therapy group* A Manuka honey dressing with viscous orange/brown topical agent at a dose of 5g/20 cm² was applied weekly. *Hydrogel group:* Received hydrogel therapy (IntraSite Gel) at a dosage of 3g/20 cm² weekly. Compression therapy (most commonly 4-layer bandages) was continued in all patients and secondary dressings were standardized. The treatment period was 4 weeks, after which all patients received variable treatments based on the clinical assessment by the investigator.
- **Source of outcome data:** Wounds were assessed at baseline and then at weekly intervals for 4 weeks. Healing was assessed at 12 weeks. The wounds were measured and the amount of slough was quantitatively assessed. The presence or absence of other tissue including granulation, epithelial and necrotic tissue was recorded at each assessment. Pain was assessed weekly using a validated 5-point visual analogue scale. Culture swabs were taken from the wound at baseline, after 1 week of treatment, and after 4 weeks of treatment.
- **Length of follow-up:** patients were treated for 4 weeks and then followed for 12 weeks to determine if the ulcer has healed.

**Validity:**
- **Blinding?** No.
- **Appropriate randomization procedures?** Yes.
- **Appropriate comparison intervention (placebo or adequate dose of accepted intervention)?** Yes.
- **Treatment/control groups comparable at baseline?** No
- **Other than intervention, was care/follow-up similar in each group?** Yes.
- **Adequate compliance with intervention?** Yes.
- **Sufficient statistical power?** No.
- **Intention to treat analysis?** Yes.
- **Completeness of follow-up: 76% complete.**
- **Industry funding?** No.
- **Conclusions regarding validity of methods:**

The study was randomized and controlled, however it was relatively small, the sample size did not reach the number calculated to provide sufficient power, and the trial was not blinded.

**Results:**

**Wound size**
Median size at baseline was 4.7 cm² for all wounds
Wound size was reduced by 23% to 3.65 cm² at week 4 for all patients (Median reduction was 34% in the Medihoney group vs. 13% in the hydrogel therapy group, p<0.001)

**Study outcomes at weeks 4 and 12 based on treatment groups**

<table>
<thead>
<tr>
<th></th>
<th>Honey therapy (n=54)</th>
<th>Hydrogel therapy (n=54)</th>
<th>P value</th>
<th>Risk ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% wound bed covered in slough (mean, SD)</td>
<td>29.0 (35)</td>
<td>43.0 (44)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>% reduction in slough* (mean, SD)</td>
<td>67 (36.41)</td>
<td>52.6 (45.1)</td>
<td>0.05</td>
<td>1.38</td>
</tr>
<tr>
<td>Healing** at 12 weeks (No %)</td>
<td>24 (44%)</td>
<td>18 (33%)</td>
<td>0.03</td>
<td></td>
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</tbody>
</table>

*After 4 weeks, 86 (80% of all wounds) had a reduction of >50% slough, with no significant difference between the two groups.
** Not clearly defined, but the investigators measured wound size, % covered in slough, and presence of other tissue

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Change in quantitative bacteriological analysis (secondary outcome)

At baseline, there was no significant difference between the two groups in the number of bacterial species.

<table>
<thead>
<tr>
<th></th>
<th>Honey group</th>
<th>Hydrogel group</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA (No %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>10/54 (18.5%)</td>
<td>6/54 (11.1%)</td>
</tr>
<tr>
<td>After 4 weeks</td>
<td>3/54 (5.5%)</td>
<td>5/54 (9.3%)</td>
</tr>
</tbody>
</table>

| Pseudomonas (No %) |                 |                 |
| Baseline           | 6/54 (11.1%)    | 10/54 (18.5%)   |
| After 4 weeks      | 4/54 (7.4%)     | 5/54 (9.3%)     |

Pain

<table>
<thead>
<tr>
<th></th>
<th>Honey group</th>
<th>Hydrogel group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.41 (1.05)</td>
<td>1.39 (1.15)</td>
<td>&lt;0.82</td>
</tr>
<tr>
<td>After 1 week</td>
<td>0.67 (1.18)</td>
<td>0.81 (1.89)</td>
<td>&lt;0.42</td>
</tr>
<tr>
<td>% reduction in wound pain</td>
<td>52%</td>
<td>34%</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Adverse events:

12 (22%) of the patients in the hydrogel therapy group, and 6 (11%) of those in the Manuka honey group withdrew from the study due to infection in the wound. Infection was diagnosed by the clinical features including increased pain, increased wound size, increased exudates and surrounding cellulitis.

Authors’ Conclusions

The authors concluded that patients treated with Manuka honey had an increased incidence of healing, more efficacious desloughing, and lower rates of infection compared to the controls treated with hydrogel.

Reviewer’s Conclusions

The study had the advantage of comparing the use Manuka honey dressings to another therapy. It was randomized, controlled and multicenter, and analysis was based on intention to treat. However, the trial was open-label, relatively small, and underpowered to detect significant differences between the two treatment groups.

Overall the results of the trial showed no statistically significant differences between the Manuka honey and hydrogel therapy in desloughing the wound (percent of wound area covered by slough) or rate of slough removal in venous ulcers at 4 weeks. The results shows however, that 44% of the ulcers treated with Manuka honey dressing healed vs. 33% of those treated with hydrogel (risk ratio 1.38, NNT =9 in 12 weeks). The authors did not discuss how they defined wound healing.

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