

# Case series of use of Manuka honey in leg ulceration

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## ABSTRACT

The historical and current literature reports the successful use of honey to manage a diversity of wound aetiologies. However, only in the last 40 years is research on its mode of action and contribution to wound healing being investigated. The challenge of managing chronic non healing wounds generated interest in researching non standard therapies. The aims of the study were to gain insight into the practical use of Manuka honey in wound management. The objective was to test the feasibility of further rigorous research into the use of honey in the management of chronic wounds. Instrumental case series were used to examine the use of Manuka honey in eight cases of leg ulceration. To collect the necessary data, photographs, acetate tracings, data monitoring and patient comments and observations were used to add greater reliability and validity to the findings. The wounds were dressed weekly with Manuka honey. The results obtained showed three males and five females with ulceration of different aetiologies were studied. A mean initial wound size for all wounds of 5.62 cm<sup>2</sup> was obtained. At the end of four-week treatment period, the mean size was 2.25 cm<sup>2</sup>. Odour was eliminated and pain reduced. The conclusions drawn were that the use of Manuka honey was associated with a positive wound-healing outcome in these eight cases. Arterial wounds showed minimal improvement only.

**Key words:** Honey • Manuka • Wound • Ulcer

## Key Points

- despite significant advances chronic ulceration remains a clinical problem
- this case series explores the use of Manuka honey
- the prevalence of leg ulceration is significant on a worldwide basis

## INTRODUCTION

Despite advances in molecular biology, the development of various tissue-engineered skin substitutes and growth factors, and a range of other therapeutic options, chronic ulceration remains a significant problem in our society (1). Wounds research continues to increase at macroscopic, microscopic and molecular level and aims to enhance our understanding of wound healing and ultimately improve patient care outcomes. The range of topical dressings available to the practitioner to promote wound healing is

enormous. This case series aims to explore the use of Manuka honey as a topical agent for ulceration of the lower limb and will lay the foundation for a more extensive study of the use of Manuka honey in wound management.

## BACKGROUND

Almost 20 years ago, studies reported prevalence of leg ulceration in the population as 1.48/1000 and 1.79/1000, and, of these, approximately 70% were because of venous disease (2,3). More recent studies reflect a small change in prevalence and aetiology. O'Brien *et al.* (4) reported a prevalence of 389 patients in a population of 317 069 (0.12%) which increased to 1.03% prevalence in patients over 70 years of age. Moffatt *et al.* (5) studied a population of 252 000 and reported a prevalence of 113 patients with ulceration (0.45/1000). However, of these, 43% were venous in origin with 15% arterial, but, more

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interestingly, 35% had a more complex aetiology including venous disease in combination with diabetes, lymphoedema and rheumatoid arthritis.

Leg ulceration, therefore, remains a significant clinical problem in terms of quality of life, duration of treatment and recurrence and resources. The study by Moffatt *et al.* (5) reported that 34% of patients had their ulcer for more than 18 months and 60% of patients had 2–10 episodes of ulceration with one patient reporting over 30 episodes.

## HONEY AND WOUND CARE

Advances in the knowledge of the healing process of chronic wounds and more effective therapeutic measures such as compression therapy for venous ulceration has led to improved healing rates. However, the presence of hard to heal chronic wound remains a challenge to health care professionals. Treating such wounds has led to an increased interest in traditional therapeutic agents such as honey as a means of treating the wound.

Reports of the use of honey in wound healing can be dated back to the Elbers Papyrus (c.1550BC) (6). The exact mode of action of honey is not yet fully understood. The promotion of granulation tissue may be because of the generation of hydrogen peroxide, low levels of which stimulate angiogenesis (7). The liquid flow created with the application of sugar where water moves from an area of high concentration to an area of low concentration contributes to the cleaning of the wound; this may also be true for the use of honey as it contains high levels of sugars such as monosaccharides and dextrose (8,9). Condon (10) argues that the antimicrobial effect lies in the physical properties of honey rather than its chemical composition. Honey is hyperosmolar, thus restricting the availability of environmental water to bacteria and other organisms (10). However, it is worth noting that unlike many modern wound dressings, honey acts intimately with the wound environment and has the ability to connect directly with all surfaces not just the more superior wound surfaces.

Five randomised controlled trials on the use of honey in acute burn wounds of less than 40% body surface area have shown faster healing rates in the honey group compared with those in other agents (11–15). A trial

comparing local honey with topical antiseptics in 50 patients with postoperative abdominal wound infections reported faster healing times, reduced hospital stay, shorter duration of antibiotic use and reduced scarring (16). Vardi *et al.* (17) reported on the use of honey in nine cases of neonatal postoperative wound infection. In Vardi *et al.*'s (17) study, wounds, which had not responded to conventional treatment for a period of two weeks, healed by day 21 following the twice-daily application of honey dressings. This report stated that no adverse reactions including hyperglycaemia, electrolyte imbalance or significant irritation to local tissues were noted (17).

## ANTIBACTERIAL PROPERTIES

Topical honey has also been reported in a multitude of case studies including MRSA-colonised hydroxyurea-induced leg ulcer, pressure ulcers, meningococcal lesions and perineal herpetic ulcers (18–21). Of note, in many of the case studies is the improvement seen when other therapeutic options had failed.

The antibacterial properties of honey have been widely studied. Willix *et al.* (22) studied seven major wound-infecting species of bacteria and compared their sensitivity with the non peroxide antibacterial activity of Manuka honey and with a honey in which the antibacterial activity was primarily because of hydrogen peroxide. It was concluded that both types of honey in quite dilute solutions could completely inhibit the growth of bacteria over an incubation period of 8 hours (22).

Cooper *et al.* (23) tested 18 strains of methicillin-resistant *Staphylococcus aureus* (MRSA), seven strains of vancomycin-sensitive enterococci (VSE) isolated from infected wounds and 20 strains of vancomycin-resistant enterococci (VRE) isolated from hospital environments against a Manuka honey and pasture honey. Manuka honey with a non peroxide activity equivalent to 18% (w/v) phenol and a pasture honey with hydrogen peroxide activity equivalent to 13.7% (w/v) phenol were used. The authors demonstrated that two natural honeys of median levels of potency were significantly more effective in inhibiting MRSA, VSE and VRE in *in vitro* tests than an artificial honey solution. In this study, 30% (w/v) artificial honey incorporated into nutrient agar failed to prevent the

## Key Points

- leg ulceration remains a significant clinical problem
- reports of the use of honey date back to 1550BC
- exact mode of action of honey is not fully understood
- five RCTs in burns have shown clinical benefit
- other clinical studies have shown benefit
- the antibacterial properties of honey are well documented

### Key Points

- the role of topical antimicrobials in wound management is the subject of much debate
- some reports state that honey can deodorise and deslough wounds
- the objectives of this study were to gain insight into the practical use of Manuka honey
- this paper presents a case series of eight consecutive cases of leg ulceration
- only non healing wounds were chosen for this study

growth of 18 strains of MRSA, whereas Manuka and pasture honey, at least 10 times more dilute than artificial honey, prevented the growth of these strains (23).

A further *in vitro* study of the effect of two types of honey on *Pseudomonas* isolated from routine swabs taken from a variety of 20 different wounds concluded that honeys with an average level of antibacterial activity could be expected to be effective in preventing the growth of *Pseudomonads* on the surface of a wound even if the honey were diluted more than 10-fold by exudation from the wound (24).

### ANTIMICROBIAL PROPERTIES

Most wounds have a polymicrobial environment, while chronic wounds support four or more pathogens (25). The development of infection delays healing, causes wound breakdown and can lead to life-threatening illness, at times resulting in amputation and even death. The role of topical antimicrobials in wound management is the subject of much discussion within the literature (26–28). The use of honey as a topical antimicrobial should follow the same rationale for use as any other antimicrobial, while reference to the infection continuum can help practitioners in the decision-making process (29).

There are many reports of honey deodorising wounds and lifting slough (30). These have significance as wound malodour adversely affects patients' quality of life, and removal of slough is a vital step in wound bed preparation.

As with any new therapy, ease of use and evidence of efficacy are required. However, the gold standard randomised controlled trial is not always available; yet practitioners require knowledge and understanding of product use. Participation in the research process

takes many forms, and many case studies, case series and *in vitro* work can stimulate future interest in large-scale trials. This study aims to add to the current body of knowledge and explore the possibility of further scientific research into the use of honey in wound management.

### METHODOLOGY

Within hierarchies of evidence, case studies are sometimes seen to be on a par with expert opinion (31). If undertaken prospectively with clearly defined multiple sources of data collection and a documented chain of evidence, case studies can add breath to our knowledge and experience of caring for patients with tissue viability problems (31). The intention of instrumental case studies is to use the phenomenon to be studied (leg ulcers) to provide insight into a particular issue (honey) (31). The aims of this study were to gain insight into the practical use of Manuka honey in wound management and document the changes in the wound with regard to size, odour and pain levels experienced by the patient. The key objective was to test the feasibility and acceptability of using Manuka honey in a randomised controlled trial.

Rather than a single case study of limited value, a case series of eight consecutive cases of leg ulceration with full consideration to clinical status and patient consent was conducted. Ethical approval for the study and informed consent from all patients were obtained. Only patients whose wound has not shown any signs of improvement in the preceding four weeks as determined by wound size and condition of the wound bed and without any clinical signs of infection were included in the study. (Table 1)

**Table 1** Patient details

| Patient ID | Age | Gender | Aetiology                             | Wound duration | Size at start        |
|------------|-----|--------|---------------------------------------|----------------|----------------------|
| A          | 62  | Male   | Diabetic foot ulcer                   | 5 months       | 8.25 cm <sup>2</sup> |
| B          | 36  | Male   | Non healed surgical excision          | 5 months       | 3.75 cm <sup>2</sup> |
| C          | 22  | Female | Full thickness burn                   | 7 weeks        | 8.75 cm <sup>2</sup> |
| D          | 83  | Female | Animal bite wound                     | 5 weeks        | 7.75 cm <sup>2</sup> |
| E          | 55  | Female | Rheumatoid ulcer                      | 12 months      | 2.50 cm <sup>2</sup> |
| F          | 59  | Female | Post excision squamous cell carcinoma | 3 weeks        | 7.25 cm <sup>2</sup> |
| G          | 66  | Female | Mixed aetiology ulcer                 | 3 weeks        | 3.00 cm <sup>2</sup> |
| H          | 82  | Male   | Venous leg ulcer                      | 18 months      | 3.75 cm <sup>2</sup> |

**Table 2** Wound size changes

| ID | Size at start        | End Week 1           | End Week 2           | End Week 3           | End Week 4           | % reduction in wound size over 4 weeks |
|----|----------------------|----------------------|----------------------|----------------------|----------------------|--|
| A  | 8.25 cm <sup>2</sup> | 8.00 cm <sup>2</sup> | 7 cm <sup>2</sup>    | 6 cm <sup>2</sup>    | 3.75 cm <sup>2</sup> | 54%                                    |
| B  | 3.75 cm <sup>2</sup> | 2.75 cm <sup>2</sup> | 2.25 cm <sup>2</sup> | 1.50 cm <sup>2</sup> | 1.00 cm <sup>2</sup> | 73%                                    |
| C  | 8.75 cm <sup>2</sup> | 5.00 cm <sup>2</sup> | 3.50 cm <sup>2</sup> | 2.50 cm <sup>2</sup> | 0.50 cm <sup>2</sup> | 94%                                    |
| D  | 7.75 cm <sup>2</sup> | 7.25 cm <sup>2</sup> | 6.50 cm <sup>2</sup> | 4.75 cm <sup>2</sup> | 4.75 cm <sup>2</sup> | 42.4%                                  |
| E  | 2.50 cm <sup>2</sup> | 2.25 cm <sup>2</sup> | 4.00 cm <sup>2</sup> | 2.50 cm <sup>2</sup> | 2.25 cm <sup>2</sup> | 10%                                    |
| F  | 7.25 cm <sup>2</sup> | 5.00 cm <sup>2</sup> | 3.25 cm <sup>2</sup> | 2.75 cm <sup>2</sup> | 2.75 cm <sup>2</sup> | 62%                                    |
| G  | 3.00 cm <sup>2</sup> | 3.75 cm <sup>2</sup> | 3.00 cm <sup>2</sup> | 2.75 cm <sup>2</sup> | 2.50 cm <sup>2</sup> | 17%                                    |
| H  | 3.75 cm <sup>2</sup> | 3.00 cm <sup>2</sup> | 2.50 cm <sup>2</sup> | 1.25 cm <sup>2</sup> | 0.50 cm <sup>2</sup> | 86.7%                                  |

All wounds were dressed once or twice weekly as necessitated by levels of wound exudate. Manuka honey (Woundcare 18+, Comvita, Natural Food Company, New Zealand) in 60 g of  $\gamma$ -irradiated tubes was used. 5 g per 20 cm<sup>2</sup> of Manuka honey was applied to Tricotex (Smith & Nephew, UK) non adherent dressing. Secondary dressings and bandages as appropriate were then used.

## DATA COLLECTION

Wounds were measured using transparent acetate tracings and fine tip permanent pen. Pain scores were recorded using the five point visual analogue scale. Odour can be a very subjective measurement, and recordings were made on no odour, odour on dressing change or odour all the time. The patient was asked to comment on any aspect of the use of honey, particularly their perception of odour associated with the wound.

Photographs were taken at the start and the end of a four-week period. 4 weeks was chosen as the time frame as the literature would recommend that if a wound shows no signs of improvement with a particular intervention over a 4-week period, then a change of treatment or further investigation may be necessary (32). As this was a single site, case report format every 4 weeks was also deemed by the practitioner/researcher to be a practical and realistic time frame for each patient to meet the aims of the study. All data were collected by the study researcher.

Blinded outcome assessment adds to the rigor of the study process and is recommended in wound management research. However, the literature fails to recommend strategies whereby practitioners can achieve blinding. Therefore, to ensure greater reliab-

ility and validity, a range of measures was employed including documentary data sources, photographic evidence, acetate tracings and patient comment and observation.

## RESULTS

Patient characteristics and wound size are summarised in Table 1. The participants included three males and five females, with an age range 22 years to 83 years and with injuries and ulceration of the lower limb of different aetiologies (Table 1). The duration of the wounds were 3 weeks to 18 months with the shorter duration wounds being the more acute injuries and the longer duration wounds being more chronic wounds. The mean initial wound size was 5.62 cm<sup>2</sup> (range 2.50 cm<sup>2</sup>-8.75 cm<sup>2</sup>). At the end of the four-week treatment period, the mean size was 2.25 cm<sup>2</sup> (range 0.5-4.75 cm<sup>2</sup>). This represented a mean reduction in wound size in all eight cases of 54.8% (range 10-94%) (Table 2).

Patient G reported stinging for up to 2 hours following application. Patient E also reported stinging but only for 30 minutes following application. This continued in both cases for the four-week period. Prior to the use of honey, patients A, B and D had noticeable malodour on dressing change. In all three cases, both patients and staff reported the absence of malodour after one week of treatment. All wounds were dressed weekly except patient B. This patient's wound did not require such frequent changes but was requested by the patient for social reasons.

## DISCUSSION

This small-scale study raised many questions and points of interest with regard to the use of

## Key Points

- all wounds were dressed once or twice weekly
- wounds were measured via tracing on to acetates
- pain was measured using a 5 point scale
- wounds were photographed and their assessment was in a blind manner.
- the mean initial wound size was 5.62 cm<sup>2</sup>
- at the end of the 4 week treatment period the mean wound size was 2.25 cm<sup>2</sup>

### Key Points

- some patients reported stinging upon application of the honey
- acute wounds improved significantly in our study
- in general the effects of honey were positive
- this is a limited clinical case series. It generated valuable information but a larger trial is needed
- in conclusion the mean reduction in wound area was 54.8% over a four week period

Manuka honey in wound management. It was interesting to note that the two patients with an arterial component to their wounds (E and G) reported stinging following application of honey and had little improvement in their wounds during this period; this may or may not be significant in terms of the use of honey in arterial wounds. Only one other reference to these phenomena is found in the literature; a statement by Molan and Betts in a review of the use of honey in wounds reported that successful healing was achieved in all patients except those with arterial insufficiency (33). However, little clarification is given; the authors offer no possible explanation for this. Further studies should focus on which wound aetiology and at which stage of the healing process, honey is most beneficial (34).

The three acute wounds (B, C and D) had significant improvements with reduction in wound size of 42–94% (Table 2). The most significant change was for patient H whose wound of 18-month duration reduced by 86.7% (Table 2). It is highly probable that the renewed interest and compliance demonstrated by this patient during the study period contributed significantly to this development. However, it also raises the possibility that with renewed interest by both the patient and practitioner, that improvements are possible, and thus, the benefit of such case studies may be greater than is recognised within the literature.

There are many reports of honey clearing malodour from wounds; this was also the outcome in this study (30). Patients were encouraged to verbalise any episodes of malodour, but none were reported or recorded after the first application.

The desired frequency of application of honey to wounds has not been established. Current management of patients with venous leg ulcers and other chronic wounds often involves once-weekly dressing change. More frequent dressing change is applied depending on the clinical need. This has resulted in improved quality of life for patients, as they are not bound to frequent appointments and leaking dressings. Thus the use of honey daily or alternate days in chronic wounds could impinge on a person's independence, unless they could change their own dressings. The benefits obtained by once-weekly dressing change with honey cannot be ignored, and thus the possibility of honey feeding bacteria

and causing infection was not borne out in this case series.

Nelson (35) highlights that an improvement seen with a new treatment does not allow one to attribute the effect to the intervention, as most wounds will eventually improve; thus, it is particularly problematic to attribute cause and effect using case reports. While this is true, descriptive research frequently precedes experimental studies, as it often serves to generate predictions (hypothesis) about the relationship among the various phenomena studied, which can then be tested in an experimental study which may confirm or reject the prediction (36).

### LIMITATIONS

As a small-scale case series, the study had a number of limitations arising principally from including a heterogeneous sample and patients with wound of various aetiologies. The lack of specific inclusion criteria such as age and morbidity, beyond non healing wounds, introduces further limitations in terms of generalisability. The inclusion of patients with healing as well as non healing wound would have provided opportunities for further comparative analysis.

### RECOMMENDATIONS

The use of case series helps to generate valuable information with regards to the use of new therapies and should be encouraged. Further research into the most appropriate aetiology in which honey is effective is required. This should include particular reference to wounds of arterial aetiology. Further studies should investigate the potential of honey in deodorising wounds, which may be of particular interest in fungating lesions. The randomised controlled trial is the gold standard to test efficacy in comparison with standard therapy and is proposed as the way forward in further studies on the use of Manuka honey in wound care.

### CONCLUSION

In this study, the use of Manuka honey was associated with a positive wound-healing outcome. Mean reduction in wound area across all wounds was 54.8% over a 4-week period. Two patients with an arterial component to their wounds reported stinging following application and had only minimal improvement in the wound size. Malodour was eliminated in all wounds. The study provided the necessary

basis for a more rigorous research into the clinical use of honey in wound management.

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