Use of honey in palliative and general wound management

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ABSTRACT

The use of traditional topical antibiotics such as metronidazole remains prevalent for the treatment of wounds in palliative care. However, over the years there has been increasing interest and adoption of the use of honey. Evidence of the effectiveness of honey and metronidazole in wound healing, especially in the palliative care environment, is limited to many small-scale studies. This paucity in high-quality evidence is restricting a more widespread adoption of the use of honey in the routine care of wounds.

This report reviewed a number of recent studies with the aim of presenting a coherent summary of current evidence on the effectiveness of honey in wound care. It is hoped that this report will encourage debate and generate quality research within institutions with regard to the effectiveness of honey in wound care.

Keywords: Honey, metronidazole, wound, topical, dressing.

Topical treatments are important in palliative care as compromised patients have weakened skin barrier¹, leaving them susceptible to skin breakdown and infection². Complications arising from wounds are a significant cause of increased hospital stay and cost². Effective wound care may decrease hospital stay, reduce costs and improve quality of life³.

In the completion of this article a number of studies have been reviewed. Characteristics of these studies have been provided in Table 1.

Metronidazole is commonly used in the management of palliative care wounds⁴. It interferes with bacterial replication, resulting in bacterial

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cell death⁵, thereby reducing odour and exudate⁶. In a randomised controlled trial of 41 patients comparing topical metronidazole with placebo there was a 100% alleviation of odour in the metronidazole group compared with 76% in the placebo group, the difference not being insignificant. The same trial also demonstrated reduction in pain and exudate levels by day three in the metronidazole group⁷.

Another trial using metronidazole 0.75% gel on 47 patients showed that 95% of patients reported decrease in odour after 24 hours compared to placebo⁸ and in another study with 16 patients, all patients showed improvement, 10 cases with complete removal of odour, and 6 cases with marked improvement of odour using 0.75% metronidazole gel⁹. Although there have been a small number of studies using limited sample size, the majority of the evidence on the effectiveness of metronidazole in palliative care patients in the community has been anecdotal⁶.

Due to increasing prevalence of antibiotic resistance, it is believed that metronidazole's use should be reduced and only reserved for brief periods of treatment³. Chronic wounds often develop a biofilm matrix, which can make them more resistant to successful treatment by topical antibiotics such as metronidazole, which only target single, specific microorganisms. This supports the need for further investigation into non-antibiotic approaches¹⁰.

In recent years, the use of medical-grade honey has received renewed interest in wound care. Some studies identify honey as more costeffective in wound care and it is fast becoming the preferred option, especially given the continued indiscriminate use of antibiotics, but no clear correlation has been made in any of these studies between the cost of honey compared to metronidazole^{3,11,12}.

Honey arrests bacterial cell division, decreases wound pH, hinders biofilm formation, and within 24 hours of honey application odour can be reduced or eradicated¹³. It also has anti-inflammatory properties which decrease oedema and exudate¹⁴. Honey not only reduces odour through reductions in various bacterial loads but also through providing glucose as a form of energy, which microorganisms use in preference to amino acids from which the malodorous substances are produced¹⁵, unlike metronidazole, which only targets odour from protozoa and anaerobic bacteria⁶.

In a systematic review¹⁶ that included 19 trials involving 2,554 subjects, there was a reduction of 4.68 days in wound healing times, when honey was compared to conventional dressings. These results were for partial thickness burns, and the authors concluded that there was insufficient evidence to make recommendations for other wound types.

A trial using honey in cancer patients with pressure ulcers showed that patients who used honey on their wounds had improved pain relief and wound healing¹¹. The trial also demonstrated that, over a period of 10 days, pressure ulcers treated with honey and metronidazole had significant improvement (39% on the Bates-Jensen wound assessment scale) over the course of 10 days when compared to wounds treated with metronidazole alone. The study arm showed steady decrease in wound severity, and the control arm showed a gradual increase in wound severity.

An in vitro study demonstrated success with honey on multiresistant microorganisms such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus (VRE) indicating that honey is an effective antibacterial agent¹⁷. The main antibacterial component of honey from the Leptospermum species is methylglyoxal, and in other types of honey (from non-Leptospermum species) is the release of hydrogen peroxide¹⁸. Both methylglyoxal and hydrogen peroxide can eradicate Gram-positive, Gram-negative species, Pseudomonas, MRSA, VRE anaerobic and aerobic bacteria as well as biofilms¹⁹. However, many studies have shown that honey from the Leptospermum species (for example, Manuka honey) which contains high levels of methylglyoxal, possess significantly greater antibacterial activity compared to non-Leptospermum species²⁰⁻²³. Recent reports^{24,25} have suggested that methylglyoxal is a potent protein-glycating agent and an important precursor of advanced glycation end products. As both these agents have roles in the pathogenesis of impaired diabetic wound healing, one may expect that Manuka honey used in diabetic patients would delay or impair wound healing. Many studies to date using Manuka honey in diabetic patients have not found any adverse effects with wound healing and, in most cases, similar rates of wound healing were observed to that of other types of wound²⁶⁻³⁰. Furthermore, in vitro studies have shown increased release of tumour necrosis factor-alpha, interleukin-beta and interleukin-6 with Manuka honey and have suggested that the effect of Manuka honey on wound healing may be in part related to the stimulation of inflammatory cytokines from monocytes³¹. These

types of cells are known to have an important role, not only in diabetic wound healing but in all wound healing. Studies have also shown that it is unlikely that bacteria will develop resistance to treatment with honey, unlike other topical treatments such as antibiotics^{13,14}.

Numerous studies have now been completed, and there is good evidence to support the use of honey in wound care^{2,3,9,10,32}. However, due to the varying methodologies used in these studies including the use of different types of honey treatments, it is difficult to ascertain which honey treatment is most efficacious. Vital to the value of any trials in honey treatment is adherence to the protocols for dressings which keep the honey in contact with the wound³³. Further well-designed comparative controlled trials are needed to better understand the role of honey in the management of wounds, and to better understand the effectiveness of honey compared to metronidazole.

This evidence-based review on the use of honey has raised important clinical questions about its future potential role in the management of wound care. In recent years the use of honey has increased substantially and many different types of honey and honey dressings are now available^{13,14}. Nurses working in wound care should consider honey as a treatment option, especially given the increasing resistance of bacteria to antibiotics in the community setting.

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Authors (year published)/ reference number	Study design/intervention/participants	Study findings	Study recommendations
Bale S, Tebble N & Price P (2004)/7	Randomised controlled trial comparing metronidazole to placebo on 41 patients.	Impact of metronidazole on odour unclear with 100% of patients in metronidazole arm, and 76% on patients in the placebo arm showing improvement in odour.	Further research is needed involving large sample size and for longer duration.
Kalinski C, Schneph M, Laboy D <i>et al.</i> (2005)/9	Prospective, single-centre open trial (not randomised) using metronidazole in 16 patients.	Metronidazole was reported to be effective for the treatment of malodorous wounds.	Further consideration is needed to the study of the use of metronidazole on fungating wounds.
Gethin G & Cowman S (2009)/20	Large, multicentre randomised controlled trial comparing Manuka honey to standard hydrogel therapy (IntraSite Gel) in 108 patients.	Manuka honey-treated wounds exhibited increased incidence of healing, more efficacious desloughing and lower rates of infection.	Manuka honey has a beneficial therapeutic effect in modern wound management.
Da Costa Santos (2010)/4	Review of 59 articles (20 studies were clinical trials, case studies or case reports) of odour control comparing metronidazole to activated carbon dressing.	Studies that fulfilled criteria showed reduction in odour. Of note was that only 10 of the 20 included studies used metronidazole.	Few studies of high quality were found. Flaws in study design, small sample size of studies and no validated odour scale were frequent found.
Molan P (2011)/14	Systemic review of 16 randomised controlled trials (honey compared to other pharmaceutical products) with 1,591 patients.	Evidence from research and studies demonstrated that honey should be considered alongside modern pharmaceutical products with regard to its effectiveness and therapeutic activities.	Manufacturers should standardise their products based upon the various therapeutic values of honey. Trials should focus on the best honey treatment for specific wound types and trials completed with the control arm being current best practice/standard treatment (as opposed to placebo).
Lee DS, Sinno S & Khackemoune A (2011)/12	Review (included 24 studies and 3 meta- analyses) using unspecified types of honey.	Every year new studies describe the action of honey, and demonstrate its efficacy in treating wounds.	Until larger, randomised controlled trials support its use, one cannot deny the great body of literature that associates honey with remarkable wound healing.
Biglari B & Linden PH (2011)/23	Prospective observational study (using Medihoney) in 20 spinal cord injury patients with chronic pressure ulcers.	Honey appears highly effective for wound management, when looking at bacterial growth and wound size.	Further studies are required to establish universal clinical medical honey guidelines.
Biglari B & Moghaddam A (2012)/22	Observational study (using Medihoney) across 10 hospitals in Germany and Austria in 121 patients over 2 years. Final analysis included 104 patients due to dropouts.	Overall wound size decreased, wounds showed less slough and reduced pain was perceived. Dressings significantly promoted wound healing.	Future comparative trials are necessary to evaluate the extent to which the observations made can be attributed to the effects of Medihoney.

Table 1: Characteristics of studies included in the literature review

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Authors year published)/ eference number	Study design/intervention/participants	Study findings	Study recommendations
iaha A, Chattopadhyay M & Sur PK (2012)/11	Randomised controlled trial (honey and metronidazole versus honey), 1 institution, 40 cancer patients with bedsore wounds. Randomised, non-blind, 20 patients in each arm.	Significant improvement in wound healing status from day 10 in the study arm, and significant reduction in pain from day 7 in the study arm.	Honey can be chosen as a safe and effective material for dressing of bedsore wounds in cancer patients in palliative settings.
ull AB, Walker N & Deshpande S (2013)/16	Systemic review of 25 randomised and quasi- randomised trials (2987 participants) which evaluated honey as a treatment for acute or chronic wounds.	Most trials evaluated were at high or unclear risk of bias. In acute wounds, honey might reduce time to healing compared with some conventional dressings, and delays healing when compared to early excision and grafting. In chronic wounds, honey does not significantly increase healing, and may decrease healing in specific identified scenarios (deep burns,	There is insufficient evidence to guide clinical practice in other types of wounds, and purchasers should refrain from providing honey dressings for routine use until sufficient evidence of effect is available

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