CLINICAL MANAGEMENT extra

Use of Honey in Wound Care: An Update

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This continuing educational activity will expire for physicians on January 31, 2012.

PURPOSE:

To enhance the clinician's competence in interpretation of research studies related to use of honey for wound healing.

TARGET AUDIENCE:

This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.

OBJECTIVES:

After participating in this educational activity, the participant should be better able to:

1. Relate the wound healing process to the antibiotic and anti-inflammatory mechanisms of honey.

2. Apply published study findings comparing honey to conventional dressings in clinical scenarios.

ABSTRACT

The therapeutic use of honey in wound care has been used since ancient times. Honey has been shown to have antibacterial properties in vitro and animal studies have demonstrated accelerated wound healing with the use of honey. In human trials, there is currently not enough strong evidence to fully support the use of honey in wound care; however, use in minor burns and prevention of radiation mucositis appear to be 2 areas where honey shows therapeutic promise.

KEYWORDS: honey use in wound care, honey use in radiation mucositis, honey use on burns, honey use in acute wounds, honey use in chronic wounds

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INTRODUCTION

A wound can result from either an external or an internal insult. Many acute wounds are caused by external insults, such as mechanical insults, thermal radiation, ultraviolet radiation, or radiation (gamma radiation) therapy. Chronic wounds (leg ulcers, diabetic ulcer, pressure ulcers), on the other hand, are largely caused by an internal insult in the form of circulatory compromise. Inadequate circulation robs tissue of necessary nutrients and potentiates proinflammatory cytokines, leading to tissues necrosis.[1]

The process of wound healing is classically divided into 4 stages: hemostasis (seconds to minutes), inflammation (3–5 days), proliferation (4–14 days), and remodeling (8 days to 1 year). There is significant overlap of the aforementioned stages.[2] After hemostasis is achieved, debris and bacteria are removed from the wound during the inflammatory phase. This is followed by blood vessel invasion and the regeneration of the connective tissue and epithelium, along with wound contraction, in the proliferation phase. During the final stage, the remodeling phase, collagen is rearranged along tension lines, and excess tissue is removed via apoptosis.[3] Older patients, infection, and poor circulation are believed to hinder this healing process.[1]

The goal of wound care is to first remove the offending insult, then to provide the best possible environment to facilitate wound healing. Controlling the bacterial load of a wound is one of the most important aspects in ensuring an optimal healing environment. A bacterial level greater than 10^5 organisms per gram of wound tissue has been found to have a deleterious effect on wound healing in surgical and chronic wounds.[4,5] Many topical products with various properties are currently being used with the intent of facilitating wound healing. Surprisingly, there is a lack of strong evidence to support the use of the majority of these products.[6–9]

By reading this article, the clinician will be better able to assess the inherent complexities of the clinical use of medical-grade honey, to evaluate the paucity of the strength-of-evidence ratings to support the use of time-honored remedies, and to select clinical entities in patients who may benefit from treatment with medical-grade honey, using the evidence indicators such as the Cochrane reviews. Consideration of the biochemical properties of honey and their discrete mechanisms of action on the wound and the bioenvironment of the wound and antibiotic and anti-inflammatory mechanisms will also be discussed.

RATIONALE FOR HONEY IN WOUND CARE

Honey has been a product that has received a growing amount of attention in wound care, especially in the care of burn wounds. Since ancient times, honey has been used by man for both food and medicine in various cultures.[6] Perhaps the first mention of honey in wound care was in ancient Egypt between 2600 and 2200 BCE.[6] Although the exact mechanism for the beneficial aspects of honey in wound healing is still unknown, research has focused on the antibacterial property of honey as a cause. Honey is hygroscopic from its high sugar content, meaning it has a dehydrating effect that is inhibitory for bacterial growth. Studies have demonstrated that the antibacterial properties of honey are more complex than just high sugar content alone.[10] Honey contains glucose oxidase, an enzyme that converts glucose to hydrogen peroxide, which may contribute to some of its antibacterial properties.[6,11,12] Furthermore, the antibacterial properties of honey appear to vary depending on the floral source. Honey derived from *Leptospermum* trees (manuka) or *Echium vulgare* bush (viper's bugloss) showed antibacterial properties independent of hydrogen peroxide.[13] It is believed that another, yet undiscovered, component of honey is responsible for the antibacterial properties.

Different types of honey have been shown to have antibacterial activity against the following bacterial species in vitro: *Alcaligenes faecalis*, *Citrobacter freundii*, *Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Mycobacterium phlei*, *Salmonella california*, *Salmonella enteritidis*, *Salmonella typhimurium*, *Shigella sonnei*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*. Interestingly, *Serratia marcescens* and the yeast *Candida albicans* were not inhibited by honey.[14] In addition, manuka honey has also been shown to have an inhibitory effect on *Pseudomonas aeruginosa*, methicillin-resistant *S aureus* (MRSA), and vancomycin-resistant enterococcus species.[15,16] In a recent report, ulmo honey showed superior anti-MRSA property compared with manuka honey.[17] Lastly, honey displayed mixed antifungal activity.[14,18]

Animal studies have demonstrated, at the histological level, that honey accelerated wound healing. In rabbits with cutaneous wounds, honey was found to decrease edema, decrease inflammation, reduce necrosis, improve epithelialization, and improve wound contraction when the wound tissue was examined histologically.[19] In mice, the use of honey also demonstrated accelerated wound healing on cutaneous wounds at the histological level.[20]

Clinical observations from human trials reported that honey-debrided wounds[21,22] facilitated formation of granulating tissue,[21–24] improved epithelialization,[21,22] and reduced inflammation.[22,25] This was consistent with what was reported in the animal study data previously discussed; however, clinical observation without the support of histological evidence is limited.

HONEY ON ACUTE WOUNDS

Although animal studies report accelerated healing time with the use of medical-grade honey,[19,20,26] results in humans have been varied. Recently, 3 small (n = 40, each study) randomized,

single-blind (examiner) controlled trial[27–29] and 1 small (n = 40) randomized, nonblinded controlled trial[30] demonstrated that honey may have some protective effects against radiation-induced mucositis in head and neck cancer patients undergoing therapy.

In a randomized, double-blind, controlled trial, honey dressing showed no difference in healing time compared with hydrogel dressings in patients who sustained abrasions or minor lacerations.[31] In a randomized, double-blind controlled trial[32] and a randomized single-blind controlled trial,[33] patients who sustained toenail avulsions showed no differences in mean healing times when honey was compared with paraffin gauze and iodoform gauze, respectively. A meta-analysis of these 3 studies confirmed no statistical difference in mean time to healing between honey and conventional dressing in these minor acute wounds.[6]

In several randomized controlled trials, using honey on minor burns (superficial to partial-thickness burns) shows accelerated healing time compared with conventional dressings, such as silver sulfadiazine dressing[25,34–36] and transparent polyurethane film dressing.[23] Figure 1 shows an example of superficial partial-thickness burns (not treated with honey). In addition, honey was found to be superior to nonconventional dressings, such as potato peels[37] and amniotic membrane.[38] However, the strength of these studies has been questioned because of the absence of the description of how randomization was achieved.[6,39] Meta-analyses of these trials showed the use of honey to accelerate healing of minor burns compared with the previously mentioned comparators.[6,39,40] In moderate burns (partial-thickness to full-thickness burns), a randomized controlled trial reported that early excision was superior to honey dressing.[41] However, this study also failed to clearly state the method of randomization, which also raises questions on the strength of the study. Clinicians must consider the available evidence when selecting dressings for burn wounds.

Figure 1.
EXAMPLE OF SUPERFICIAL PARTIAL-THICKNESS BURN

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HONEY ON CHRONIC WOUNDS

As stated earlier, many chronic wounds have their origins from circulatory compromise. Because topical agents do not adequately address the underlying circulatory compromise, it is not surprising that there is little evidence that supports the use of many products currently used.

Two randomized, open-label, controlled trials were reported on the use of honey on venous leg ulcers. In the larger study, honey-impregnated dressing did not significantly improve venous leg ulcers compared with conventional dressing at 12 weeks.[42] Compression was used in both groups. In the second trial, honey dressing was compared with hydrogel in sloughy venous ulcers. At 12 weeks, honey was found to have a slightly higher rate of healing (44%) versus hydrogel (33%).[43] The method of randomization was reported in both studies. A meta-analysis based on these 2 studies concluded that there is no statistical difference in healing between honey and conventional dressing in venous leg ulcers.[6]

In a poor-quality randomized controlled trial, honey dressing compared with saline-soaked dressing was found to accelerate healing in Stages I and II pressure ulcers.[44] In another, poor-quality trial, honey was found to accelerate healing in Stage II or III pressure ulcers.[45] In yet another randomized controlled trial of poor quality, honey dressing was found to be equivocal to iodine dressing in Wagner type II diabetic foot ulcers.[46] The method of randomization was not described for any of these previously mentioned studies, which raises questions on their strength.

DISCUSSION

There is a paucity of strong evidence to support the use of many topical agents and dressings currently used in wound care. In systematic reviews, there was not enough evidence to support the use of the following: silver-containing dressing to promote wound healing,[47,48] topical agents or dressings to promote healing in arterial ulcers,[9] topical agents or dressings in minor burns to promote healing (superficial to partial-thickness burns),[7] systemic or topical antibiotics in venous ulcers to promote healing,[8] and topical agents or dressing in promoting postoperative wound healing by secondary intention.[49] Failure to report the method of allocation concealment, failure to blind participants and/or

outcome assessors, and inadequate follow-up were cited as limiting the strength of the randomized controlled trial.[7–9,47]

Despite some evidence that medical-grade honey may be beneficial in superficial and partial-thickness burns, many randomized controlled trials failed to report the method of randomization, which limited their strength.[6,39,40] In addition, many of these trials were performed by the same researcher.[23–25,36–38,41] In several trials on minor burn wounds, the use of honey was compared with silver sulfadiazine.[24,25,34–36] Although silver dressings are currently used in burn wound care owing to its antibacterial properties, there is little support that silver is effective in promoting wound healing.[47,48] Furthermore, several poor-quality studies reported that silver sulfadiazine may delay wound healing, putting in question its use as a suitable comparator.[7] Although the evidence is poor, owing to the potential for silver sulfadiazine dressing to artificially skew results in favor of honey, future studies should exercise caution when considering using silver sulfadiazine as a comparator.

The antibacterial property of honey has been the focus regarding its use in wound healing; however, it is important to realize that honey is not a substitute for antibiotics. The current standard of care dictates that unless the wound is infected, prophylactic use of antibiotics is not recommended. There is little support that prophylactic antibiotics correlates with accelerated healing.[8] For this reason, the antibacterial property alone may not explain the beneficial effects. Further *in vitro* studies and animal research need to be done to identify other components of honey involved in antibacterial, debriding, and anti-inflammatory properties. This may shed more light for the reason behind the variation between the different types of honey and may lead to the standardization of the type of honey used in therapy.

SUMMARY

There are some promising results with the use of honey in minor burns and protection from radiation mucositis. However, large, multicenter, randomized controlled trials with at least single blinding (examiner) are needed prior to clinical recommendations being given. In addition, these studies should clearly indicate the method of allocation concealment and have adequate follow-up time.

After reading this article, the clinician should be better able to assess the inherent complexities of the clinical use of medical-grade honey, to evaluate the paucity of the strength-of-evidence ratings to support the use of time-honored remedies, and to select clinical entities in patients who may benefit from treatment with medical-grade honey, using the evidence indicators such as the Cochrane reviews.

PRACTICE PEARLS

- Consider the available evidence when selecting dressings for burn wounds.
- Use of honey in minor burns and the prevention of radiation mucositis show therapeutic promise.
- The potential benefits of honey in wound healing may be due to its antibacterial property.
- Different types of honey have been shown to have antibacterial activity against a number of bacterial species.
- Studies show that honey-debrided wounds facilitated formation of granulating tissue, improved epithelialization, and reduced inflammation.

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