

# Honey vs povidone iodine following toenail surgery

Caroline Marshall, Janet Queen, Jane Manjooran

## Abstract

**Background:** Anecdotally, honey is useful in wound healing, but there is limited empirical evidence. **Objective:** This single-blind, randomised, controlled trial compared a medicated honey dressing vs an iodine dressing on post-operative healing following toenail surgery with matrix phenolisation. **Method:** Participants (n=51, with 61 operated toes) were randomly assigned to receive honey or iodine dressings. The primary outcome was the time (days) taken for complete re-epithelialisation to occur following surgery. **Results:** Mean healing times were 33 days (SD=15.71) for honey, and 25 days (SD=8.70) for iodine (P = 0.04). Total avulsion wounds healed statistically significantly faster with iodine (30 days) compared with honey (44 days), but no significant difference in healing time was found for partial avulsion wounds (18 days with honey vs 23 days with iodine). **Conclusion:** Despite a small sample size, these results indicate that healing time following toenail avulsion surgery is accelerated with iodine dressings vs honey dressings. **Declaration of interest:** None

## KEY WORDS

Honey dressings  
Iodine dressings  
Toenail surgery  
Podiatry  
Randomised controlled trial

The use of honey in medicine dates as far back as c. 50 AD where Dioscorides is cited as describing honey as being 'good for all rotten and hollow ulcer' (Molan, 2001b). Since ancient times, honey products have continued to be used across the world in wound management, however; their use in modern wound care has diminished, particularly over the last half a century. This has primarily been attributed to the introduction of systemic antibiotics and the advent

Caroline Marshall is Lecturer in Podiatry, Centre for Health and Social Care Research, University of Huddersfield, Queensgate, Huddersfield, HD1 3DH, and Janet Queen and Jane Manjooran are Senior Podiatrists, Department of Podiatry and Foot Health, Scarborough, Whitby & Ryedale Primary Care Trust, UK

of a plethora of modern wound care products (Molan, 2001a). With the vast use of antibiotics and the subsequent development of anti-microbial drug resistance, a major crisis in health care has occurred which clearly highlights the need for alternative treatment options (Al-Waili and Saloom, 1999).

## Povidone iodine

Povidone iodine is a long established antiseptic used in wound care. Current literature surrounding the use of iodine is conflicting; topical application is known to provide effective antibacterial prophylaxis in wound care, particularly burns (Lawrence, 1998); however, based on *in vitro* and *in vivo* animal studies, concern has been raised as to its cytotoxic effect (Close-Tweedie, 2001). Questions remain as to its therapeutic use in wound care. Often studies relate to a single application of povidone iodine, however, in podiatric practice particularly following toenail surgery, application may continue for a number of weeks. Few studies have examined healing rates with povidone iodine products, particularly after toenail surgery, despite the fact that povidone

iodine is frequently used as a first choice post-operative dressing by podiatrists (Martin, unpublished observations).

## Honey

Interest in the antibacterial properties of honey has arisen as a result of its reported inhibitory action against various major wound-infecting species of bacteria, including *Staphylococcus Aureus* and methicillin-resistant *Staphylococcus Aureus* (Phuapradit and Saropala, 1992; Cooper et al, 1999; Natarajan et al, 2001). Anecdotally, rapid clearance of infection is a common clinical observation following the use of honey dressings, particularly when used on complex wounds where conventional methods have failed (Dunford et al, 2000).

Furthermore, Marshall (2002) suggested that the chemical and physical properties of certain honeys may have a positive effect on wound healing. This is primarily due to its antibacterial properties, but honey is also thought to assert an anti-inflammatory action (Molan, 1999), a debriding action (Subrahmanyam, 1998; Vardi et al, 1998) ►►

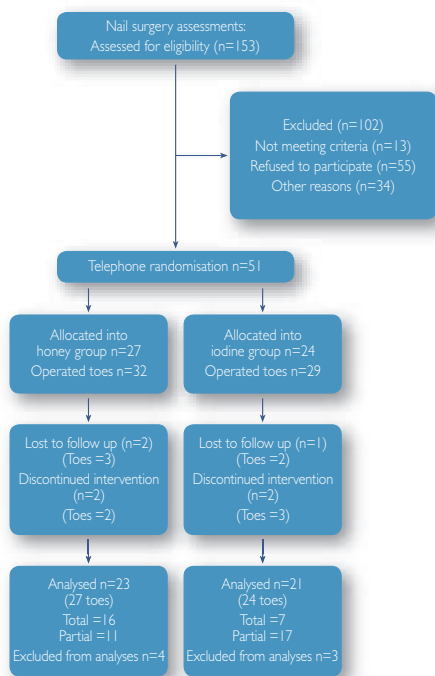


Figure 1. Participant flow through the study.

and play a role in the stimulation of tissue growth. Molan (1999) attributes the latter to stimulation of angiogenesis by the production of low levels of hydrogen peroxide, and the nutritional content of honey introduces trace elements, amino acids, and vitamins to the wound interface.

**Literature review**

A recent systematic review concluded that confidence in the use of honey in wound management is low due to a limited and poor quality evidence base (Moore et al, 2001). Only eight randomised controlled trials have been conducted to investigate the effect of honey on wound healing, one of which investigated the use of manuka honey following toenail surgery (Marshall and Thomson, 2004). In all cases, honey was compared to an alternative dressing material. Comparators included polyurethane film and silver sulfadiazine on burns (Subrahmanyam, 1993; 1998) and paraffin-impregnated tulle (Marshall and Thomson, 2004).

One trial, conducted in the United Arab Emirates, compared crude undiluted honey to povidone iodine in infected post-surgical wounds (Al-Waili and Saloom, 1999). This study

was a randomised controlled trial to investigate the effect of topical honey on post-operative wound infections due to Gram-negative and Gram-positive bacteria following caesarean sections and hysterectomies. For all outcomes, including healing times and eradication of bacterial infection, honey was significantly better than iodine. Al-Waili and Saloom (1999) found that honey-treated wounds healed, on average, 11 days earlier than those with iodine. Eradication of bacterial infection was reported after a mean duration of 6 days with honey vs 15 days with iodine.

Of the 8 studies, 6 gave positive results, and, in terms of healing rates and eradication of infection, honey was superior to the comparator. Two studies yielded negative results, whereby tangential excision (Subrahmanyam, 1999) and paraffin-impregnated tulle (Marshall and Thomson, 2004) were found to be superior to honey.

**Justification for the study**

Accelerated wound healing following toenail surgery with matrix phenolisation, would be of great clinical benefit. A recent randomised controlled trial with concurrent economic evaluation was conducted to evaluate the effectiveness and cost-effectiveness of toenail surgery performed by podiatrists in the community setting, and surgeons in the hospital setting (Thomson et al, 2002). Results showed that podiatric intervention was more effective in all outcomes, with the exception of healing rates, with the surgeon's group healing on average 1.6 weeks earlier than the podiatry group. This can be explained by the corrosive nature of phenol, frequently used by podiatrists for matrix ablation. Wound healing following toenail avulsion with matrix phenolisation takes approximately 6-weeks following partial avulsion, and 8-weeks following total avulsion (Thomson et al, 2002; Marshall and Thomson, 2004).

There are currently few quality controlled trials to investigate the most effective post-operative dressing material following toenail surgery in podiatric and general medical literature. This is despite the fact that toenail pathologies are

common debilitating conditions, which frequently require podiatric surgical intervention (Thomson et al, 2002).

It is evident from the published literature that honey has potential in wound healing but, currently, limited evidence exists to support the use of honey in clinical practice. Furthermore, in a climate of clinical effectiveness and evidence-based practice, further research is required to investigate the efficacy of dressing materials following toenail surgery. In particular, randomised controlled trials with blinded assessment of useful clinical outcomes and comparison with standard wound treatments are needed (Moore et al, 2001).

**Aim**

The aim of this study is to test the hypothesis that medicated honey is superior to iodine in reducing post-operative healing time following nail surgery with matrix phenolisation.

**Methods**

This pragmatic trial took place at a general hospital in the north east of England. All patients referred to the Department of Podiatry and Foot Health for assessment for toenail surgery between August 2003 and April 2004 were invited to participate in the trial. All surgery and all follow-up consultations were undertaken within a podiatry outpatients setting. ➤

**Table 1**

**Baseline demographics**

	Honey	Iodine
Age	Mean 39.67 days (SD=20.54) n=27	Mean 44.96 days (SD=23.67) n=24
Gender	16 Males 11 Females	10 males 14 females
Smokers	n=7	n=3
Diabetics	n=9	n=4
Total avulsion	n=16	n=7
Partial avulsion	n=11	n=17

Eligible patients were those deemed suitable for toenail surgery following pre-surgical assessment, and who were to undergo unilateral or bilateral, or total or partial toenail removal with matrix phenolisation, performed by a registered podiatrist.

Patients with peripheral vascular disease or peripheral neuropathy, patients with communication difficulties and patients unable or unwilling to give informed consent or attend follow-up appointments were excluded before randomisation.

Ethical approval was sought from Scarborough General Hospital, local and regional ethical committee and granted in May 2003.

### Interventions and follow-up

Patients received either total or partial toenail removal with phenolisation depending on clinical needs.

Two post-operative wound care interventions were compared:

- ▶▶ Medicated Jarrah honey dressing (B Naturals, Perth Australia)
- ▶▶ Iodine dressing (Inadine, Johnson & Johnson, Skipton UK).

All participants undertook daily redressing according to normal clinical practice following instruction.

Participants were reviewed weekly until complete healing had occurred. An outcome measures form was completed at each consultation, which involved an assessment of wound healing described in previous studies (Schwarztraub and Raymond 1991; Subrahmanyam, 1993). Blind assessments were undertaken, by a registered podiatrist, after removal of dressings and cleansing of the wounds by the investigator to reduce the likelihood of observer bias.

### Outcome measures

The primary outcome measure was the total number of days taken for complete re-epithelialisation of the nail bed. Sub-group analyses compared healing times for total and partial avulsion. Secondary outcome measures included the incidence of post-operative infection, the occurrence of any adverse

**Table 2**

Mean healing times (SD) for the main and sub-group analyses

	Honey	Iodine
Overall	Mean 33 days (SD=15.71) n=27	Mean 25 days (SD=8.70) n=24
Total avulsion	Mean 44 days (SD=7.88) n=16	Mean 30 days (SD=10.62) n=7
Partial avulsion	Mean 18 days (SD=8.45) n=11	Mean 24 days (SD=7.23) n=17

events in each group, the level of post-operative pain experienced generally during the post-operative period and the level of pain experienced in each group at dressing change, measured by a visual analogue scale (VAS) 10 cm (Breivik et al, 2000).

### Sample size

A power calculation showed that 78 subjects (operated toes) would be required. This was based on the ability to detect a clinically important difference between main groups on the primary outcome measure with a power of 80% at the 5% significance level.

### Randomisation

Participants were invited into the study two days post-surgery. Those giving written informed consent were randomly assigned to the intervention groups by telephone randomisation. This involved a phone call to an independent assistant located outside of the clinical setting with no prior knowledge of the participants; random tables were used to determine group allocation. Baseline assessments were completed by the assessor.

### Masking

The study was a single blind trial. While the operating clinician and the patient could not be blinded to the intervention, the outcomes assessor was unaware of group allocation. All dressings were removed and wounds were cleansed by

the investigator before the outcomes assessor entered the room.

### Data analysis

The data were processed with Minitab version 12, using a non-parametric statistical test (Mann Whitney's U test) (Greenhalgh, 2001) to compare average times to complete healing and levels of post-operative pain, with the significance level set at 5%.

### Results

#### Participant flow and follow-up

Figure 1 shows the flow of participants through the trial. From a total of 153 potentially eligible patients, 51 participants were randomised, of whom 27 received honey dressings and 24 received iodine dressings. A similar loss to follow-up in each arm led to 23 participants in the honey arm and 21 participants in the iodine arm completing the trial.

A total of 7/51 participants withdrew from the trial: 4/27 in the honey group, of which 2/4 were lost to follow up and 2/4 were withdrawn due to non-compliance. In the iodine group, 3/24 withdrew from the trial; 1/3 lost to follow up, 1/3 withdrawn for non-compliance, and 1/3 required further surgical intervention. All seven participants were excluded from primary analyses.

#### Baseline demographics

Baseline analyses (Table 1) showed that data relating to age were similar in both groups; mean values were 39.67 (SD=20.54) and 44.96 (SD=23.67) years in the honey and iodine groups, respectively. Distribution of gender across both groups was different; 16 males and 11 females in the honey group and 10 males and 14 females in the iodine group. In respect of prognostic factors, randomisation allocated more patients who smoked (7 vs 3), and more patients with diabetes (9 vs 4) to the honey group.

#### Primary outcome measures

The results are presented in Table 2. Participants randomised to receive honey dressings had a mean healing time of 33 days (SD=15.71), while those randomised to receive iodine dressings had a healing time of 25 days (SD=8.70). This difference was statistically significant (P = 0.04).

In the sub-group analysis, participants having total nail avulsion had a mean healing time of 44.25 days (SD=7.88) in the honey group and 30.14 days (SD=10.62) in the iodine group, indicating that the iodine dressing group healed on average 14.11 days quicker than the honey group. This difference was found to be statistically significant ( $P = 0.01$ ). Participants having partial nail avulsion had a mean healing time for the honey group of 18.45 days (SD=8.45), and 23.55 days (SD=7.23) for the iodine group. Although the honey group appeared to have healed 5.1 days quicker on average, the difference was not statistically significant ( $P=0.16$ ).

### Secondary outcome measures

One participant in the honey group developed a clinically diagnosed post-operative infection requiring referral for antibiotics, but no post-operative infections occurred in the iodine group. No significant adverse events were recorded in either group in relation to the wound dressings used. With respect to general pain experienced in the post-operative period, the mean values recorded on the VAS were 1.86 cm (SD=1.67) for the honey group and 1.99 cm (SD=1.41) for iodine; this difference was not statistically significant ( $P=0.56$ ).

### Discussion

This randomised comparative trial found a statistically significant difference between honey and iodine dressings for post-operative healing time following toenail avulsion surgery. Sub-analyses suggest that there is a statistically significant difference in post-operative healing times following total nail avulsion favouring the iodine dressings, but that did not hold true for partial avulsion surgery.

The incidence of infection was low, with only one instance (in the honey group), and no significant adverse events were recorded with regard to either dressing product. Both dressings were well tolerated by participants in terms of post-operative pain.

### Limitations

A number of limitations to this interpretation must be acknowledged.

A priori power calculation determined 78 operated toes were required to maximise the chance of detecting a statistically and clinically significant difference between the interventions. Unfortunately, due to a lack of funding and resources, only 51 participants (61 operated toes) were recruited into the trial, thereby risking a failure to demonstrate a true difference overall. Results therefore should be interpreted with caution. However, the study aimed to determine whether honey dressings were superior to the more conventional iodine dressings, and with the exception of partial avulsion, iodine dressings led to shorter healing times, so it is unlikely that the hypothesis (overall superiority of honey) would be supported with a larger sample size.

Completing numbers within each group were different; 16 in the honey group and 7 in the iodine group following total avulsion, and 11 in the honey group and 17 in the iodine arm of the study following partial avulsion. Despite the fact that there were fewer participants in the iodine group following total nail avulsion, results indicate that iodine is significantly superior to honey after total avulsion in terms of healing times.

The trial was pragmatic in that it intended to reflect a patient population typical of UK hospital practice. The groups transpired to be heterogeneous in nature with diverse demographic factors and prognostic factors. Participants with stable diabetes mellitus and current smokers (factors that could impact on wound healing), were included in the study, yet the numbers involved would be unlikely to threaten internal validity.

The single-blind design, in which patients undertook their own re-dressing, raises the issues of assessment bias and compliance. A double-blind design with practitioner-administrated redressing was not feasible, though a blind outcomes assessor was used and there is no reason to believe compliance differed between the groups.

Overall, the results of this study add to the findings from the only previous study of healing time after toenail

surgery, suggesting that honey dressings do not accelerate healing (Marshall and Thomson, 2004). While Al-Waili and Saloom (1999) found that honey-treated wounds healed, on average, after 10.73 days compared to 22.04 days for iodine-treated wounds, the surgical procedure in that trial (gynaecological) is quite dissimilar to toenail avulsion surgery. It may be that honey dressings have a role in the management of infected wounds (Molan, 1999), and it remains to be seen if they have a role in post-operative infections following toenail surgery.

A formal cost-benefit analysis was not incorporated within the trial design, but, the unit costs per dressing of honey (£0.30) compared favourably with £0.35 for iodine.

### Conclusion

Despite its limitations, this trial can reasonably be interpreted as offering no support for the general use of honey dressing over iodine dressing following toenail avulsion surgery with phenolisation. Nevertheless, the marginal advantage of honey dressings for partial avulsion surgery deserves further study in a larger sample with formal cost-benefit analysis. **WUK**

### Acknowledgements

The authors would like to thank David Bliss and B Naturals, Australia, for supplying B Naturals medicated trial for the study, Julie Cammish for her assistance in the randomisation process, Scarborough Primary Care Trust, particularly Simon Valente, Podiatry Services Manager for facilitating the study, Jon Blacktop at the University of Huddersfield for statistical advice and Professor Kim Burton, Centre for Health and Social Care Research, University of Huddersfield for invaluable guidance. **▶▶**

### Key Points

- ▶▶ Healing time is accelerated after toenail avulsion surgery with iodine vs honey dressings.
- ▶▶ The marginal advantage of honey dressings on healing following partial avulsion therapy deserves further study.
- ▶▶ Due to a limited sample size, results should be interpreted with caution.

## References

- Al-Waili NS, Saloom KY (1999) Effects of topical honey on post-operative wound infections due to gram positive and gram-negative bacteria following caesarean sections and hysterectomies. *Eur J Med Res* **4**(3): 126–30
- Breivik EK, Bjornsson GA, Skovlund E (2000) A comparison of pain rating scales by sampling from clinical trial data. *The Clinical Journal of Pain* **16**(1): 22–8
- Close-Tweedie J (2001) The role of povidone-iodine in podiatric chronic wound care. *J Wound Care* **10**(8): 339–42
- Cooper RA, Molan PC, Harding KG (1999) Antibacterial activity of honey against strains of staphylococcus aureus from infected wounds. *JR Soc Med* **92**: 283–5
- Dunford C, Cooper R, Molan P (2000) Using honey as a dressing for infected skin lesions. *Nursing Times* **96**: 7–9
- Greenhalgh T (2001) How to read a paper. In: *The Basics of Evidence-based Medicine*. 2nd Ed. BMJ Books, Wales: 45–7
- Lawrence JC (1998) The use of iodine as an antiseptic agent. *J Wound Care* **7**(8): 421–5
- Marshall C, Thomson CE (2004) *The Effect of Honey Dressings on Post-operative Healing following Toenail Surgery: A Randomised Controlled Trial*. Oral Communication. 2nd World Union of Wound Healing Societies' Meeting, Paris
- Marshall CD (2002) The use of honey in wound healing: a review article. *Br J Podiatry* **5**(2): 47–9
- Martin K. A Comparison of Post-operative Dressings following Nail Avulsions in the Schools of Podiatry throughout the United Kingdom. (Unpublished observations). BSc (Hons) Thesis, University of Southampton, New College, Southampton: 22–5
- Molan P (2001a) *Honey as a Topical Antibacterial Agent for Treatment of Infected Wounds*. www.worldwidewounds.com (online) (accessed on 9/3/02)
- Molan PC (2001b) Treatment of wounds and burns with honey. *Current Therapeutics* **9**: 33–39
- Molan PC (1999) The role of honey in the management of wounds. *J Wound Care* **8**(8): 415–18
- Moore OA, Smith LA, Campbell F, Seers K, Mcquay HJ, Moore RA (2001) Systematic review of the use of honey as a wound dressing. *BMC Complementary and Alternative Medicine* **1**(2): 1–8
- Natarajan S, Williamson D, Grey J, Harding KG, Cooper RA (2001) Healing of an MRSA-colonised, hydroxyurea-induced leg ulcer with honey. *Journal of Dermatological Treatment* **12**: 33–6
- Phuapradit W, Saropala N (1992) Topical Application of Honey in Treatment of Abdominal Wound Disruption. *Australia and New Zealand Journal of Obstetrics and Gynaecology* **32**(4): 381–5
- Schwarzenraub PH, Raymond GA (1991) Foot ulcers: a 54-month retrospective study. *Journal of Foot Surgery* **30**(5): 437–42
- Subrahmanyam M (1999) Early tangential excision and skin grafting of moderate burn is superior to honey dressing: a prospective randomised trial. *Burns* **25**: 729–31
- Subrahmanyam M (1998) A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. *Burns* **24**(2): 157–61
- Subrahmanyam M (1993) Honey impregnated gauze versus polyurethane film (Opsite) in the treatment of burns; a prospective randomised study. *Br J Plastic Surgery* **46**(4): 322–3
- Thomson CE, Paterson-Brown S, Russell IT (2002) A Clinical and Economical Evaluation of Toenail Surgery performed by Podiatrists in the Community and Surgeons in the Hospital Setting: A Randomised Controlled Trial. www.show.NHS.uk/cso/ (online) (accessed 11/03/03)
- Vardi A, Barzilay Z, Linder N, Cohen HA, Paret G, Barzilay A (1998) Local application of honey for treatment of neonatal post-operative wound infection. *Acta Paediatr* **87**(4): 429–32