A honey-based dressing for diabetic foot ulcers: A controlled study

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This study's objective was to establish the efficacy of a honey-based dressing in the treatment of diabetic foot ulcers. A well-known moisture-retention dressing was used as the control dressing, and factors influencing wound healing were controlled. There was no significant difference in healing rates of diabetic foot ulcers between honey and the conventional dressing, and the honey had no significant effect on glycaemic control. It was concluded that honey is at least as effective as conventional dressings in healing diabetic foot ulcers.

Amputations are common following diabetic foot ulceration. A main aim of the diabetic foot care clinic in the University of Malaya Medical Centre in Kuala Lumpur, Malaysia, is to prevent and treat diabetic foot ulcers so that amputation rates are reduced. Conventional dressings are used in most cases, but honey-based ones have also been used and are claimed to be better than a conventional dressing by many of its proponents.

A systematic review by Moore et al (2001) found seven randomised trials on the use of honey in the treatment of burns or wounds. Six of the studies were conducted by the same researcher (Subrahmanyam 1991, 1993, 1994, 1996, 1998, 1999). Although the studies in the review were of limited quality, six of the seven showed honey to be superior for wound healing. A more recent review (Molan, 2006) quoted positive findings in 17 randomized controlled trials on the use of honey in various wounds. Reports of honey being used to treat a variety of wounds ranging from various wounds in infants to post-vulvectomy wounds also give credence to the therapeutic use of honey (Cavanagh et al, 1970; Efem, 1993; Vardi et al, 1998).

The wound healing properties of honey have been attributed to various factors, including antibacterial action and endogenous antiseptic properties (Zumla and Lulat, 1989; Harris, 1994; Lione, 1998; Subrahmanyam, 1998; Cooper and Molan, 1999).

However, to date, no formal randomised controlled trial on the use of honey in diabetic foot ulcers have been published.

Aim of the study

This study's objective was to ascertain whether honey was a viable dressing for diabetic foot

Article points

1. Honey has been used for wound healing since ancient times.
2. Over the past three decades, there have been reports of the effective use of honey as a dressing for diabetic foot ulcers.
3. This controlled study found honey-based dressing to be as effective as a conventional moisture-retention dressing in the treatment of diabetic foot ulcers.
4. The use of honey-based dressings in people with diabetic foot ulcers had no significant effect on their glycaemic control in this study.

Key words

- Honey
- Diabetic foot ulcer
- Dressing

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Page points

1. Capilano™, a common commercial brand of honey from Australia, was used for the study; the control dressing was Granuflex™.
2. Ulcer breadth, length and depth were measured weekly using a calibrated rule.
3. The end point was a 50% reduction in any two of these dimensions.
4. When the end point was reached, the healing rate of each dimension was calculated by dividing the dimension by the number of weeks taken to achieve the reduction. Healing rates of the two dimensions were then averaged to give an average healing rate.

ulcers. The effect of the use of honey on glycaemic control in people with diabetes was also investigated.

Materials and method

Selection of participants

This study was carried out on people with diabetic foot ulcers who attended the Wound Management Centre of the University of Malaya Medical Centre (UMMC), which is a teaching hospital. The majority of these people were referred from the hospital's diabetic clinic and primary care clinic. The approval of the hospital's medical ethics committee was obtained before the study was carried out. Funding was obtained from a short-term research grant provided by the University of Malaya.

People with diabetic ulcers who met the following criteria were included in the study:

- age 40 years or more, with previously known diabetes mellitus.
- a diabetic foot ulcer of Wagner classification grade I or II, below the ankle measuring 1 cm or more in any of three dimensions: length, breadth and depth. Measurements were made using a calibrated rule.

People with biomechanical factors that were difficult to correct, an ankle–brachial pressure index (ABPI) of <0.45 or Wagner grade III–IV wounds were excluded from the study.

Hospitalisation and ulcer deterioration as evidenced by hypergranulation, increasing size of wound or infection were considered adverse events necessitating discontinuation of the treatment protocol. Adherence with the use of the dressing was assessed by giving participants a fixed quantity of dressing material and assessing the amount left at follow-up. Participants who did not turn up to follow-up appointments more than twice were considered non-adherent.

Dressings were assigned according to the sequence of case enrolment. Odd-numbered patients were allocated the honey dressing and even-numbered patients the control dressing.

Capilano™, a common commercial brand of honey from Australia, purchased from a local supermarket, was used for the study. This brand was used for all those in the honey group at all times. A well-known brand of moisture-retention dressing from Convatec, namely Granuflex™ (marketed in Malaysia as Duoderm™), was used as the control dressing.

Baseline assessment

Before the study, all participants had a history taken and were given a physical examination. History consisted of demographic details, diabetes complications, duration of ulcers and lifestyle habits such as smoking. A neurological and vascular assessment of the foot was carried out during physical examination. Neurological examination consisted of a sensory examination using a 10 g monofilament for pressure and a 128 Hz tuning fork for vibration sense. Vascular status was assessed by palpation of the anterior tibialis, dorsalis pedis and posterior tibial pulses, and was reconfirmed by Doppler where the pulse was difficult to palpate. ABPI was also measured.

Dressing protocols

The ulcers were cleaned and debrided before the dressings were applied. Surrounding callosities were also debrided. The ulcer was then dressed or packed with pieces of honey-impregnated gauze and kept in place with a piece of occlusive dressing placed over the gauze. The moisture-retention dressings were applied according to the manufacturer's instructions.

All participants had their footwear adjusted using paddings and strappings to reduce pressure around the ulcers.

Participants were taught to do ulcer dressings at home. They were advised to change the dressing every other day, or sooner if exudate had seeped through the dressing (for the honey-based dressing).

Wound assessment

The ulcers were assessed weekly. The parameters measured were breadth, length and depth. The end point was a 50% reduction in any two of these three parameters.

When the end point was reached, each of the two chosen dimensions was divided by the number of weeks it took to achieve the 50% reduction, to obtain the healing rate of each dimension. The healing rates of the two

dimensions were then averaged to give an average healing rate. This method was devised as it was felt that the end point of wound healing is difficult to determine and is usually subjective. Rate of healing calculated in this way was considered to be a more objective method than using an end point such as a healed wound and finding how long it would take the wound to heal completely.

Post-study assessment

Participants were asked a few questions at the end of their treatment regarding the dressing used. The questions were designed to establish whether participants experienced:

- absence or presence of pain
- absence or presence of odour
- difficulty or ease in applying the dressing.

Biochemical analysis

Blood samples were taken at the start of the study, before the dressing was applied, and analysed for albumin concentration to assess nutritional status of participants. Fructosamine and random blood glucose levels were also measured before starting the dressing and every 4 weeks thereafter.

Analysis of results

Results were analysed using the Fisher's Exact test and Mann–Whitney U test as the samples were non-parametric. The chi-squared test was used when possible. The statistical software used for analysis was SPSS Version 8.0.

Results

Seventeen people took part in this study: nine were treated with the control dressing and eight with the honey-based dressing. One person was withdrawn from the honey group because of hypergranulation of the wound, which led to delayed wound contraction and required withholding the use of honey. This person was eventually referred to the plastic surgeon for skin grafting.

The remaining 16 people in the study had a total of 23 ulcers, of which 12 were dressed with the honey-based dressing and 11 were dressed with moisture-retention dressing.

Table 1. Demographics and other characteristics of people with diabetic foot ulcers enrolled in the study.

	No. of participants (n = 16)		
Demographic	**Honey group**	**Control group**	**Total**
Gender:			
Female	3	4	7
Male	4	5	9
Age (years):			
40–59	3	6	9
60–79	4	3	7
Duration of diabetes (years):			
<9	3	5	8
≥9	4	4	8
Previous surgery	2	7	9
Footwear:			
Indoor and outdoor	3	6	9
Outdoor only	4	3	7
Daily foot check	1	6	7

There were no significant differences in demographic data between the groups (Fisher's Exact test, $P>0.05$).

Other factors that could potentially affect the rate of wound healing were considered, namely duration of diabetes, vascular and neurological findings and footwear. In Malaysia, it is customary for most people to go barefoot at home because of the humid weather, and so the majority of people in this study did not wear any form of footwear at home. Some of these characteristics are summarised in *Table 1*. There were no significant differences between the groups in these characteristics using the Fisher's Exact test ($P>0.05$).

There was also no significant difference between the two groups in terms of the medical complications considered, namely ischaemic heart disease, hypertension and stroke (chi-squared test, $P>0.05$).

Physical findings are summarised in *Table 2*. There was no significant difference between the two groups of patients (Fisher Exact Test, $P>0.05$). There was also no significant difference in ABPI between the groups (Mann–Whitney U test, $P>0.05$).

Page points

1. The two groups were evenly matched in terms of demographics, physical findings, nutritional level, and blood glucose control.
2. There was no statistically significant difference in healing rates between the honey group and the control group.
3. The only patient withdrawn from the study was one from the honey group who developed wound hypergranulation; this is an adverse effect, causing a delay in wound healing.
4. There were no reports of pain with either dressing, but this was to be expected in people with sensory neuropathy.

The two groups were similar in terms of albumin concentration (honey group: 19–42 g/litre; control group: 18–39 g/litre), which was chosen as a nutritional marker to control for nutritional effect on wound healing; fructosamine (honey group: 281–496 µmol/litre; 267–663 µmol/litre); and random blood glucose levels (honey group: 6.3–29.6 mmol/litre 5.9–20.1 mmol/litre) (Mann-Whitney U test, $P>0.05$). Fructosamine was chosen over HbA_{1c} as it gives a better indication of blood glucose control (over 2 weeks) in a short-term study such as this.

In addition, pre- and post-treatment fructosamine levels in the honey group were compared to see whether the honey used in the dressings affected blood glucose control in this group. No significant difference in levels was found (mean fructosamine level = 381.3 mmol/litre at the start of the study and 409.0 mmol/litre at the end of the study; Mann–Whitney U test, $P>0.05$).

Overall, therefore, the two groups were evenly matched in terms of demographics, physical findings, nutritional level and blood glucose control.

Average ulcer healing rates ranged from 0.11 cm to 1.0 cm per week (mean 0.35 cm per week, median 0.25 cm per week) for the control group, and from 0.13 cm to 0.45 cm per week (mean 0.24 cm per week, median 0.25 cm per week) for the honey group. However, these differences were not statistically significant (Mann–Whitney U test, $P>0.05$).

Participants did not report any pain with either type of dressing. However, this was to be expected as this population has sensory neuropathy. No complaints were made regarding odour, although one person on hydrocolloid dressing complained persistently that he could not stand the smell. None of the participants or caregivers complained about the need to change dressings themselves.

Table 2. Salient physical findings of people enrolled in the study (n = 16).

Physical finding	No. of participants (n = 16)		
	Honey group	Control group	Total
Palpable arteries:			
Anterior tibial*	6	7	13
Dorsalis pedis*	6	7	13
Posterior tibial*	7	8	15
Delayed capillary refill time	1	1	2
Absent vibratory sense	3	5	8
Reduced pressure sensation	7	9	16

* All the pulses that were not palpable were detected using the Doppler

Discussion

This study was designed to control for the influence of confounding factors on wound healing, as far as possible, so that a honey-based and moisture-retention dressing could be compared on their own merit. This was achieved by means of the eligibility criteria, for example by restricting the age of participants to 40 years or above, excluding those with ABPI<0.45, choosing wounds at more or less the same location (below the ankle) and using paddings and strapping to ensure that foot pressure differences were offset.

At the end of the study, blood investigations and physical examination were also done to see whether these two groups were similar with regard to factors that could not be controlled for, but were felt to exert an influence on wound healing, such as medical complications, nutritional level and blood glucose level. Albumin level was used to assess nutritional level, and fructosamine and random blood glucose levels were used to assess glycaemic control. All of these measures have proved succcessful in controlling for possible confounding factors that could have affected the eventual wound-healing rates.

This study failed to prove that honey was superior to conventional dressing in healing diabetic foot ulcers, despite earlier findings with other wounds. Previous studies, however, did not control for confounding factors very well, which admittedly is not an easy task with studies on wound healing.

This study showed that honey-based are a possible alternative to a modern dressing: even though it did not demonstrate superior healing, it proved equally effective in healing diabetic

foot ulcers when compared with a conventional dressing. In addition, honey is cheaper and more readily available, especially in third-world countries. It is disturbing that the only patient withdrawn from the study was one from the honey group who developed wound hypergranulation. This is considered to be an adverse event as it delays wound contraction despite good granulation tissue formation. Our experience with conventional dressings is similar, in that we do see cases with hypergranulation. However, hypergranulation is easily treatable. Further research on hypergranulation due to honey and other moisture-retention dressings is needed.

Limitations of the study

This study was limited in two respects. First, the sample size was small. This was felt to result from the very strict inclusion and exclusion criteria employed in an attempt to control for confounding factors. The ideal sample size could not be calculated, as similar studies had not been done previously. Thus type I statistical error could not be ruled out.

Second, it was difficult to devise a suitable protocol for the honey dressing, as there was no standard protocol available.

Conclusion

Honey was shown to be as effective for the treatment of diabetic foot ulcers as a conventional moisture-retention dressing, and may therefore be used as an alternative to moisture-retention dressing, especially in areas where modern conventional dressings are not readily available.

Furthermore, honey did not affect the glycaemic control of participants in the study and was very well tolerated. However, more research needs to be done, especially in establishing a standardised protocol of application and in cost analysis of honey dressing compared with conventional wound dressings. ■

Acknowledgements

This study was carried out with the help of a short-term research grant (Vote F) from the University of Malaya, and the assistance of nurses from the diabetic foot care clinic.

Cavangah D, Beazley J, Ostapowicz F (1970) Radical operation for carcinoma of the vulva. A new approach to wound healing. *Journal of Obstetrics and Gynaecology of the British Commonwealth* **77**: 1037–40

Cooper RA, Molan PC (1999) The use of honey as an antiseptic in managing Pseudomonas infection. *Journal of Wound Care* **8:** 161–4

Efem SE (1993) Recent advances in the treatment of Fournier's Gangrene: Preliminary observations. *Surgery* **113:** 200–204

Harris S (1994) Honey for the treatment of superficial wounds: A case report and preview. *Primary Intention* **2:** 18–23

Lione A (1998) Folk remedies (letter). *Journal of the American Medical Association* **279:** 149

Molan PC (2006) The Evidence Supporting the Use of Honey as a Wound Dressing. *International Journal of Lower Extremity Wounds* **5:** 40–54

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 & Alternative Medicine* **1:** 2

Subrahmanyam M (1991) Topical application of honey in treatment of burns. *British Journal of Surgery* **78:** 497–8

Subrahmanyam M (1993) Honey impregnated gauze versus polyurethane film (OpSite) in the treatment of burns – a prospective randomised study. *British Journal of Plastic Surgery* **46:** 322–3.

Subrahmanyam M (1994) Honey-impregnated gauze versus amniotic membrane in the treatment of burns. *Burns* **20**: 331–3.

Subrahmanyam M (1996) Honey dressing versus boiled potato peel in the treatment of burns: a prospective randomized study. *Burns* **22**: 491–3.

Subrahmanyam M (1998) A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. *Burns* **24**: 157–61.

Subrahmanyam M (1999) Early tangential excision and skin grafting of moderate burns is superior to honey dressing: a prospective randomised trial. *Burns* **25:** 729–31.

Vardi A, Barzilay Z, Linder N, Cohen HA. Paret G, Barzilai A (1998) Local application of honey for the treatment of neonatal postoperative wound infection. *Acta Paediatrica* **87**: 429–32

Zumla A, Lulat A (1989) Honey – a remedy rediscovered. *Journal of the Royal Society of Medicine* **82:** 384–5

CAUTION

It is important to use medical grade honey for wound dressings. Over-the-counter honey is not licensed for use on wounds in the UK.

Page points

1. Difficulties were experienced with the honey dressing protocol, as there was no standard protocol available.
2. The sample size was small, owing to the very strict inclusion and exclusion criteria employed to control for confounding factors.
3. The ideal sample size could not be calculated, as similar studies had not been done previously; consequently a type I statistical error could not be ruled out.