The Efficacy and Safety of Natural Honey on the Healing of Foot Ulcers: A Case Series

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Abstract: This clinical observation investigated the efficacy, cost-effectiveness, and acceptability of natural honey on the healing of a variety of chronic foot ulcers at the primary care level. Materials and Methods. A total of 12 patients with foot ulcers utilizing natural honey as an effective alternative to more expensive, advanced wound products were followed. Cases were referred to Umghailinah Primary Health Care Center, Doha, Qatar from different health centers and from Hamad General Hospital, Doha, Qatar. There were also self-referred cases. After rinsing the site with normal saline, natural honey was applied and the wound was covered by glycerin-impregnated gauze (Adaptic Non-Adhering Dressing, Systagenix, San Antonio, TX) to prevent the absorption of honey into the cotton gauze and away from the wound site. Patients were followed on a daily basis for an average of 4 weeks. Results. All ulcers healed with no contractures or scars with a mean healing time of 3 weeks. There was a 75% reduction in the dressing budget of the health center and a high level of satisfaction among both health professionals and patients. Patients’ pain levels were reduced significantly after using natural honey, as evidenced by the use of the Visual Analog Scale. Conclusion. The use of natural honey in the management of chronic foot ulcers proved to be efficacious, cost-effective, and acceptable by both clinicians and patients.

Key words: natural honey, efficacy, safety, foot ulcers

Natural honey dressings have been used to treat wounds throughout the ages.¹ This case series describes the use of natural honey in patients with a variety of chronic foot ulcers. A wound assessment was carried out daily and used to decide upon the continuation of treatment with natural honey. Numerous preparations of honey have been...
previously studied and categorized according to the floral origin. And while leptospermum honeys are the most widely studied, a local regional honey was used to treat the patients in this case series. Natural honey is a viscous, supersaturated sugar solution derived from nectar gathered and modified by the honeybee. It has high osmolarity and acidity, flavonoids, beeswax, hydrogen peroxide, and inhibit. Natural honey has been shown to possess antibacterial potency well in excess of that needed to stop the growth of clinically important organisms such as methicillin-resistant 
Staphylococcus aureus and vancomycin-resistant Eschericia coli.\textsuperscript{5}

Natural Honey in Wound Care

Mechanism of effectiveness. Due to its therapeutic characteristics, natural honey has been used in wound care as a topical treatment for infected wounds for stimulating tissue regeneration, debriding necrotic tissues, reducing edema, and promoting rapid wound healing.\textsuperscript{6,7} Furthermore, natural honey leads to suppression of inflammation, minimization of scarring, and stimulation of angiogenesis.\textsuperscript{6} The acidic pH of honey (3.2 to 4.2) inhibits growth of most pathogenic bacteria within wounds,\textsuperscript{8} and increases production of hydrogen peroxide from the enzyme glucose oxidase at 1:1000 concentration. This is less than the conventional rinse solutions but just enough to inhibit bacterial growth without compromising the new granulation tissue.\textsuperscript{9} Natural honey also provides bacteria with glucose and fructose as an alternative to the amino acids from dead cells and serum, thereby deodorizing infected wounds.\textsuperscript{10} Compounds such as ammonia, amines, and sulphur, which are the cause of malodor in wounds, are replaced by lactic acids.\textsuperscript{11,12} According to histological studies,\textsuperscript{13-15} natural honey is thought to possess anti-
inflammatory properties. The definitive mechanism is yet to be identified although preliminary data suggests natural honey may activate monocytes within the wound. Additionally, natural honey provides moisture to wounds, thereby aiding fibroblast migration and epithelialization, reducing scarring and hypertrophy, and working as a physical barrier to external pathogens, especially when the wax content in the honey is high. Furthermore, honey reduces pain and promotes granulation tissue formation. Clinical and laboratory data indicate natural honey is effective against a variety of common pathogens such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Psuedomonas aeroginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter*, *Stenotrophomonas*, methicillin-resistant *S. aureus*, and vancomycin-resistant *E. coli*. Natural honey with high wax content forms a semisolid medium offering a better wound contact thereby preventing the development of biofilms without compromising the newly forming fibroblasts. It should also be noted that recent in vitro studies have demonstrated limited cytotoxicity to human keratinocytes and dermal fibroblasts when compared to conventional silver dressings.

**Evidence for natural honey.** Natural honey has been assessed in many laboratory and clinical studies and demonstrated an effective bacterial barrier against external pathogens. Also of note is that it causes minimal pain during application and removal, and maintains the wound at optimum temperature and pH. Natural honey has a low adherence to the wound bed upon removal thereby preserving the newly forming granulation tissue. In addition to hampering the development of biofilms, natural honey has a limited keratinocyte and fibroblast cytotoxicity compared to conventional silver dressings. It limits the amount of edema and reduces scarring and contractures in patients with burn wounds. Natural honey lowers the alkaline pH of wounds, thereby enhancing healing outcomes, and deodorizes infected wounds as the amino acids from dead cells and serum that cause malodor.

**Figure 3.** (A-D) Case 3. Diabetic neuropathic ulcer with 8 weeks time to healing.

**Figure 4.** (A-C) Case 4. Diabetic neuropathic ulcer with 4 weeks time to healing.
Table 1. Patient and wound characteristics.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age</th>
<th>Wound etiology and comorbidities</th>
<th>Smoking status</th>
<th>Wound measurement at presentation (L x W x D, cm)</th>
<th>Previous treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>Spontaneous, diabetes, hypertension</td>
<td>Non smoker</td>
<td>3.0 x 3.0 x 0.7</td>
<td>Cadexomer iodine paste</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>Spontaneous, chronic venous insufficiency</td>
<td>Smoker</td>
<td>3.0 x 2.0 x 0.2</td>
<td>Povidone iodine</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>Trauma, diabetes peripheral vascular disease, hypertension</td>
<td>Smoker</td>
<td>2.5 x 2.0 x 0.5</td>
<td>Hyrogel and nonadherent silver dressing (Nu Gel Hydrogel and Silvercel Non-Adherent Dressing, Systagenix, Gatwick, UK)</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>Spontaneous, coronary artery disease, hypertension, renal impairment</td>
<td>Smoker</td>
<td>3.0 x 2.5 x 0.3</td>
<td>Hyrogel and nonadherent silver dressing</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>Traumatic, diabetes, peripheral vascular diabetes, hypertension, obesity, hypercholesterolemia</td>
<td>Non smoker</td>
<td>2.5 x 2.5 x 0.3</td>
<td>Silver sulfadiazine (Flamazine, Smith &amp; Nephew, St. Petersburg, FL)</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
<td>Trauma, diabetes peripheral vascular disease, hypertension</td>
<td>Non smoker</td>
<td>4.0 x 1.5 x 1.0</td>
<td>Nonadherent silver dressing</td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>Trauma, diabetes, hypertension</td>
<td>Non smoker</td>
<td>3.0 x 1.0 x 0.1</td>
<td>Silver-impregnated dressing (Acticoat Flex 7, Smith &amp; Nephew, St. Petersburg, FL)</td>
</tr>
<tr>
<td>8</td>
<td>55</td>
<td>Trauma, diabetes peripheral vascular disease, hypertension</td>
<td>Non smoker</td>
<td>3.0 x 2.0 x 0.2</td>
<td>Povidone iodine</td>
</tr>
<tr>
<td>9</td>
<td>47</td>
<td>Thermal burn, contact dermatitis diabetes, hypertension</td>
<td>Non smoker</td>
<td>10.0 x 4.0 x 0.1</td>
<td>Dry cotton gauze</td>
</tr>
<tr>
<td>10</td>
<td>37</td>
<td>Burn, diabetes</td>
<td>Non smoker</td>
<td>5.0 x 4.0 x 0.2</td>
<td>Dry cotton gauze</td>
</tr>
<tr>
<td>11</td>
<td>64</td>
<td>Spontaneous, diabetes, Charcot foot</td>
<td>Non smoker</td>
<td>1.5 x 1.5 x 1.5</td>
<td>Silver sulfadizine (Allevyn Advanced Foam Wound Dressing, Smith &amp; Nephew, St. Petersburg, FL), nonadherent silver dressing</td>
</tr>
<tr>
<td>12</td>
<td>76</td>
<td>Trauma, diabetes</td>
<td>Non smoker</td>
<td>4.0 x 1.3 x 0.2</td>
<td>Antibacterial spray</td>
</tr>
</tbody>
</table>

*Pain was assessed using the Visual Analogue Scale in which 1 = minimal pain and 10 = maximum pain.
<table>
<thead>
<tr>
<th>Duration of previous wound</th>
<th>Glycemic control</th>
<th>Infection status elevated protease activity (EPA)</th>
<th>Duration of honey treatment</th>
<th>Average epithelialization rate</th>
<th>Pain* before vs during treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>HbA1C = 7.8% Suboptimal control</td>
<td>Not infected</td>
<td>3 weeks</td>
<td>1.2 mm per day</td>
<td>1/10 vs 1/10</td>
</tr>
<tr>
<td>2 months</td>
<td>HbA1C = 4% Normal</td>
<td>Infected</td>
<td>6 weeks</td>
<td>0.6 mm per day</td>
<td>7/10 vs 1/10</td>
</tr>
<tr>
<td>3 months</td>
<td>HbA1C = 7.9% Suboptimal control</td>
<td>Low EPA</td>
<td>8 weeks</td>
<td>0.4 mm per day</td>
<td>1/10 vs 1/10</td>
</tr>
<tr>
<td>One month</td>
<td>HbA1C = 7.4% Suboptimal control</td>
<td>Infected</td>
<td>4 weeks</td>
<td>1.1 mm per day</td>
<td>8/10 vs 1/10</td>
</tr>
<tr>
<td>2 months</td>
<td>HbA1C = 7.5% Suboptimal control</td>
<td>Not infected</td>
<td>3 weeks</td>
<td>1.2 mm per day</td>
<td>1/10 vs 1/10</td>
</tr>
<tr>
<td>4 months</td>
<td>HbA1C = 7% Good control</td>
<td>Low EPA</td>
<td>5 weeks</td>
<td>0.8 mm per day</td>
<td>1/10 vs 1/10</td>
</tr>
<tr>
<td>3 months</td>
<td>HbA1C = 6.9% Good control</td>
<td>Low EPA</td>
<td>3 weeks</td>
<td>1.1 mm per day</td>
<td>7/10 vs 1/10</td>
</tr>
<tr>
<td>2 months</td>
<td>HbA1C = 8% Suboptimal control</td>
<td>Low EPA</td>
<td>2 weeks</td>
<td>1.4 mm per day</td>
<td>2/10 vs 1/10</td>
</tr>
<tr>
<td>1 week</td>
<td>HbA1C = 8.5% Suboptimal control</td>
<td>Infected</td>
<td>3 weeks</td>
<td>0.7 mm per day</td>
<td>5/10 vs 1/10</td>
</tr>
<tr>
<td>1 week</td>
<td>HbA1C = 8% Suboptimal control</td>
<td>Not infected</td>
<td>1 week</td>
<td>1.9 mm per day</td>
<td>8/10 vs 2/10</td>
</tr>
<tr>
<td>6 months</td>
<td>HbA1C = 8% Suboptimal control</td>
<td>Not infected</td>
<td>3 weeks</td>
<td>0.55 mm per day</td>
<td>1/10 vs 1/10</td>
</tr>
<tr>
<td>1 week</td>
<td>HbA1C = 7% Good control</td>
<td>Not infected</td>
<td>3 weeks</td>
<td>0.66 mm per day</td>
<td>4/10 vs 1/10</td>
</tr>
</tbody>
</table>

*Pain was assessed using the Visual Analogue Scale in which 1 = minimal pain and 10 = maximum pain.
such as sulphur compounds, ammonia, and amines, are replaced by lactic acids.\textsuperscript{29,30} Furthermore, natural honey debrides slough, stimulates angiogenesis,\textsuperscript{31-34} and stimulates immunomodulation by up-regulating tumor necrosis factor alpha, interleukin (IL)-1 beta, IL-6, and prostaglandin E2 from monocytes.\textsuperscript{35} Finally, natural honey is bactericidal and antifungal against approximately 70 bacterial strains, both gram-positive and gram-negative, and some yeasts.\textsuperscript{36,37}

The performance of natural honey was evaluated previously\textsuperscript{38-40} in a case series that included patients with complex comorbid conditions, locally infected wounds which failed hospital management including diabetic foot ulcers, postexcisional malignant melanoma ulceration,\textsuperscript{10} contact dermatitis, burns, and Charcot foot ulceration. There was excellent tolerability, and no trauma caused to the wound bed.

**Materials and Methods**

**Patients.** All patients were seen in a primary care health center (Umgwailinah Primary Health Care Center, Doha, Qatar) and had been receiving various therapies for their chronic and acute wounds. Wound etiologies, timelines, and wound products applied prior to the use of natural honey are summarized in Table 1. All patients were treated with topical natural honey purchased from the local market. The honey was a homogeneous, thick, white honey mixed with royal jelly and produced by Russian bees (ie, *Apis mellifera*) native to the Primorsky Krai region of Russia. Prior to use with patients, the honey was sent to the microbiology laboratory of the Ministry of Health in Qatar. After rigorous testing, it was found to be sterile and free from *Clostridium difficile* spores. The wounds were cleaned with normal saline and surgically debrided using a sharp scalpel if they had necrotic tissues or callosities until a clean wound bed was achieved (ie, no necrotic tissue was present). At that point, treatment with natural honey was commenced by applying it directly on the wound bed and covering it with a nonadherent dressing made of knitted cellulose acetate fabric (Adaptic Non-Adhering Dressing, Systagenix, San Antonio, TX) and impregnated with specially formulated petroleum emulsion. When natural honey is applied to the wound bed it becomes less viscous and is diluted through exudation. As a result, wounds were covered with a cotton wool bandage and a light crepe bandage to contain the natural honey in the wound bed environment. The natural...
honey dressing was changed on a daily basis and offloading was provided using a multilayered incontinence pad which was applied around the periwound area. This option was chosen since total contact or removable casts are not available at the primary care level, but only if the patient is admitted to the hospital. At each daily review the wounds were debrided if necessary and assessed for signs of infection and pain level. No systemic or local antibiotics were administered except in case 4 which had signs of infection on presentation, and case 9 in which the patient had sustained a thermal burn and was started on oral ciprofloxacin to cover for *P. aeruginosa*.

The study consisted of 12
patients with a variety of acute and chronic wounds secondary to type II diabetes, peripheral vascular disease, chronic venous insufficiency, type I diabetes, and burns, although secondary diagnosis included trauma, contact dermatitis, and Charcot foot. Age, gender, wound etiology, related comorbidities, pain score, and wound size are listed in Table 1. Patients were managed according to the etiology of the wound. Treatment included cleaning with normal saline and sharp debridement of necrotic tissue, application of natural honey covered by 3 layers of a paraffin-based dressing to prevent absorption of honey onto the secondary cotton gauze, and offloading. All patients showed complete healing with a mean healing time of 3 weeks.

Results

From 2011 to 2014, 12 patients with various chronic and acute wounds (Figures 1-12) presented to Umgwailinah Primary Health Care Center, Doha, Qatar. They were subsequently managed on an outpatient basis and treated daily with natural honey as previously described. Table 1 shows ages, wound etiology, clinical history, smoking status, clinical history, size of wound, previous wound products used, duration of wound prior to treatment, glycemic control, infection status, duration of natural honey application until wound closure, average epithelialization rates calculated from daily wound dimension measurements, and patients’ reported local pain prior to and during treatment with natural honey. Pain was assessed using the Visual Analog Scale (VAS), a unidimensional measure of pain intensity which has been widely used in diverse adult populations, including those with chronic painful conditions. The VAS is a continuous scale comprised of a horizontal and a vertical line, usually 10 cm in length, anchored by 2 verbal descriptors, one for each extreme. For pain intensity, the scale is most commonly anchored by “no pain” (score of 1) and “worst imaginable pain” (score of 10).

Clinically, patients 1, 2, 4, 5, 6, 7, 8, 10, 11, and 12 had a marked response to the treatment regimen, while patient 3’s wound failed to respond in such a swift manner, and required about 8 weeks of treatment to achieve complete closure (Table 1). However, it should be noted that patient 3 was a chronic heavy smoker of 40 cigarettes per day, with chronic diabetic complications including diabetic retinopathy. He also had been living with hypercholesterolemia and peripheral vascular disease. Patient 9 had sustained a second degree burn complicated by cellulitis and the wound was heavily infected with a high level of protease activity as measured by a point of care test (Woundchek Protease Status test, Woundchek Laboratories, North Yorkshire, UK). The attending consultant family physician with a special interest in diabetic foot management started the patient on oral ciprofloxacin, debrided the wound, took a deep swab, intensified his insulin regimen, and ordered a twice-daily dressing change due to high exudate. These factors produced swift results and the wound was closed in 3 weeks time. Average wound duration prior to the natural honey treatment
for all 12 patients was 120.2 days (range 14-180 days). Average natural honey treatment duration was 23.8 days including patients 3 and 9. Average wound epithelialization rate was 0.6 mm per day.

When comparing local pain symptoms with the natural honey treatment regimen compared to previously used wound products, 6 patients (patients 2, 4, 5, 6, 7, and 11) had no local pain symptoms on the VAS before or during the natural honey treatment, since they had diabetic peripheral neuropathy and were unable to feel pain, and patient 11 had Charcot foot. Patient 2 was experiencing a high level of pain measured as a 7 on the VAS. That score fell to 2 after 1 week of treatment with honey, and to 1 after 6 weeks of treatment with honey. Similarly, patient 4 presented with high intensity pain and a score of 8 on the VAS, which dropped to 3 after 1 week of treatment with honey, and to 1 after 2 weeks of treatment with honey. Patient 9 had a VAS score of 5 on presentation which dropped to 1 after 2 weeks of treatment with honey. Finally, patient 12 presented with a VAS score of 8 and dropped to 2 after 1 week of natural honey. This finding is quite encouraging as the pain in wounds results from the nerve endings being sensitized by prostaglandins produced in the process of inflammation, as well from the pressure on tissues resulting from edema. Due to its high sugar content, honey also prevents pain during dressing changes as it keeps the wound surface moist by mobilizing the edema from the surrounding tissues.

Wound infection status was assessed using a point of care protease status test since, although chronic wounds with elevated protease activity (EPA) have a 90% probability of not healing without appropriate intervention, and 28% of nonhealing wounds have EPA, there are no visual cues to detect EPA. Patients 1, 5, and 12 had no elevated EPA throughout their treatment regimen while patients 2, 3, 6, 8, and 11 had minimal EPA prior to treatment with natural honey which subsided to no activity 2 weeks after beginning treatment with honey. Patient 4 experienced EPA due to the presence of osteomyelitis. The EPA dropped 2 weeks post-initiation of systemic ciprofloxacin at presentation and then increased again for another week due to the presence of osteomyelitis as evidenced by a positive probe-to-bone test. Clinicians seeing patients in a similar setting (ie, a specialized diabetic foot unit with a high prevalence of osteomyelitis in the patient population) can confidently diagnose diabetic foot osteomyelitis when either the probe-to-bone test or a plain x-ray, or especially both, are positive. However, after proper antibacterial coverage coupled with a natural honey dressing, the EPA became minimal at week 3. Similarly, patient 7 had an elevated EPA, the wound was malodorous, and necrotic tissue was present in the wound bed. Amoxicillin clavulanate coupled with natural honey dressing resulted in the EPA to be brought to a minimum on week 2. Patient 9, who had a second degree burn complicated by cellulitis, had high EPA activity and was prescribed oral ciprofloxacin to cover for P. aeruginosa; this regimen resulted in the reduction of the EPA activity to a minimum amount 2 weeks later.

Discussion

This case series raised many points of interest with regard to the use of natural honey in wound management. It was interesting to note there was no report of adverse effects with the use of honey from either patients or health professionals. Even stinging sensation, which had been reported elsewhere among patients with arterial insufficiency, was not reported in the authors’ patients with peripheral artery disease. This could be due to the varying pH of different types of honey, coexistent peripheral neuropathy, and different composition and floral source of the honey used. There are many reports of honey deodorizing malodorous wounds, especially among chronic diabetic
wounds. Health professionals and patients were encouraged to report no malodor, and it was evident that many cases, including patients 4, 6, 7, and 8, had reported improvement and disappearance of malodor in the first week similar to charcoal-based advanced wound products. Although the desired frequency of application of natural honey has not been established, the authors opted for daily application for the purpose of this study as it was convenient for the patients to visit the health center on a daily basis since they lived nearby.

The usage of honey in this clinical study amounted to about 1 kg in weight with a cost of approximately $100, compared to treating a diabetic foot ulcer in the United States, which costs an average of $48,000 per year. This is quite significant, especially in underdeveloped countries where diabetes is becoming an epidemic and a major health and financial burden. The pain score utilizing the VAS demonstrated a lower score with the application of natural honey, showing the anesthetic effect of natural honey. This finding is in agreement with earlier reports utilizing honey for the management of radiation-induced mucositis following head and neck radiotherapy.

Reference

Mohamed et al

Conclusion

Although silver-based dressings are currently extensively used to treat a variety of acute and chronic wounds, a recent study and 2 Cochrane reviews have concluded there is insufficient evidence to show that silver dressings improve healing rates. Furthermore, silver ions released by silver-containing dressings were found to be cytotoxic to keratinocytes and fibroblasts, and to impair epithelialization in animal wound models. While silver-based products are used extensively in the market, randomized controlled trials supporting its efficacy are lacking.

Natural honey is emerging as the ideal dressing in the market in comparison to advanced wound products due to the collective properties it contains including an osmotic gradient which inhibits microbial growth, an ability to release hydrogen peroxide at 1:1000 dilution thereby inhibiting microbial growth and stimulating angiogenesis without causing damage to health granulation tissue; increased lymphocytic and phagocytic activity; and an ability to release tumor necrosis factor-alpha; IL-1 beta, and IL-6. Finally, natural honey deodorizes wounds, provides moisture, and initiates tissue repair.

References


