Healing potential of propolis and bee’s honey on diabetic foot ulcers in Jabir Abu Eliz Diabetic Center- Khartoum

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Abstract Background: Propolis is a naturally occurring anti-inflammatory bee derived protectant resin. It had been tried on humans with reported promising results in wound healing. We aimed to study its effect on diabetics with foot ulcer.

Methods: A randomized case control clinical trial was conducted among diabetic patients presenting to JADC-Khartoum. The study included 86 diabetics with foot ulcers, 43 patients as case group and treated with propolis and honey mixture application to the ulcers and 43 patients as controls treated with tap water.

Results: The mean healing period in study group was significantly shorter (11.55 weeks) compared to the control group (15 weeks) (p=0.02). Minor toe amputation rate was significantly lower in the case subjects (p=0.039). Major amputation rate was lower in the study group, but this was not significant.

Conclusion: Propolis and bee’s honey dressing in diabetic foot ulcers lead to early healing and reduction of rate of minor toe amputation in diabetic foot ulcers.

Keywords: Propolis, bee’s honey, diabetic foot, Sudan

Introduction
Foot ulceration secondary to diabetes occurs in up to one quarter of people with diabetes(1) and it is the commonest cause of lower limb amputation(2). Diabetes increased the risk of lower extremity amputation by 10 to 20 times(3) and the estimated cost to the US healthcare system of diabetic foot ulceration and related amputations was more than $10.9 billion annually(4). Thus diabetic foot ulceration is a cause of significant morbidity and financial burden.
Propolis is a resinous bee-hive product consisting of plant materials that is initially collected on the hind legs of worker bees. The material is then masticated, salivary enzymes are added and mixed with wax to produce propolis\(^5\).

Propolis has multiple properties that makes it an attractive agent for treatment of diabetic foot ulcers, including being anti-inflammatory\(^6\), anti-oxidant and anti-microbial\(^8\). Its most biologically active fractions are flavanoids and esters of caffeic acid\(^7\).

Although the propolis is known dressing material since before Christ, its use in diabetic ulcers is limited.

**Patients and Methods**

A randomized clinical trial study was conducted among diabetic patients in Jabir Abu Eliz Diabetic Center Khartoum (JADC). The study included 86 patients with diabetic foot ulcers, 43 patients (study group) used propolis and honey as dressing material, and 43 patients (control group) used tap water. Patients evidence limb ischaemia manifested as absent pedal pulses or Doppler Ankle/Brachial Index <0.9 were excluded. Wagner classification was used for grading of the wounds. Dressing was conducted by trained nurses and senior general practitioner and was supervised by consultants. Wound swab was done for culture and sensitivity and antibiotics were given accordingly. Wound dressing was done on daily basis for one week, every other day for another week and then according to the wound status. All patients were covered by empirical systemic antibiotics for 3 days and then according to swab culture and sensitivity. Dressing continued until wounds healed or ended by amputation. In the case group the wounds were initially debrided and treated till there was no sepsis or cellulitis then a thick layer of propolis and honey paste was applied. Wounds were covered with sterile gauze and wrapped with non-elastic crepe bandage. In the control group after debridement dressing done using tap water and wounds covered by the same way. Both groups had similar off-loading with proper shoes used to promote wound healing. Manual technique was used to measure the wound size.

**Results**

Table 1 shows that both the study and control groups were matched for age, duration of diabetes, gender, wound size, ulcer depth and prior amputation rate. All patients in the two groups had Ankle /Brachial Index >0.9.

The mean healing period in study group was 11.55 weeks and in control group was 15 weeks (P= 0.02). Minor toe amputation was done in one patient of the case subjects and in six patients in the control group (P= 0.039). In the study group there was no major limb amputation and in control group there were three major amputations (P= 0.24).

**Table 1: Demographic and ulcer characteristics of the study and control groups**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Study group</th>
<th>Control group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>57.04 yr</td>
<td>53.86 yr</td>
<td>0.255</td>
</tr>
<tr>
<td>Mean duration of diabetes</td>
<td>13.11 yr</td>
<td>12.02yr</td>
<td>0.509</td>
</tr>
<tr>
<td>Mean size of the wound</td>
<td>27.18 cm</td>
<td>24.37 cm</td>
<td>0.680</td>
</tr>
<tr>
<td>Males</td>
<td>33</td>
<td>34</td>
<td>0.795</td>
</tr>
<tr>
<td>Females</td>
<td>10</td>
<td>9</td>
<td>0.795</td>
</tr>
<tr>
<td>Wagner 1</td>
<td>1</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Wagner 2</td>
<td>42</td>
<td>42</td>
<td>1.000</td>
</tr>
<tr>
<td>Commonest organism</td>
<td>15</td>
<td>17</td>
<td>0.655</td>
</tr>
<tr>
<td>(pseudomonas)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous amputation</td>
<td>5</td>
<td>4</td>
<td>1.000</td>
</tr>
</tbody>
</table>

**Discussion**

One of the most common complications of diabetes in the lower extremity is the diabetic foot ulcer. The number of patients suffering from this complication still remains high stimulating researches that focused on more effective treatment and dressing methods. The basic function of the wound care materials is providing protection against infection and to promote wound healing\(^8\). A myriad of dressings have been applied to wounds since ancient times. The list of naturally occurring materials and topical applications used were abundant but lacked controlled trials\(^9\). The
20th century had seen a revolution in wound management. Wound dressings can be divided into two broad groups: inert/passive and interactive/bioactive. Honey dressings promote moist wound healing, autolytic and osmotic debridement and have antimicrobial activity claimed to be from the slow release of low levels of Hydrogen peroxide, so honey is one of the bioactive dressing agents. However, it is difficult to draw overall conclusions regarding the effects of honey as a topical treatment for wounds due to the heterogeneous nature of the patient populations and comparators studied and the mostly low quality of the evidence(10). In the case group of full-thickness burn injuries and chronic wounds such as pressure ulcers, venous ulcers and diabetic foot ulcers, the influx of growth factors secreted by macrophages, and fibroblast proliferation and subsequent synthesis and remodeling of collagenous dermal matrix are damaged and new technologies should have to develop to improve the healing in these conditions(11). No one dressing agent is suitable for the management of all types of wounds, and few are ideally suited for the treatment of a single wound during all stages of the healing cycle. Successful wound management therefore depends upon a flexible approach to the selection and use of products based upon an understanding of the healing process combined with knowledge of the properties of the various dressings available(12).

Bee’s products (honey and propolis) to some extent are available in rural societies and hospitals which make it easy to use. Bee’s and its products reported in Holy Quran so Islamic societies believe that it’s a source for many treatments. Propolis represents a virgin material to be used as dressing material in diabetic foot ulcers. Topical propolis is a well-tolerated therapy for wound healing; however, very few studies were reported on its effect(13,14).

The biological activity of propolis and bee’s honey (newly formed vessels, fibroblasts and the presence of plasma cells) accelerate the healing process and is also supported by antibacterial and anti-inflammatory effects of propolis on the wounds. The application of propolis should be preceded by good surgical debridement, and it's only be used in clean wounds.

In a similar study from JADC Afaf(15) studied 30 patients with diabetic foot ulcer using propolis and another 30 patients as control using tap water dressing. The feasibility of her study was not powered to determine if propolis may be effective in foot ulcer healing and minor amputation because there was no comparison of the control subjects with propolis treated subjects. In 2010, a study from Egypt using bee’s honey alone in diabetic ulcers where 30 patients have been studied, all with chronic wounds (three months and more). The honey dressing was applied for three months until healing, grafting, or failure of treatment. The end result was 43% of wounds healed completely within three months, a decrease in wound size and healthy granulation were significantly observed in another 43.3% of patients(16). In our study, 65% of wounds healed completely within three months so it is better to use propolis with honey in diabetic ulcers than honey alone.

In a study from Nigeria, 50 patients with septic wounds were treated with lotion made from honey and powdered propolis mixed in a ratio of 7:3, applied to the wound 3 times a day. Eighty per cent of patients showed remarkable improvement of the wounds at the end of day 4, 60% healed completely at the end of day 10 and the remaining 40% healed completely by day 15(17).

In a study from Australia, including 24 patients with diabetic foot ulcer as case group and 84 patients as control group, 19% of propolis wounds healed in 3 weeks compared to 12% in the control group who healed in 7 weeks (P<0.05)(18).

In conclusion, propolis and bee’s honey dressing in diabetic foot ulcers lead to early healing and enables a higher rate of toes salvage in diabetic foot ulcers.
References:


15. Afaf ME. Chemical analysis of Sudanese propolis and its effect on bacteria isolated from diabetic wounds. Ph D degree Faculty of Veterinary University of Khartoum, 2010.

