# Comparing active Leptospermum honey dressing with conventional dressing in skin graft donor sites

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**Background:** Active Leptospermum honey has non-peroxide antibacterial and anti-inflammatory effects, rendering it suitable for wound healing. Leptospermum honey is endemic in New Zealand belonging to the manuka bush (Leptospermum scoparium). The objective of the present research was to compare the efficacy of manuka honey dressing with conventional dressing regarding skin graft donor sites following a burn injury.

**Methods:** This study was carried out in the department of surgery, Iran University of Medical Sciences, Tehran, Iran. It is a non-controlled prospective trial, and an open-label study, analyzing Leptospermum honey and conventional dressing for the treatment of donor site areas for skin grafts. Data were collected from 15 eligible patients with burn wound. Two independent donor sites were formed, one of which was treated with active Leptospermum honey dressing and the other covered through the conventional method. Further collected was information regarding subjects' demographics, self-reported pain (VAS scale), wound surface areas and bacterial wound culture.

**Results:** In the treatment of skin graft donor sites, honey proved to be less painful compared with the conventional group (P=0.001). Three and seven days following treatment, a significant decrease was observed in the mean wound surface areas in the honey group (P=0.001). There was no significant difference between honey and conventional dressings with regards to the rate of infection (20% in honey dressing versus 40% in conventional group; P=0.068).

**Conclusions:** Active Leptospermum honey dressing accelerates the healing process, decreases pain and has antimicrobial activity and can be used for care of skin graft donor sites.

**Keywords:** wounds, honey, burn

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## INTRODUCTION

Employing honey as a wound treatment was primarily acknowledged by the ancient Greeks and Egyptians [1]. It is a known fact that honey prevents a wide spectrum of bacterial infections [2,3]. Honey contains glucose, fructose, sucrose, amino acids, vitamins, minerals, enzymes, and water [4]. These materials combined with a number of other factors, such as low water activity, and low pH generate a high antimicrobial effect [5,6]. Studies have recently reported an increase in the incidence of resistance to antibiotics and ineffectiveness of antibacterial topical dressings, an issue which requires alternative care options [7].

Evidence supports the use of honey as a dressing

material for a broad spectrum of wounds [8,9]. Honey provides moist wound healing and inhibits or quickly clears the existing wound infections [10]. Moreover, it has been successfully used for many types of disease in certain centuries [11].

Honey has been employed as a dressing substance for many broad wounds such as burn wounds, chronic ulcers, decubitus ulcers, traumatic wounds and wound dehiscence [12]. It is also applied on skin grafts, and infected skin graft donor sites [13]. Special honey is now obtainable in various sterile types licensed for use in wound treatment in Australia, Canada, the European Union, Hong Kong, New Zealand and the USA [14]. New Zealand and Australian honey, known as active Leptospermum honey, is marketed as Medihoney [15], which has antibacterial activity without the peroxide activity and osmolarity of normal honey [16].

In a study, methylglyoxal was the reason for non-peroxide activity [17]. The antimicrobial activity in Leptospermum honey is similar to ionic silver, minus the latter's toxicity [18]. Medihoney calcium alginate was employed for the management of moderately to heavily exuding wounds [15]. It has the capacity to facilitate wound healing via pH modulation, suppression of protease activity, high osmolarity, production of very low levels of hydrogen peroxide, and augmenting the stimulation of inflammatory cytokines, such as inherent antibacterial properties [19].

This study evaluated the antimicrobial properties of Leptospermum honey dressing and its potential to accelerate the wound healing process, decrease pain, and treat skin graft donor sites following a burn injury, compared with conventional dressing.

## MATERIALS AND METHODS

This study was conducted in the department of surgery, Iran University of Medical Sciences, Tehran, Iran. It is a non-controlled prospective trial, and an open-label study, assessing Leptospermum honey and conventional dressing with regards to the treatment of donor site areas for skin grafts. Data were collected from 15 eligible patients with burn wound. For each patient, two independent donor sites were formed, one of which was treated with active Leptospermum honey dressing and the other with conventional method from May 2015 to April 2016. Ethical approval was gained from the Ethics Committee of Iran University of Medical Sciences. Moreover, written informed consent was obtained from all patients, who were later interviewed as per a predesigned pretested form. A complete clinical examination was further carried out. Information regarding subjects' demographics, self-reported pain (VAS scale), wound surface area and bacterial wound culture was collected.

The donor site with an area of 20*10 $cm^2$ and not deeper than 0.4 mm, was randomly divided into two sites. The test group was covered with Leptospermum honey dressing and the control group was covered with nitrofurazone ointment. Most donor site areas belonged to the thigh region, and the frequency of the donor site was 33.3% on the lateral right thigh, 26.7% on the left thigh, 13.3% on the medial left thigh, 13.3% on the foreside right thigh, 6.7% on the foreside left thigh, and 6.7% on the lateral right arm. The skin was removed by charging Dermatomes, and all patients received appropriate and routine treatment of burn ointment. Donor site assessment and dressing change were done postoperatively, on Days 3 and 7. Using Image J software, photographs were taken during the dressing change for the assessment of wound surface areas. Patients were asked by two anesthesiologists and a trained nurse to specify the degree of dressing pain on a visual analog scale (VAS) of 0 (no pain) to 10 (excruciating pain). The wound was assessed by two surgeons and an infectious disease specialist, 3 and 7 days post treatment. Wound culture taken during the dressing change was sent for bacterial wound culture testing.

Patients allergic to honey, or having systemic disease or chronic alcoholism were excluded from the study.

Descriptive statistics were used to summarize the demographics of the patients. Quantitative variables were compared between groups using Wilcoxon and Friedman test. For qualitative data, Fisher's exact test was used, and data were analyzed through the use of SPSS 20 software (SPSS, Chicago, IL, USA). A P-value less than 0.05 was considered statistically significant.

## RESULTS

Fifteen patients (thirty wounds) were included in this study. The Mean±SD age of the participants

**Table 1.** The wounds' surface areas according to dressing type and the day of follow up

| Wounds' surface areas | Dressing group | | Diff. (95% CI) | *P*-value |
|---|---|---|---|---|
| | Honey | Conventional | | |
| Day 1 | 82.1±22.95 | 86.8±22.78 | -4.7 (-21.8 to 12.4) | 0.173 |
| Day 3 | 1.69±2.5 | 36.15±23.55 | -34.46 (-46.99 to -21.93) | 0.001 |
| Day 7 | 0.76±1.65 | 19.1±21.89 | -18.33 (-30.48 to -6.18) | 0.001 |

**Table 2.** The wounds' surface areas comparison between groups

| Dressing group | Wounds' surface areas | | Diff. (95% CI) | *P*-value |
|---|---|---|---|---|
| | diff (Day 3-Day 1) | diff (Day 7-Day 1) | | |
| Honey | -80.41±22.52 | -81.34±22.6 | 0.93 (0.35 to 1.51) | 0.001 |
| Conventional | -50.67±33.75 | -67.73±31.39 | -17.06 (-24.93 to -9.19) | 0.001 |

was 37.00±15.68 years, and the mean of burn in patients was 21.00±12.10 % (Table 1).

Table 1 shows the wound surface areas of the study samples on days 1, 3, and 7. On day 1, the mean wound surface areas of the honey group and conventional group were 82.1±22.95 $cm^2$ and 86.8±22.78 $cm^2$, respectively. No significant difference was observed between the groups with regards to the wound surface areas on day 1 (P=0.173). On day 3, the mean wound surface areas of the honey group and conventional group were 1.69±2.5 $cm^2$ and 36.15±23.55 $cm^2$, respectively (P=0.001). Finally, on day 7, the mean wound surface areas in the honey group and conventional group were 0.76±1.65 $cm^2$ and 19.1±21.89 $cm^2$ (P=0.001) (Table 1). There was a significant decrease in the mean wound surface areas in the honey group, 3 and 7 days after the treatment (P=0.001).

Table 2 shows the wound surface areas of the patients. The mean difference of days 3 and 1 regarding the wound surface areas of the honey group and conventional group was -80.41±22.52 $cm^2$ and -50.67±33.75 $cm^2$ (P=0.001). The mean difference between Days 7 and 1 regarding the wound surface areas of the honey group and the conventional group was -81.34±22.6 $cm^2$ and -67.73±31.39 $cm^2$ (P=0.001) (Table 2). In the treatment of skin graft donor sites, a significant reduction was observed in the wound surface areas of both groups three and seven days post treatment.

Three wounds (20%) in the honey group and six wounds (40.0%) in the conventional group had a positive bacterial wound culture. No association was found between the two groups concerning bacterial wound culture (P=0.064) (Table 3).

On Day 3, the mean of pain was 3.67±1.45 in the honey group, and 8±1.36 in the conventional group, indicating a significant difference (P=0.001). On day 7, 2.67±1.29 was the pain mean of the honey group and 7.13±1.5 was that in the conventional group (P=0.001). There was a significant difference in pain between groups, 3 and 7 days after the treatment (P=0.001 and 0.006 respectively) (Table 4).

## DISCUSSION

Honey is available in most countries, but its medical potential remains grossly underutilized. It is increasingly used for antibacterial activity and wound healing, and recent studies have reported

**Table 3.** Distribution of bacterial wound culture in the two groups

| Group | Bacterial wound culture | | | | *P*-value |
|---|---|---|---|---|---|
| | Positive | | Negative | | |
| | N | % | N | % | |
| Honey | 3 | 20 | 12 | 80 | 0.064 |
| Conventional | 6 | 40 | 9 | 60 | |
| Total | 9 | 30 | 21 | 70 | |

**Table 4.** Pain in patients according to dressing group and the day of follow up

| Pain | Dressing group | | Diff. (95 % CI) | *P*-value |
|---|---|---|---|---|
| | Honey | Conventional | | |
| Day 3 | 3.67±1.45 | 8±1.36 | -4.33 (-5.26 to -3.4) | 0.001 |
| Day 7 | 2.67±1.29 | 7.13±1.5 | -4.47 (-5.33 to -3.6) | 0.001 |
| Diff. (95 % CI) | 1 (0.58 to 1.42) | 0.87 (0.36 to 1.37) | | |
| P-value | 0.001 | 0.006 | | |

that the applications of the honey are of several sorts [20-22]. The aim of the present study was to investigate the effect of active Leptospermum honey on skin graft donor sites following a burn injury, and to provide a comparison with conventional dressing. Many studies corroborate the effectiveness of honey in healing various types of wounds [25,27,28].

In this study, there was no significant difference, on Day 1, between the two groups regarding wound surface areas. On days 3 and 7, on the other hand, a significant decrease was seen in the honey group compared with the conventional group. An almost complete healing occurred in honey group after seven days, indicating that Leptospermum honey heals wounds more rapidly comparisons with the conventional treatment.

Subrahmanyam et al. showed that all superficial burn wounds treated with honey healed within 21 days, compared to the 84% of those treated with silver sulfadiazine [23]. The rate of wound healing increased after treatment with honey in other studies [24-26].

In the present study, Leptospermum honey had less pain compared with the conventional group, in the treatment of skin graft donor sites. A significant difference was observed between the groups regarding the degree of pain, 3 and 7 days post treatment. Certain studies have analyzed the pain involved in wound healing with honey dressing [25,27-30], many of which reported that honey dressing entailed less pain in patients [25,26,31,32]. Dunford and Hanano investigated whether or not Medihoney is an acceptable treatment for patients with leg ulcers with respect to pain reduction, odour control and overall patient satisfaction; they reported that the pain was reduced, odorous wounds became deodorized promptly and, in many cases, the healing process was expedited. Overall, they concluded that Medihoney treatment has a positive effect on patient satisfaction [33]. In one study, the conclusion was that the pain experienced in honey dressing is not related to the wound healing [25]. In some studies, in line with the present research, the pain relief was better than the speed of wound healing [25,26,31,32]. Pain in burn patients is a very important factor and the dressing change is, more often than not, accompanied by pain, especially in skin graft donor sites. An important factor in burn treatment is to control pain during dressing change. Accordingly, in addition to accelerating the wound healing process, appropriate dressing helps reduce pain [31].

In this study, 20% in the honey group, and 40% in the conventional group had a positive bacterial wound culture, which indicates no significant difference between the groups. The evidence provided in this study suggests that active Leptospermum honey is an antibacterial honey that is a promising agent in the management of skin graft donor sites following a burn injury.

Moghazy et al. reported that bacterial ulcer load was significantly reduced in diabetic foot ulcers following the use of honey dressings [34]. Recent studies have shown that in addition to antimicrobial effects, honey has a low pH and a high osmolarity and induces the enzymatic production of hydrogen peroxide [22,35-37].

In his laboratory studies conducted in 2015, Molan reported that honey has antibacterial activities [19]. A number of studies have shown that the non-peroxide antibacterial effects of Leptospermum honey are more special compared to other sorts of honey [38]. Moreover, the antibacterial activity of Leptospermum honey was related to methylglyoxal [17,39].

No adverse effects have been reported with regards to the wound healing of honey [40]. Neither did our study find any negative effects associated with honey. Taken together, the present study showed that Leptospermum honey, with its antimicrobial activities, offers advantages in accelerating the healing process and decreasing pain. Some studies have reported similar results with Leptospermum honey from New Zealand [41-44].

## CONCLUSION

Honey offers advantages in accelerating the healing process, decreasing pain, and antimicrobial activities as far as the treatment of skin graft donor sites is concerned. Given the small sample size of this research, it is recommended that future studies be of larger sample sizes.

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**Conflict of Interest:** None declared.

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