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The effects of topical honey dressing versus silver sulfadiazine dressing for the treatment of burn wounds contaminated by *Pseudomonas aeruginosa*

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ABSTRACT

The management of microbial contamination of burns in order to prevent sepsis is a routine requirement of acute care that led to the development of different therapeutic agents for topical use. This study was performed with the aim to compare the effects of topical honey dressing versus silver sulfadiazine dressing for the treatment of burn wounds contaminated by *Pseudomonas aeruginosa*. This animal study was performed in the central laboratory of Zahedan University of Medical Sciences in 2014. A total of 40 Hindi pigs were randomly divided into two groups of honey and silver sulfadiazine. After six hours of the inoculation of 108 *Pseudomonas aeruginosa* in the area of burn wound, in the honey group, the wound was dressed with honey, and in the silver sulfadiazine group, the wound was dressed with silver sulfadiazine. Then, after 30 daily dressings, the extent of the remaining wound was measured, and the results were compared between two groups. A $P < 0.05$ was considered significant. The honey group had less mortality than the silver sulfadiazine group (30% vs. 40%). Within 10 days, more granulation tissue was formed in the honey group than in the silver sulfadiazine group (90% vs. 20%). The extent of the remaining wound was significantly smaller in the honey group than in the silver sulfadiazine group (the percentage by which the wound shrunk was 74% in the honey group vs. 29% in the silver sulfadiazine group). The honey group had less contamination than the silver sulfadiazine group (20% vs. 95% at the 10th days of dressing). The honey dressing was shown to be significantly more effective than the silver sulfadiazine dressing for the treatment of burn wounds.

Introduction

Infections in burn wounds continue to be the main cause of morbidity and mortality. Burn wounds result in the loss of the protective function of the skin as a barrier to microorganisms, leading to high risk of infection [1]. Although significant improvement has been made in the survival of burn patients, infectious complications are still a major cause of morbidity and mortality worldwide [2]. Due to a reduced immune response, burn patients are at a high risk of wound infection, sepsis, and ventilator-associated pneumonia. *Pseudomonas aeruginosa* is a predominant pathogen cultured from burn wounds [3-5]. P. aeruginosa, with mortality rates of up to 80%, is an opportunistic pathogen; it takes advantage of the compromised defense mechanisms in burn patients, due to the loss of the skin barrier and the suppression of the innate and adaptive immune system [6,7]. Since *P. aeruginosa* has multi-drug resistance, it forms biofilms and survives in many hostile environments, so it is difficult to eradicate from burn wounds [8,9]. Topical use of antimicrobial

agents plays an important role in the management of a burn wound infection. Also, management of the microbial contamination of burns to prevent sepsis has led to the development of a variety of therapeutic agents for topical use [10]. Topical use of antimicrobial agents has reduced the overall mortality rate in the typical burn population from 38–45% to 14–24% [11]. Among the variety of therapeutic agents, honey has been used in wound care since ancient times [12]. After having served an important role in the medical tradition, honey was "rediscovered" by modern medicine as a topical agent for treating wounds and burns [13]. Its high sugar content gives it the ability to absorb water from a wound (osmolarity), and this deprives bacteria of the moisture they need to thrive. Honey provides a non-adherent interface between the dressing and the wound bed, which creates a moist healing environment and prevents the dressing from tearing away the newly formed tissue when removed [14]. Therapeutic properties of honey have been scientifically proven by many studies, laboratory experiments, and clinical trials during the last century. The antimicrobial properties of honey are mediated by high sugar content, low pH, hydrogen peroxide, methylglyoxal, and bee defensin [15]. In addition, the activation of enzymes in the host, and the osmotic ability of honey, stimulate the autolysis of necrotic tissue [16]. Moreover, honey optimizes epithelialization and angiogenesis, promotes the formation of healthy granulation tissue, and induces oxygen uptake [17]. Hydrogen peroxide is produced by glucose oxidase in honey and fibroblasts, and epithelial cell growth is stimulated [18]. Silver sulfadiazine is one of the topical agents for the treatment of burns, because silver is an effective, broad-spectrum, antimicrobial agent [19]. Topical silver, due to its toxicity to keratinocytes, delays wound healing [20]. Silver sulfadiazine is used for a limited period in the treatment of burns, rather than for the entire treatment period. Despite its advantages, including reduced use of systemic antibiotics and slow release of silver ions to promote healing, cellular toxicity remains a problem [21].

However, the management of the burn wounds is still under debate, and an ideal dressing for burn wounds has not been discovered [22]. Therefore, this study was performed with the aim to compare the effects of topical honey dressing versus silver sulfadiazine dressing for the treatment of burn wounds contaminated by *Pseudomonas aeruginosa*.

Materials and Methods

This animal study was performed in the burn ward of central laboratory of Zahedan University of Medical Sciences in 2014. A total of 40 Hindi pigs were randomly divided into two, honey and silver sulfadiazine groups, of 20 cases in each group. First, after weighing them, the skin of the right groin of each animal was carved, and then the antiseptic process was performed using alcohol and Betadine. The pigs were anesthetized using ketamine and atropine, and special gated containers, that were prepared in advance, were fixed at the site using zero nylon.

After rinsing the site with saline, this limited area of the skin, which had an approximate area of 5.8 cm/m2, was exposed to boiling water for 10 seconds, and then after complete cooling of the site, 108 P. aeruginosa bacteria, separated from one of the patients of Zahedan Khatamolanbia hospital, which was resistant to all available antibiotics, was inoculated onto the wounds.

Dressing began after an interval of six hours of inoculation, dressing with honey and silver sulfadiazine in each group. The honey used in this study was natural honey made from beehives in Taftan Mountain pastures in Sistan and Baluchistan, that had no additional process performed on it, and its purity was confirmed by the Food Administration of the province. All wounds were daily dressed and based on a predetermined table, and the pigs' weight, condition, and the extent of the wounds were recorded on certain days; qualitative and quantitative cultures were prepared from the wounds.

Daily dressing was continued up to 30 days after the burn, and at the end of 30-day period, after pigs' re-weighing, the extent of the remaining wound was measured. All of the obtained information was recorded in predetermined tables, and the cultures' results, obtained by the

Department of Microbiology of University of Medical Sciences, were used in the total results of the study.

The data were analyzed by SPSS software (version 12). A student t-test and an analysis of variance test were used to compare the study groups. A $P < 0.05$ was considered statistically significant.

Results

The mean weight of the pigs in the two groups of honey and silver sulfadiazine before the study was 640 and 628 g, respectively, and after 30 days of dressing, that was reduced to 491 and 505 g, respectively. The percentage of weight loss in the honey group was 23% and in the silver sulfadiazine group it was 19 %.

From a total of 40 pigs during the 30-day treatment period, 14 died, and the overall mortality rate was 35%. Except for 2 cases of death in the silver sulfadiazine group, no mortality was observed within 10 days after a burn. The mortality rate in the honey group was 6 deaths from 20 pigs (30%), and in the silver sulfadiazine group, it was 8 deaths from 20 pigs (40%).

The clinical status of the wounds on the 10th day after burn was assessed in two groups. Table 1 demonstrates the infections in the wounds and the granulation tissue formation. The clearly infectious wound is defined as a quite purulent exudate on the wound, or smelly *P. aeruginosa* bacteria.

The extent of the wounds was measured after 30 days of daily dressing and compared with the first day of burning. In both groups, the wounds' surface was covered by favorable granulation, but the extent of the wound in the honey group was clearly smaller compared to the silver group. The average size of the wound after 30 days of dressing was 26 cm^2 in the silver dressing group, and in the honey dressing group, it was 2.25 cm^2 (Table 2).

In the silver group, from 12 remaining pigs (alive) at the end of 30 days after burning, hair loss was seen in 11 cases (92%), of which 4 cases (36%) were serious. That finding was not found in the honey group.

Wounds' status 10 days after burn (clinical view): Without any exudate or infection-based evidence: Silver group, 5 of 18 (2 had died) (28%), Honey group, 9 of 20 (45%)

The formation of granulation (G1 = good) (G2 = is forming); Silver group, G2 = 8 (44%), honey group, G1 = 10 (50%), G2 = 8 (40%).

Ten days after burn, the provided cultures of wounds showed that the lowest level of contamination is related to the honey group (20% in the honey group and 100% in the silver sulfadiazine group) (Table 3).

Table 1. infection in wounds and granulation tissue formation in two studied groups

Groups	Variables				
	Good granulation	Granulation is forming	Wounds with granulation (%)	Clearly infectious wounds	Wounds without any infection
Silver sulfadiazine	0	8	40	11	5
Honey	10	8	90	2	9

Table 2. the extent of the wounds after 30 days of dressing in two studied groups

Wound's status	Silver sulfadiazine	Honey
Mean extent of wound	6 cm2	2.25 cm2
Percentage of wound being smaller	29%	74%

Table 3. Cultures of wounds in two studied groups

Culture	Quantitative				
	4th days	6th days	10th days	14th days	17th days
Honey	100%+	100%-	80%-	100%-	90%-
Silver sulf.	100%+	100%+	100%+	10%-	50%-

*Positive quantitative culture shows contamination> 105 per 1 g soft tissue.

Discussion

Various dressing materials have been used for dressing burn wounds' amniotic membrane, such as banana leaf, skin grafting, boiled potato peel, epidermal growth factor, soframycin cream, silver

sulfadiazene (SSD), honey dressing, etc. Honey has been used since ancient times as a remedy in wound healing, and a lot of evidence from animal studies and some trials has suggested that honey accelerates wound healing [23].

The present study was performed with the aim to compare the effects of topical honey dressing versus silver sulfadiazine dressing for the treatment of burn wounds contaminated by Pseudomonas aeruginosa.

According to the results of present study, the honey group had less mortality than silver sulfadiazine group (30% vs. 40%). Within 10 days, more granulation tissue was formed in the honey group than in the silver sulfadiazine group (90% vs. 20%). The extent of the remaining wound was significantly smaller in the honey group than in the silver sulfadiazine group (the percentage by which the wound shrunk was 74% in the honey group vs. 29% in the silver sulfadiazine group). The honey group had less contamination than the silver sulfadiazine group (20% vs. 95% at the 10th day of dressing).

A survey conducted in 2010 by Malik and colleagues to compare honey with silver sulfadiazine in the treatment of burn wounds, showed that 6 patients had a positive culture for Pseudomonas aeroginsa in the honey-treated site, whereas 27 patients had a positive culture in the SSD-treated site; it was concluded that the efficacy of honey for treating superficial and partial-thickness burns was greater than SSD cream [24]. Their results were consistent with the findings of our study.

Despite the use of antibiotics and modern sterilization techniques, infection is one of the most frequent complications of wound healing, which accounts for considerable patient morbidity, discomfort, and prolonged hospitalization and delayed healing [24]. In the presence of infection, antibiotics are ineffective and the situation becomes worse, and antiseptics cause tissue damage, further slowing the wound healing. On the other hand, honey causes no tissue damage, promotes the healing process, and decreases the average duration of wound healing [25]. Subrahmanyam *et al*., in a prospective randomized clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine, concluded that patients treated with honey had a significantly lower mean duration of wound healing than those who were treated with silver sulfadiazine [26-27]. Similar results were reported in the study of Gupta *et al*., who performed a retrospective study in 2011 to evaluate the effects of honey dressing versus silver sulfadiazine dressing for wound healing in burn patients, and they concluded that honey dressings make the wounds sterile in less time, enhance healing, and have a better outcome in terms of the hypertrophic scars and post burn contractures, as compared to SSD dressings [28].

Also, Baghel and colleagues, in a comparative study in 2009 in which evaluated the effect of honey dressing and silver sulfadiazine dressing on wound healing in burn patients, reported that honey dressing improves wound healing, makes the wound sterile in lesser time, has a better outcome in terms of the prevention of hypertrophic scarring and post-burn contractures, and decreases the need of debridement irrespective of time of admission, when compared to SSD dressing [29]. In terms of healing and making the wound sterile, SSD dressing did not have any added benefits over honey dressing. There is evidence of an antibacterial effect of SSD dressing, but no direct evidence of improved healing or reduced infection is found [30].

Moreover, many controlled clinical trials have compared honey with different products (silver sulfadiazine, Betadine, saline compresses, paraffin dressings, hydrogel etc.) for the treatment of burns wounds, and they have found robust evidence for the use of topical honey to reduce healing times in burns [31-35]. Also, experimental research on animals has shown the effectiveness of topical administration of honey in wound healing compared to the control, or to silver sulfadiazine [36].

One of the limitations of the present study is the evaluation of the mortality rate in the two groups of honey and silver sulfadiazine, which has been assessed in few limited studies. On the other hand, time duration of healing is not compared between the two groups.

Conclusions

According to our results, this study indicates that a honey dressing is significantly more effective compared with a silver sulfadiazine dressing for the treatment of burn wounds. Therefore, in regards to honey being economical and easily available, it is a reasonably ideal dressing material in developing countries, including Iran. However, further research is needed in the future.

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