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Research Article

The Comparative Efficacy of Honey, Turmeric and Silver Sulfadiazine Dressing on the Healing of Burn Wounds in Rabbits

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Abstract

In this study, the healing potential of turmeric and honey dressings on rabbit burn wounds was compared to that of silver sulfadiazine treatment. Four equal groups of sixteen rabbits were randomly assigned. All surgical burn lesions had the same size (1.8 cm x 1.8 cm) and were created on the dorsal back skin of rabbits. Every day, the burns were dressed with sterile Phosphate Buffer Saline (PBS) in control group C, sterile silver sulfadiazine in group S, turmeric in group T and honey in group H. By measuring the bacterial load, tissue response to healing, wound contraction rate and histology, the effectiveness of the treatment was assessed. In comparison to the group treated with silver sulphadiazine and turmeric, full healing occurred far sooner in the lesion treated with honey due to the wound's much higher rate of epithelialization. During the histoarchitecture analysis of the wound biopsy, reactive cells were found and slower keratinization in the lesion treated with Silver Sulphadiazine and turmeric demonstrated signs of slow healing. In terms of the difference in wound surface area, the honey group healed more quickly (22 ± 0.957 days), whereas the silver sulfadiazine group healed more slowly (26 ± 1.291 days). On the other hand, full recovery occurred in the control group and those who received turmeric treatment after 28.00 ± 1.826 and 39 ± 1.291 days, respectively. In contrast to burn skin treated with silver sulfadiazine and turmeric, our research indicated that the re-epithelialization process was more rapid in burn skin treated with honey.

Keywords: *Burn Wound; Honey; Turmeric; Silver Sulfadiazine; Rabbit*

Abbreviations

µl: Microliter; °C: Degree Celsius; Cm: Centimeter; Kg: Kilogram; H&E: Haematoxylin and Eosin; %: Percentage; Mg: Milligram; µm: Micrometer; ml: Milliliter

Introduction

Skin burns pose difficult clinical concerns because the skin's surface loses its ability to act as a barrier to microorganisms, increasing the risk of infection [1]. Burns may be full thickness, including all layers of the skin and extended deeper structures, or superficial, only

affecting the epidermal layer of the skin [2]. The meticulous care that burn wounds require to progress results in significant financial and medical costs. Graft or materials for covering burn wounds play an essential part among the many elements that affect how well a burn lesion heals [3]. The use of natural remedies to quicken burn wound healing is a long-standing practice around the world and the results are promising [4].

From a scientific standpoint, numerous *in vitro* studies, lab tests and clinical trials conducted over many years have shown the therapeutic value of honey [5]. In the past, people have used honey as an adjuvant to hasten the healing of burns, infected wounds and skin ulcers. Honey has been shown to have strong adhesive properties for skin transplant adhesion and speed up wound healing [6]. When honey is applied to superficial and partial-thickness burns, less pain is felt when changing the dressing, there is less inflammation and healthy granulation forms [7]. Honey primarily functions as a hyperosmolar medium that prevents bacterial development [8]. Its high nutritional content enhances the availability of substrate in the immediate environment, promoting angiogenesis and epithelialization. Additionally, honey creates a moist environment for the best conditions for healing [9]. Because it is affordable and widely available, honey makes a respectable dressing for burn patients in developing nations [10].

Since it contains antibacterial qualities, silver sulfadiazine (SSD) has been used as the gold standard in topical burn therapy [11]. As a broad-spectrum antibacterial, silver is frequently utilized in medical equipment and wound dressings. Some silver-containing dressings, silver nitrate, nano crystalline silver and other substances have anti-inflammatory properties that promote neovascularization [5,12].

For the treatment of cutaneous wounds, it has been claimed that the traditional spice turmeric, a natural product made from the rhizomes of *Curcuma longa* that are chemically related to its main constituent, curcumin, is effective [13]. The re-epithelialization and migration of cells like myofibroblasts, fibroblasts and macrophages are enhanced by curcumin. Curcumin reduces pain and inflammation by obstructing the arachidonic acid cascade specifically [2]. Nitric oxide is scavenged by curcumin, which also inhibits the pro-inflammatory cytokine cyclo-oxygenase (COX-2) [14]. Numerous studies have demonstrated that when taken along with antibiotics for the treatment of infections, turmeric has beneficial synergistic effects [15]. There is disagreement over the best dressing for covering burn wounds, preventing or controlling infection, or promoting wound healing. The experiment was therefore conducted with the following goals in mind: to investigate the therapeutic effect, tenderness of the wound and healing potential of topical application of honey dressing, turmeric dressing and silver sulfadiazine dressing on burn wound.

Materials and Methods

The experiment was performed to assess the effect of two herbal medicines on healing of deep second degree burns in rabbits and their comparison with silver sulfadiazine group. The study was conducted in the department of Medicine, Surgery and Obstetrics, Faculty of Veterinary and Animal Sciences, Hajee Mohammed Danesh Science and Technology University (HSTU), Dinajpur, Bangladesh. Histopathological study was conducted in the department of Pathology, Faculty of Veterinary Sciences, Bangladesh Agricultural University (BAU), Mymensingh.

Experimental animals

Sixteen rabbits that appeared to be in good health were used for this experiment with the approval and in accordance with the recommendations and guidelines of the department of Medicine, Surgery and Obstetrics, Faculty of Veterinary and Animal Science, Hajee Mohammed Danesh Science and Technology University, Dinajpur. The animals' average body weight was 1.5 - 1.8 kg. The animals were kept without any limits on food or water under regular laboratory conditions and veterinary supervision. The rabbits were quarantined for two weeks before to the trial.

Experimental design

A total of sixteen full-thickness cutaneous burn wounds were made on dorsal side of the vertebral column of rabbits. They were studied under four groups:

1. Group H or honey group: Honey was applied on the burn wound surface twice daily with sterile cotton swabs following burning.
2. Group- S or Silver sulphadiazine group: Silver Sulfadiazine was applied on the burn wound surface twice daily with sterile cotton swabs following creation of burn wound.
3. Group T or turmeric group: Turmeric was applied on the burn wound surface twice daily with sterile cotton swabs following post wounding.
4. Group C or control group: Animals of this group received sterile phosphate buffered saline (PBS) on the burn wound surface twice daily with sterile cotton swabs following post wounding.

Creation of burn wound

Five centimeters away from the spinal column, the surgical site was chosen. To lessen the microbial load in the wound area, the operation sites were trimmed with sharp scissors and cleaned with soap and water in this technique. The remaining hair was thoroughly shaved off with a razor to expose the flesh beneath. The animal was then positioned on the operating table in lateral recumbency. Following inverse "L" blocks at the surgical site, local anesthetic was infiltrated using lidocaine hydrochloride 2% and epinephrine 0.005% (Jasocaine-ATM, Jayson Pharmaceuticals Ltd. Bangladesh). In order to inflict a deep second-degree burn, wound on the rabbit, a 4 cm^2 (2 cm × 2 cm) iron rod that had been heated on a Bunsen burner for one minute was placed there for three seconds. The burn wound wasn't stitched up and was left uncovered.

Assessment of wound healing

Every day, wounds were checked for any alterations in their appearance, the color and smell of any discharge and the timing of scar separation. If an animal started to become lethargic, activity was also noted. Digital photography was used to measure therapy responses up to day 40 of the treatment. To evaluate the tissue response during the healing process, histological parameters (epithelialization, fibrosis and angiogenesis) were measured at days 14 and 21 after the experiment was started from a wound biopsy.

Burn wound microbiology

On days 3, 8, 13 and 18 following wounding, wound swab samples were taken and inoculated into nutritional agar medium before being placed onto 100 µl, 50 µl and 10 µl agar plates and incubated at 37^0C overnight. 0.05 mg/ml Fungizone (amphotericin B, Thermo Fisher Scientific INC, NY) was utilized to prevent contaminating fungus development in nutrient broth and nutrient agar plates. Using a marker pen, the agar plates were divided into four separate quarters and colonies from each quarter were counted. Each time, the total number of bacterial colonies per cotton swab (1 ml of nutritional broth) was counted.

Tissue biopsy

For a better understanding of the wound healing process, tissue samples were taken on the fourteenth and twenty-first day after the burn injury. The tissues were embedded in paraffin after being fixed in 10% buffered neutral formalin for 24 hours. Hematoxylin and eosin was used to stain sections that were 5 µm thick. After that, the slides were examined with a photographic microscope (Micros®, Austria).

Statistical analysis

All data were presented as mean ± SD. To compare data among groups, one-way ANOVA (Analysis of Variance) factor analysis was performed by IBM SPSS (Version 25.0) at $P < 0.05$.

Results

Time required for healing (epithelialization) in different treatment groups

Every day, the burn injuries were checked for any discharge, edema around the site and wound healing. While other treated groups had a considerably ($P < 0.05$) longer time to heal out, the honey-treated group demonstrated faster healing and completed complete healing in 22 ± 0.957 days. In terms of healing time, the silver sulfadiazine group came in second place (26 ± 1.291 days). On the other hand, full recovery occurred in the control group and those who received turmeric treatment after 28.00 ± 1.826 and 39 ± 1.291 days, respectively. It was clear from examining the images taken during the experiment that the wound had healed the fastest in the honey group compared to the silver sulfadiazine group, the turmeric group and the control groups (Figure 1). There was a statistically significant difference in the rate of burn wound healing across all groups. When the parameters used to assess the three topical burn treatments were analyzed, honey and silver sulfadiazine were shown to be more effective than turmeric (Figure 2).

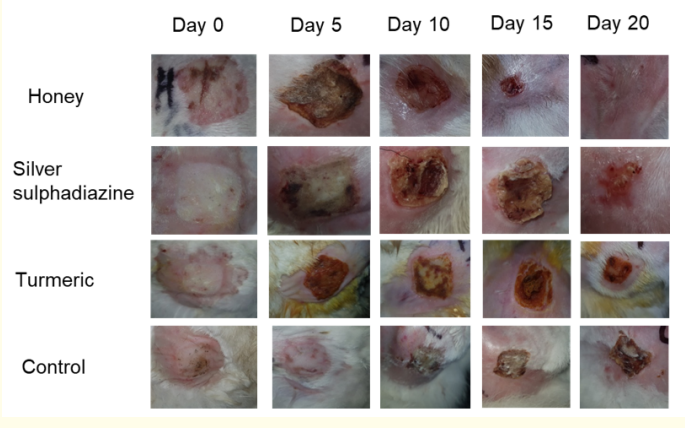

Figure 1: *Macroscopic evolution of wound contraction process in all groups at different time-points of the experiment.*

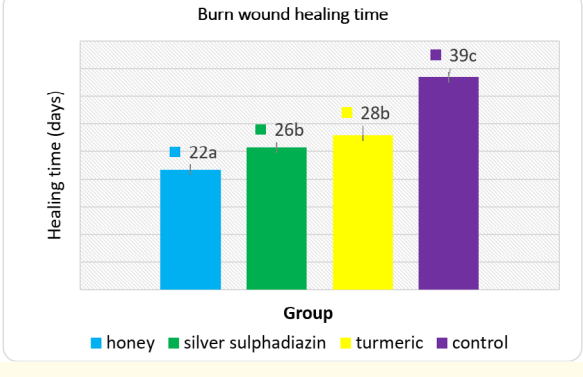

Figure 2: *Comparison between different treatment groups with mean of healing-time.*

Microbiology of wound

All samples had bacterial colonies visible on nutrient agar, however group H consistently had the lowest bacterial load (CFU), followed by group S, group T and group C. Following day 3 of the experiment, group C had the highest bacterial load (16.15×10^2 CFU/ml), while group H had the lowest count (4.08×10^2 CFU/ml). On day 18, the bacterial burdens of groups H, S and T appeared reduced, although group C's wounds appeared less infected and less likely to heal (Table 1).

Groups	Day 3	Day 8	Day 13	Day 18
Honey (H)	4.08×10^2	2.75×10^2	1.8×10^2	0.42×10^2
Silver sulphadiazine (S)	4.28×10^2	3.13×10^2	2.19×10^2	0.54×10^2
Turmeric (T)	5.12×10^2	3.57×10^2	2.62×10^2	0.76×10^2
Control (C)	16.15×10^2	14.00×10^2	11.92×10^2	10.20×10^2

Table 1: *Colony forming unit (CFU/ml) in different treatment groups.*

Biopsy examination of experimental burn wound healing

Skin biopsies taken and inspected on days 14 (Figure 3) and 21 (Figure 4) after wounding revealed that control skin had not healed because there was a significant gap between the cutting edge and the wounded skin's lack of keratinization. Additionally, the cutting edge of the control wound, when inspected at days 14 and 21, revealed the deposition of neutrophils, indicating a higher level of bacterial infectivity. In contrast, wounds treated with honey (H), silver sulphadiazine (S) and turmeric (T) exhibited neutrophil infiltration, albeit to a lesser extent. On day 14 after wounding, the densities of neutrophils in the skin were low in the groups treated with honey and silver sulphadiazine. From day 14 after wounding, there was the growth of fibrous connective tissues; the densities were larger in untreated control wounds than in the turmeric, silver sulphadiazine and honey-treated groups. Fibrous tissue proliferation in wounds treated with honey appeared to be reduced on day 21 after injury. The development was still more pronounced in the groups treated with turmeric and silver sulphadiazine.

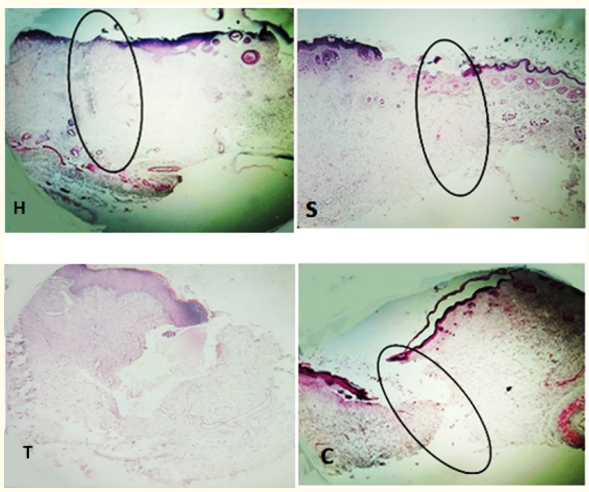

Figure 3: *Histopathology of burn wound biopsies collected on day 14.*

A biopsy was taken from the skin of the untreated control (C), honey (H), silver sulphadiazine (S) and turmeric-treated skin on day 14 after the wounding, stained with H and E and examined under low magnification (4x). The wound treated with honey (H, circle), silver sulphadiazine (S, circle) and turmeric (T, circle) showed signs of progressing wound healing in the form of gap filling and incomplete keratinization over the wounding surface, in contrast to the untreated skin (C, circle), which showed no signs of healing at all. Honey, Silver Sulphadiazine and wounds treated with turmeric seemed to improve the reaction.

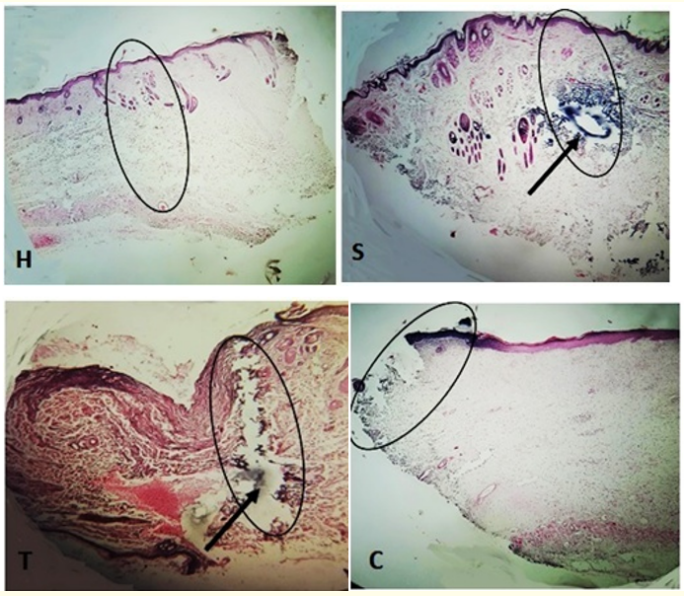

Figure 4: *Histopathology of burn wound biopsies collected on day 21.*

On day 21 after the wound, a biopsy was taken from the untreated control (C), the skin that had been treated with honey, silver sulphadiazine and turmeric and it was stained with H&E and viewed under a low-power microscope (4x). Skin that had not been treated exhibited no signs of healing and the wound margin was still raw and disconnected after the tissue was processed (C, circle). On day 21, there was keratinization across the incised surface of the wound that had been treated with honey (H, circle), providing evidence that the wound had fully healed. There were dead tissues under the repaired dermis (S, arrow) and significant gaps between tissue ends (T, arrow) of the incised skin, indicating that the wound treated with Silver Sulphadiazine (S, circle) and Turmeric (T, circle) had not fully healed (Figure 4).

Discussion

The honey, turmeric and silver sulfadiazine dressing for healing has been a staple in indigenous medicine and has cemented its place in the wound care toolbox [16]. In order to promote healing, the use of honey, turmeric and silver sulfadiazine dressings is becoming increasingly important in the treatment of burns. This is because burn lesions are more susceptible to localized and spreading infections, which can result in a variety of local and systemic detrimental effects [17]. In this experimental investigation, data on burn wound extent were initially recorded every five days, but as the burn wound's healing process advanced, data were kept up until the day the burn wound completely contracted. In order to help a defects, heal after injury, centripetal movement of the wound margins is known as contraction [18].

The study's findings demonstrated that when honey, silver sulphadiazine and turmeric were applied topically for the post-wounding days, the burn wound area of the experimental animals did not enlarge. The results concur with earlier reporters [19]. According to this study, honey was the first treatment to show a substantial increase in the rate of contraction, epithelialization and maturation of burn wounds in rabbits when compared to other therapies. Burns treated with honey recovered in 22 days. The outcome of a recent study is comparable to [20]. Honey's anti-inflammatory properties would lessen the harm done by free radicals produced by inflammation and stop further necrosis [14]. It has been demonstrated that acidification can speed up the healing of wounds by inducing hemoglobin to release oxygen when applied topically with honey [17]. Additionally, honey contains a variety of antioxidants, including flavonoids, monophenolics, polyphenolics and vitamin C, all of which are crucial for the processes involved in tissue regeneration [21]. Commercial honey that has not been boiled appears to speed up wound healing when applied topically due to its antibacterial, hygroscopic and energy-producing qualities [13].

This study also supported the idea that honey helps open wounds heal faster by lowering the bacterial load. According to several earlier studies, Alpha® ointment [22] and hydrocolloid dressing are two common wound care treatments that can be used in conjunction with honey to promote wound healing [4]. According to the results of this investigation, honey can lower the bacteria burden in experimental wounds. The reduction of microbial load, development of a thin scar and completion of keratinization within 21 days of wounding all contributed to the topical application of honey's ability to speed up wound healing [3]. Due to the viscosity and high sugar content of honey, a moist environment is generated that promotes the production of thin scars. Burn wound healing is accelerated by the thinner scabs that form throughout the healing process because they act as smaller barriers for epithelialization [20,22].

However, in the group that received silver sulfadiazine treatment, wound healing took 26 days. These findings are very comparable to those of earlier research [15]. The only mechanism supporting the ongoing use of silver sulphadiazine in burn injuries is its antibacterial action. The sulphonamide, which kills microorganisms, is released when the silver ion connects with an organism's DNA [5]. When compared to other therapies, Silver Sulphadiazine was found to be the pioneer in promoting the healing of cutaneous burn wounds in rabbits, greatly speeding up the pace of wound contraction, epithelialization and maturation [9].

Burn burns treated with turmeric healed completely in about 28 days. Similar results have been reported elsewhere [1,23]. Re-epithelialization of the burn in the rabbit model that had been treated with turmeric, per the research, was finished after 21 days. The average healing period in our study is a little bit longer than in the prior report. It might be because turmeric treats deep second-degree burns so effectively. There is another study that is comparable to the one under consideration here [14,24]. The increased migration of myofibroblasts, fibroblasts and macrophages as well as re-epithelialization in the curcumin-treated groups indicated that curcumin was crucial to the wound healing process following burn injury [16]. At day 21, the interstitial edema and bleeding in the control group were accompanied by a loose collagen matrix with round to polygonal fibroblasts. Additionally, lymphocytes and polymorphonuclear cells were infiltrated and adipose tissue occupied the dermal layers.

Conclusion

It is reasonable to draw the conclusion that honey promoted burn wound healing better than silver sulfadiazine and turmeric with smaller lesions and quicker healing times based on the findings of wound morphometry and histological features. The exceptional effectiveness of honey in healing burn wounds can be attributed to its antibacterial, cell-proliferative and anti-inflammatory properties. For burn wound healing, honey may be utilized as an alternative to haphazard topical antibiotic administration. Silver Sulphadiazine shown effective burn wound healing and turmeric demonstrated wound healing activity as well, however it was more time-consuming than using honey and Silver Sulphadiazine. These two traditional substances are suggested for extensive study at various doses for going to field practice for topical burn wound care in animals rather than a Silver Sulphadiazine.

Conflict of Interest

The authors declare no conflict of interest.

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