THE EFFECT OF MOIST EXPOSED BURN OINTMENT ON MAINTAINING A PHYSIOLOGICAL MOIST ENVIRONMENT IN TREATING BURN WOUND

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SUMMARY. Objective: To investigate the effect of moist exposed burn ointment (MEBO) on the maintenance of a physiological moist environment in burn wound treatment. Methodat: A rabbit model with deep-second degree burn wound was used in this study. Observations were conducted at 0 hours (before burn), at 0.5, 6, 24, 48, 72 hours and 7 days post-burn, and after wound healing. Water evaporation, gross appearance, pathological changes, and the healing time of burn wounds treated with MEBO were studied, and the findings were compared with those of burn wounds treated respectively with either Vaseline or conventional dry exposed therapy. Results: It was found that water evaporation in MEBO-treated wounds was similar to that in normal skin and significantly less than that in wounds treated with dry exposed therapy (p < 0.01). MEBO did not obstruct proper water evaporation from wound as Vaseline did (p < 0.01). MEBO-treated wounds retained good breathing properties and adequate drainage and healed faster than dry exposed wounds. The difference was statistically very significant (p < 0.01). Conclusion: MEBO provided burn wounds with a physiological moist environment that promoted tissue regeneration and wound repair.

Introduction

Many controlled studies have confirmed that wounds heal more readily in a moist, physiological environment. Maintenance of a moist wound environment facilitates the wound-healing process.1,2 In contrast, prevention of dehydration results in a marked delay in the healing of partial-thickness burn wounds. Moist exposed burn therapy (MEBT) was developed in China by Professor Rong-xiang Xu. The essential purpose of MEBT is to keep the burn wound in an optimal physiological moist environment by using a specially designed ointment, i.e. moist exposed burn ointment (MEBO). Composed of natural plant extracts dissolved in refined sesame oil as base with beeswax as preservative, MEBO ointment is topically used for burn treatment, promoting the discharge and removal of debris (liquefaction of necrotic tissues) and enhancing the regeneration and repair of residual viable tissues and wound healing.4 This feature distinguishes MEBO from dry exposed therapy and other conventional topical medications for treating burn wounds. In an experimental model, Ioannovich et al. found that MEBO provided a moisturizing environment for a longer period that significantly accelerated the wound-healing process in partial-thickness burns compared with silver sulphadiazine and povidone iodine.5 Recently, in a multicentre clinical trial in 25 study centres in six Middle Eastern countries, it was reported that MEBO enhanced and expedited healing when applied to acute burn wounds. Epithelialization was sufficient for
epidermal regeneration in nearly all second-degree cases. Even some third-degree burns, with limited total body surface area, healed without skin grafting. Conversely, excessive wetness of the burn wound may induce secondary tissue injury by maceration. It also promotes bacterial colonization and is the major cause of wound infection, including wound sepsis. The basic requirement of moist exposed burn therapy/moist exposed burn ointment (MEBT/MEBO) is therefore the capacity to maintain optimal wound moisture without affecting good drainage. This paper presents the results of an experimental study on a rabbit model designed to observe the different degree of water evaporation in burn wounds of same degree but treated with different methods. It also evaluates the effects of MEBT/MEBO on burn wound water evaporation and the wound healing process.

Materials and methods

Forty-two healthy adult rabbits of both sexes (pregnant females were excluded) were used in the study (weight, 2.1-3.0 kg). The animals were depilated on the dorsum by applying 8% sodium sulphide solution. Anaesthesia was achieved by intraperitoneal injection of pentobarbital sodium (40 mg/kg). One deep second-degree (deep partial-thickness) burn wound was inflicted on each side of the back by contact for 4 seconds with a 100 heated copper plate, 3 cm in diameter. Wound depth was verified by pathological examination. MEBO ointment was supplied by the Beijing Guangming Chinese Medicine Institute for Burns, Wounds and Ulcers. Vaseline for medicinal use was produced by the Yangzizhou Pharmaceutical Plant of Nanchang City of China. The model used for measuring wound water evaporation was an EPIC evaporometer (Servomed).

Experiment 1 - MEBO treatment as auto-control

Ten rabbits were used in this experiment. The water evaporation value of normal skin was measured before injury. The animal was then burned on both sides of the dorsum. The wound on one side was treated with MEBO, while the wound on the other side was left exposed to dry spontaneously as an auto-control. MEBO was directly smeared on the wound to a thickness of 0.5-1 mm and renewed at an interval of 6 to 8 h. Residual ointment and the white liquefied products of necrotic tissues were wiped off gently with a tongue-depressor before re-application of MEBO. No disinfectant or saline was used to clean the wound. A principle of injury was enforced throughout the course of wound treatment, i.e. no method or agent was used that might irritate the wound or cause secondary injury. Measurement of wound water evaporation was performed at 0.5, 6, 24, 48, 72 h, and 7 days post-burn.

Experiment 2 - Blind assignment

Twenty-four rabbits were randomly divided into two groups after injury: a MEBO treatment group and a dry exposed therapy group (12 per group). The method of treatment and measurement of wound water evaporation were as in Experiment 1. The healing time of each wound was recorded. After observation of gross pathological changes and water evaporation in the wound, the wound tissues were sampled at 0.5, 6, 24, 48, 72 h, and 7 days post-burn, and after healing. Specimens were fixed in 10% neutral formalin, embedded in paraffin, sectioned at 10 , stained with haematoxylin and eosin, and studied by light microscope for micropathological changes.

Experiment 3 - Vaseline treatment as negative control

Eight rabbits with deep second-degree burn wounds on both sides of the back were topically treated with Vaseline. The method of treatment and observations were the same as for Experiment 1 with MEBO treatment, except that Vaseline replaced MEBO. The ambient temperature was 25-28 and humidity 50.5%. Data are presented as mean value standard error and analysed statistically using analysis of variance and t-test. Results were considered significant if p < 0.05 and highly significant if p < 0.01.

Results

Wound water evaporation

Compared with values in normal skin, water evaporation values in burn wounds treated with dry exposed therapy in both Experiments 1 and 2 increased.
progressively post-injury and reached a peak of 19 times the value of normal skin at 6 h, after which they tended to decrease slowly but never returned to normal values until wound healing. In MEBO-treated wounds, water evaporation values also dramatically increased post-burn compared with values in normal skin (p < 0.05) but were significantly less than values in dry exposed wounds (p < 0.01). After wound healing, wound water evaporation returned to normal values (Tables I, II). Water evaporation in wounds in the Vaseline-treated group remained at a very low level, significantly different from that of normal skin, as also in MEBO-treated wounds in Experiment 2 (p < 0.01) (Table III). Determination of water evaporation in wounds treated with Vaseline was not performed 7 days post-burn because most of the wounds were infected.

<table>
<thead>
<tr>
<th>Wound (No.)</th>
<th>Before injury</th>
<th>Times after injury</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.5 h</td>
</tr>
<tr>
<td>Corrected</td>
<td>4.48±0.67</td>
<td>83.70±1.22</td>
</tr>
<tr>
<td>Corrected</td>
<td>4.48±0.81</td>
<td>5.69±0.21ε**</td>
</tr>
</tbody>
</table>

Compared with the value before injury εp < 0.05, εεp < 0.01.; Compared with the value of dry exposed control ** p < 0.01.

**Table I- Water evaporation of wounds in Experiment 2 (g/m²/h, x±s)**
<table>
<thead>
<tr>
<th>Wound (No.)</th>
<th>Before injury</th>
<th>Times after injury</th>
<th>0.5 h</th>
<th>6 h</th>
<th>24 h</th>
<th>48 h</th>
<th>72 h</th>
<th>7 d</th>
<th>Healing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry exposed (n = 124)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16.27±0.54¢¢</td>
</tr>
<tr>
<td></td>
<td>4.48±0.67</td>
<td>82.38±0.54¢¢</td>
<td>85.92±0.11¢¢</td>
<td>79.58±0.06¢¢</td>
<td>74.41±0.04¢¢</td>
<td>69.54±0.14¢¢</td>
<td>56.62±0.60¢¢</td>
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<td></td>
</tr>
<tr>
<td>MEBO (n = 24)</td>
<td>4.67±0.75</td>
<td>5.32±0.09¢**</td>
<td>5.37±0.04¢**</td>
<td>5.29±0.97¢**</td>
<td>5.18±0.84¢**</td>
<td>5.18±0.84¢**</td>
<td>5.30±0.93¢**</td>
<td>4.84±0.39**</td>
<td></td>
</tr>
</tbody>
</table>

Compared with the value before injury ¢p < 0.05, ¢¢p < 0.01.; Compared with the value of dry exposed control ** p < 0.01.

| Table II- Water evaporation of wounds in Experiment 2 (g/m²/h, x±s) |

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<table>
<thead>
<tr>
<th>Wound (No.)</th>
<th>Before injury</th>
<th>Times after injury</th>
<th>0.5 h</th>
<th>6 h</th>
<th>24 h</th>
<th>48 h</th>
<th>72 h</th>
<th>168 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaseline (n = 16)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.48±0.87</td>
<td>1.60±0.35¢¢</td>
<td>1.76±0.51¢¢</td>
<td>1.64±0.34¢¢</td>
<td>1.78±0.55¢¢</td>
<td>1.77±0.50¢¢</td>
<td>1.79±0.32¢¢</td>
<td></td>
</tr>
<tr>
<td>MEBO (n = 24)</td>
<td>4.67±0.75</td>
<td>5.32±0.09¢**</td>
<td>5.37±0.04¢**</td>
<td>5.29±0.97¢**</td>
<td>5.16±0.82¢**</td>
<td>5.18±0.84¢**</td>
<td>5.30±0.93¢**</td>
<td></td>
</tr>
</tbody>
</table>

Compared with the value before injury ¢p < 0.05, ¢¢p < 0.01.; Compared with the value of Vaseline treatment ** p < 0.01.

| Table III- Water evaporation of Vaseline-treated wounds (Experiment 3) and Mebo-treated wounds (Experiment 2) (g/m²/h, x±s) |
**Gross observation**

In the early phase after injury, wounds in all three experimental groups looked pale or red-white, with inflammatory swelling over the level of the wound edges. Wound surfaces treated with dry exposed therapy were then gradually dried, lower than wound edges with contractive crust formation. Wounds treated with MEBO were always kept moist, and tissue swellings subsided 48-72 h post-burn. Necrotic tissues then began to liquefy from the surface inwards and were removed. In Experiment 2, MEBO-treated wounds healed more quickly than dry exposed wounds, the difference being statistically very significant (p < 0.01) (Table IV). The wounds treated with Vaseline in Experiment 3 became macerated after 6-8 h and further deteriorated, with serious and long-persisting tissue oedema. Seven days post-burn most of the Vaseline-treated wounds were infected, and even normal skin surrounding the wound showed a serious inflammatory reaction.

<table>
<thead>
<tr>
<th>Wounds</th>
<th>Number of wounds</th>
<th>Healing time days</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry exposed</td>
<td>24</td>
<td>19.80 ±2.61</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>MEBO</td>
<td>24</td>
<td>15.00 ±1.16</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

**Table IV** - Comparison of healing time of different wounds in (Experiment 2) (x±s)

**Pathological examination**

All the wounds in the three experimental groups proved to have the pathological changes of deep second-degree burn injury, and these pathological changes were almost the same half an hour post-burn. After 6 h, the injured tissue became loose, and there was vacuolar degeneration of cells, together with rarefaction of fibre tissues. The changes were most serious in Vaseline-treated wounds. Micro blood vessels were dilated and presented thrombi and infiltration of a few white blood cells. After 24 h, in dry exposed treated wounds, the coagulation zone of necrosis expanded and deepened continuously. The microcirculation was further blocked with thrombi, and there was infiltration of a large number of inflammatory cells, mainly neutrophils. After 48 h, a zone of leukocyte infiltration formed around the junction of necrotic and surviving viable tissues. This phenomenon became increasingly obvious as time passed. In MEBO-treated wounds, tissues in the zone of stasis began to recover. Micro blood vessels were still in a state of dilation and congestion. The infiltration of inflammatory cells spread around the micro blood vessels, after which these cells concentrated at the junction of necrotic tissue and where MEBO was applied, forming a dense area after 48 h.

Pathological changes in Vaseline-treated wounds were quite different from those seen in MEBO-treated wounds. The vacuolar degeneration of tissues was more serious and inflammatory reactions were diffuse. Seven days post-burn, most of the Vaseline-treated wounds were infected. Wounds MEBO-treated healed with integral structure and very few scars. Dry exposed therapy treated wounds healed with capillary proliferation and incomplete regeneration of the epidermis and dermis.

**Discussion**
The skin is the largest organ and one of most important in the human body. Burn injury destroys the body surface barrier. In the early post-burn period, one of the most important pathophysiological changes is the increase in capillary permeability. Injured skin loses its ability to prevent over-evaporation of water from the body. This results in an excessive loss of body fluid, as also of a large amount of plasma protein and electrolytes from the lesion area, plus a decrease in the effective circulatory blood volume - this is an important cause of the onset and development of burn shock.

After a burn, some body fluid exudes into the intercellular space and causes oedema, owing to high capillary permeability, and part of the body fluid is lost through wound evaporation. The inhibition of loss of body fluid through wound evaporation is therefore an important measure for the reduction of burn shock morbidity and for lessening the severity of shock. In addition, if nothing is done to prevent over-evaporation, the burn wound will deepen and be aggravated by dehydration and progressive necrosis. In deep second-degree burn wounds, injured tissue in the stasis zone is revivable, although excessive drying will cause irreversible pathological changes in the tissue. This is the disadvantage of conventional dry exposed therapy.

It is well known in pathophysiology that a moist environment is favourable to the regeneration and repair of injured tissue. Great effort has therefore been devoted to the creation of an environment in which the burn wound can be exposed without dehydration or maceration. One of the key ways to maintain water in burn wounds is to prevent over-evaporation. We found that wounds treated with dry exposed therapy had a very high evaporation capacity after burns, i.e. 19.05 times that of normal skin and 15.72 times that of MEBO-treated wounds. The results of this study showed that both MEBO and Vaseline were capable of inhibiting wound evaporation. In the early post-burn period, the evaporation capacity of wounds treated with MEBO was close to that of normal skin (1.19 times that of normal skin) and significantly lower than that of wounds treated with dry exposed therapy (p < 0.01).

Conversely, the inhibitory capacity of Vaseline was excessively strong and the water evaporation of Vaseline-treated wounds was much lower than in normal skin. MEBO is different from other medical lubricants or ointments, such as Vaseline or Vaseline-based ointments. It retains wound moisture but preserves good venting quality in the wound surface. Excess water can permeate through the MEBO ointment layer and evaporate or be removed. In contrast, Vaseline treatment induces over-wetness of the burn wound and maceration. The difference between water evaporation in MEBO-treated wounds and Vaseline-treated wounds was very significant (p < 0.01). What attracted our attention was the finding that although water evaporation in MEBO-treated burn wounds was significantly increased compared with that of normal skin (p < 0.05), the difference between the mean values was not marked. This suggested that MEBO has a sebum-like water-retaining ability. MEBO maintains wound moisture without affecting drainage and is therefore good for creating a moist environment for wound repair and healing.

It is known that after a burn there is a zone of thermally injured but viable tissue in the deep part and the surroundings of coagulated tissue, i.e. the zone of stasis. Blood flow in micro blood vessels in this zone reduces progressively post-burn and is very susceptible to further injury. Dehydration or mechanical injury will cause tissue necrosis in this stasis zone. In this study, the pathological process of wound tissues treated with conventional dry exposed therapy was consistent with this process. On the contrary, MEBO inhibited the development of the process because secondary injuries such as dehydration were avoided, and MEBO promoted tissue recovery in the stasis zone. MEBO has been shown to promote wound tissue regeneration and repair. In this study, MEBO-treated burn wounds healed more quickly than wounds treated with dry exposed therapy (p < 0.01). This result cannot be attributed to the moisture-maintaining effect of MEBO alone, but without a moist environment it is hard for any medication to succeed. Vaseline treatment also kept the wound wet, but maceration caused pathological...
changes in wound tissues quite different from those seen with MEBO treatment. On the basis of the results of our experiment, we consider that MEBO provided a moist physiological environment that was favourable to wound tissue regeneration and repair. After healing, water evaporation in MEBO-treated wounds returned to normal levels, without any statistical difference (p > 0.05). In dry exposed wounds, water evaporation remained at a higher level after healing (about 3.60 times that of normal skin). We believe that this finding may have been due to the structure of rabbit skin, which has very few sweat glands in skin tissues - water evaporation does not depend so much on sweating as on the skin structure. MEBO-treated wounds healed with integral structure and very few scars. The sebaceous glands regenerated with good function and few proliferated capillaries. In contrast, dry exposed therapy treated wounds healed with capillary proliferation and incomplete regeneration of the epidermis, dermis, and skin appendages. The results of our study indicated that MEBO effectively prevented excessive loss of body fluid from wound evaporation throughout the course of burn wound treatment. It was beneficial to shock resuscitation and the prevention of hypertonic dehydration after thermal injury. The unique dosage form and pharmacokinetic features of MEBO are considered to be responsible for its moisture-maintaining effect. The following aspects may account for the mechanism of its action:

1. MEBO has a unique dosage form with a frame structure; when applied to a wound, it warms up and creates an equilibrium of two phases, liquid and semi-solid. The ointment layer isolates the wound from external irritation and prevents excessive water evaporation from the wound surface.
2. The MEBO base contains hydrophilic and lipophilic groups and has high surface activity. It has a higher affinity to the wound tissues than water and thus forms a strong adsorptive film on the wound surface, protecting it from maceration and dehydration.

Conclusions

This study showed that burn wounds treated with MEBO had markedly less water evaporation than burns treated with conventional dry exposed therapy, while wound water evaporation was nearly the same as that of normal skin. Unlike Vaseline, MEBO offered good air permeability and allowed active drainage. Excess water and exudate can thus evaporate or be removed. MEBO can provide a moist physiological environment that is favourable to wound healing.

Bibliography

