Abstract

One hundred and thirty-eight (138) patients, with five hundred and sixty-six (566) different burn sites with different degrees, severity and locations, were enrolled to a multicenter clinical trial at 25 study centers. The goal of this trial was to evaluate the efficacy of MEBO (Moist Exposed Burn Ointment) in the treatment of burn wound. Various parameters were studied including: (i) healing time, (ii) need for pain killers, (iii) consumption of i. v. Fluids, (iv) use of systemic antibiotics and (v) aesthetic appearance. There was remarkable decrease in the healing time and most patients either did not need any pain killer or were relieved with only mild analgesics, except in few cases of deep second degree and third degree burns. A decrease in the volume of i. v. fluids needed was also reported. Only 19% of cases developed clinical infection, especially in those who were not treated with MEBO immediately post burn. Even though systemic antibiotic treatment was prophylactically implemented in most cases as a routine measure, 32 cases did not receive any antibiotic prophylaxis with MEBO and yet did not develop any infection. The aesthetic appearance reported was very acceptable. This treatment modality was not associated with any side effects, and patient discomfort during application and change was negligible. Thus, MEBO treatment was associated with excellent and relatively faster healing, low incidence of wound infection, and excellent patient compliance.

Key words: MEBT, MEBO, Multicenter, Middle East, Julphar

Introduction:

Changes in wound care over the past thirty years including the use of effective topical antimicrobial chemotheraphy and excision of the burned tissue to achieve timely closure of the burn wound, have significantly reduced the occurrence of invasive burn wound infection and its related morbidity and mortality. Many modalities have been followed under both the exposure and the occlusive techniques. The exposure technique is based on drying the burn wound to enhance the formation of a scab underneath which the burn heals either with scarring or with skin grafting after excision(1, 2). Topical antibiotics, including silver sulfadiazine are used to prevent bacterial invasion (3, 4). The limitations of the exposure technique are:

(i) loss of body fluids is high
(ii) the semi-viable cells are forced to die (6)
(iii) topical antibiotics delay healing (7), and
(iv) relatively high scar formation (8)

Recently, carefully controlled experiment studies as
well as clinical experience have supported the belief that wounds heal better in the moist environment provided by the occlusive dressings (9-12). This belief is based on the fact that wound healing in terms of epithelialization, i.e. keratinocytes migration, proliferation and differentiation, is favored in a moist-rich environment (11). Thus, the better understanding of the wound pathophysiology lead to the development of more effective treatment.

In line with this better understanding was the development of MEBT (Moist Exposed Burn Treatment) and MEBO (Moist Exposed Burn Ointment) in the mid 80's by Professor Xu Rongxiang of the Beijing Guangming Chinese Medicine Institute for Burns, Wounds and Surface Ulcers (13). Composed of b-sitosterol as a major active constituent in addition to other constituents including baicalin and berberine, all of natural herbal origin, dissolved in refined sesame oil as base with beeswax as preservative, MEBO provides the optimum physiological environment for wound healing (13). By virtue of its active ingredients and special formula, MEBO isolates the wound bed from the invasive environmental factors and reduces body fluids loss, produces an anti-inflammatory and anti-edema effect, reduces pain tremendously, controls bacterial and fungal invasion, improves local microcirculation and thus recovery of the semi-viable cells and promotes healing with minimal scarring and acceptable aesthetic results (6, 13). Many studies have confirmed the above effects of MEBO, whether in experimental models (14, 15) or in clinical practice (16, 17).

The aim of this study was to explore the therapeutic effectiveness of MEBO and to gain more experience in its use in the Middle East.

**Materials and Methods**

A total of 138 patients 2 months to 70 years of age having different degrees of burn injuries with an average total body surface area (TBSA) of 15.1% were enrolled and completed the study at 25 centers in the Middle East (United Arab Emirates, Saudi Arabia, Kuwait, Qatar, Egypt and Jordan). The study protocol was prepared in accordance with FDA guidelines and in line with the declaration of Helsinki and was presented to and approved by the participating doctors before its initiation. Written informed consent was obtained form participating patients or their guardians. The study was designed as phase IV post marketing trial to evaluate the efficacy, safety and cost effectiveness of MEBO in acute burn wounds. Wound management was assessed in terms of time needed for healing, i.v. fluids consumed, need for analgesics, control of infection, need for skin grafting, aesthetic appearance, adverse reactions, patient compliance and overall cost of treatment.

Patients were 65% males and 35% females, and 35% of them had dark skin complexion. The source of thermal injury was direct flame in 44% of cases, scald in 45%, and the rest were due to either electric burn, chemical burn or friction.

The number of burn sites treated was 566, as follows:

- Upper arm: 21 sites
- Fore arm: 69 sites
- Hand: 61 sites
- Thigh: 60 sites
- Leg: 66 sites
- Foot: 49 sites
- Buttocks: 21 sites
- Genitalia: 7 sites
- Head: 63 sites
- Neck: 57 sites
- Anterior trunk: 72 sites
- Posterior trunk: 20 sites

The range of body surface area treated was 0.5%-40%, with the following distribution:

- 65%<15%
- 27%<15%-30%
- 8%<30%-40%

Most of the cases were deep second degree burns, as follows:

- 9% were first degree
- 71% were second degree (20% superficial and 51% deep)
20% were third degree
Initiation of treatment was within the first 8 hours postburn in 75% of first degree burns and 92% of second and third degree burns, but few reported rather late to the different centers (3-4 days), especially those with first degree burns.

Test Material
MEBO (Moist Exposed Burn Ointment) manufactured by Gulf Pharmaceutical Industries-Julphar under licence from Beijing Guangming Chinese Institute for Burns, Wounds and Surface Ulcers, RP China.
Pack size: 30 gm.

Results
Various parameters were studied to assess burn wound management in this multicenter study. Table 1

1-Analgesia
Five to ten minutes after application, MEBO induced a strong analgesic effect that 58% of first degree, 41% of second degree and 39% of third degree patients did not need any pain killer concomitantly with MEBO. The rest who asked for pain killers were relieved by mild analgesics, mostly paracetamol, and only 14% of second degree and 21% of third degree patients needed strong analgesics (pethadine).

2-Control of Infection
Although prophylactic use of systemic antibiotics was initiated in most of the cases as a routine regimen, 35% of second degree burn cases and 11% of third of third degree did not receive any systemic antibiotic with MEBO and did not develop any infection, except in one cases of second degree burn which developed local infection at the beginning, but maintained on MEBO alone which controlled the infection thereafter.

3-Healing Time
First degree burns healed within an average of 6 days, second degree burns 20 days and third degree burns 35 days. The end point for healing was complete epithelialization and retain of functions in movable parts (hand, neck).

4-I. V. Fluids
There was a remarkable reduction in the volume of fluids needed, and 47% of patients with second degree burns and 18% of those with third degree burns, all with TBSA between 1% and 19%, did not receive any infusion.

5-Skin Grafting
Almost all of second degree burns, with TBSA ranging between 0.5%-35% epithelialized without grafting, except in 2 cases, one with 6% TBSA and the other with 12.5%, where grafting was initiated. 6 cases of third degree burn with TBSA range of 16%-28% also did not need grafting.

6-Complication
a. Infection: 112 cases, 32 of them were on MEBO alone without receiving systemic antibiotic, did not develop any signs of infection during the course of treatment with MEBO until healing. Local infection was reported only in 15.9% of the cases, systemic infection in 1.4% and systemic and local in 1.4%. Infected cases were maintained on topical MEBO treatment but their systemic antibiotic treatment was changed.
b. Scar Formation: 84% of the cases of second and third degree burns healed with acceptable cosmesis and negligible or no scars. Only 14 cases with second degree burns and 6 cases with third degree burns developed scar, but even in those scars the quality of scar tissue was acceptable as far as tensile strength, color and retain of function are concerned.
c. Hypopigmentation: Only 4% of second degree burns and 7% of third degree burns developed hypopigmentation.

7-Safety
No adverse events were reported with the use of MEBO. Two cases developed hypersensitivity reactions and treatment was discontinued, and two patients complained from the strong odor of the ointment.

Discussion
This study confirms the results of a vast number of studies conducted in China that have shown MEBO to be an effective and safe modality in wound
management (6, 13-17). MEBO enhanced and expedited healing when applied to the acute burn wound. Epithelialization was sufficient for epidermal regeneration in almost all second degree cases which did not require skin grafting. Even some third degree cases, with limited TBSA, healed without grafting. The analgesic effect of MEBO was fast and strong enough to relieve most of the patient within 5 to 10 minutes. Even those who asked for pain killers were mostly satisfied with paracetamol, which usually is not sufficient for severe burn pain. Another indication of MEBO's analgesic effect was the reported ease of dressing change especially in children; some slides showed children sleeping or playing while changing dressing.

32 cases were treated with MEBO alone without systemic antibiotic and yet, did not develop any signs of infection. The anti-infective effect of MEBO has been well documented in China (18). This effect is partly due to the ingredients of MEBO and partly due to the proper method of application. In this study cases which developed infection, mostly local, were maintained on MEBO as topical treatment and only the systemic antibiotic was replaced. Knowing the limitations of the effectiveness of systemically administered antibiotics due to the avascularity of the burned tissue as a result of thermal thrombosis (19), the role of MEBO as local anti-infective is to be considered.

Intravenous fluids are an essential measure in the resuscitation of severely burned patients and is routinely maintain due to excessive fluids loss from the burn wound. With MEBO, it was reported that less volume of fluids is needed to maintain the balance between fluids intake and urinary output. Furthermore, almost one third of the patients with second and third degree burns (47% of second degree, 18% of third degree) were maintained without i.v. supplementation. MEBO isolates the wound and limits fluids loss. This has been well documented in an experimental study on rabbits, using the Servomed Evaporimeter EPIC type to measure wound evaporation (20). It was found that an intact skin has a rate of evaporation 4.48g/m²h. Postburn, evaporation rate was increased 20 fold i.e. to 83.70g/m²h. Covering the wound with MEBO reduced the evaporation rate to 5.69g/m²h. (20).

As MEBO enhances the natural healing processes, proper application reduces tremendously the possibility of scar development, especially when used immediately postburn. In this study, only 15% of the cases developed scar (20 cases), out of which 5 were on different treatment modality and then shifted to MEBO. The quality of scar tissue reported was acceptable, and no contractures have been reported. Almost all cases retained normal skin color after healing with MEBO, and hypopigmentation was reported only in rare cases.

To evaluate the overall cost of wound management with MEBO, the following parameters were taken into consideration: (i) the cost of the medicament, (ii) hospitalization time, (iii) use of dressing, (iv) use of analgesics, (v) use of antibiotics and (vi) i.v. fluids volume needed.

Taking into consideration the reported values and comments on those parameters as discussed earlier, MEBO was found to be a cost effective modality in wound management.
Table 1: Summary of variables and data collected

<table>
<thead>
<tr>
<th>Study Group</th>
<th>First Degree</th>
<th>Second Degree</th>
<th>Third Degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No. Of cases</td>
<td>12</td>
<td>98</td>
<td>28</td>
</tr>
<tr>
<td>2. TBSA</td>
<td>2%-23% (av. 10.0%)</td>
<td>0.5%-35% (av. 14.5%)</td>
<td>1.5%-40% (av. 21.3%)</td>
</tr>
<tr>
<td>3. No Pain Killer</td>
<td>59%</td>
<td>41%</td>
<td>39%</td>
</tr>
<tr>
<td>- Only paracetamol</td>
<td>41%</td>
<td>45%</td>
<td>40%</td>
</tr>
<tr>
<td>- Pethadine</td>
<td>-</td>
<td>14%</td>
<td>21%</td>
</tr>
<tr>
<td>4. No Systemic Antibiotic</td>
<td>100%</td>
<td>35%</td>
<td>11%</td>
</tr>
<tr>
<td>5. Healing Time</td>
<td>6 days</td>
<td>20 days</td>
<td>35 days</td>
</tr>
<tr>
<td>6. No L.V. Fluids</td>
<td>100%</td>
<td>47%</td>
<td>18%</td>
</tr>
<tr>
<td>7. Skin Grafting Initiated</td>
<td>-</td>
<td>2%</td>
<td>79%</td>
</tr>
<tr>
<td>8. Infection</td>
<td>-</td>
<td>19%</td>
<td>25%</td>
</tr>
<tr>
<td>- Systemic</td>
<td>-</td>
<td>1%</td>
<td>4%</td>
</tr>
<tr>
<td>- Local</td>
<td>-</td>
<td>18%</td>
<td>14%</td>
</tr>
<tr>
<td>- Systemic and Local</td>
<td>-</td>
<td>-</td>
<td>7%</td>
</tr>
<tr>
<td>9. Scar</td>
<td>-</td>
<td>14%</td>
<td>21%</td>
</tr>
<tr>
<td>10. Hypopigmentation</td>
<td>-</td>
<td>4%</td>
<td>7%</td>
</tr>
</tbody>
</table>

References:

8. Hammond MA. Moist wound healing: breakdown the dry barrier. Nurs Mirror 1979 Nov I; 149(18):38