What is the Safety and Efficacy of Biobrane Versus Silver Sulfadiazine in the Treatment of Low Body Surface Area Partial-thickness Burns?

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“What is the safety and efficacy of Biobrane versus Silver Sulfadiazine in the treatment of low body surface area partial-thickness burns?”

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ABSTRACT:

OBJECTIVE: To determine how the synthetic skin substitute Biobrane® compares to silver sulfadiazine (SSD, Silvadene®) in the treatment of patients with low body surface area partial thickness burns.


DATA SOURCES: Randomized controlled trials comparing Biobrane with silver sulfadiazine were identified from MEDLINE, The Cochrane Central Registrar of Controlled Trials, and BioMed Central.

OUTCOMES: Measured outcomes included: healing time, length of hospital stay, amount of pain, and development of treatment complications.

RESULTS: Three trials comparing Biobrane to silver sulfadiazine found a significantly decreased amount of healing time in those subjects treated with Biobrane. Two of the three trials studied and found a significantly decreased length of hospital stay and a significantly decreased amount of pain in the Biobrane-treated subjects. Each of the three trials reported complications, which were not significant when comparing Biobrane to SSD. After combining the studies, calculations showed an overall decrease in the healing time, pain scores, and length of hospital stay.

CONCLUSIONS: Evidence provided by these three trials suggests Biobrane is more effective than silver sulfadiazine at reducing healing time, length of hospital stay, and amount of pain in the treatment of partial-thickness thermal burn injuries. Although Biobrane does not have the anti-bacterial effects of silver sulfadiazine, the decreased number of dressing changes with Biobrane likely decreases pain and lessens the opportunity for wound exposure to infectious organisms or contaminants. Two of the three studies focused primarily on pediatric patients, however the results were similar throughout all age ranges.
INTRODUCTION:

There are roughly 1 million burn injuries that occur each year, 700,000 of these result in visits to the emergency department.\(^1\) In the United States, as well as much of the world, treatment of partial-thickness burns is accomplished through the use of topical antimicrobials— one of the most common and popular of these being silver sulfadiazine (SSD, Silvadene®). SSD treatment usually consists of daily or twice daily dressing removal, wound debridement, and reapplication of SSD.\(^2,3\) This process is commonly painful and time consuming for the patient or caregiver. A potential alternative to topical antimicrobials is the use of synthetic materials such as Biobrane® to cover the wound site.\(^4\) Biobrane is a semipermeable membrane with porcine (swine) dermal collagen bonded to a nylon and silicon mesh.\(^5\)

A systematic review was conducted to determine how Biobrane compares to SSD with use in the treatment of low body surface area (BSA) partial-thickness (2\(^{nd}\) degree) thermal burns.

METHODS:

Literature searches were performed using the following databases: MEDLINE (1990-2004), The Cochrane Central Register of Controlled Trials (through 4\(^{th}\) quarter 2004), and BioMed Central (1997-2004). Searches were restricted to the English language and human subjects, using the key-words: “burns,” “silver sulfadiazine,” “Biobrane,” “biocompatible materials,” “occlusive dressings,” and “biological dressings.” All randomized controlled trials (RCT) that compared Biobrane with SSD were attempted to be located.

Trials that were included met the following inclusion criteria: (1)-Compared Biobrane with SSD, (2)-Randomization was used, (3)-Studied subjects with partial-thickness thermal burns less than 20% total BSA, (4)-Studied, at minimum, healing time of burn wounds and complications. Exclusion criteria consisted of: (1)-No randomization evident, (2)-Comparing products other
than Biobrane with SSD, (3)-Studied subjects with superficial or full thickness burns, (4)-Studied subjects with burns greater than 20% BSA, (5)-Studied subjects with burn injuries over 48 hours old or wounds that were grossly contaminated or obviously infected.

Each trial was reviewed for the inclusion and exclusion criteria and trial data was reviewed for statistical significance—which was considered a p-value less than 0.05.

RESULTS:

Included Studies

Literature searches and subsequent review revealed three randomized controlled trials. The characteristics of each included RCT study are shown in Table 1. Each of the three trials specifically studied Biobrane and SSD in the treatment of partial-thickness burns. All three of the studies reported wound healing times and complications of treatment. In addition, two of the three trials studied duration of hospital stays, pain levels and the use of analgesics. Two of the three trials focused primarily on pediatric and adolescent subjects, the third included subjects of all ages.

The inclusion criteria for the individual studies allowed percent BSA burned to be as high as 29%; however, the mean burned BSA for each study ranged approximately between 2% and 12%. The limit of 20% burned BSA was observed for this review.

A fourth trial was excluded because it studied TransCyte®—a product that uses a biological material derived from newborn human foreskins cultured on the Biobrane mesh—compared to SSD. Although this trial did show similar results as the included three, it did not specifically study Biobrane; therefore, it was not possible to determine to what extent the results were affected by the biological material coating the Biobrane mesh.
<table>
<thead>
<tr>
<th>Study</th>
<th>Barret 2000</th>
<th>Gerding 1990</th>
<th>Lal 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Study</td>
<td>Prospective, Randomized Controlled Trial (RCT)</td>
<td>Prospective RCT</td>
<td>Prospective RCT</td>
</tr>
<tr>
<td>N-value</td>
<td>20</td>
<td>64</td>
<td>89</td>
</tr>
<tr>
<td>Age (mean yrs)*</td>
<td>Biobrane: 3.1 +/- 0.5 SSD: 3.7 +/- 0.6 (Range: Not reported)</td>
<td>Biobrane: 18.3 +/- 2.6 SSD: 22.1 +/- 3.5 (Range: 8 mo-79 yrs)</td>
<td>Biobrane: 2.8 +/- 0.5 SSD: 3.4 +/- 0.6 (Range: Not reported)</td>
</tr>
<tr>
<td>Burn BSA (mean %)*</td>
<td>Biobrane: 8.9 +/- 4.9 SSD: 7.8 +/- 0.9</td>
<td>Biobrane: 2.0 +/- 0.3 SSD: 2.4 +/- 0.5</td>
<td>Biobrane: 11.8 +/- 1.1 SSD: 11.5 +/- 0.9</td>
</tr>
<tr>
<td>Inclusion Criteria</td>
<td>-0-17 yrs old -Partial-thickness burn -Thermal or scald injury -Burned BSA 2-29% -Admitted within 24 hrs -Clean, non-infected wound</td>
<td>- &gt;2 mo of age -Partial-thickness burn -Burn &lt;24 hrs old -Wounds with “moist, sensate surface” and appropriate capillary refill</td>
<td>- &lt;17 yrs old -Hot fluid, non-grease burns -Superficial 2nd degree (partial-thickness) burns -5-25% of total BSA -In hospital within 48 hrs of burn injury</td>
</tr>
<tr>
<td>Exclusion Criteria</td>
<td>- &gt;17 yrs old -Causes other than thermal or scalding -Full-thickness burns -Time to admission &gt;24 hrs -Contaminated or infected wounds</td>
<td>- &lt;2 mo old -Pregnant -Chemical or electrical burns -Full-thickness burns -Wounds &gt;24 hrs old -History of sulfa sensitivity -Gross contamination -Treated with any topical agent before Emerg Dept arrival</td>
<td>- &gt;17 yrs old -Grease burns and non-scald burns -Burns &lt;5% or &gt;25% BSA -Appear initially to need skin grafting -Full-thickness burns -Burns &gt;48 hrs old</td>
</tr>
<tr>
<td>Withdrawals</td>
<td>0</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Interventions</td>
<td>1% SSD versus Biobrane application</td>
<td>1% SSD versus Biobrane application</td>
<td>1% SSD versus Biobrane application (Note: Burns to head / neck in SSD group were Wanner, Biobrane vs SSD, Pg 4)</td>
</tr>
</tbody>
</table>

* Differences in age and total burn body surface area were not statistically significant, as reported by each study

**Data Analysis**

Data from each study was examined for healing times, amount of pain, length of hospital stay, and number of complications. Two of the trials did not specifically study amount of pain and
length of hospital stay. An overall review of the outcomes from each study can be found in Table 2.

### Table 2

**Overall review of outcomes from studies comparing Biobrane to SSD**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healing time</td>
<td>Decreased in Biobrane group (p &lt; 0.001)</td>
<td>Decreased in Biobrane group (p &lt; 0.01)</td>
<td>Decreased in Biobrane group (p &lt; 0.05)</td>
</tr>
<tr>
<td>Pain scores</td>
<td>Decreased in Biobrane group (p &lt; 0.001)</td>
<td>Decreased in Biobrane group (p &lt; 0.001)</td>
<td>---</td>
</tr>
<tr>
<td>Complications</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>Decreased in Biobrane group (p = 0.017)</td>
<td>---</td>
<td>Decreased in Biobrane group (p &lt; 0.05)</td>
</tr>
</tbody>
</table>

Differences noted were all statistically significant

“---” indicates that the study did not report or specifically study the outcome

“NS” indicates no statistically significant difference between the Biobrane and SSD groups

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### Healing Time

Healing time was defined relatively similarly in each of the three studies as the time required to attain complete wound closure or re-epithelialization. One of the studies estimated wound healing time as the midpoint between the date when wound closure was documented in the follow-up note and the previous visit.

After taking into account the number of subjects and combining the mean healing times from each study, an overall mean average healing time was attained, as well as a percentage change between the Biobrane and SSD treatments (Table 3). Overall, healing times were reduced by approximately 61% in subjects treated with Biobrane.

### Length of Hospital Stay

The length of hospital stay was reported in two of the three studies. The total number of subjects were taken into account and mean lengths of stay were combined to produce an overall mean length of hospital stay for each treatment group. The overall length of hospital stay was reduced by approximately 48% in the Biobrane-treated group (Table 3).
Amount of Pain

Pain scores were assessed in two of the three included studies. Each of these two studies assessed pain on a 5 level linear scale, with lower numbers correlating to less pain and higher numbers more pain. Because the Barret study assessed pain on a 0 to 4 scale, and the Gerding study on a 1 to 5 scale, a uniform scale ranging from 1 to 5 was adopted during analysis and the Barret scores were adjusted to reflect the change. The mean total pain scores were combined, taking into account the number of subjects, and produced an overall mean pain score. The overall pain scores were reduced by 54% in the group treated with Biobrane (Table 3).

<table>
<thead>
<tr>
<th>Outcomes</th>
<th># of studies</th>
<th># of subjects</th>
<th>Biobrane</th>
<th>SSD</th>
<th>Change in Biobrane group (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healing Time</td>
<td>3</td>
<td>151</td>
<td>13.2 *</td>
<td>21.5</td>
<td>- 61.4</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>2</td>
<td>99</td>
<td>2.5 *</td>
<td>5.2</td>
<td>- 48.2</td>
</tr>
<tr>
<td>Pain Scores</td>
<td>2</td>
<td>72</td>
<td>2.1 **</td>
<td>3.9</td>
<td>- 54.0</td>
</tr>
</tbody>
</table>

* Heating time & Hospital stay are reported in days
** Pain scores are reported on a linear scale (1=least pain; 5=most pain)

Complications of Treatment:

Complications of treatment were defined as the apparent development of infection or need for skin grafting after the treatment method had begun. Each of the three studies reported complications. The number of complications were combined, and produced an overall complication of treatment percentage (Table 4). Overall, 5 subjects in the Biobrane group and 4 subjects in the SSD group had complications of treatment. In the Biobrane group 7.1% of subjects experienced a complication, whereas in the SSD group 4.9% had a complication of treatment. For the purpose of complication analysis, Biobrane was considered the “treatment” group and SSD was considered the “control” group. The relative risk of complication was
increased in the Biobrane group, and the absolute risk of complication was 2.2% higher in the Biobrane treatment group. Chi-square analysis shows that the increased number of complications in the Biobrane group is not statistically significant compared with the complications experienced in the SSD group (p=0.33). It should be noted that Biobrane, compared to SSD, has the potential for a unique type of complication: non-adherence to the wound. Two subjects in the Lal study experienced non-adherence of the Biobrane and were analyzed in the Biobrane group as intent-to-treat. For this review, these two subjects were not counted as complications in the Biobrane treatment group because infection or the need for skin grafting did not occur. Had the two non-adherence complications been included, the number of Biobrane complications was still not statistically significant as compared to SSD complications.

**Table 4**

<table>
<thead>
<tr>
<th>Outcome</th>
<th># of studies</th>
<th># of subjects</th>
<th>Subjects w/ Outcome (%)</th>
<th>Relative Risk</th>
<th>Absolute Risk Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications of treatment *</td>
<td>3</td>
<td>151</td>
<td>Biobrane 7.1, SSD 4.9</td>
<td>1.45</td>
<td>- 2.2</td>
</tr>
</tbody>
</table>

* Complications were considered development of infection or need for skin grafting after beginning specific treatment.

**DISCUSSION:**

The findings from this review support the use of Biobrane in the treatment of partial-thickness burns affecting a body surface area of less than 20%. Compared to silver sulfadiazine, Biobrane appears to have a clinically significant reduction in healing time, length of hospital stay, and amount of pain. Fewer dressing changes are necessary and the need for daily debridement of
wound sites is not necessary in patients using Biobrane—this likely has an impact on this lower pain scores demonstrated in the Biobrane treatment group. Complications experienced between the two groups were not significantly different in terms of number of complications. Users of Biobrane, however, must be aware of the potential for the material to become non-adherent to the wound—essentially making a closed wound into an open wound and likely increasing the chance for infection.

**Limitations**

This review has some limitations that should be noted. Attempts to find all available data comparing Biobrane to SSD revealed a number of studies and total number of subjects that remains small. The included studies also focused on varying age ranges and fairly large differences in the percent BSA burned. Therefore, this review has limited power to detect the differences present in a specific age group or a specific percentage of BSA burned.

Each of the included trials appeared to be of fair to good quality, however there were a few limitations noted. All three of the trials did not study each of the outcomes addressed in this review—in fact only two of the outcomes (healing time and complications) were addressed by all three of the included studies. Because of this, results dealing with pain scores and hospital stay have a smaller total sample size and likely have less ability to predict outcomes in the general population. Only one of the three studies (Lal7) specifically mentioned how subjects who withdrew from the study were analyzed.

Although this review suggests that Biobrane appears to reduce the healing time, length of hospital stay, and pain level of subjects; caution must be taken in applying the results of this review to the general population, as the results may be significantly different.
It should also be noted that the American Burn Association recommends referral of partial thickness burns >10% BSA to a burn specialty center. Because a number of the subjects studied in these trials had burns near or slightly above 10% total BSA, the transferability of results to patients with significantly lower percent burned BSA—as may be seen and managed in a primary care or local emergency department setting—must be interpreted cautiously.

Conclusions

Data from this review implies that Biobrane is more effective than SSD at reducing healing time, pain scores, and length of hospital stay in patients with partial-thickness burns affecting a BSA less that 20%. Although complications encountered with Biobrane are similar in number to those encountered with SSD, extra care must be taken when using Biobrane to ensure adherence of the Biobrane mesh to the wound site. In order to more accurately apply these results to the general population, future research employing a larger sample population size and addressing a more specific age range or size of burn wound would be beneficial.

REFERENCES:


