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BIOBRANE® IMPROVES WOUND HEALING IN BURNED CHILDREN WITHOUT INCREASED RISK OF INFECTION

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ABSTRACT—A synthetic bilaminar membrane used as a skin substitute (Biobrane®) has been shown to decrease pain and hospitalization in superficial second-degree burns. Despite these benefits, it has not been utilized universally, particularly in young children, due to a perceived increase in related infections. We propose that when this synthetic membrane is applied to superficial scald burns <25% of the total body surface area (TBSA), decreased healing times are expected without increased risk of infection. Between 1994–1999, 89 children treated within 48 h after receiving superficial partial thickness scald burns covering 5–25% TBSA with no indication of infection were seen at our hospital. Forty-one were assigned randomly to receive treatment with the skin substitute Biobrane and 48 to receive conservative treatment with topical antimicrobials and dressing changes. Comparisons of treatment were made between groups for length of hospitalization, wound healing times, and infectious complications. Children treated with Biobrane or topical antimicrobials were similar in age, race, sex, %TBSA burned, and location of burn. Those receiving Biobrane had shorter hospitalizations and healing times, which was significant for both infants and toddlers and older children. Treatment groups were not different in the use of systemic antibiotics or readmissions for infectious complications. Biobrane was removed in 5.9% of cases for non-adherence. The application of Biobrane within 48 h of superficial burns provides for shorter hospitalizations and faster healing times in children of all ages without increased risk of infection.

KEYWORDS—Scald burns, partial thickness burns, silver sulfadiazine, Biobrane, synthetic skin substitute, burn infection

INTRODUCTION

The skin acts as a protective barrier to evaporative fluid losses and against bacteria and other microbes normally present in the environment. This is done by mechanical exclusion of microbes by the epidermis and immediate activation of host defense mechanisms when bacteria invade into the vascular dermis. Burns pose major threats to this system because of skin barrier destruction, which leads to fluid and electrolyte losses and local invasion of proliferating microbes on the wound that can lead to systemic infection. In the past, these events were managed by administration of increased fluid volumes along with topical antimicrobials to make the burn wound hostile to microbial growth (1).

A skin substitute, Biobrane® (Bertek Pharmaceuticals, Sugar Land TX), has been commercially available since 1979 for the treatment of burn wounds. In the 1980s, this synthetic membrane was recommended for use in partial thickness injuries (2–4) and subsequently has been shown to be effective as a temporary cover to reduce pain and provide a barrier to substantial water loss and bacterial colonization while improving the rate and quality of healing (5–10). Biobrane is a translucent bilaminar flexible silicone membrane bonded to an ultrathin collagen layer, which allows for visualization of the wound bed and allows excellent range of motion when applied over joints (1). Some of its prominent features include nonpenetrance of tissue into the collagen coated silicone surface, resulting in rapid epidermal growth in the wound and easy removal (1) and its ability to adhere to wound surfaces to prevent proliferation of bacteria endogenous to wounds (11). Clinical results show that this skin substitute is effective in controlling bacterial growth in wounds initially containing $<10^5$ bacteria per gram of tissue when good adherence is achieved (1). It is readily available in most hospitals and normally does not require periodic dressing changes which keeps the overall costs low (1, 8, 9).

Despite these reported advantages, some clinicians have been reluctant to use Biobrane in partial thickness burns because of anecdotal evidence of increased wound infection in wound areas where the Biobrane is not adherent. Since Biobrane has no inherent antimicrobial properties, the condition of non-adherence provides a moist protected environment for bacterial overgrowth and potential for invasion. This condition is thought to be particularly prevalent in toddlers and infants who are generally more active, causing non-adherence through shear forces. Soiling of the wounds from excrement is also common in this population. Nonetheless, Biobrane would

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be considered an optimal treatment for this age group, since the most common burn type in these patients is a superficial scald from hot liquids (12).

With this concern in mind, the aim of this study was to determine whether treatment with Biobrane in superficial scald burns covering 5–25% total body surface area (TBSA) will decrease hospitalization and wound healing times without increased risk of infection in all children compared to standard conservative treatment with topical antimicrobials.

MATERIALS AND METHODS

In this prospective study performed from 1994 through 1999, 89 children with scald burns were assigned randomly to receive either Biobrane or conservative treatment consisting of twice-daily dressing changes with topical antimicrobials, typically silver sulfadiazine (Silvadene®). The children studied had 5–25% TBSA partial-thickness scald burns that were treated within 48 h of injury and showed no initial signs of cellulitis or need for grafting. A computer-generated randomization table was used to assign patients to either the Biobrane group or the antimicrobial group. Of the 1280 children admitted acutely to our hospital between 1994 and 1999, 230 received non-grease superficial second-degree scald burns. Our inclusion criteria consisted of superficial second-degree hot fluid scald burns that were 5–25% TBSA and were brought to the hospital within 48 h of injury who did not appear to need grafting. Our exclusion criteria consisted of scalded patients who had burns <5% TBSA or >25% TBSA, arrived later than 48 h from injury, had third-degree burns in addition to their second-degree injuries or were burned by grease. In addition, six patients that otherwise fit the inclusion criteria received grafts and were, therefore, excluded from the study (Fig. 1). Discharge criteria for study patients was not altered from clinical hospital protocol. The Institutional Review Board of the University of Texas Medical Branch, Galveston, Texas, approved this study. Each patient's parent/next-of-kin signed an informed consent form prior to entry into this study.

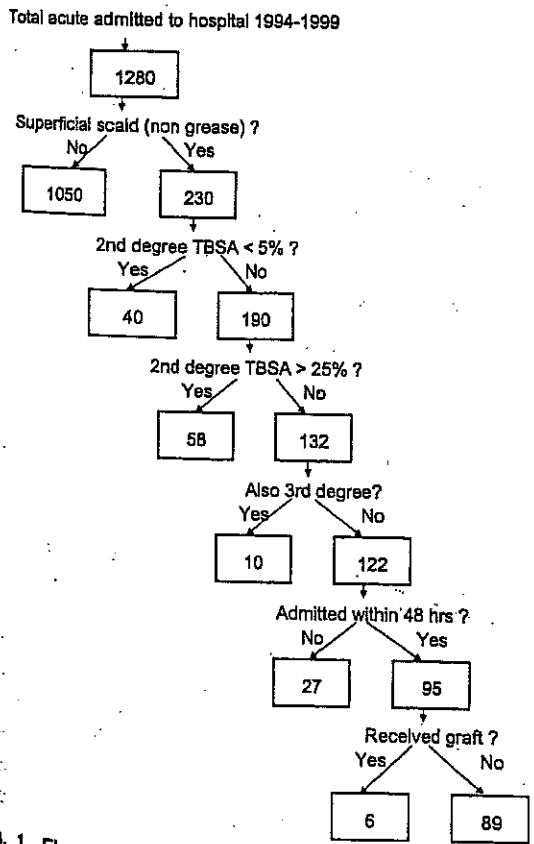

FIG. 1. Flow diagram of patient population broken down to reveal patients included in study versus those excluded from study.

Treatment

Subjects were brought to the treatment room upon arrival to the hospital where intravenous (i.v.) medications, usually morphine (0.03 mg/kg/dose i.v. or 0.1–0.2 mg/kg/dose p.o.) were administered every 2–4 h as needed to control pain. In all subjects, wounds were debrided to remove overlying epidermis using sharp and blunt dissection. If necessary, conscious sedation with ketamine (1–2 mg/kg/dose i.v. or 3–7 mg/kg/dose intramuscularly) was used. Wounds were cleaned with Betadine® followed by copious irrigation. All wounds to the head and neck in both groups were treated similarly with a 1:1 mixture of fine mesh gauze impregnated with 2% polymyxin B-bacitracin ointment (Burroughs Wellcome, Morris Plains, NJ) and 1% nystatin ointment, USP (E. Fougera and Co., Melville, NY).

The Biobrane group received sheets that would be either stapled to the skin or wrapped circumferentially around the extremities and the torso. If hands were covered in Biobrane gloves, they were maintained in an elevated position. After application, the wounds were wrapped with fine mesh gauze impregnated 2% polymyxin B-bacitracin ointment and 1% nystatin ointment followed by dry cotton dressings and elastic bandages. The dressing would remain intact for 12–24 h before an evaluation by the attending surgeon. At this time, if Biobrane was adherent without signs of underlying infection, wounds were covered with dry gauze once a day or left open based on attending surgeon's discretion. If the Biobrane did not adhere to the wound surface, it was removed and conservative treatment was implemented.

Wounds in subjects randomized to topical antimicrobials received silver sulfadiazine (Hoechst Marion Roussel, Inc., Kansas City, MO) following superficial debridement of debris and blisters and cleansing. The dressing changes were done twice a day, which consisted of washing the wounds with soap and water followed by application of Silvadene-impregnated fine mesh gauze and dry cotton dressings and elastic bandages until full wound healing was achieved. While in the hospital, dressing changes were done by hospital staff. Upon discharge, parents were given instructions for its application.

Outcomes

The outcomes used for comparison were; length of hospital stay, number of days for wound(s) to heal, need for oral antibiotics after acute hospital discharge, hospital readmission for infection/sepsis, or need for skin grafting. Patients were seen in the clinic at regular intervals after hospital discharge. Wound healing times were based on the midpoint between the date of physician's clinic note stating that all wounds were closed and the previous visit. We interpolated that the wounds finally closed between these last two visit dates. Subjects were excluded if they did not return to follow-up clinic after discharge or the time between their final two visits was greater than two standard deviations from the population's average (i.e., the final visit was at least 21 days after the previous visit). This extreme length of time does not allow adequate clinical monitoring of the wound and would have resulted in vague assessment of its healing time.

A post-hoc stratification of subjects into toddlers and infants (ages 0–3) and children (age >3) was done to assess differential effects among age groups. Statistical analysis was by t test, χ^2, or Fisher's Exact test where appropriate.

RESULTS

Eighty-nine patients randomly assigned to receive Biobrane ($n = 41$) or Silvadene ($n = 48$) for treatment of their superficial second-degree scald burns were studied. There were seven subjects who were admitted late at night by on-call surgery residents. These residents consistently chose a treatment type based on the preference of their on-call attending. Therefore, the treatment for these patients depended on the rotating attending call schedule, removing overall biased assignments to a particular group. We felt that since those subjects received unbiased treatment they could be enrolled in

TABLE 2. Treatment complications

Silvadene (n = 45)	
Oral antibiotics*	1/45 (2.2%)
Hospital readmission	0
Skin graft required	0
Biobrane (n = 34)	
Oral antibiotics*	1/34 (2.9%)
Hospital readmission	0
Skin graft required	0
Biobrane failure†	2/34 (5.9%)

*Outpatient clinic evaluation resulted in prescription of oral antibiotics for suspected infection.
†Biobrane was removed early due to non-adherence without suspicion of underlying infection.

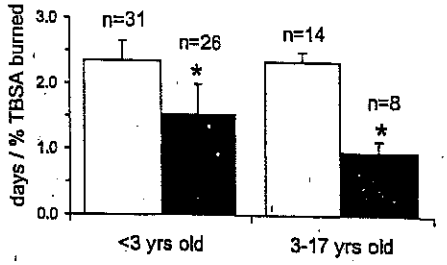

FIG. 4. Comparison of time to heal per % TBSA burned for Biobrane (filled bars) versus Silvadene (open bars) treatment in children <3 years of age and 3–17 years of age. Mean + SEM; *P < 0.05 by Student's t test.

generates less pain than dressing changes necessary for topical antimicrobial treatment of second-degree burns (5–9), providing another potential advantage. We have shown that Biobrane treatment is efficacious and safe in terms of infectious complications for toddlers and infants as well as older children. We therefore recommend the use of Biobrane regardless of age in the treatment of partial thickness scald burns.

Our study was not blinded. It is possible that there was a potential bias during discharge evaluation of the patient. This sort of problem arises in clinical trials since some degree of blindness may not be feasible in a trial where the variables are grossly visible, as with Biobrane. However, blindness is an important strengthening feature that should be used whenever possible. We could have included variables such as histological slides that could have been blinded to the examiner (13). Despite these limitations, we feel that our results are valid because clinical criteria not specific to the study were used for discharge evaluation.

In this study, we chose to include only patients with superficial scald burns. We did not include patients who were initially assessed with second-degree wounds of intermediate or deep depth. However, two applications of Biobrane failed complete adherence. It is probable that the *zone of stasis* in these wounds proceeded to coagulative necrosis because local blood flow was not maintained (14), converting a superficial to an intermediate or deep second-degree burn. At this point, Biobrane may lose its adhesive capability. It is possible that other patients' wounds experienced this same type of transition from superficial to deep second degree burn and Biobrane still succeeded as a temporary covering. On the other hand, it must be emphasized that scald burns can be of an indeterminate depth on initial examination, and are problematic in terms of the optimal treatment because even the most experienced practitioners cannot accurately predict their behavior. The safe course of treatment for such wounds may still lie in conservative treatment until wound depth can be accurately estimated. Currently, burn wound depth is most accurately assessed by the judgment of experienced practitioners (14).

Biobrane treatment failed in 5.9% of cases in this study due to non-adherence. The potential for invasive wound infection is likely to be much higher in these cases if the Biobrane was left in place. Therefore, in these cases we removed the Biobrane in accordance with good medical practice. It must be emphasized that routine surveillance of Biobrane treated wounds avoids complication(s) and ensures the results of this study in routine burn practice.

While no increase in infectious complications was found between groups, type II error for lack of statistical power is one explanation. However, when using our chosen outcome measure for infection (systemic antibiotic use), we showed 2.9% in the Biobrane group and 2.2% in the topical antimicrobial group. As a model for a power analysis, we determined that over 8200 patients would need to be enrolled to determine an increase in infectious complications with Biobrane treatment. A difference requiring this many subjects is probably not clinically significant.

Our study lost 10 of 89 patients to follow-up. Seven of the ten were in the Biobrane group. Attempts were made to contact the patients or their families for follow-up. Many times parents indicated that they saw no open areas after the Biobrane had fallen off and they did not want to return to clinic. The antimicrobial group lost three patients to follow-up. Again, attempts were made to follow up via phone or letter. Once again, parents were satisfied with their child's healing wounds. Demographics were not different in the group that was lost to follow up compared to the group that was studied.

The enrollment criteria for this study went beyond other investigations by extending the time limit from 24 to 48 h after injury. It has been shown that once wound colony counts are $>10^5$ organisms/gram of tissue, Biobrane is not likely to adhere (1). It is also known that burn wound colony counts increase to this range after 24 h (2); therefore, the 24-h time point has been empirically used as a break point for the use of Biobrane. Our results show that Biobrane can be applied up to 48 h after injury, and indicate that further liberalization of this time point might be justified. Further studies to test this contention are currently underway. We did not include a cost analysis in this study. Our non-profit hospital owned by the philanthropic society Shriners International does not charge patients for their care. Therefore, it is difficult to compare our no-cost hospital to the majority of medical care facilities. However, previous investigators have shown that Biobrane's overall cost is less than that of antimicrobial use (1, 8, 9).

Since dressing changes can be very painful and since Biobrane typically does not require more than one dressing change, then it would be expected that patients who have Biobrane would experience less pain. In fact, this has been

phone and/or letter. On a brief review of these attempts, it appears that sometimes the parents did not feel that they needed to bring their child back to the hospital because their child was healed.

In this study we did not evaluate pain, which has been evaluated many times in past studies. These studies have shown a clear benefit of Biobrane over topical antimicrobial treatment in terms of diminished problems with pain. For these reasons, we did not repeat this analysis. Biobrane comes in three different size sheets. The price range is usually between a $100 and $120 per sheet. It sounds expensive, but when you add up the price of antimicrobials plus dressing changes and the nurse's time, medications needed because dressing changes are very painful and that the child stays in the hospital longer, incurring extra hospital cost, it serves to reason that the overall cost is higher for the antimicrobials than for the Biobrane.

The last question was who should not be included in this group for use of Biobrane. I attempted to be as specific as I could in describing the inclusion group. Only superficial second degree burns <25% TBSA admitted within 48 h were included, and I think we have shown that Biobrane treatment is effective in this kind of patient. To extend these parameters, Biobrane might be used in larger burns with a greater period of time between burn and initial treatment. These studies are currently underway. Thank you.