
Randomized Clinical Study of SilvaSorb® Gel in Comparison to Silvadene® Silver Sulfadiazine Cream in the Management of Partial-Thickness Burns

Paul M. Glat, MD, Wade D. Kubat, DO, John F. Hsu, DO, Tarek Coptly, MD, Brooke A. Burkey, MD, Wellington Davis, MD, Isak Goodwin, MD

This prospective, randomized study assessed the clinical, microbiological, and patient comfort characteristics of two silver-based topical agents in the management of partial-thickness burn wounds. Pediatric patients were randomly assigned to treatment with either SilvaSorb® Gel (Medline Industries, Munedelein, IL) or Silvadene® silver sulfadiazine cream (King Pharmaceuticals, Bristol, TN) for up to 21 days or to the point of full reepithelialization of the wound. Inclusion criteria were patients ranging in age from 2 months to 18 years with TBSA ranging from 1 up to 40%. A total of 24 patients were enrolled and completed the study. Findings demonstrated that the use of SilvaSorb Gel was associated with less pain and greater patient satisfaction when compared with Silvadene. No statistically significant differences were found when assessing the rate of infection, time to reepithelialization, or the number of dressings changes required during treatment. The reduction of pain and improved overall patient satisfaction with the use of SilvaSorb Gel compared with Silvadene indicates an important role for SilvaSorb Gel in treatment of partial-thickness burns in a pediatric population. (*J Burn Care Res* 2009;30:262–267)

Topical antimicrobials are the standard of care in the treatment of burn wounds because of their ability to reduce the incidence of wound sepsis. Silver sulfadiazine (SSD) cream is the definitive standard in the treatment of burns because of their relative ease of application, wide efficacy profile, and availability in most hospital formularies. SSD cream is a soft, white, and water-soluble topical, which contains 10 mg of active silver antimicrobial (silver sulfadiazine). Aside from the active antimicrobial, SSD contains a mixture of white isopropyl myristate petrolatum, sorbitan monooleate, stearols, polyoxyl 40 stearate, propylene glycol, and water. SSD cream is generally considered a good choice for partial-thickness wounds as it allows wounds to heal without the need for surgical intervention or skin grafting. Offsetting the bene-

fits of SSD topical treatments are the reported side effects that include allergic reactions or sensitivity, frequent and painful dressing changes, delayed healing, and staining/discoloration of the wound bed, which confound wound evaluation and depth determination.¹

Advances in burn management have greatly improved survivability from severe burn injuries, with new wound care products focusing on effective moisture management,² control of infection and improved healing, while resolving limitations and/or side effects of current treatments. Newer topical treatments such as SilvaSorb® Gel (Medline Industries) have been developed to address the potential side effects of SSD, while maintaining rapid healing, increasing ease in application, ability to reduce bioburden, and improving patient comfort.³ SilvaSorb Gel is an amorphous, biocompatible hydrogel with a unique Micro-Lattice structure in which the scaffolding stabilizes the silver ions. The product is effective for 3 days thus not requiring daily dressing changes.³ The hydrogel has the advantage of being transparent, nonirritating, nonsensitizing, and excellent with fluid management. The product has also been shown in vitro to possess excellent fluid management and wound healing properties, while controlling wound bioburden

From the Department of Plastic Surgery, St. Christopher's Hospital for Children, Philadelphia, Pennsylvania.

Address correspondence to Paul M. Glat, MD, St. Christopher's Hospital for Children, Erie Ave at Front Street, Philadelphia, PA 19134.

This research was supported through Drexel University School of Medicine by Medline Industries.

Copyright © 2009 by the American Burn Association. 1559-047X/2009

DOI: 10.1097/BCR.0b013e318198a2e8

without being toxic to host cells such as fibroblasts and keratinocytes.^{4,5} It also functions without staining the surrounding skin and wound or forming a pseudoeschar. However, SilvaSorb Gel has not been extensively studied in a clinical burn setting. As a result, this study was designed to compare SilvaSorb Gel to the standard of care topical burn treatment, SSD, in the treatment of partial-thickness burn wounds in pediatric patients.

METHODS

Pediatric patients presenting to our unit with superficial and mid-dermal burn wounds were considered eligible if they were at least 2 months of age and not greater than 18 years of age and sustained their burn injuries within 36 hours of enrollment. The burn size needed to range from 1% but not greater than 40% of TBSA and the patients or their parents were able to consent to both inclusion in the study and treatment until their wounds were completely healed. The study was designed to be carried out for 21 days, but all patients were followed until complete healing. Major exclusions included burn wounds associated with either electrical or chemical injury, deep or full-thickness burns, the subject's prognosis was unlikely for survival past the study duration, the patient's burn site had been previously treated with an antimicrobial agent or a debriding with an enzymatic agent, the patient had been previously entered into a similar study, or was pregnant. Burn injuries progression with an increase in burn depth requiring wound closure or surgical intervention was criteria to withdraw patients from further participation in the study. All patients were recruited into the study from a population of

patients at the Burn Unit at St. Christopher's Hospital for Children, Philadelphia, Pennsylvania. Patients were provided with informed consent to participate in the study and the protocol was approved by the institutional review board.

A total of 24 patients were prospectively enrolled into the study, with a goal of at least 20 patients meeting the definition of "protocol correct," prior to randomization into either a control group with treatment with Silvadene® silver sulfadiazine cream (King Pharmaceuticals) or into a study arm with treatment with SilvaSorb Gel. Eligibility was established by completion of the written informed consent, fulfillment of the inclusion criteria, and with no exclusions being met. The study was scheduled until full reepithelialization of the wound occurred.

After eligibility was established, an initial evaluation was performed on each patient, which included subject demographics, medical history, and a baseline assessment of the burn injury with photographic documentation. TBSA standard formulas, as appropriate for the age of the subject, along with Lund and Browder charts were provided in the Clinical Research Form and used in the determination of the extent of the burn injury.

Patients were randomly assigned to a protocol of care that included either SSD cream or SilvaSorb Gel, without blinding of the physician investigator or other medical personnel to the type of treatment. Figure 1 summarizes the treatment protocol for each arm of the study.

Under the study protocol, patients received an initial evaluation that included medical history, subject demographics, and baseline assessment of the burn

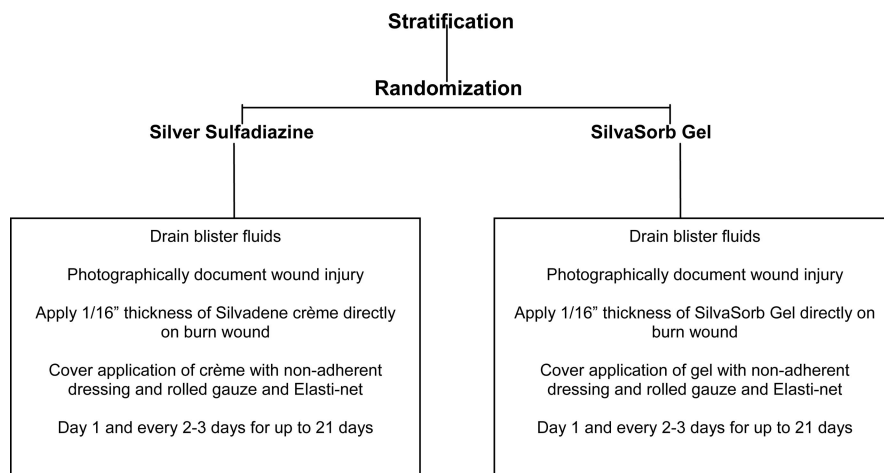


Figure 1. Treatment Protocol—SilvaSorb gel vs silver sulfadiazine (SSD). Each product was used in a similar fashion with daily dressing changes until complete reepithelialization was observed.

injury. Dressing changes were scheduled to continue until complete healing. Subjects were instructed to visit the clinic for evaluation once every 2 to 3 days and complete requisite dressing change forms. Outpatients and/or their guardians were allowed to change their own dressing and were provided with general practice instructions of the burn center and on the use of the topical treatments.

The initial treatments as well as each dressing change were documented on the wound assessment, dressing change, home dressing change forms and included in the CRF. Data were recorded during the initial treatment and subsequent changes included details on the treatment application, status of the burn, number of dressing changes between evaluations and any adverse findings or events. Study endpoints that were recorded included the following: a) time to full reepithelialization, b) pain during dressing changes utilizing an age-specific pain rating scale measured just after the first postdebridement dressing change, c) number of dressing changes, and d) patient satisfaction as assessed by a parental or patient questionnaire.

A descriptive statistical analysis was used to examine the distribution of continuous variables and included frequency histograms for categorical variables for each of the treatment groups. In nonnormal distributions, transformations were used to normalize the data for statistical analysis. In some cases, exact methods were employed when the expected frequencies were small. Statistical significance was defined as a two-sided P -value with 95% confidence intervals. For all study endpoints, a P -value of less than or equal to 0.05 was considered significant. Substantial equivalence of the treatment groups with respect to wound infection was assessed via Blackwelder's method of testing equivalence. The percentage of patients achieving full reepithelialization within 21 days was assessed utilizing a chi-square test, with exact test being used in

cases where expected frequencies are small. The percentage of reepithelialization at 21 days was compared between groups using t -test or Wilcoxon's rank sum test, with the time to full reepithelialization compared utilizing Kaplan-Meier estimates and a log-rank test. The number of dressing changes was assessed via the use of Wilcoxon method.

RESULTS

A total of 24 pediatric patients were enrolled into the study and randomly assigned to a protocol of care that included either SSD cream ($n = 12$) or SilvaSorb gel ($n = 12$). Baseline characteristics were comparable between the treatment and control arms of the study with the exception of patient age. Overall mean age of the patients in the Silvadene arm was 22.78 months, with a standard deviation of 13.51 months, compared with the mean age of patients in the SilvaSorb arm at 43.00 months, with a standard deviation of 29.10 months with a significant difference being noted ($P = 0.0291$). Patients ranged in age from 13 months to 5 years in the SSD treatment arm compared with 9 months to 9 years in the SilvaSorb arm. TBSA for the wound injury site was comparable for both study arms and ranged from 1 to 10% TBSA.

Overall pain ratings were recorded based on an age-specific pain rating scale. In older children, the patient's were asked directly to rate their pain on a scale of 1 to 10 or using the Wong-Baker Pain Scale (Figure 2).⁶ In infants and toddlers, pain was determined by the observational pain assessment scale.⁷ Pain ratings were found to be significantly less in the SilvasorbGel group when compared with SSD (Table 1), and the results were statistically significant (2.33 vs 5.33, $P = 0.0001$). Also relevant was that proportionately more patients (50%) in the SilvaSorb cohort experienced less pain as registered by a rating between

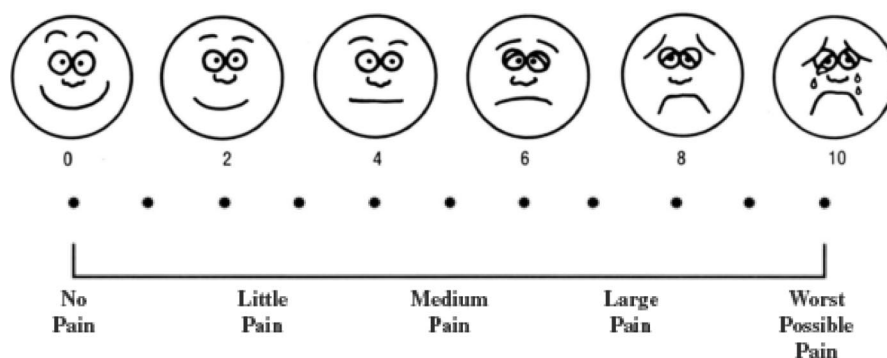


Figure 2. Wong/Baker Faces Pain Scale.

Table 1. Pain rating

Treatment	Mean	Median	SD
SilvaSorb (n = 12)	2.33	2.00	1.07
Silver sulfadiazine (n = 12)	5.33	5.00	1.44
Total (n = 24)	3.83	4.00	1.97

$t(22) = -5.80; P = .0001.$

1 and 4, when compared with the same range in the SSD group (17%). Although there is no specific definitive standard infantile or toddler pain assessment tools, the two scales that were used in this study have been extensively used in previous studies in the burn literature.⁸

The study was designed to be carried out for 21 days but all patients were followed until complete healing was observed. When comparing patients in the SilvaSorb Gel treatment group, proportionately more reached reepithelialization within the 21-day study duration than those in the SSD treatment group, although the difference in mean time to reepithelialization between groups was not significantly different with a *P*-value of 0.949 (Table 2). In two cases, patients in the SSD treatment group reached reepithelialization after the 21-day study duration, (26 and 28 days) whereas all patients in the SilvaSorb Gel cohort experienced healing within the study duration. In contrast, the furthest point of reepithelialization occurred at only 18 days in one patient in the SilvaSorb Gel group. However, because of small sample sizes, these differences were not demonstrated in the statistical comparisons.

Dressing changes were documented throughout the course of treatment, whether administered within the context of inpatient or outpatient care. Dressing change forms included in the CRF included wound assessment, dressing change (inpatient care), and home (outpatient) dressing change forms. The distribution of the number of dressing changes by treatment arm varied slightly, although there were virtually no differences seen in the total number of dressing being applied, as evidenced in the nonstatistically significant *P*-value of 0.449 (Table 3).

Table 2. Days to re-epithelialization

Treatment	Mean	Median	SD
SilvaSorb (n = 12)	12.42	12.50	3.58
Silver sulfadiazine (n = 12)	12.75	9.50	7.45
Total (n = 24)	12.58	10.50	5.72

$S = 136.50; P = .449.$

Table 3. Number of dressing changes

Treatment	Mean	Median	SD
SilvaSorb (n = 12)	13.50	13.00	4.70
Silver sulfadiazine (n = 12)	13.42	10.00	8.26
Total (n = 24)	13.46	11.50	6.57

$S = 165.50; P = .383.$

Patient satisfaction was evaluated by questionnaire using a 1 to 4 point scale, with 1 equating to being “unsatisfied” and 4 being “extremely satisfied,” reflective of the highest possible evaluation. Patients in the SSD treatment arm were found to have a lower satisfaction rating when compared with the patients in the SilvaSorb (Table 4). These data were found to be statistically significant (*P* = 0.004).

Finally, neither group had any burn wound infections or adverse events occur during the course of the study.

DISCUSSION

Topical antimicrobials remain the standard of care in the treatment of partial-thickness burn wounds because of their ability to reduce the incidence of wound sepsis. SSD cream has been the definitive standard in the treatment of burns.¹ However, in this study, the use of SSD was associated with significantly more pain and patient discomfort when compared with the study medication, SilvaSorb Gel. Not surprisingly, this translated to a patient satisfaction rating which was higher with the use of SilvaSorb Gel. The comfort and satisfaction profile are likely due to the unique polymer microlattice composition of SilvaSorb, which provides more moisture to the wound while simultaneously controlling the amount of exudate.³ In addition, the formation of pseudoeschar with the use of SSD would account for increased pain upon removal of the pseudoeschar during the dressing changes.

The microlattice structure of SilvaSorb gel is unique. It is composed of polyacrylamide, cross linker, water, glycerol, and polysaccharide. These components together serve to provide scaffolding for silver stabilization and regulating the moisture within the gel. The

Table 4. Patient satisfaction rating

Treatment	Mean	Median	SD
SilvaSorb (n = 12)	3.25	3.00	0.75
Silver sulfadiazine (n = 12)	2.17	2.00	0.72
Total (n = 24)	2.71	3.00	0.91

$S = 198.00; P = .004.$

microlattice allows oxygen to penetrate to the wound surface while minimizing the moisture from escaping to the surface. Moisture enters the gel and interacts with the silver within the scaffold. The interaction mobilizes the silver component and allows the silver to be diffused to the wound site. Previous study demonstrated ionic silver reservoir release at an average rate of 1.5 ppm. SilvaSorb gel maintains a level of ionic silver that is effective against a wide-spectrum of microbes without harming healthy tissues within and around the wound site.^{4,5,9}

This study measured the number of dressing changes for each patient was recorded, with the goal of comparing the cost of each treatment. Two previous studies authored by Caruso et al previously demonstrated the cost effectiveness of utilizing a 7-day burn dressing compared with SSD in partial-thickness burns.^{10,11} The cost savings are related to decreased nursing and physician time associated with fewer dressing changes needed with the 7-day product, despite the increased cost of the product itself. In this study, the number of dressing changes was relatively equivalent; however, SilvaSorb Gel is normally prescribed as a 3-day product and can potentially be left in place for up to 7 days. This study was designed to allow each group to change dressings on a daily basis in order to maintain consistency between groups. The direct costs for this study were not calculated. It can be extrapolated that, similar to the Caruso studies,^{10,11} SilvaSorb Gel when used as recommended every 3 days would have a significant cost savings due to less manpower required for dressing changes. This is despite a slightly increased product cost for the SilvaSorb Gel when compared with SSD.

Reepithelialization rates were found to be equivalent between the two study groups. Because of the above-mentioned recommended 3-day wear time, less frequent dressing changes would occur in clinical practice and this could impact rates of reepithelialization. Less frequent dressing changes allows reepithelialization to progress without disruption, and therefore may correlate with a decrease in the overall time for healing. It must be stressed, however, that in the case of time to reepithelialization (in days) and the number of dressing changes in this study neither endpoint yielded a significant difference. Improvement in these parameters can only be hypothesized in clinical practice with a less frequent dressing change regimen. The small cohort of patients enrolled in this study makes it difficult to compare reepithelialization rates as well as complications between the two groups. However, there were no adverse events seen in this study (including no infections) and there was no significant

difference in rates of reepithelialization. Therefore, for these two variables the two groups demonstrated equivalency. Larger study size would be required to demonstrate significant differences in these areas. The authors also acknowledge the potential bias created from patients changing their own dressings but this should be balanced against the beneficial advantages of data collection and limitations encountered in patient follow-up logistics.

CONCLUSIONS

SilvaSorb Gel was safe and effective at treating partial thickness burns and was associated with significantly less pain and greater patient satisfaction over the course of treatment. Proportionately more patients in the SilvaSorb Gel study group reached reepithelialization within the 21-day study duration when compared with those in the Silvadene treatment group, although the difference in mean time to reepithelialization between groups was not significantly different ($P = 0.949$). All patients in the SilvaSorb Gel cohort reached full reepithelialization before the scheduled 21-day study duration, whereas two patients in the Silvadene arm reached this healing endpoint at 26 days and 28 days. No differences were seen in either the number of dressings. Although no significant differences were noted in the infection rates between the two study groups, this data demonstrated that SilvaSorb Gel showed equivalence with the standard of care in this regard.

Given the sensitive nature of treatment required for burn wounds, especially in the pediatric population, the ability to reduce pain associated with dressing changes and to decrease the number of dressing changes is extremely valuable. This, combined with the ability to improve patient comfort with the use of SilvaSorb Gel, warrants additional investigation of this product in the care of the burn patient. Further analysis in larger patient populations is necessary and should provide more data, including cost analyses, which may prove beneficial in the treatment of burn wounds with this product.

REFERENCES

1. Hollinger MA. Toxicological aspects of topical silver pharmaceuticals. *Crit Rev Toxicol* 1996;26:255–60.
2. Madden MR, Nolan E, Finkelstein JL, et al. Comparison of an occlusive and a semi-occlusive dressing and the effect of the wound exudate upon keratinocyte proliferation. *J Trauma* 1989;29:924–30; discussion 930–1.
3. Gibbons BL, Manetka M, Hopman LD. Pre-clinical and clinical evaluation of a new silver antimicrobial wound dressing. Available from <http://www.acrymed.com/Aug2002/SilvaSorbSheet0802.html>, page 2–8. Accessed July 1, 2008.

4. Castellano JJ, Shafii SM, Ko F, et al. Comparative evaluation of silver-containing antimicrobial dressings and drugs. *Int Wound J* 2007;4:114–22.
5. Heggers J, Goodheart RE, Washington J, et al. Therapeutic efficacy of three silver dressings in an infected animal model. *J Burn Care Rehabil* 2005;26:53–6.
6. Whaley L, Wong D. *Nursing care of infants and children*. Mosby; 1991; p. 1148.
7. Barone M, McCall J, Jenkins M, Warden G. The development of an observational pain scale (OPAS) for pediatric burns (Abstr 230), Presented at the 32nd annual meeting of the American Burn Association, Las Vegas, NV, March 14–17, 2000.
8. Duhn LJ, Medves JM. A systematic integrative review of infant pain assessment tools. *Adva Neonatal Care* 2004;4:126–40.
9. Product information and description taken from Medline Industries website: <http://www.medline.com/literature/Silvasorb%20Brochure.pdf>.
10. Caruso DM, Foster KN, Hermans MH, Rick C. Aquacel Ag in the management of partial-thickness burns: results of a clinical trial. *J Burn Care Rehabil* 2004;25:89–97 [Ovid Full Text Bibliographic Links].
11. Caruso DM, Foster KN, Blome-Eberwein SA, et al. Randomized clinical study of hydrofiber dressing with silver or silver sulfadiazine in the management of partial-thickness burns. *J Burn Care Research* 2006;27:298–309.