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An Open, Parallel, Randomized, Comparative, Multicenter Study to Evaluate the Cost-Effectiveness, Performance, Tolerance, and Safety of a Silver-Containing Soft Silicone Foam Dressing (Intervention) vs Silver Sulfadiazine Cream

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An open, parallel, randomized, comparative, multicenter study was implemented to evaluate the cost-effectiveness, performance, tolerance, and safety of a silver-containing soft silicone foam dressing (Mepilex Ag) vs silver sulfadiazine cream (control) in the treatment of partial-thickness thermal burns. Individuals aged 5 years and older with partial-thickness thermal burns (2.5–20% BSA) were randomized into two groups and treated with the trial products for 21 days or until healed, whichever occurred first. Data were obtained and analyzed on cost (direct and indirect), healing rates, pain, comfort, ease of product use, and adverse events. A total of 101 subjects were recruited. There were no significant differences in burn area profiles within the groups. The cost of dressing-related analgesia was lower in the intervention group ($P = .03$) as was the cost of background analgesia ($P = .07$). The mean total cost of treatment was $309 vs $513 in the control ($P < .001$). The average cost-effectiveness per treatment regime was $381 lower in the intervention product, producing an incremental cost-effectiveness ratio of $1688 in favor of the soft silicone foam dressing. Mean healing rates were 71.7 vs 60.8% at final visit, and the number of dressing changes were 2.2 vs 12.4 in the treatment and control groups, respectively. Subjects reported significantly less pain at application ($P = .02$) and during wear ($P = .048$) of the Mepilex Ag dressing in the acute stages of wound healing. Clinicians reported the intervention dressing was significantly easier to use ($P = .03$) and flexible ($P = .04$). Both treatments were well tolerated; however, the total incidence of adverse events was higher in the control group. The silver-containing soft silicone foam dressing was as effective in the treatment of patients as the standard care (silver sulfadiazine). In addition, the group of patients treated with the soft silicone foam dressing demonstrated decreased pain and lower costs associated with treatment. (J Burn Care Res 2011;32:617–626)

Partial-thickness burns are among the most frequently reported thermal injuries. They are painful, difficult to manage, and, particularly when deeper, may have a negative effect on quality of life through scarring, permanent disfigurement, and loss of function.[1] The aims of burn treatment are to save lives, promote rapid healing, decrease pain and suffering, and enable patients to return to productive activity.[2]

Every year in the United States, approximately 700,000 patients are treated for burns, of which at

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least 45,000 require hospitalization.[3] Burn centers are subject to growing pressures to improve services, whilst maintaining optimal outcomes and decreasing treatment costs.[4]

Burn infection continues to be the primary source of morbidity and mortality. Topical antimicrobial therapy remains the central tenet of wound care: controlling microbial colonization and avoiding/reducing burn wound infections[5] while maintaining an environment in which tissues can repair at their optimum rate.

Silver sulfadiazine (SSD) creams such as Silvadene® (Keltman Pharmaceuticals, Inc., Flowood, MS), Flamazine® (Smith & Nephew, Hull), and Geben® (Mitsubishi Pharma, Tokyo) combine a fairly broad antimicrobial spectrum[6] with ease of availability and have been used as the standard treatment for partial-thickness burns management for over 30 years.[5] A recently undertaken international survey revealed that SSD remains the most frequently used topical preparation for the treatment of both superficial and deep partial-thickness burns.[7] However, a number of side effects of this treatment have been documented.[8] With respect to the safety profile, leukopenia has been described to occur when the material is used on, and absorbed through, large burn surfaces.[8–11] Other side effects that are known to occur are hypersensitivity, allergic reactions,[8,12] discoloration of the wound bed,[8,13] microorganism resistance,[8,12] and pain during application and removal of the material. Infrequently occurring events include skin necrosis, erythema multiforme, burning sensation, rashes, and interstitial nephritis.[14] Changes to the appearance of the wound bed can pose significant clinical problems; maceration and the development of stained pseudoslough over the wound bed makes accurate determination of the depth of tissue damage difficult. Consequently, an alternative approach to the topical treatment of partial-thickness burn injury is justified. This requires healing and economic outcomes to be at least as good as those achieved with the current standard (ie, SSD) but associated with reduced side effects.

A variety of silver-containing dressing types (ie, alginates, films, foams, and hydrofibers) have been developed in an attempt to offer practical benefits in use such as accelerated healing and reduced pain. One example of such a product is a silver-containing foam dressing with a soft silicone wound contact layer (Mepilex® Ag; Molnlycke Health Care, Gothenburg). Foam dressings possess a number of important characteristics of the "ideal" dressing, ie, they provide good exudate management, help to provide a moist environment at the surface of wounds while providing thermal insulation, do not shed particles or fibers, and are easily cut or shaped. Furthermore, they are gas-permeable, comfortable to wear, and can be impregnated with topical agents such as antimicrobials.[15] Mepilex Ag (MAg) is one of a number of dressings that incorporate Safetac®, a patented soft silicone technology. The presence of Safetac on the surface of this dressing means that it readily adheres to intact dry skin but does not stick to the surfaces of moist wounds, thereby facilitating atraumatic dressing changes and minimizing pain to the patient.[16]

An open, parallel, randomized, comparative, multicenter study was implemented to evaluate the use of MAg vs SSD (Silvadene) in the treatment of partial-thickness thermal burns. Further details about the two products are given in Table 1. The primary objective of the study was to compare the incremental costs (direct and indirect) and healing outcomes of the two treatments from the perspective of the healthcare provider. The secondary objectives were to compare the two treatments in terms of their performance, tolerance, and safety, including pain.

METHODS

Patient Selection

Patients were considered as eligible for inclusion in the study if they were aged at least 5 years; had a burn injury (thermal origin) within 36 hours of enrollment; and had a second-degree burn area of 2.5 to 20% of TBSA. Patients with burns covering between 3 and 25% of TBSA, allowing for up to 10% of TBSA to be third-degree burn, were considered suitable for enrollment with just the second-degree burn area treated as per study protocol. Key exclusion criteria included chemical or electrical burn; clinically infected burn; treatment of the burn with an active agent before study entry (ie, SSD within 24 hours of randomization); and pregnancy. The inclusion and exclusion criteria are presented in full in Table 2.

Recruitment took place in 10 centers across mainland United States. All patients (or their legal representatives) were provided with written information and written consent obtained. The study was conducted in accordance with the Declaration of Helsinki and the protocol was approved by a review board or ethics committee at each site.

Interventions

Enrolled subjects were assigned randomly to a treatment regimen that included either SSD or MAg. This was achieved through the use of sealed envelopes that were opened at the time of randomization. The randomization schedules were designed to ensure that

Table 1. Product descriptions

Mepilex Ag	Silvadene Cream
The product consists of: —a conforming Safetac soft silicone wound contact layer, which reduces wound bed trauma on application and removal.[16] —an absorbent polyurethane foam pad containing activated carbon and silver sulfate (1 mg/cm^2). In vitro studies have demonstrated that silver ions are released from the product to kill a wide range of wound-related pathogens (bacteria and fungi) for up to 7 days.[16] —an outer surface consisting of a vapor-permeable waterproof film that prevents exudate leakage and provides a barrier to microbial ingress. MAg is indicated for the management of low- to moderately exuding wounds such as leg and foot ulcers, pressure ulcers, and partial-thickness burns.[16]	The product consists of a soft, white, water-miscible cream containing silver sulfadiazine in micronized form. It is indicated as an adjunct for the prevention and treatment of wound sepsis in patients with second- and third-degree burns. Each gram of Silvadene cream 1% contains 10 mg of micronized silver sulfadiazine. The cream vehicle consists of white petrolatum, stearyl alcohol, isopropyl myristate, sorbitan, monooleate, polyoxyl 40 stearate, propylene glycol, and water.[14]

equal numbers of patients were assigned to each treatment group at all participating centers. The study treatment was not blinded. Treatment was initiated at the baseline visit. In the MAg treatment group, the burn was cleansed according to standard practice and the periwound skin dried thoroughly. The adherent side of the dressing was applied to the wound, without tension and with an overlap of at least 2 cm onto intact skin. Where necessary, the dressing was cut to enable conformity to body contours. An additional light bandage was used as needed to ensure fixation. Dressing changes of MAg were performed every 5 to 7 days (3–5 days during the acute phase) depending on the status of the burn. In this study, two sizes of dressing were used: 20 × 20 cm and 20 × 50 cm. Once discharged from hospital, this group had dressing changes undertaken at the burn clinic.

For the study, SSD cream was available in 400-g jars with application performed in accordance with the manufacturer's instructions; the burn area was cleansed and covered with SSD cream once to twice daily to a thickness of approximately 2 mm, then covered with a gauze pad and gauze wrap or other fixation. At dressing change, previously applied SSD was removed before reapplication. On discharge from hospital, the SSD group had dressings changed daily at home by a nurse or family member and once a week at the burn clinic.

Observation of dressings in both groups continued until 21 days postburn or until full reepithelialization occurred, alternative therapy for infection was initiated, or significant change in burn depth required surgical intervention. Sharp debridement was carried out at baseline visit only. Outcomes were measured at every scheduled visit: ie, days 0 (at inclusion in study), 7, 14, 21, and 35 (±1 day) until study discontinuation.

Outcomes Measured

At the baseline visit, patient demographics, medical and surgical history, and burn characteristics were collected for each subject. A validated burn estimate record (Lund and Browder Chart[17]) was completed for each patient at the baseline visit and at the second visit to ascertain if there had been any increase in the proportion of third-degree burns. During burn status assessment, the investigator considered the color of the burn tissue (pink, red, yellow, black, other), the presence of blistering (intact, broken, debrided), exudate level (none, slight, moderate), nature of exudate (clear, yellow, serosanguinous, purulent), wound odor (no, yes), clinical signs of local secondary infection in study burn, and acceptability at each dressing change. In addition, the investigator was required to make a subjective assessment of treatment efficacy at each formal assessment (excluding baseline). This consisted of the following: "100% healed," "'71 to 99% healed," "31 to 70% healed," "0 to 30% healed," "no healing," and "deterioration." In addition, the investigator considered the ease of application (extremely easy, very easy, somewhat easy, not very easy, and not at all easy), the subjects' anxiety (not at all anxious, a little anxious, somewhat anxious, a lot anxious, and extremely anxious), and pain during dressing changes (measured using the John Hopkins visual analog scale),[18] dressing adherence (lack of) to the wound bed (extremely good, very good, somewhat good, not very good, not at all good), bleeding on dressing removal (not at all, a little,

Table 2. Inclusion/exclusion criteria

Inclusion Criteria	Exclusion Criteria
Patients with a second-degree burn area as the target burn, covering 2.5 to 20% BSA. TBSA covered with burn at least 3% and up to 25%, allowing a maximum of 10% to be third-degree burn. Only the second-degree burns were treated	Burns equal to or older than 36 hours
Burn of thermal origin	Burns of chemical and electrical origin
Both gender with an age ≥5 yr at randomization	Clinically infected burn (as judged by the investigator)
Signed informed consent	Treatment of the burn with an active agent before study entry, SSD was allowed up to 24 hr before randomization
Subjects who were younger than the legal consenting age had to have a legally authorized representative	Patients with necrotizing leukocytic vasculitis or pyoderma gangrenosa
	Diagnosed underlying diseases (eg, HIV/AIDS, cancer, and severe anemia) judged by the investigator to be a potential interference in the treatment
	Patients with insulin-dependent diabetes mellitus
	Patients treated with systemic glucocorticosteroids, except patients taking occasional doses or doses <10 mg prednisolone/d or equivalent
	Use of immunosuppressive agents, radiation, or chemotherapy within the past 30 d
	Known allergy/hypersensitivity to any of the components of the investigation products
	Patients with physical and/or mental conditions that were not expected to comply with the investigation
	Participation in other clinical investigations within 1 mo before the start of the investigation
	Pregnancy
	Previous randomization to this investigation

somewhat), and the flexibility and conformability of the dressing (extremely good, very good, somewhat good, not very good, not at all good).

Patients were asked to record their pain at dressing change (during removal, during wear, and during application of dressing) measured using the Wong Baker Faces scale[19] (for children) and the Johns Hopkins visual analog scale (for adults). Patients were asked to rate their experience of apprehension during dressing change (frequently, sometimes, rarely, never), their ease of movement (extremely easy, very easy, somewhat easy, not very easy, not at all easy), and any stinging or burning (frequently, sometimes, rarely, never) while wearing the dressings. Between clinic visits, these were recorded in a patient diary which was provided for each patient to use once discharged home.

A microbiological swab was taken at the baseline visit and subsequently if infection was suspected. Although tissue biopsy is generally considered to be the most appropriate sampling method for identifying wound infection and its causative pathogens, the procedure is potentially traumatic; furthermore, a number of studies have demonstrated that the less-invasive swab technique is sufficient for burn wound monitoring.[20,21] Records were kept of time to discharge from clinic (days) (from inpatient to outpatient). Cost-related data were recorded at each dressing change.

Statistical Methods

An evaluable patient was defined as a patient completing the investigation with 3 weeks of treatment or a patient who healed before 3 weeks of treatment or a patient who was excluded because of the need for skin graft. Patients who discontinued the investigation because of an adverse event were also considered valid. The "intention-to-treat" (ITT) population included all patients subjected to at least one postrandomization treatment and that provided some data for the primary endpoint. Patients not fulfilling the inclusion and exclusion criteria were included in the ITT population. Primary conclusions were drawn from the ITT population. Treatment groups were compared descriptively with respect to baseline demographic and medical history characteristics. The proportion of burn wounds healed after 3 weeks was analyzed using a nonparametric test. The time to skin grafting was analyzed in the same way as time to healing.

All costs were documented by a research assistant via an activity-based costing worksheet from a random sample of patients in each treatment group. Descriptive statistics were calculated for each treatment group stratified by adult and pediatric patients. All patient costs were pooled by treatment group with similar descriptive statistics compiled. An independent *t*-test highlighted any significant differences in costs between each group.

Table 3. Patient demographics

Variable	Mepilex Ag (n = 49)	Silvadene (n = 51)	*P*
Age (yr)	37.0 (18.1)/31.5 (8.4:88.1)/n = 49	39.2 (18.2)/36.5 (8.7:86.0)/n = 51	.49
Gender, n (%)			
Male	36 (73.5)	41 (80.4)	
Female	13 (26.5)	10 (19.6)	.56
Race, n (%)			
Caucasian	43 (87.8)	37 (72.5)	
African-American	3 (6.1)	6 (11.8)	
Hispanic	2 (4.1)	7 (13.7)	
Other	1 (2.0)	1 (2.0)	.24
Use of nicotine, n (%)			
No	24 (49.0)	32 (62.7)	
Yes	25 (51.0)	19 (37.3)	.24

For categorical variables, n (%) is presented. For continuous variables, mean (SD)/median (min:max)/n is presented. For comparison between, Fisher's exact test was used for dichotomous variables, Mantel-Haenszel χ^2 test was used for ordered categorical variables, χ^2 test was used for nonordered categorical variables, and Mann-Whitney *U* test was used for continuous variables.

For the cost-effectiveness evaluation, time to 100% reepithelialization was calculated by survival analyses using the Kaplan-Meier method, with both log-rank and Wilcoxon statistics to test for differences between groups. The actual date of healing could not be captured because the patients were assessed weekly.

An incremental cost-effectiveness ratio (ICER) was computed reflecting change in costs of the MAg intervention (compared with SSD) to the change in effects on the interventions. The ICER of MAg treatment vs the standard (SSD) treatment was defined as $ICER = (K_2 - K_1)/(E_2 - E_1)$ and estimated the additional costs, which must be invested to achieve one additional clinical benefit unit under MAg treatment instead of the standard.

In line with a previously reported randomized controlled trial which also compared a silver-containing dressing with SSD,[22] the primary objective of this study was to compare the incremental costs (direct and indirect) and healing outcomes of the two treatments from the perspective of the healthcare provider. Sixteen evaluable patients (ie, patients completing the investigation with 3 weeks of treatment, patients who healed before 3 weeks of treatment, patients who were excluded due to the need for skin graft, and patients who discontinued the investigation because of an adverse event) were needed in each treatment group to provide 80% power for the primary analysis at a two-sided significance level of .05.

A sample size calculation for the incremental cost-effectiveness method was used as basis for a determination of sample size in the study. A willingness to pay based on incremental cost-effectiveness was used in the sample size determination compared with a minimally important difference based on incremental cost-effectiveness. Both have a foundation from a formula for health economic studies alongside clinical trials.[23] Sites that were to complete the activity-based costing worksheet were randomly selected before enrollment. In total, 20 patients from each treatment group were needed to be able to apply the costing methodology documenting the costs of treatment by health state, ie, noninfected burn, infected burn, and surgery (skin graft).

RESULTS

Study Population

The study was undertaken from September 2008 to October 2009. One hundred and one subjects were assigned to the study and randomized to treatment with MAg (n = 49) or SSD (n = 51). One individual never received treatment as the burn was incorrectly classified. In total, 50 subjects were randomized to the MAg arm of the study, 49 of which received the proposed treatment. Two patients did not provide any follow-up data and are therefore only valid for the safety population. Fifty-one subjects were randomized to SSD and went on to receive treatment; these are therefore valid for both safety and ITT populations. "Final visit" was defined as the last visit undertaken by the subject even if this was before the formal close of the study. In such cases, the results were carried forward to the study close date (Table 3).

The mean age of patients in the ITT populations was 37.5 years in the MAg group and 39.2 years in the SSD group. Seventy-five males (34 MAg and 41 SSD) were included in the ITT population (76.5% of the total trial population); 93.9% of subjects in the MAg

Table 4. Patient characteristics (health status and burn type) in the safety population

Variable	Mepilex Ag (n = 49)	Silvadene (n = 51)	*P*
General health before injury, n (%)			
Excellent	30 (61.2)	29 (56.9)	
Good	16 (32.7)	21 (41.2)	
Fair	3 (6.1)	1 (2.0)	.99
Type of burn injury, n (%)			
Scald	17 (34.7)	9 (17.6)	
Flash	17 (34.7)	16 (31.4)	
Flame	13 (26.5)	19 (37.3)	
Contact	2 (4.1)	4 (7.8)	
Other	0 (0.0)	3 (5.9)	.12
Hours since burn injury	16.3 (7.7)/17.0 (1.0:38.0)/n = 49	16.1 (7.9)/16.0 (1.0:34.0)/n = 51	.95

For categorical variables, n (%) is presented. For continuous variables, mean (SD)/median (min:max)/n is presented. For comparison between, Fisher's exact test was used for dichotomous variables, Mantel-Haenszel χ^2 test was used for ordered categorical variables, χ^2 test was used for nonordered categorical variables, and Mann-Whitney *U* test was used for continuous variables.

group and 98.1% in the SSD group described their general health status before the burn injury as good to excellent (Table 4).

The mean time period elapsed between injury and initial assessment was 16.4 hours (range, 1.0–38.0 hours) in the MAg group and 16.1 hours (range, 1.0–34.0 hours) in the SSD group. The distribution of burn types can be seen in Table 4.

Some subjects had parts of their burn injury considered to be full thickness. These areas were not considered part of the calculated burn value for the purposes of the study. The size of partial-thickness burn calculated values used within the analysis were as follows:
MAg: mean, 5.64% BSA; median, 4.5 (2.5–24); and SSD: mean, 4.93% BSA; median 4 (2.5–15).

An independent *t*-test analysis to demonstrate parity within the two groups showed no significant differences in group burn area profiles ($P = .13$).

Health Costs

A representative sample of 40 subjects (20 in each treatment arm) from across study facilities were used to calculate total cost. These were estimated from average wholesale prices taken from the 2009 Pharmacy Red Book.[24] Average wholesale costs of primary and secondary dressings and supplies were compiled from manufacturers and discount suppliers. Hourly labor rates for physicians, registered nurses, physician assistants, and others were taken during activity-based costing procedures and compared with national statistics from U.S. Government Bureau of Labor and Statistics (http://www.bls/wages.htm).

The mean total cost of wound management per patient was calculated at $309 for the MAg group and $514 for SSD group (Figure 1). The difference in costs between the two groups is statistically significant at $P < .001$. Primary dressing costs accounted for 70.1% of MAg wound management costs. Dressing costs in the SSD group (cream, gauze, and retention bandages) accounted for 11.1% of the total cost. Labor used in wound management accounted for 21.3% of the costs in the MAg group compared with 63.1% in the SSD group.

A higher weekly average cost of pain medications for SSD dressing changes was noted compared with MAg (Figure 2). The percentage of pain medications given per week for dressing changes accounted for 15.3% of wound management costs in the SSD group with the likelihood of trauma at dressing removal.

Within this study, the average cost-effectiveness in each group was calculated by determining the total cost of in-clinic treatment and then dividing by the rate of full reepithelialization (taken from the survival curve) at 20 days. For the MAg group, the average cost-effectiveness per burn healed is $395 and for the SSD group $776. Therefore, the net savings per burn healed is $381 with a protocol of care using MAg dressing instead of SSD.

The ICER was used to estimate the cost per unit of effectiveness with the use of one treatment (MAg) in place of another (SSD). Because the use of MAg saves $204 per patient and is associated with a 12.1% improvement in reepithelialization than SSD, the ICER is calculated to be −$1688 in favor of MAg dressing protocol (Table 5).

Clinical Outcomes

The mean time to discharge from inpatient hospital care was 5.62 days in the MAg group (median: 3.0, range: 1.0–30.0) and 8.31 (median: 5.0, range: 1.0–35.0) in the SSD group ($P = .034$). Of these, 97.6%

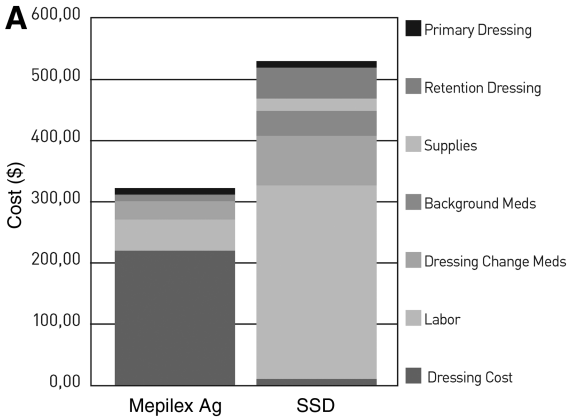

Figure 1. Total cost of care for MAg and SSD treatment groups.

of MAg subjects required no nursing or skilled nursing interventions in the community with 7.2% of the SSD group requiring further healthcare input.

Healing rates within the ITT population reveal that at visit 2 (1 week postburn) 16 (34.8%) of subjects within the MAg group had achieved complete healing, whereas only 10 (20%) of subjects within the SSD had achieved the same status. At visit 3 (2 weeks postburn), 31 (75.6%) of the MAg group had healed completely, compared with 23 (56.1%) in the SSD group. By the final visit, 33 (71.7%) subjects in the MAg group had complete healing, with 31 (60.8%) achieving this status in the SSD group. The average healing time was 13.44 days for the MAg group and 17.11 days for the SSD group (difference not statistically significant).

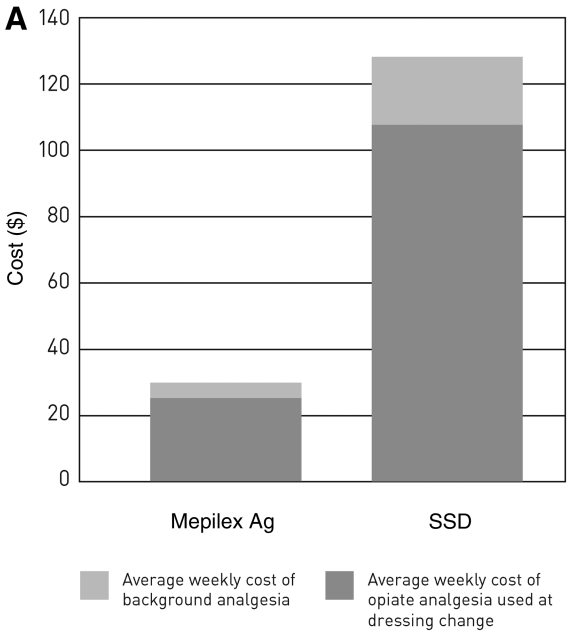

Figure 2. Total mean weekly cost of analgesia.

Table 5. Cost-effectiveness for each treatment regime

	MAg (n = 47)	SSD (n = 51)
Total cost of care ($), mean (SD)	309 (144)	514 (282)
Full reepithelialization in 21 days, n (%)	38 (78.3)	34 (66.2)
Average cost-effectiveness ($) (95% CI)*	395 (344–450)	776 (659–892)
Incremental cost-effectiveness ratio ($)†	−1688	

* Calculated from the total cost of care, divided by the proportion of patients with full reepithelialization.
† Calculated from the difference in total cost of care, divided by the difference in the proportion of patients with full reepithelialization.

Ease of Use

Clinicians considered MAg to be superior to SSD in terms of ease of application (rated extremely well to very well in 95.6% [MAg] and 78.4% [SSD]; $P = .028$) and flexibility (rated extremely well to very well in 97.8% [MAg] and 74.6% [SSD]; $P = .038$).

The mean number of dressing applications undertaken in the first week after injury was 1.54 in the MAg group and 6.82 in the SSD group. During this period, no MAg subject required more than four dressing changes, the majority (54.3%) requiring only one dressing change. The majority (52.9%) of SSD patients required daily dressings; however, one required 14 dressing changes.

By study week 2, 94.7% of patients in the MAg population required once a week dressing with none requiring more than two dressings per week. In the SSD group, 48.6% required daily dressing changes. By week 3, only 7 patients required dressings in the MAg group compared with 17 in the SSD group. The total mean number of dressing applications per subject during the study was 2.24 (median: 2.0, range: 1.0–5.0) in the MAg group and 12.4 (median: 13.0, range: 1.0–29.0) in the SSD group.

Pain

The mean pain scores were significantly different (MAg group, 19.1; SSD group, 40.0; $P = .018$) during dressing application at the end of the first week of treatment, as were pain scores during wear (MAg group, 22.0: SSD group, 35.5; $P = .048$). On dressing removal, no statistical significance was found ($P = .097$) between the study groups.

The use of analgesia both during active wound care interventions and in response to background pain is a

measure of perceived pain. Across most of the study facilities, fentanyl was the primary analgesic used to alleviate pain at dressing change. The trend in pain reduction at dressing change incurred by using MAg is further supported by a significant reduction in average weekly costs of pain medication (opiates) associated with dressing changes. This analysis was extrapolated from a representative sample group. The average weekly cost of opiate medication for dressing change per patient was $28.69 in the MAg group compared with $107.20 in the SSD group (P = .031). This finding is also supported by the use of medication to manage background pain levels. The average weekly cost of background pain medication (excluding fentanyl) per patient was $5.80 in the MAg group and $20.67 in the SSD group ($P$ = .078; Figure 2).

Pain, and the anticipation of pain, associated with wound care intervention is a factor in patients' perception of anxiety. Within the study, the overall investigator assessed anxiety at dressing change was reduced in the MAg group with 84.8% of patients reported they had little or no anxiety compared with 78.4% in SSD. Although there is no significant difference in anxiety measures (P = .54), it does favor the MAg intervention and supports the findings of pain perception.

Wound Swabs for Microbiological Analysis

Of the wound swabs taken at baseline, 14 showed microbiological growth (MAg, n = 6; SSD, n = 8). Throughout the rest of the study period, microbiological growth was evident on only eight of the swabs taken (all from the MAg group).

Safety

During the course of the study, 81.6% of subjects within the MAg group and 76.5% of subjects within the SSD completed the allotted course of treatment. Only two patients from each group required discontinuation of the allotted treatment because of an adverse incident (*Staphylococcus aureus* infection [n = 1] and coumadin reversal [n = 1] in the MAg-treated group; need for split-thickness skin grafting [n = 2] in the SSD-treated group). The total incidence of reported adverse events was 51% in the patients treated with SSD, compared with 38.8% in those assigned to MAg. Adverse events involving the skin were more frequent in the SSD-treated group (n = 12) than in the MAg-treated group (n = 6). The number of patients needing a skin graft was higher in those assigned to SSD (four vs two). Infectious complications were similar in the two treatment groups. One patient in the MAg dressing group died (myocardial infarction) during the course of the study; no relationship to the study treatment was detected.

DISCUSSION

In this study, the use of MAg was associated with significantly lower total costs to healthcare financers (Figure 1). These findings are consistent with the results of other studies that have compared the cost-effectiveness of silver-containing dressings with SSD.[22,25] From a healthcare funding perspective, the clinical management of burns injury needs to consider the financial implications of treatment. Although the achievement of optimal wound healing outcomes is of primary importance, the need to provide therapies that have sound financial prudence is also of importance. Interventions have a number of key financial components including the length of time a patient requires inpatient treatment. Hospital care is costly; so treatments that can reduce the length of time needed in hospital must therefore be considered. Within this study, it was found that the average length of inpatient stay in the MAg group was nearly 3 days shorter than in the SSD group. Although not statistically significant (at the P = .05 level), this finding has major implications for healthcare funding in that it demonstrates a potential means of reducing costs per burn victim considerably.

The topical management of partial-thickness burns remains an area of debate amongst clinicians. Since the research by Winter in the 1960s,[26] the central core of wound management is accepted as the maintenance of a moist wound environment which facilitates the optimum reparative potential for damaged tissues. However, in burns injuries, the role of topical antimicrobial preparations has held a wider significance, and the use of topical antimicrobial products has been widely accepted as a gold standard. From a clinician's perspective, it is essential that a successful burns dressing should in the first instance promote healing, be easy to apply, control bacterial burden effectively, not interfere with further burn assessment or tertiary treatment modalities, and manage the sequestra of injury effectively, notably wound exudate. Although SSD can offer some of these key characteristics, it is notably lacking in others.

Photographic evidence from the study demonstrates the ease of application and removal of the product and the lack of cream-based debris permitting uncomplicated burn assessment. A key problem with SSD is its effect on the appearance of the burn wound. Many clinicians now delay application of SSD onto partial-thickness burns wounds for 48 to 72 hours because of the difficulty experienced in reas-

sessing burn depth, instead using relatively inert wound care products such as tulle gras (gauze dressings impregnated with paraffin). Although this prevents the formation of discolored soft eschar, it fails to provide a bacterial barrier or antimicrobial action and can adhere to the wound bed. In comparison, it has been shown that MAg has a broad-spectrum antimicrobial action with a rapid and sustained action.[16] The low incidence of growth on microbiological swabs taken during this study are indicative of the antimicrobial properties of the two treatment regimes.

Pain is a factor that impacts not only perception of dressing effectiveness but also has an effect on total health economics. In this study, it was possible to demonstrate that the MAg product group had significantly lower mean pain scores at dressing application ($P = .02$) and during wear time ($P = .048$) during week 1. It can be argued that in the acute burn this period is the most crucial as the inflammation process is at its most expressive in the burn wound. The fact that patients treated with MAg required less background and dressing-related analgesia is however noteworthy and from a healthcare economics perspective significant as it further drives down associated costs. The results of assessment of bleeding on dressing removal, although not statistically significant ($P = .13$), indicate a positive trend toward the MAg product, supporting the implication that dressings with soft silicone technology can have a significant role in minimizing trauma on dressing removal. This supports the findings of Meuleneire[27] which showed that in clinical situations the dressing accounted for significantly reduced pain ($P < .0001$) at dressing change and ongoing (background) pain.[27]

A potential limitation to the design of this study was the time period over which subjects were evaluated. Although a timeframe of 21 days postburn enabled the investigators to observe the effects the treatments had on wound healing in the majority of subjects, a small subgroup (5 in the MAg group and 8 in the SSD group) were assessed to have achieved 30% healing or less. In this group, an extended treatment period may have resulted in further progression to healing. In addition, a longer follow-up period would have permitted assessment of scar quality in the healed burn-injured individuals. Both of these issues were considered when constructing the study design but discounted due to logistical issues. It was noted that in studies such as that carried out by Caruso et al,[22] attendance at follow-up clinic was poor with insufficient numbers to obtain significant results. It was also considered that wounds that had not healed by 21 days were highly likely to require surgical intervention to achieve closure.[22] The fact that healing was assessed by nonblinded observation could also be seen as a study limitation.

For practical reasons (ie, to ensure that the study was completed within a reasonable time frame and excessive administrative costs were avoided), the investigators agreed to compare the cost-effectiveness of the two interventions by analyzing data relating to 20 patients in each treatment group. Although subsampling could be seen as a potential weakness in the study methodology, it is important to point out that sites at which cost data were collected were randomly selected before patient enrollment. Furthermore, subsampling is widely used in clinical research as a practical, but reliable, means of evaluating interventions.

Another potential limitation in the study is a calculation of the economic impact of home carer input in treatment regimes. The use of SSD in the home setting has serious implications for carers in terms of the necessity to take time from work to undertake care and procedures. Although not an issue for health insurance companies, this does have implications for the wider community and the occult cost of burns management.

CONCLUSION

The results of this study strongly indicate that the silver-containing soft silicone foam dressing can be considered efficacious (eg, healing outcomes), safe, and cost-effective in the treatment of partial-thickness burns. The dressing offers a number of benefits over and above the use of SSD, including minimizing pain associated with dressing change, increased flexibility, and ease of application.

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