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ARTICLE**Comparison of Effects of 0.5% Silver Nitrate and 10% Sucralfate on the Healing of Second-degree Burn Wounds in Burn Patients: A Randomized Controlled Clinical Trial Study**

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Received: June 03, 2025

Revised: September 01, 2025

Accepted: September 13, 2025

Abstract

Introduction: This study aimed to compare the effects of silver nitrate and sucralfate on the healing of second-degree burn wounds in burn patients at Imam Reza Hospital in Birjand.

Methods: This randomized controlled clinical trial was performed on 60 patients with second-degree burns. Participants were randomly assigned to two groups: group A, which consisted of patients treated with a 0.5% silver nitrate dressing, and group B, which included those treated with a 10% sucralfate dressing. Initially, the Kolmogorov-Smirnov test was used to assess the normal distribution of the data. If the data were found to be normal, one-way analysis of variance and independent t-tests were employed. In the absence of normality, the Friedman and Mann-Whitney tests were used.

Results: Based on the findings, in the intervention group (B), 5 cases of bacterial colonization were positive, while 25 were negative. However, in the control group (A), 11 individuals had positive bacterial colonization. In both the intervention and control groups, the mean Bates-Jensen wound score on day 3 was significantly higher than on days 7 and 21 ($p < 0.001$). Additionally, the mean Bates-Jensen wound score on day 7 was significantly higher compared to day 21 ($p < 0.001$). In terms of pain score, the median score on day 3 was significantly higher than on days 7 and 21 ($p < 0.001$).

Conclusion: Based on this study, the administration of 10% sucralfate, compared to the conventional approach, significantly enhanced wound healing.

Key words: Burns, Silver Nitrate, Sucralfate, Wounds and Injuries

Introduction

Burn injuries arise from the transfer of energy from a heat source to bodily tissues, resulting from direct contact or exposure to heat, chemicals, electricity, or radiation (1). Severity of burns can range from minor to extensive and deep, frequently imposing substantial physical and economic burdens on both the affected individual and their family (2). Individuals sustaining burn injuries often experience significant physical pain and psychological distress as a consequence of the trauma (3).

This issue exhibits a higher incidence in developing countries, compared to developed nations, constituting approximately 5% of hospital admissions in such regions. Notably, in the United States and Europe, an estimated 1.1 million individuals annually undergo treatment for burn injuries. In Iran, regional disparities in burn prevalence are evident. For instance, a study conducted in Western Azerbaijan, Iran, reported a burn incidence rate of 21.6 per 100,000 people (4).

Burn injuries are frequently complicated by infections, both local and systemic, which are recognized as the primary contributors to morbidity and mortality, particularly in cases involving burns exceeding 20% of the total body surface area. Presence of burn infection poses significant challenges to patient care and treatment, culminating in prolonged hospitalization, increased healthcare expenditures, and elevated mortality rates.

Second-degree burns extend beyond the epidermis, encompassing the dermis. This dermal involvement leads to fluid accumulation between the epidermis and dermis, culminating in the characteristic blister formation. In severe cases, the burn injury may extend through the entire thickness of the cutaneous layers (5). To date, a diverse array of therapeutic approaches for burn management has been established. These interventions primarily concentrate on fluid resuscitation and safeguarding the skin from microbial invasion. Notably, substances, such as silver nitrate and sucralfate, play a significant role within this therapeutic landscape.

Extensive research has investigated the therapeutic approaches concerning burn management. For instance, a study performed by Mahim Koshariya explored the analgesic properties of sucralfate in burn treatment, demonstrating its efficacy in patient pain reduction without associated adverse effects (6). While a substantial number of studies have examined the use of silver

nitrate in burn treatment, a comparative analysis of sucralfate and silver nitrate in this context has not yet been conducted. Consequently, this study aimed to conduct a comparative assessment of the efficacy of these two substances in healing the second-degree burn wounds in burn-affected individuals.

Methods

This study was approved by the Research Ethics Committee of the Birjand University of Medical Sciences, Birjand, Iran (IR.BUMS.REC.1400.107). The present randomized controlled clinical trial followed CONSORT guidelines and was registered in the Iranian Registry of Clinical Trials (IRCT) website to obtain an IRCT code (IRCT20250316065099N1) (Figure 1).

A sample of 60 patients with second-degree burns was recruited for this study through simple random sampling from the burn ward and the clinic at Imam Reza Hospital in Birjand, Iran. Participants were randomly assigned to two groups: a control group including patients treated with a 0.5% silver nitrate dressing (Group A), and an intervention group consisting of patients treated with a 10% sucralfate dressing (Group B). This randomization process was conducted in a blinded manner, ensuring that neither the researchers nor the patients were aware of the group assignments prior to treatment initiation.

The intervention in this study was conducted to evaluate the efficacy of two topical treatments for second-degree burns. Participants were randomly assigned to two groups. The control group received a routinely used treatment with 0.5% silver nitrate ointment, applied at a thickness of 1.5 mm during dressing changes. Conversely, the intervention group underwent treatment with 10% sucralfate ointment, applied at a thickness of 1.5 mm during dressing changes. Prior to application of either treatment, the wounds were cleansed with a normal saline solution. To mitigate potential bias, the study was conducted in a single-blind manner, where patients were unaware of the type of treatment they were receiving.

The intervention was administered by a qualified and experienced registered nurse. The present study assessed wound size utilizing the Bates-Jensen Wound Assessment Tool (BWAT), which has 15 items. Two items pertaining to wound site and shape were not categorized, while the remaining 13 items employed a 4-point Likert scale to assess wound condition. Scores ranged from 1 to 4, with lower scores indicative of optimal wound

using the evi ne technique, involving a wound condition. The minimum and maximum possible scores on this scale are 13 and 40, respectively. Consequently, lower scores on the questionnaire represent improved wound healing, whereas higher scores indicate greater wound deterioration.

Wound size measurement was assessed using a plastic tape measure with a precision of approximately 1 mm. At the initial clinic visit and subsequently on days 3, 7, and 21 of the treatment period, wound measurements were recorded as length × width. Concurrently, the BWAT was employed to evaluate burn wound parameters, including wound size, burn degree (depth), tissue damage, type of necrotic tissue, type of exudate, and surrounding skin conditions (color, induration, edema, granulation tissue presence, and epithelialization status). The collected data facilitated an in-depth analysis of the wound healing progression based on the assigned scores.

Additionally, patient demographic information, including gender, age, length of hospital stay, and place of residence, was collected at the outset of the study. Concurrently, nurses assessed and documented subjective symptoms related to the wound, including itching, pain, and burning at the wound site. These initial findings were subsequently corroborated through examination by a physician. Moreover, the pain measurement was carried out using the Numerical Rating Scale.

To evaluate bacterial colonization, the presence of *Pseudomonas aeruginosa* and *Staphylococcus aureus*, the predominant bacterial agents of burn wound infections, was assessed on days 3 and 7 post-admission. Prior to sampling, the wounds were cleansed with sterile normal saline. Bacterial sampling was performed using the evi ne technique, involving a 4 cm² area of each wound. A sterile swab was employed, applying sufficient pressure to obtain wound exudates. In instances of dry wounds, the swab was moistened with sterile normal saline before sampling. Subsequently, the swab was transferred to a tube containing sterile Stuart's transport medium and immediately transported to the microbiology laboratory for further analysis.

In the laboratory, wound specimens were subjected to vortexing and homogenization within a designated transport medium. Subsequently, a series of serial dilutions (10^{-1} , 10^{-2} , 10^{-3}) was prepared from the original sample. An amount of 0.1 mL of both the original and diluted samples was then uniformly distributed onto blood agar and eosin-methylene blue agar plates. Incubation of these plates was conducted at 37 °C for 24-48 h.

Bacterial colonies were subsequently counted, incorporating the respective dilution factors, and ultimately expressed as CFU/mL in the original sample, which was then extrapolated to represent CFU/cm² of the wound surface area. Furthermore, the identification of bacterial isolates, including *S. aureus* and *P. aeruginosa*, was achieved by implementing a battery of complementary tests. These tests encompassed Gram staining, catalase, coagulase, oxidase tests, and other relevant tests specifically designed for the characterization of Gram-negative bacterial species.

In accordance with the literature reviewed by Schwartz and Sayeston (14,15), the prophylactic administration of antibiotics in burn patients was deemed unnecessary. Consequently, neither study group received prophylactic antibiotics prior to postoperative day 7. However, if there was clinical evidence of wound infection on days 2 or 7, therapeutic antibiotics would be prescribed. Data collected subsequent to the commencement of therapeutic antibiotic treatment were not included in the final analysis.

During the study period:

1. Antibiotic Initiation: Seven patients (11.7%) required therapeutic antibiotics: five in the control group (16.7%) and two in the intervention group (6.7%)

Indications: a) Culture-positive wound infection ($> 10^5$ CFU/g), b) Systemic signs (fever > 38.5 °C + leukocytosis)

2. Analysis Method: Time-to-event outcomes were analyzed using Kaplan-Meier curves. Between-group comparisons were performed with the Log-rank test ($p=0.042$). Cox regression was applied to adjust for %TBSA and age

3. Dropout Management: Four participants (6.7%) were excluded after initiation of antibiotics. Intention-to-treat analysis preserved all randomized patients, and missing data were handled via multiple imputation.

Patients who required corticosteroid therapy within the initial 7 days of hospitalization were not excluded from the study. This decision was made based on the understanding that the immunosuppression associated with high-dose corticosteroid administration typically requires at least one week to manifest. Consequently, corticosteroid use within this timeframe was not anticipated to significantly compromise the immune system, enabling continued patient participation in the study. This decision was supported by the temporal premise that wound cultures were evaluated on postoperative days 3

and 7. Initially, the Kolmogorov-Smirnov test was used to assess the normal distribution of the data. If the data were found to be normal, one-way analysis of variance (ANOVA) and independent t-tests were employed. In the absence of normality, the Friedman and Mann-Whitney tests were used. A significance level of 0.05 was considered.

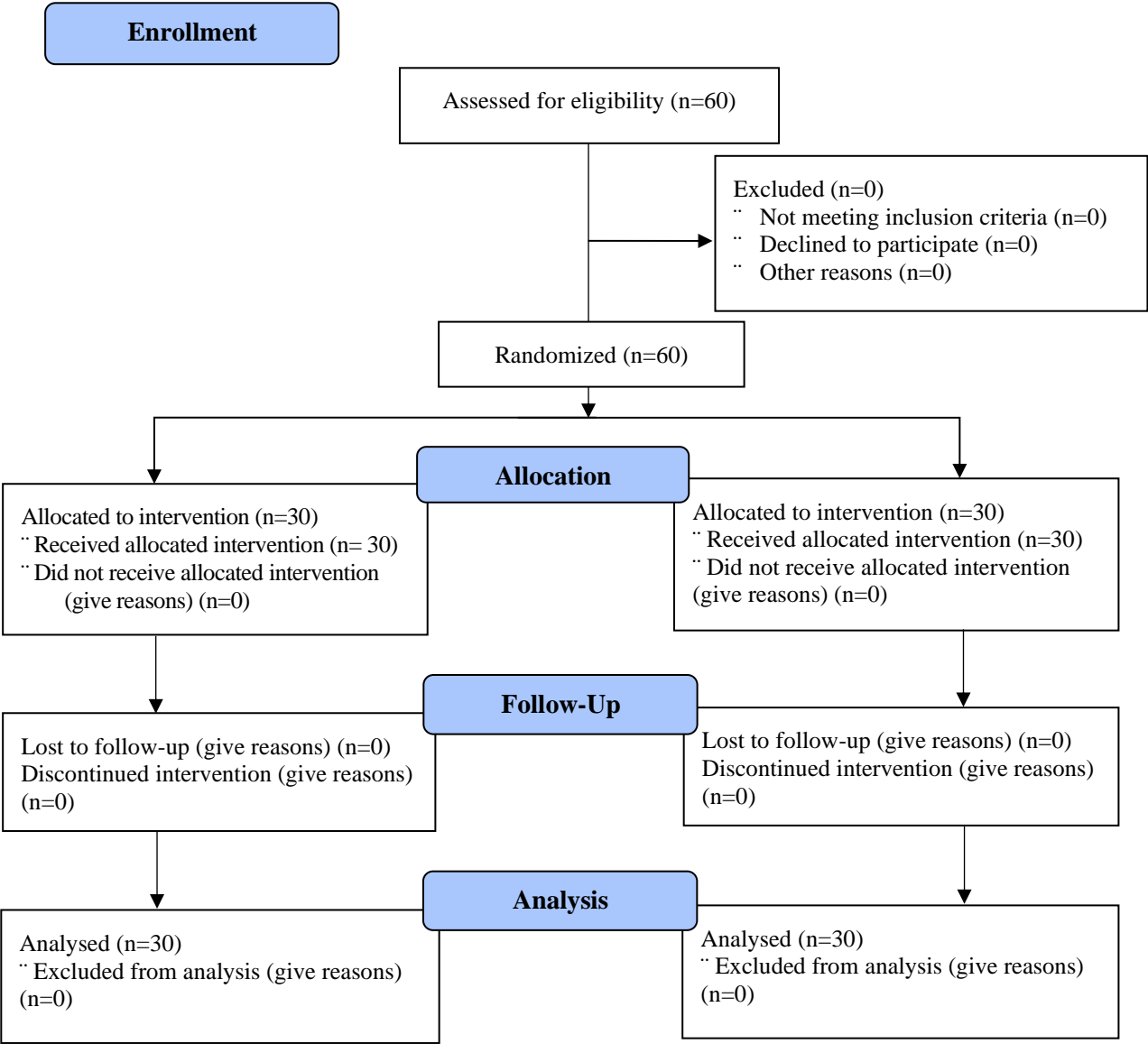


Figure 1. Flowchart of the study

Results

Analysis revealed that the mean BWAT scores for the intervention group on days 3 and 21 were 31.76 ± 3.25 and 31.06 ± 0.36 , respectively. A repeated-measures ANOVA demonstrated a statistically significant difference in mean BWAT scores across the three time points between the intervention and control groups. Subsequent

analysis indicated that the mean BWAT scores for both groups were significantly higher before treatment and on day 3, compared to days 7 and 21. Additionally, the mean BWAT score on day 7 was significantly higher than that on day 21 ($p<0.05$). The independent samples t-test revealed that participants in the intervention group exhibited significantly lower mean BWAT scores, compared to the control group, on days 3, 7, and 21 post-

treatment ($p < 0.05$) (Table 1).

Table 1. Comparison of the Mean Benson-Jensen wound status in the intervention and control groups on days 3, 7, and 21.

Variable	Group	Before intervention (Mean \pm SD)	Day 3 (Mean \pm SD)	Day 7 (Mean \pm SD)	Day 21 (Mean \pm SD)	<i>p</i> value**
Bates-Jensen Wound Assessment	Intervention	45.4 \pm 3.65	31.76 \pm 3.25	18.8 \pm 2.55	13.06 \pm 0.36	<0.001
	Control	51.98 \pm 2.21	42.2 \pm 2.65	37.07 \pm 5.31	26.2 \pm 3.81	
<i>p</i> value*		<0.001	<0.001	<0.001	<0.001	<0.001

* Independent t-Test

** Repeated-measures analysis of variance (the time*group interaction effect)

Analysis revealed a median pain score of 4 in the intervention group on day 3, decreasing to 0 by day 21. The Friedman test demonstrated significant differences in median pain scores within both the intervention and control groups across the three time points. Subsequent post-hoc analysis using Kendall's text confirmed a significant elevation in

median pain scores on day 7, compared to day 21 in both groups. Furthermore, Mann-Whitney U tests consistently indicated significantly lower median pain scores in the intervention group, compared to the control group on days 3, 7, and 21 ($p < 0.0001$) (Table 2).

Table 2. Comparison of pain scores in the intervention and control groups on days 3, 7, and 21.

Variable	Group	Before intervention	Day 3	Day 7	Day 21	<i>p</i> value**
Pain	Intervention	8.2 (6-11)	4 (3-5)	1.5 (1-2)	0 (0-0)	<0.001
	Control	11 (9-14.3)	8 (6-8)	6.5 (5.75-7)	5 (3.5-6)	
<i>p</i> value*		<0.001	<0.001	<0.001	<0.001	<0.001

* Mann-Whitney U test, ** Friedman test

Data are expressed as median and interquartile range

Subsequent analysis revealed a significantly lower incidence of bacterial colonization in the intervention group, compared to the control group. Specifically, the intervention group exhibited 5 positive and 25 negative cases, while the control group demonstrated 11 positive cases of bacterial colonization. Subsequent analysis using Fisher's exact test (two-tailed) revealed significantly lower bacterial colonization in the intervention group (5/30 positive, 16.7%), compared to the control group (11/30 positive, 36.7%) ($p = 0.042$, 95% CI for difference: 3.5% to 36.5%). It should be mentioned that the relative risk was 0.45 (95% CI: 0.18-0.97). Moreover, a notable reduction in the mean duration of hospitalization was observed in the intervention group, compared to the control group.

Discussion

The prevalence of burns is higher in low-income

and developing countries. Annually, 250,000 people suffer from moderate to severe burns in developing countries, and burns are among the most common severe injuries with a high mortality rate (7, 8). This investigation assessed the therapeutic efficacy of a sucralfate-silver nitrate combination in the management of second-degree burn injuries over a defined timeframe. The findings revealed a statistically significant reduction in both BWAT scores and pain intensity among subjects treated with the combination therapy. These improvements were consistently observed on post-treatment days 3, 7, and 21. However, this study identified significant disparities in bacterial colonization rates between the intervention and control groups. Similarly, a previous study conducted by Godhi AS et al. demonstrated the effectiveness of sucralfate in promoting the healing of second-degree burn wounds, potentially surpassing the efficacy of silver-based compounds in this context (9).

In another study involving 116 participants, P. J.

Gupta et al. explored the local analgesic and wound-healing properties of topically applied sucralfate in patients who had undergone hemorrhoidectomy. The participants were divided into two equal groups, and the study concluded that sucralfate exhibited significant wound-healing and analgesic benefits (10).

Banati et al. in their research investigated the efficacy of topically applied sucralfate in 60 patients with third-degree burn wounds. The participants were randomized into two groups: one receiving sucralfate treatment and the other receiving a placebo. Pain was assessed using the Visual Analog Scale, and the outcomes demonstrated significantly lower pain levels in the sucralfate group, compared to the placebo group, on days 7 and 18 post-burn. Concomitantly, the sucralfate group exhibited reduced analgesic medication consumption. Notably, wound healing was accelerated in the sucralfate group, further substantiating the beneficial effects of sucralfate in both wound healing and pain management (11).

In a study conducted by Hassanzadeh et al., the localized impact of sucralfate was assessed on burn injuries in 80 female rats. The experimental cohort was evenly divided into five groups: the first group received a base ointment, the second group received sucralfate, the third group received silver sulfadiazine, and the fourth group received *Brassica oleracea* extract. There was also a control group. By the conclusion of the two-week observation period, the groups treated with sucralfate and *Brassica oleracea* exhibited significantly accelerated angiogenesis and epithelialization, strongly suggesting that these agents possess efficacious wound-healing properties (12).

A comparative study conducted by Bahashti et al. investigated the therapeutic efficacy of sucralfate cream and silver sulfadiazine in second-degree burn wounds in a rat model. In their study, 48 male rats were randomly assigned to three equal groups and subjected to burn injuries on their backs. Subsequently, the burn wounds were topically treated with either sucralfate cream, silver sulfadiazine cream, or a cold cream (as a control), respectively. Histological assessments were conducted on skin samples collected on post-treatment days 7, 14, 21, and 28. By the end of the study period, both the silver sulfadiazine and sucralfate groups demonstrated complete regeneration of the epidermis and keratin layer. However, only the sucralfate group exhibited complete skin adherence. The aforementioned study revealed a significantly higher wound healing

percentage in the sucralfate group (100%), compared to the silver sulfadiazine group (91%) and the control group (76%), underscoring the potential of sucralfate as a promising therapeutic agent for wound healing (13).

This study was limited by its small sample size and single-center design, which may affect the generalizability of the findings.

Conclusions

The findings corroborated by previous research and highlighted the efficacy of sucralfate in promoting wound healing. Similarly, silver nitrate has exhibited substantial therapeutic benefits in numerous studies. Given the complementary mechanisms of action of these agents, their combined application may offer a promising approach to enhance wound healing outcomes in clinical settings. In future studies, it is recommended to evaluate the combined use and effectiveness of these two ointments.

Acknowledgments

The authors gratefully acknowledge all research team members for their contributions.

Funding

None.

Conflict of Interest

None.

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