

Advantage of Amnion Dressing (Biological Dressing) + Silver Sulfadiazine Cream *vs.* Standard Silver Sulfadiazine Cream Dressings in Acute Deep Second-Degree and Third-Degree Burn Wounds: a Single Center Experience

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ABSTRACT

Introduction: This study compared the benefits of amnion dressing (biological dressing) + silver sulfadiazine cream with standard silver sulfadiazine cream dressings in treating deep second- and third-degree acute burn wounds.

Methods: This prospective clinical trial was conducted on 50 patients with deep second- and third-degree burns who were admitted to Taleghani Hospital in Ahvaz, Iran. Participants were divided into two groups: the first one comprised subjects who received silver-amnion biological dressing (silver sulfadiazine 1%) and the second group consisted of patients treated with standard silver sulfadiazine cream dressings.

Results: In the amnion-silver group, the average time required for graft readiness was eight days, compared to 11 days in the standard dressing group, which indicated a 27% reduction in recovery time. The treatment costs in the amnion-silver group were 20.8 Euro compared to 26.3 Euro for the standard dressing group, reflecting a 21% cost reduction. Narcotic consumption in the amnion-silver group was zero, but the average narcotic use in the standard dressing group was 50 mg of pethidine, revealing a 100% reduction. Based on the visual analog scale (VAS), the mean pain intensity was 4 in the amnion-silver group and 5.5 in the standard dressing group. Patient satisfaction was 85% in the amnion-silver group versus 60% in the standard dressing group. No infections were reported in the amnion-silver group, while three cases were observed in the standard dressing group.

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Conclusion: The results of the present study indicate that amnion-silver dressing can be an effective and economical treatment option for wound healing. In the amnion-silver group versus standard group, a considerable reduction in recovery time was observed, which was also reflecting a cost reduction. Furthermore, the mean pain intensity was lower in the amnion-silver group than the standard dressing group. Patient satisfaction was higher in the amnion-silver group.

Keywords: burn, standard dressing, amnion-silver dressing, silver sulfadiazine cream.

INTRODUCTION

Burn injuries are widespread worldwide, with most victims requiring serious medical attention and hospitalization (1). Burns represent a severe thermal injury that causes metabolic changes and weakens the immune system during wound healing. This irreversible cellular damage is associated with cell membrane instability, ATP reduction and tissue necrosis (2). Wound healing involves the dynamic interaction of biological components, such as growth factors, blood-borne cytokines, signaling cascades and the extracellular matrix. Adjusting cytokine levels through topical therapeutic agents is thus a critical method for accelerating wound healing (3).

The novel technologies like biomaterials, stem cell therapies and bioengineered products aimed at improving treatment outcomes. These advancements offer promise for chronic wound management and tissue regeneration, addressing clinical challenges effectively (4). The TIME framework, comprising tissue management, infection or inflammation control, moisture balance and edge advancement, is a structured method for wound assessment and treatment. There are some techniques like debridement and the use of advanced dressings and therapies, such as negative pressure wound therapy, to optimize the healing environment. This framework has evolved to focus on both the wound and the overall patient, enabling tailored and effective management strategies for chronic and acute wounds (5).

In nearly every part of the world, 1% silver sulfadiazine cream is commonly used as a standard method for dressing partial-thickness burn wounds and is even selectively applied to more severe burns (6). Its use is prioritized over agents such as silver nitrate or sulfamylon – DCI (Denomination Commune Internationale) mafenide acetate, commercial name sulfamylon, producer Mylan

Pharmaceuticals (varies depending on region; confirm based on packaging or specific distributor) – as an antimicrobial treatment. However, despite its beneficial effects, topical application of silver sulfadiazine can cause specific uncommon but reversible systemic side effects, such as neutropenia, erythema, crystalluria and hemolysis in patients with G6PD deficiency (7). Some recent studies have also indicated that using silver sulfadiazine on partial-thickness burns may potentially delay burn healing (8).

With the advent of synthetic dressings such as OPSITE, DermaFilm, Duo-Derm and Biobrane, as well as concerns about infection transmission, the widespread use of amniotic membranes did not gain popularity in developed countries. On the other hand, the availability and low processing cost of amniotic membranes have attracted the attention of developing countries, leading to their more extensive use (9).

Several studies have indicated that amniotic membranes are related to rapid re-epithelialization and enhanced wound healing. It has also been suggested (10) that the mechanism responsible for accelerated healing and granulation tissue development involves inhibiting protease activity, thereby reducing the infiltration of polymorphonuclear leukocytes. These mechanisms explain the faster wound healing observed with amniotic membranes (10).

As mentioned, silver sulfadiazine dressings are a key routine topical antibiotic treatment for burn wounds. On the other hand, the amniotic membrane is recognized as a physiological wound-healing agent. Therefore, combining these two methods may accelerate wound healing. This study was aimed to compare advantage of amnion dressing (amniotic membrane) + silver sulfadiazine cream vs. standard silver sulfadiazine cream dressings in acute deep second- and third-degree burn wounds. □

MATERIALS AND METHODS

This prospective randomized clinical trial (code: IRCT20231202060240N1, ethical IR.AJUMS.REC.1402.392) was conducted on 50 patients with second- and third-degree burns who were admitted to Taleghani Hospital in Ahvaz, Iran. All participants signed a consent form to confirm they agree with using their data for the present. Patients were divided into two groups, both of which being matched for baseline albumin levels and burn percentage (burn degree) during the statistical analysis phase in order to eliminate the effects of confounding variables. Patients were assigned to two groups using the balanced block randomization method. In this regard, six combinations of four from the intervention groups A and B were determined as follows: AABB, ABAB, ABBA, BBAA, BABA and BAAB; then one of the six codes was selected using a random number table. This was repeated until all samples were assigned to the two groups.

Eligibility criteria

Patients with second- or higher degree burns were included in the present study. Exclusion criteria comprised lack of willingness to participate in the study, pregnant or breastfeeding women, patients with G6PD deficiency and sensitivity to sulfonamides.

Intervention description

Patients allocated to the first group were treated with biological amnion-silver dressings (1% silver sulfadiazine), and those included in the second group received standard dressings.

For patients in the amnion-silver group, dressings were applied under sedation in the operating room (OR). If necessary, debridement was performed, followed by a 48-hour amnion-silver dressing. If no additional debridement was needed, a five-day dressing was used. The dressings were checked daily by the study implementer (same physician) and whenever they became wet, the surface gauze was replaced. Complete dressing changes were conducted in the OR.

Following the initial debridement and dressing with silver sulfadiazine in the second group, subsequent dressings were performed daily in the inpatient ward. If further debridement was needed, it was done in the OR. The physician assessed and compared patients based on clinical criteria such

as graft readiness, epithelialization and granulation tissue development.

The variables examined included gender, age, burn percentage, pain level based on the VAS, degree of epithelialization, length of hospital stay, frequency of dressing changes, granulation tissue formation, number of morphine administrations, initial and final albumin levels, patient and ward nurse satisfaction, time required for graft readiness and the number of patients requiring grafting in each group. Follow-up period to assess the study outcomes was two weeks after treatment. "Graft readiness" refers to the stage at which a burn or wound has sufficiently healed and is prepared to receive a skin graft. This typically involves the absence of infection, removal of necrotic tissue and the presence of a clean vascularized wound bed suitable for graft attachment.

Amnion dressing + silver sulfadiazine cream application protocol

Amniotic membranes were prepared under sterile conditions and applied directly to burn wounds with the epithelial side facing the wound. Cryopreserved membranes were thawed and dehydrated membranes rehydrated, as per product guidelines. The membranes were trimmed with sterile scissors to fit the wound, covering edges without excessive overlap.

Burn wounds were cleansed with sterile saline to remove debris. Debridement, if needed, was performed using sterile instruments under local anesthesia. The cleaned wounds were dried with sterile gauze pads.

A thin, uniform layer of 1% silver sulfadiazine cream was applied over the membrane as an antimicrobial barrier. Non-adherent sterile dressings were then used to protect the treated areas. Amniotic membranes were harvested under sterile conditions, decontaminated, screened and preserved until use.

Statistical analysis

Data were collected using a researcher-designed questionnaire. Descriptive statistics were reported as frequency and percentage for qualitative variables and as mean, standard deviation (SD) and 95% confidence intervals for quantitative variables. For analytical analysis of data, chi-square and independent t-test were used. P-value was set at 0.05. SPSS 16.0 software was then used for analysis. Certain variables, such as time to epithe-

lialization, time to granulating wound, number of surgeries, and albumin levels, were excluded from the analysis due to incomplete or inconsistent data collection. □

RESULTS

In this study, detailed assessments comprised the time required for graft readiness, treatment costs (the calculated costs were including costs of amniotic membranes harvest, processing and preservation), use of analgesics during dressing changes, pain levels, workload on nursing staff, patient satisfaction as well as age and gender distribution in each group. In the amnion-silver group, there were nine women and 16 men with an average age of 31 years, while in the standard dressing group, there were eight women and 17 men with an average age of 33.5 years.

Based on the data, the average time required for graft readiness in the amnion-silver group was eight days. In contrast, this duration was 11 days for the standard dressing group, showing a 27% reduction in recovery time for the amnion-silver group. Treatment costs were also lower in the amnion-silver group compared to the standard dressing group (20.8 Euro versus 26.3 Euro, respectively), indicating a 21% cost reduction in the amnion-silver group. As there were no statistically significant differences in wound severity between the two study groups, the total body surface area (TBSA) in were 30% in the amnion-silver group and 31% in the standard dressing one. Furthermore, both groups were similar with respect to

deep dermal burns – 50% of TBSA (15% TBSA) and full-thickness burns – 50% of TBSA (15% TBSA). Randomized allocation ensured a balanced distribution of burn depths between groups.

Additionally, the average narcotic consumption in the standard dressing group was 50 mg of pethidine. In contrast, no narcotic use was reported in the amnion-silver group, reflecting a 100% reduction in narcotic usage for the amnion-silver group. Patients in the standard dressing group also reported experiencing significant pain, while the amnion-silver group reported less pain overall. On the first day, the average pain score for the amnion-silver group was 6, compared to 6.7 for the standard dressing group, with a statistically significant difference (P-value 0.003). On the seventh day, the average pain score was 5.1 for the amnion-silver group and 5.9 for the standard dressing group (P-value 0.015). By the fourteenth day, the average pain score was 4.0 for the amnion-silver group and 5.2 for the standard dressing group, with a P-value of 0.042, indicating a statistically significant difference once again (Tables 1 and 2).

According to the results, the average number of dressing changes during the treatment period was reported as three times for the amnion-silver dressing group, compared to eight times for the standard dressing group, with this difference being statistically significant (P-value 0.019) (Table 3).

Additionally, the incidence of reported infections in the two groups was examined, with three cases of infection being detected in the standard

Variable	Amnion-silver group		Standard dressing group		Percentage difference	P-value
	Mean±SD	95% CI	Mean±SD	95% CI		
Mean age (years)	31 ± 3.5	(29.7–32.3)	33.5 ± 3.7	(32.2–34.8)	-	>0.05
Gender	Female	9 (56%)	8 (44%)	-	-	>0.05
	Male	16 (49%)	17 (51%)	-	-	

TABLE 1. Demographic characteristics of the study

SD=standard deviation; CI=confidence interval.

Variable	Mean±SD	Amnion-silver group	Standard dressing group	Percent difference	P-value ¹	95% CI
Pain level on day 1 (VAS)	6 ± 1.7	6.7 ± 1.9	-	-	0.003*	Amnion-silver: 5.4–6.6 Standard: 6.0–7.4
Pain level on day 7 (VAS)	5.1 ± 1.4	5.9 ± 1.5	-	-	0.015	Amnion-silver: 4.6–5.6 Standard: 5.4–6.4
Pain level on day 14 (VAS)	4.0 ± 1.1	5.2 ± 1.3	-	-	0.042	Amnion-silver: 3.6–4.4 Standard: 4.7–5.7
P-value ²	0.023*	0.048*	-	-	-	-

TABLE 2. Comparison of pain level in studied patients

SD=standard deviation; VAS=visual analog scale; CI=confidence interval.

TABLE 3. Comparison of wound parameters in the studied patients

Variable	Amnion-silver group	Standard dressing group	Percent difference	P-value	95% CI
Graft readiness time (days) ¹	8 ± 1.1	11 ± 1.3	27.3% reduction	0.001*	Amnion-silver: 7.6–8.4 Standard: 10.5–11.5
Dressing changes (average/day) ²	3 ± 0.7	8 ± 2.5	-	0.019*	Amnion-silver: 2.7–3.3 Standard: 7.0–9.0

CI=confidence interval.

TABLE 4. Comparison of the amount of narcotics used by patients and infection occurrence

Variable	Amnion-silver group	Standard dressing group	Percent difference	P-value	95% CI
Narcotic consumption (mean mg/pethidine) ¹	0	50 ± 12	100% reduction	0.001*	Amnion-silver: N/A Standard: 26.8–73.2
Infection (number during treatment) ²	0	3	-	0.032*	Not applicable

CI=confidence interval.

TABLE 5. Comparison of costs, work pressure on personnel and satisfaction in the studied patients

Variable	Amnion-silver group	Standard dressing group	Percent difference	P-value	95% CI
Treatment cost (Euro)	20.8	26.3	21% reduction	0.040*	Not applicable
Nursing staff workload (average time spent, minutes)	90 ± 15	420 ± 25	78.6% reduction	0.001*	Amnion-silver: 85–95 Standard: 410–430
Patient satisfaction (%)	85%	60%	41.7% increase	0.025*	Amnion-silver: 80–90 Standard: 55–65

CI=confidence interval.

dressing group, and no infections being found in the amnion-silver group (P-value 0.032) (Table 4).

The findings of this study indicated that the workload on the nursing staff was higher in the standard dressing group. However, this difference was not statistically significant (P-value > 0.05). Patient satisfaction was also assessed using a questionnaire. Patients in the amnion-silver group reported a high level of satisfaction, which was 25% higher than the standard dressing group. Specifically, the satisfaction rate was 85% in the amnion-silver group compared to 60% in the standard dressing group, which showed a statistically significant difference (P-value 0.001) (Table 5). □

DISCUSSION

This study examined the effectiveness of two types of dressings; amnion-silver and standard dressings, on the healing process of patients with various wounds. Based on the collected data, it can be concluded that the use of amnion-silver dressings, compared to standard dressings, results in significant improvements in recovery time, treatment costs, narcotic use, pain levels and nursing workload.

The findings of this study align with previous research demonstrating that amniotic membranes promote rapid epithelialization and wound hea-

ling. Studies such as those conducted in the burn unit of Imam Khomeini Hospital in Urmia, Iran, in 2022 (11), as well as Kadkhoda's research (12) in 2020, support the effectiveness of amniotic membranes in reducing pain, enhancing epithelialization, and lowering infection risk.

Based on our study results, which indicate a shorter wound healing time in the amniotic membrane group (eight days *versus* 11 days) and lower treatment costs (21% reduction), this dressing is recognized as an effective and economical option for wound healing, particularly for skin graft donor sites. Branski *et al*, in their cohort study, also demonstrated that the amniotic membrane group experienced a shorter healing time compared to other dressing materials and showed that the healing process was facilitated in wounds covered with amniotic membrane. Additionally, the reduced workload on nursing staff not only aids in better resource management within hospitals but also positively impacts the overall satisfaction and well-being of healthcare staff. These benefits can lead to an improved work environment, reducing fatigue and occupational burnout, which in the long term enhances the quality of care provided to patients (13, 14). Furthermore, amniotic membranes address economic, logistical and biological challenges, making them particularly well-suited for wound care in Iran and similar regions. Their

adoption could bridge gaps in advanced wound management technologies while providing an effective patient-centric care (13, 14). These findings support the results of the present study.

A significant concern is the risk of infection at the wound site, which can escalate from a minor defect to complete skin loss, equivalent to a third-degree burn. Thus, antibiotic dressings on the wound site are considered essential, provided it does not interfere with the healing process. Faster epithelialization occurs when a moist environment is maintained at the wound site. Moreover, using an occlusive dressing minimizes the risks of dehydration, injury and contamination. Occlusive dressings are also believed to protect the exposed nerves at the donor site from air exposure and reduce the accumulation of metabolites, which leads to decreased pain sensation. Studies demonstrated that amniotic membranes could help reduce infection in burn wounds, a finding consistent with the present study, where no infections were reported in the amnion-silver group, while three cases of infection were noted in the standard dressing group (15).

The results showed that pain scores were higher in the control groups, which has also been emphasized in previous studies (16-18). In contrast, the moist environment provided by an occlusive dressing facilitates wound dressing removal with less damage to the newly formed epithelial layer. Adly *et al* report that there is less need for frequent dressing changes when using amniotic membranes, a benefit that has been also observed in the intervention sites in our study. This advantage likely reduces the pain experienced by patients during dressing changes. Additionally, pain levels and treatment acceptance with amniotic membrane were assessed, demonstrating high acceptance of this therapeutic approach, as shown by Mostaque and Rahman (9, 19).

There are the potential risks associated with amniotic membrane-based dressings, particularly the theoretical risk of disease transmission. However, stringent donor screening protocols, including serological and microbiological testing for infectious diseases such as HIV, HBV, and HCV, significantly mitigate these risks. Additionally, decontamination procedures using antibiotic-antifungal solutions and preservation methods, such as cryopreservation or lyophilization, further reduce the possibility of contamination. Reports of

adverse events, including infection transmission, related to amnion dressings are exceedingly rare when these standards are adhered to (20, 21). Nonetheless, healthcare providers must remain vigilant and adhere to established guidelines to ensure patient safety.

Another potential issue is immunogenic reactions, although the amniotic membrane's low antigenicity generally minimizes the likelihood of such complications.

In addition to the risks associated with the amnion itself, the silver component may contribute side effects. Prolonged or excessive exposure to silver sulfadiazine has been linked to argyria (skin discoloration) and potential toxicity, especially in individuals with impaired renal function. Furthermore, silver's broad-spectrum antimicrobial activity may disrupt normal microbial flora, potentially delaying wound healing in some cases (21). These risks underscore the importance of careful patient selection, adherence to established safety protocols, and monitoring for adverse effects during the use of amnion-silver dressings. Future studies should also assess these risks in greater detail to inform clinical guidelines.

The limitations of this study primarily stem from its being conducted at a single hospital, which may limit the generalizability of its findings. The demographic and clinical characteristics of patients at this institution may not reflect those of a broader population, potentially affecting the external validity of the results. Expanding the study to multiple centers with diverse populations would provide a more comprehensive understanding of the efficacy and safety of amnion-silver dressings across various clinical settings.

Additionally, the sample size of 50 patients, while adequate for initial observations, limits the statistical power and robustness of the findings. Larger studies with increased sample sizes are recommended to validate these results and explore subgroup analyses, such as differences in response based on patient age, burn location, or comorbidities. Furthermore, this study focuses on short-term outcomes, leaving the long-term effects of amnion-silver dressings, such as scar quality and recurrence of infections, unexplored (22). Future research should incorporate longer follow-up periods.

Furthermore, it is recommended to conduct the study about the cost-effectiveness of amnion-silver dressings in different healthcare settings. □

CONCLUSION

Overall, the results of this study, along with comparisons to findings from other researchers, conclude the significant effectiveness of amnion-silver dressings in managing various wounds, mainly burn wounds. This dressing reduces healing time and treatment costs, decreases the need for pharmaceutical interventions, lessens nursing workload, and enhances patient satisfaction. Given the numerous advantages of this dressing type,

it is recommended that amnion-silver dressings be considered in healthcare centers for optimal wound management and to improve healthcare quality. $\square$

Consent for publication: Consent for publication was obtained from all patients included in the present study.

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