

## Original Article



# A Comparative Study of the Impacts of Aloe vera Gel and Silver Sulfadiazine Cream 1% on Healing, Itching and Pain of Burn Wounds: A Randomized Clinical Trial

Maryam Mahboub<sup>1</sup>, Ahmad Mirza Aghazadeh Attari<sup>2</sup>, Zahra Sheikhalipour<sup>1</sup>, Mohammad Mirza Aghazadeh Attari<sup>3</sup>, Babak Davami<sup>4</sup>, Alireza Amidfar<sup>1</sup>, Mojgan Lotfi<sup>1\*</sup>

<sup>1</sup>Department of Medical and Surgical Nursing, Faculty of Nursing and Midwifery, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Department of Basic Sciences, Faculty of Paramedicine, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>3</sup>Faculty of Medicine, Medical Imaging Center, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>4</sup>Plastic Surgeon, Sina Hospital, Tabriz University of Medical Sciences, Tabriz, Iran

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#### \*Corresponding Author:

Mojgan Lotfi,

Email: mojgan.lotfi@yahoo.com

### Abstract

**Introduction:** Although several studies have highlighted the beneficial effects of Aloe vera on burn wounds, limited clinical evidence exists in this regard. This study aimed to evaluate the impact of the Aloe vera gel on healing, itching and pain of burn patients.

**Methods:** This clinical trial was conducted at Sina Hospital in Tabriz, Iran. The patients with second and first degree burn wounds on symmetrical organs, were randomly assigned to control (n=34) and experimental (n=34) groups. The Aloe vera gel and silver sulfadiazine cream were used in the experimental and control groups, respectively. To assess the healing effects, the Bates-Jensen Wound Assessment Tool (BWAT) was employed. Regarding itching and pain, visual analogue scale (VAS) was used for precise evaluation and comparison on days 1, 3, 5, 7, 9 and 14. The data were analyzed using SPSS version 13.

**Results:** Although the wounds in both groups healed up completely within two weeks, the healing process among the patients in the experimental group was faster. The peak of wound itching was on day 7 in both groups. The wound itching significantly reduced half an hour after being dressed with Aloe vera gel. The wound pain in the experimental group was less than control group during the study period. Moreover, there was no pain in either experimental or control group on day 14.

**Conclusion:** Aloe vera is an effective agent in reducing itching and pain, and it can substantially increase the rate of healing. Accordingly, this agent can be considered in the treatment of burn wounds.

### Introduction

A burn episode is associated with significant physical, mental, and financial distress for any individual and their immediate family.<sup>1,2</sup> Regardless of the quality of care and the duration of an individual's treatment, they may face various long-lasting complications.<sup>3</sup>

Healing a burn wound is a complex and dynamic process that restores typical cellular structures and tissue layers.<sup>4,5</sup> Clinicians aim to treat wounds in the most timely manner, with minimal pain and long-lasting sustenance of bodily functions.<sup>6</sup> In this regard, one of the main treatment options for burn patients is topical ointments and lotions.<sup>7</sup>

Among different treatments, Silver sulfadiazine cream 1% is the most commonly used treatment option with a broad-spectrum antimicrobial activity; this topical antibiotic is commonly used as a chemoprophylaxis agent against wound infections, which are one of the most

important causes of increased mortality in burn patients.<sup>8</sup> Due to surface-adhesion of the agent, dressing with this cream leaves a pseudo-scar and also has a toxic effect on the reconstruction process of keratinocytes, resulting in delayed wound healing.<sup>9</sup> Some uncommon side effects of this cream include leukopenia, renal toxicity, methemoglobinemia, silver poisoning (argyria), and skin discoloration. Also, patients with hypersensitivity reactions to sulfonamide groups have limitations in receiving this treatment.<sup>10-12</sup>

Aloe vera is one of the medicinal plants used as a topical agent for various local and systemic skin pathologies. In vitro, in vivo, and clinical studies have shown that this agent inhibits thromboxane (i.e., wound healing inhibitor), reduces inflammation, and leads to a swift healing process.<sup>13,14</sup>

Among the recommended herbs, Aloe vera is the

only plant which has undergone three evaluation types including the laboratory, animal, and clinical studies and the overall results of the aforementioned studies have determined positive impacts of the Aloe vera gel on wound and burn healing processes. Studies have indicated that Aloe vera is the first and most recommended herbal remedy for burn wounds.<sup>15-17</sup> Since no complications have been reported for Aloe vera gel, this herbal substance is perfectly safe for topical usage.<sup>18</sup> Despite the mentioned impacts of Aloe vera, literature reviews suggest that the corroborative evidence for Aloe vera effects on wound healing and pain are not sufficient enough.<sup>19</sup>

On the other hand, the healing, itching, and pain factors of burn wounds have often been studied separately and the relation of these factors or whether faster healing of the wound results in pain and itching reduction have not been considered. For example, Malekhosseini et al compared the effects of silver sulfadiazine 1% and Aloe vera gel dressing on burn wound healing,<sup>20</sup> although they did not assess other variables. Such studies provide the necessary knowledge and information to adopt therapeutic protocols and also provide a profound understanding of the healing process or confirmation of what is said in textbooks regarding healing. As far as the researchers of this study investigated, there is no study on the impacts of Aloe vera gel on wound itching. Therefore, this study aimed to evaluate the impacts of Aloe vera gel on healing, itching, and pain of burn wounds.

**Materials and Methods**

This randomized single-blind clinical trial was conducted in two different groups at Tabriz University of Medical Sciences, Tabriz, Iran in 2019. It was carried out as a research project under the direct supervision of Tabriz University of Medical Sciences, and the study protocol was approved by the Research Ethics Committee.

First- and second-degree burn patients were selected

through convenience sampling and were randomly (simple random) divided into two groups of control and experimental based on burn in the side of body part (left or right side). The experimental group was treated with Aloe vera gel and the control group was treated with silver sulfadiazine cream 1% as a routine treatment. The wounds were observed by researcher (MM) and evaluated carefully for 14 consecutive days until complete healing. Pictures of all the wounds were taken on a daily basis after washing them with water and detergent with a neutral PH.

First- and second-degree burn patients with an extent of  $\geq 20\%$  total body surface area on symmetrical body parts within the same depth were selected. The selected patients did not have any underlying diseases such as diabetes mellitus, skin allergy diseases, malignancy, acquired immunodeficiency syndrome (AIDS), hypertension, and infectious diseases and they were not under treatment with cytotoxic drugs. The burned areas were apart from the genital area and face. The patients had been admitted to the hospital within a maximum of three hours after burn and not due to chemical and electrical factors, and they had not been transferred from other hospitals. The wounds were not infected with contaminating agents and no substances other than drinking water had been applied to the wounds before hospital admission. Exclusion criteria included patients discharged from or transferred to other hospitals for any reason and patients allergic to Aloe vera gel.

The total number of participants in each group was 35 patients (one patient excluded), finally 17 males and 17 females were selected based on a comparison of the total healing score for two dependent groups containing six measurements of 0.85 power and a significant level of  $\alpha = 0.01$  using G\*Power software (Figure 1). A pilot study was conducted on one male and one female patient with 4 wounds. If the participants were eligible for the study, comprehensive information about the aims and

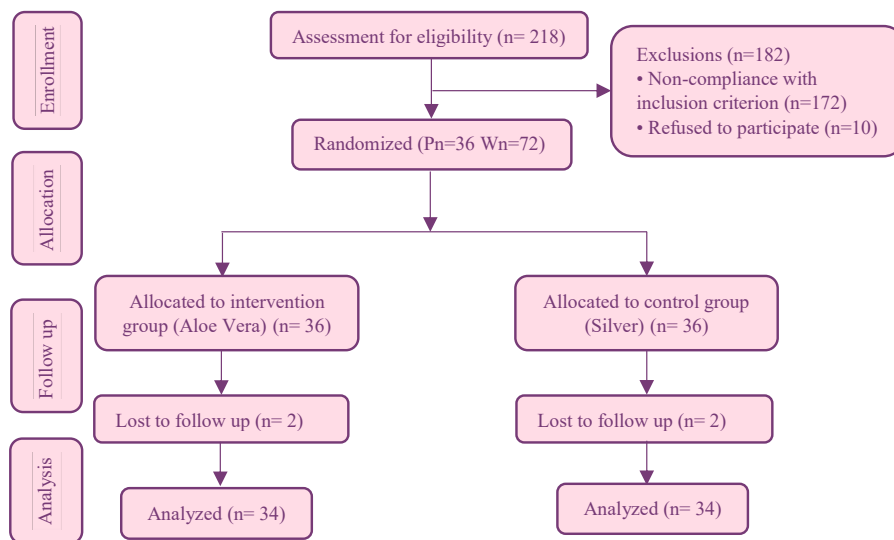


Figure 1. Flow chart of the study. Pn: Patient number, Wn: Wounds number.

confidentiality of the study was provided to them. An informed consent was obtained from all participants prior to data collection.

In both experimental and control groups, the wounds were washed with room temperature normal saline, and a detergent solution with a neutral pH was used subsequently. In case of having intact blisters, the wounds were washed without popping them, and if the blisters were pierced, they were washed without removing the blister wall. All wounds were gently dried with sterile gauze. The wound size was measured using a sterile plastic ruler.

Assigning patients to two groups was performed in two stages. During the first stage, eligible patients were selected based on the convenience sampling method. To randomize the 'Control' and 'Experimental' groups, the patients were randomly assigned to experimental and control groups using four envelopes labeled as control, experimental, left, and right. Envelopes were chosen by a person who had no direct contact with the patients. First, the person was told to select one of the two envelopes labeled as 'experimental' and 'control'; then she/he chose another envelope among the envelopes labeled as 'left' and 'right'. Accordingly, it was determined whether the experimental or control patients would be on the left or right side.

After selecting eligible patients and including them in the study, symmetrical wounds were randomly assigned to two groups of experimental and control. The wounds assigned to the experimental group were dressed with Aloe vera gel and the symmetric ones in the control group were dressed with silver sulfadiazine 1%. The wounds had been washed on a daily basis without removing the blisters. In the experimental group, a layer of Aloe vera gel with a thickness of 3 mm was applied on the wound. According to the instructions of the manufacturer, the gel had been prepared from the lower leaves of the plant and, like filleting fish, after separating the middle glaze, the prepared mucilage had been used for the treatment process. For the control group, a layer of silver sulfadiazine cream 1% with a thickness of 3 mm was applied on the wound. Then, Vaseline gauze was applied on each wound in both groups and the wounds were bandaged similarly in both groups. The dressing was changed daily at 9 AM. All the steps were taken by one of the research team members who was a registered nurse trained for burn care. The healing rate of the wounds was first photographed in the following days after the wounds were washed. Then, using the Bates-Jensen Wound Assessment Tool (BWAT), they were evaluated and recorded by another member of the research team who was blind to the patient's group and the dressing materials. The pain and itching intensity score in both groups were evaluated and recorded by the same individual using visual analogue scale (VAS) half an hour before and after dressing in the morning, as well as at 8:00 PM. During the study, if the patient developed a fever

or was suspected to be infected, a sample was taken from the wound; if the test result was positive, the patient was excluded from the study. Fortunately, no case with fever and infection was observed (Figure 1).

The tools used in this study included a demographic form, the BWAT, and VAS. Healing, itching, and pain scores in both experimental and control groups were measured within 14 days and compared on days 1, 3, 5, 7, 9, and 14 (Figure 1).

Wound healing scores were measured by the BWAT, which is a 15-item questionnaire with two items related to the location (anatomical site) and shape of the wounds not classified based on the Likert scale. However, the other 13 items of wound evaluation including size, depth, edges, undermining, necrotic tissue type, necrotic tissue amount, exudate type, exudate amount, skin color surrounding wound, peripheral tissue edema, peripheral tissue induration, granulation tissue and epithelization. The scores for the questions are in the range of one to five, with a score of one indicating the best condition and five indicating the worst condition. Based on this tool, the minimum score attainable is 13, and the maximum score is 65. The higher scores indicate deterioration and lack of wound healing, whereas the lower scores indicate improvement in the wound healing process. For measuring the size of the wound, a disposable ruler was used with a precision of 1:200. The wound healing scores were recorded and verified by two individuals through direct clinical and wound image observation daily.

A 10-point VAS was used for assessing pain and itchiness, in which zero indicates no pain and itching at all and ten indicates the highest pain intensity and severity of itching. Accordingly, the pain severity and itching in the range of 0-2 is mild, 3-5 is moderate, 6-8 is severe, and nine or higher indicates the highest pain and itching severity.

Statistical analysis was done by SPSS (version 13, Chicago, IL, USA). Descriptive variables were presented as frequency and percentage, and quantitative variables were represented as mean and standard deviation (SD). For comparing the total scores of healing, itching, and pain on days 1, 3, 5, 7, 9, 11, and 14, one-way analysis of variance (ANOVA) with repeated measures and multiple testing in case of meaningful measures were used. If the obtained data did not have a normal distribution, the Friedman test was used; otherwise, multiple comparative analysis was used. To determine content validity, the questionnaires were distributed among 15 academic members to gather their opinions. To measure reliability, in a pilot study, two questionnaires were completed for 20 burn patients, and the Cronbach's coefficient alpha was calculated. For the VAS questionnaire, Cronbach's coefficient alpha was 0.85,<sup>23</sup> and for BWAT it was 0.91. It should be noted that the reliability coefficient among assessors (graders) was 0.99, which was considerably higher than that reported in previous studies (0.89).<sup>24,25</sup>

**Results**

In this study, 36 patients with first- and second-degree burn wounds were included. Two cases left the study due to severe pain after applying Aloe vera gel and the patient's unwillingness to continue the treatment. Accordingly, 34 patients entered our final analysis (Figure 1).

The mean (SD) age of the participants was 36.32 (2.02) years. The most common cause of burn injury in females was scalds (32.35%), while it was contact with fire in males (26.50%). In females, seven cases had hand burns (41.30%), and six cases had burns on their feet. In males, eight cases had hand burns (47.10%).

For comparing the healing scores of the burn wounds in both experimental and control groups, two-way ANOVA with repeated measures was performed on days 1, 3, 5, 7, 9, and 14. The results are shown in Table 1. To determine whether there is a significant difference between the total pain scores of both experimental and control groups on different days before and after dressing and at 8:00 PM, two-way ANOVA with repeated measures was used. The results are shown in Table 2. The pain score in both groups on the first day of treatment was equal. Thirty minutes after dressing with Aloe vera in the experimental group and silver sulfadiazine in the control group, the pain had relieved in both groups; however, it had a gentler slope in the experimental group compared to the control group. Pain levels were also lower in the experimental group during 14 days and reached zero on day 14.

For evaluating whether there was a significant difference between the itching scores of two groups on different days, two-way repeated measures ANOVA was used. The results are summarized in Table 3. The average score of itching in both groups was identical on the first day of treatment, with the average score increasing gradually until days 5-7 when it started to decline in both groups. According to Table 3, the decline in itchiness was greater in the experimental group. After the third day, the experimental

**Table 1.** Results of wound healing scores in both experimental (Aloe vera) and control (Silver sulfadiazine) groups

Healing	Medication	Mean (SD)	95% CI	
			LL	UL
Day1	Aloe vera	24.91)1.29(	22.28	27.53
	Silver	23.14)1.15(	20.79	25.50
Day 3	Aloe vera	22.73)0.97(	20.76	24.70
	Silver	24.29)1.04(	22.16	26.42
Day 5	Aloe vera	16.52)1.50(	13.46	19.59
	Silver	19.05)1.62(	15.76	22.35
Day 7	Aloe vera	11.61)1.70(	8.14	15.08
	Silver	12.97)1.88(	9.13	16.80
Day 9	Aloe vera	5.35)1.38(	2.53	8.17
	Silver	6.08)1.56(	2.91	9.26
Day 14	Aloe vera	0.52)0.52(	-0.54	1.60
	Silver	0.52)0.52(	-0.54	1.60

LL, lower limit; UP, Upper limit.

**Table 2.** Results of pain scores in experimental (n= 34) and control (n=34) groups

Pain	Mean (SD)		95% CI			
	Aloe vera	Silver	Aloe vera		Silver	
			LL	UL	LL	UL
<b>Day 1</b>						
30 Mins before	9.20(0.47)	9.20(0.47)	8.25	10.16	8.25	10.16
30 Mins after	4.64(0.58)	7.41(0.42)	6.55	8.26	3.45	5.83
8:00 PM	6.08(0.48)	7.58(0.56)	6.43	8.73	5.09	7.08
<b>Day 3</b>						
30 Mins before	5.97(0.56)	6.55(0.52)	5.48	7.63	4.82	7.11
30 Mins after	3.67(0.48)	5.05(0.54)	3.95	6.15	2.69	4.66
8:00 PM	4.20(0.45)	5.44(0.51)	4.39	6.48	3.27	5.13
<b>Day 5</b>						
30 Mins before	3.85(0.61)	3.85(0.60)	8.25	10.16	8.25	10.16
30 Mins after	2.14(0.49)	2.88(0.56)	6.55	8.26	3.45	5.83
8:00 PM	3.38(0.48)	2.97(0.53)	6.43	8.73	5.09	7.08
<b>Day 7</b>						
30 Mins before	1.85(0.43)	2.05(0.46)	8.25	10.16	8.25	10.16
30 Mins after	0.85(0.31)	1.35(0.37)	6.55	8.26	3.45	5.83
8:00 PM	0.91(0.27)	1.41(0.37)	6.43	8.73	5.09	7.08
<b>Day 9</b>						
30 Mins before	0.64(0.25)	0.85(0.29)	8.25	10.16	8.25	10.16
30 Mins after	0.08(0.08)	0.44(0.17)	6.55	8.26	3.45	5.83
8:00 PM	0.38(0.16)	0.52(0.20)	6.43	8.73	5.09	7.08
<b>Day 14</b>						
30 Mins before	0.00(0.00)	0.00(0.00)	0.00	0.00	0.00	0.00
30 Mins after	0.00(0.00)	0.00(0.00)	0.00	0.00	0.00	0.00
8:00 PM	0.00(0.00)	0.00(0.00)	0.00	0.00	0.00	0.00

LL, lower limit; UP, Upper limit.

group had a greater downward slope compared to the control group. Also, the itching scores in experimental group were lower compared to the control group.

**Discussion**

This study aimed to determine the effects of Aloe vera gel on healing, itching, and pain of patients with first- and second-degree burn wounds. Our results indicated the favorable effects of Aloe vera in this regard.

Similar results were reported by Malekhosseini et al indicating that Aloe vera significantly improved the healing process.<sup>20</sup> In a clinical study conducted by Thamlikitkul et al two groups of patients were enrolled: 20 patients were treated with Aloe vera and 18 patients with silver sulfadiazine. Healing in the Aloe vera group was 95%, which was significantly higher compared to Silver sulfadiazine group (85%).<sup>21</sup> Sabaghzade Irani and Varaie compared the effects of Aloe vera gel and nitrofurazone 2% on epithelialization and granulation of the burn wounds. Their results showed that the formation of granulation tissue and re-epithelialization was faster in patients treated with Aloe vera gel.<sup>22,23</sup>

**Table 3.** Results of wound itching in experimental (n=34) and control (n=34) groups

Itching	Mean (SD)		95% CI			
	Aloe vera	Silver	Aloe vera		Silver	
			LL	UL	LL	UL
<b>Day 1</b>						
30 Mins before	0.00(0.00)	0.00(0.00)	0.00	0.00	0.00	0.00
30 Mins after	0.00(0.00)	0.00(0.00)	0.00	0.00	0.00	0.00
8:00 PM	0.00(0.00)	0.00(0.00)	0.00	0.00	0.00	0.00
<b>Day 3</b>						
30 Mins before	0.23(0.11)	0.23(0.14)	0.007	0.46	0.53	-0.06
30 Mins after	0.00(0.00)	0.14(0.08)	0.00	0.00	0.32	-0.02
8:00 PM	0.50(0.13)	0.52(0.19)	0.22	0.77	0.93	0.12
<b>Day 5</b>						
30 Mins before	1.17(0.24)	1.17(0.28)	0.68	1.66	1.74	0.60
30 Mins after	0.20(0.11)	0.73(0.22)	-0.01	0.43	1.19	0.27
8:00 PM	1.08(0.14)	1.76(0.29)	0.77	1.37	2.36	1.16
<b>Day 7</b>						
30 Mins before	2.08(0.35)	2.44(0.40)	1.36	2.80	3.26	1.62
30 Mins after	0.50(0.14)	1.76(0.35)	0.21	0.78	2.47	1.05
8:00 PM	1.73(0.32)	2.85(0.47)	1.06	2.40	3.82	1.88
<b>Day 9</b>						
30 Mins before	1.29(0.36)	1.91(0.51)	0.54	2.04	2.95	0.87
30 Mins after	0.29(0.14)	1.32(0.38)	0.002	0.58	2.10	0.54
8:00 PM	1.08(0.31)	1.94(0.51)	0.45	1.72	2.99	0.88
<b>Day 14</b>						
30 Mins before	0.08(0.08)	1.17(1.17)	-0.09	0.26	0.53	-0.18
30 Mins after	0.00(0.00)	0.08(0.08)	0.00	0.00	0.26	-0.09
8:00 PM	0.05(0.05)	0.14(0.14)	-0.06	0.17	0.44	-0.15

LL, lower limit; UP, Upper limit.

Moreover, Akhoondinasab et al showed that rats treated with Aloe vera had better healing scores compared to the rats treated with silver sulfadiazine. Also, the recovery process of Aloe vera group was faster than the sulfadiazine group.<sup>24</sup> Similar to our results, all these studies confirm the positive effect of Aloe vera gel on burn wounds.

The results of this study indicated the positive effects of Aloe vera on reducing pain and other undesired sensations in burn wounds. Daily evaluation of the wound healing process showed that Aloe vera caused no damage to the blister membrane and blister wall. In the group treated with Aloe vera, after the appearance of the pink epithelization tissue in the wound bed, the wound membrane of the blister was gently removed while the underlying tissue had undergone the final stages of healing, resulting in less pain.<sup>21</sup> However, in the group treated with silver sulfadiazine, the membrane had ruptured faster and wound discharge was greater. With blisters tearing up earlier, the restorative tissue directly contacted the dressing, which increased pain scores. It is worth mentioning that using Aloe vera on the wounds with pierced blisters caused severe pain and irritation, which

led to the exclusion of one of the participants. The blister membrane is a suitable dressing for burn wounds and if it can be preserved without being infected or pierced, it can reduce the amount of experienced pain and also increase the pace of the healing process.<sup>22,24</sup> Similar results were also shown by Varaei et al., regarding the comparison of Aloe vera and nitrofurazone.<sup>25</sup>

The results of this study indicated the effect of Aloe vera gel on reducing the wound itching. Although itching was at its peak in both groups on days 5 and 7, the experimental group had better itching scores than the control group. This observation is of importance as no study has focused on the effects of Aloe vera on itching, which is directly correlated with the healing process. Notably, various studies have shown that most patients with a second-degree or higher burn wounds have severe itching during the treatment process.<sup>26-28</sup> So, Aloe vera may even be considered as an adjuvant treatment to reduce itching in these patients.

This study was conducted on the first- and second-degree burn wounds with little or intact blisters. Therefore, it cannot be generalized to burn wounds that

## Research Highlights

### What is the current knowledge?

- Aloe vera is among natural products being included for wide-scale clinical use.
- Clinical studies have shown that Aloe vera inhibits thromboxane healing, reduces inflammation, and leads to a swift healing process.

### What is new here?

- Aloe vera gel contributed to faster healing of the wounds and reduced pain and itchiness in the process of treatment without any severe complications.

have blistering at the time of admission.

### Conclusion

Aloe vera gel contributed to faster healing of the wounds and reduced pain and itchiness in the process of treatment without any severe complications. This treatment could be considered as an adjuvant therapeutic agent in treating first- and second-degree wounds.

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### Authors' Contributions

ML, MM: Conception and design; ZSH, MM, BD: Acquisition of data; AMAA: Analysis and interpretation of data; AA, ML, BD: Drafting the article; MM, MMAA: Review of article and final approval. All authors have agreed final version of manuscript.

### Ethical Issues

This study was conducted after obtaining the written permission of the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1395.1052) and the study was registered in IRCT (IRCT20160424027561N10).

### Conflict of Interest

The authors declare that they have no competing interests.

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