

The Effects of *Aloe Vera* Cream on Split-thickness Skin Graft Donor Site Management: A Randomized, Blinded, Placebo-controlled Study

Ghasemali Khorasani, MD;¹ Ali Abmadi, MD;^{1,2} Seyed Jalal Hosseinimehr, PhD;³ Amirhossein Abmadi, PharmD;⁴ Abmadreza Taberi, MD;¹ Hamidreza Fathi, MD¹

WOUNDS 2011;23(2):44–48

From the ¹Department of Surgery, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran; ²Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran; ³Department of Radiopharmacy, Faculty of Pharmacy, Traditional and Complementary Medicine Research Center, Mazandaran University of Medical Sciences, Sari, Iran; ⁴Research Student Committee, Mazandaran University of Medical Sciences, Sari, Iran

Address correspondence to:

Ghasemali Khorasani, MD

Imam Khomeini Hospital

Keshasvarz Boulevard

Tehran, Iran

Phone: +98 21 66418885

E-mail: khorasani@tums.ac.ir

Abstract: *Purpose.* Split-thickness skin graft donor site management is an important patient comfort issue. The present study examined the effects of *aloe vera* cream compared to placebo cream and gauze dressing on the rates of wound healing and infection at the donor site. *Methods.* Forty-five patients were enrolled in this randomized clinical trial and divided into three groups: control (without topical agent), placebo (base cream without *aloe vera*), and *aloe vera* cream groups. All patients underwent split-thickness skin grafting for various reasons, and the skin graft donor site wounds were covered with single-layer gauze without any topical agent, with *aloe vera*, or with placebo cream. The donor sites were assessed daily postoperatively until complete healing was achieved. *Results.* Mean time to complete re-epithelization was 17 ± 8.6 , 9.7 ± 2.9 , and 8.8 ± 2.8 days for control, *aloe vera*, and placebo groups, respectively. Mean wound healing time in the control group was significantly different from the *aloe vera* and placebo groups ($P < 0.005$). The healing rate was not statistically different between *aloe vera* and placebo groups. *Conclusion.* This study showed a significantly shorter wound care time for skin graft donor sites in patients who were treated with *aloe vera* and placebo creams. The moist maintenance effect of these creams may contribute to wound healing.

Skin grafting is a reconstructive procedure in plastic surgery designed to accelerate the healing of wounds, such as burns and trauma wounds. The donor sites created after harvesting a split-thickness skin graft present an additional wound to manage. The management of the donor site after removing the skin graft is an important patient comfort issue. A suitable wound dressing helps to achieve wound healing and to satisfy patients barring any complications, such as infection or pain. A suitable dressing should also facilitate physiological recovery.^{1,2} There are two dressing strategies for wound healing after skin grafting: dressing with high humidity at the wound harvesting surface (moist dressing) and non-moist dressing (dry dressing).²⁻⁴ Dressing material that adheres to the wound causes bleeding, and removing the dressing is often painful. A moist dressing has a

KEYPOINTS

- *Aloe vera* topical skin gel has been found to provide healing support for the skin
- *Aloe vera* has pharmacological properties including antioxidant, wound healing, antibacterial, antifungal, antiviral, and immunomodulating effects

greater effect on wound healing and pain relief than a dry dressing.⁵ Various types of dressing materials have been recognized based on ease of use, cost, optimal healing environment, and pain relief, eg, paraffin gauze dressing,⁶ hemicellulose dressing (Veloderm®, BTC srl, Torino, Italy),¹ lipido-colloid wound dressing (Urgotul®, Laboratoires Urgo, Chenôve, France),⁷ polyurethane film,⁸ carboxymethyl cellulose dressing (Aquacel®, ConvaTec, Skillman, NJ),⁹ ionic-containing hydrofiber dressing,¹⁰ alginate (Kaltostat®, ConvaTec),³ and polyvinyl pyrrolidone-iodine liposome hydrogel.¹¹ These dressing materials induce moisture on the wound surface by absorbing and maintaining water. In 2009, Voineskos et al⁴ conducted a comprehensive systematic review of skin graft donor site dressings. They concluded that the evidence supporting moist wound dressings is weak, and more methodologically sound, randomized, controlled trials are needed to determine the optimal dressing for split-thickness skin graft donor sites. Trials with parallel evaluations are necessary to answer this question.⁴ Although numerous dressings have been studied, there is not one perfect dressing for use on the donor site that is easy to use, provides patient comfort, prevents infection, is inexpensive, and promotes faster re-epithelization.

Aloe vera (family: *Liliaceae*) has been used in traditional medicine for a long time. *Aloe vera* gel, which is obtained by breaking or slicing its leaf, is the principle part of the plant that is used in herbal medicine. *Aloe vera* contains many important nutrients including amino acids, B group vitamins, polysaccharides, and other nutrients that support general health. It also has many pharmacological properties including antioxidant, wound healing, antibacterial, antifungal, antiviral, and immunomodulating effects.^{12,15,16} The topical skin gel provides healing support for the skin. Recently, the authors demonstrated that *aloe vera* cream treatment could reduce healing time in patients with burn injury compared to silver cream,¹⁷ and it has been demonstrated that this cream facilitates wound healing in posthemorrhoidectomy patients.¹⁸

In light of the potential uses for *aloe vera* in wound

healing, the present clinical study was aimed to examine the effect of *aloe vera* cream in comparison with gauze dressing and placebo cream on the rate of donor site wound healing.

Materials and Methods

***Aloe vera* cream preparation.** Pure spray-dried *aloe vera* powder was used for preparing the *aloe vera* cream. White liquid paraffin (2 g), stearyl alcohol (7.5 g), cetyl alcohol (7.5 g), solid white paraffin (3 g), and propylene paraben (0.015 g) were mixed and heated to a boil (oil phase). *Aloe vera* powder (0.5 g) and 70 mL deionized water was added to the mixture with propylene glycol (7 g), sodium lauryl sulfate (3 g), and methyl paraben (0.025 g). The mixture was heated until it reached an aqueous state (liquid phase). Next, the oil and liquid were mixed continuously while being gradually cooled. The uniform cream (500 g), once it had cooled, was stored in a plastic package. The cream contained 0.5% of the *aloe vera* gel powder. The preparation was carried out under sterile conditions. The cream was tested for contaminating microbes, and none were found.

Patients and study protocol. Permission to perform the study was granted from the Ethical Committee at Tehran University of Medical Sciences (no. 130-362), and was carried out in the Plastic Surgery ward at Imam Khomeini Hospital (Tehran, Iran) during 2009 and 2010. The inclusion criterion was undergoing skin graft harvest of the thigh due to trauma, tumor, or scar. Patients were aged between 12 and 70 years. Exclusion criteria were diabetes mellitus, immunodeficiency state, pregnancy, and kidney disease. The patients and attendants were given information regarding the drug (*aloe vera* cream) and written informed consent was obtained from all patients. Forty-five patients were enrolled into this study. After the patients were administered general anesthesia, the donor site was prepared with 10% povidone-

KEYPOINTS

- The test cream contained 0.5% of the *aloe vera* gel powder
- Study patients were those who had a skin graft harvest from the thigh because of trauma, tumor, or scar
- The *aloe vera* and placebo groups received *aloe* or base cream on single-layer gauze three times daily, respectively; no topical treatment or dressing was applied in the control group

Table 1. Patient demographics.

Characteristic	Control group (n = 15)	Aloe group (n = 15)	Base group (n = 15)	P*
Male/female	13/2	11/4	13/2	0.05*
Age (years) mean ± SD	38.2 ± 13.5	35.5 ± 15.6	32.6 ± 15.2	0.05*
Reason (%)				
Trauma	26.7	40	60	
Scar	26.7	26.7	20	
Bedsore	13.3	6.7	13.3	
Tumor	20	20	6.7	
Reconstruction	13.3	6.7	60	
Area (skin harvest) mean ± SD (cm ²)	146 ± 104	140 ± 103	114 ± 89	0.05*

*Not significant

layer of petrolatum gauze along with several sterile gauzes. After 2 days, the top dressing layer was removed leaving the first gauze layer in place to prevent damage to the wounds. No treatment or dressing was applied in the control group. The *aloe vera* and placebo groups received *aloe vera* or base cream on single-layer gauze three times daily, respectively. Donor site re-epithelization was evaluated postoperatively on a daily basis until complete re-epithelization and until separation of the single layer gauze could be performed without causing the patient further trauma or pain. The time to complete re-epithelization was recorded

for each patient. Wound infection was subjectively measured based on clinical signs of infection (edema, heat, pain, pus discharge, or smell). Another physician, who was blinded to the treatments, clinically assessed all patients.

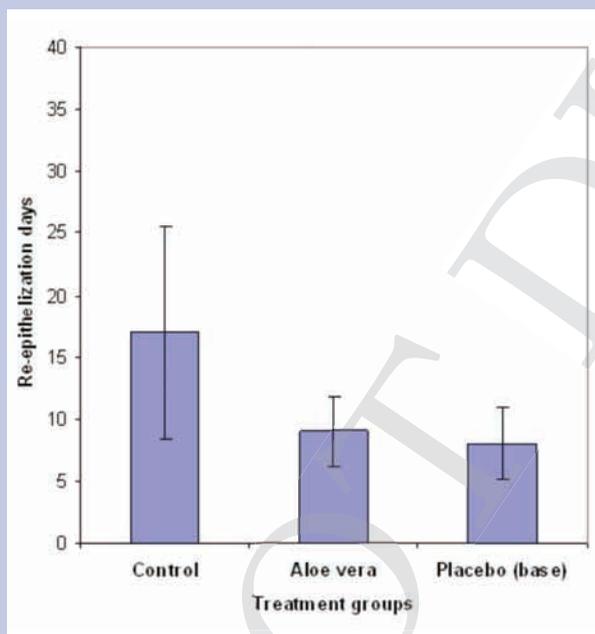
Statistical Analysis

The data were analyzed using SPSS version 10.0 software. Student's *t* test and ANOVA test were used to compare the wound size and healing time between two groups and all three groups, respectively. The significance level was determined less than $P < 0.05$. A Chi-square test was used for descriptive analysis.

Results

A total of 45 patients (45 donor sites) were enrolled in this study with follow-up until complete healing (Table 1). There were 37 (82.2%) men and 8 (17.8%) women. Significant differences were not found between groups in relation to age or sex. Average total skin graft size was similar between control, *aloe vera*, and placebo groups (Table 1). The re-epithelization time in the control group was 17 ± 8.6 days (range, 8–37), while in the *aloe vera* group and placebo group it was 9.7 ± 2.9 days (range, 5–18) and 8.8 ± 2.8 days (range, 4–14), respectively (Figure 1). Mean time to wound healing was significantly different in the control group compared to the *aloe vera* and placebo groups ($P < 0.005$). There was not any significant difference in mean re-epithelization time between *aloe vera* and placebo (base) groups ($P = 0.9$).

There were no allergic reactions or other adverse events (eg, donor site infection) related to the dressings.

**Figure 1.** Mean time from application of dressing to complete re-epithelization.

iodine solution. All skin grafts were harvested from anterolateral and posterior thigh regions with an electric Padgett Dermatome (Olympus), which was adjusted to 0.014 in. A nurse generated the allocation sequence, and patients were randomly allocated to one of three groups: *aloe vera* cream (group A [n = 15]), placebo cream (base cream without *aloe vera* powder, group B [n = 15]) and the control (without topical agent, group C [n = 15]). The dressing was similar for all groups and at the end of skin harvesting, wounds were dressed and bandaged with a

Discussion

This study showed that *aloe vera* and base creams had wound healing effects on the donor sites after harvest. Re-epithelization time was faster among patients treated with these creams as compared to patients who did not use any topical agent. Conversely, a significant difference in healing times between aloe and base groups was not observed. In cream-treated groups, the creams were applied continuously to the donor sites, which induced a moist wound environment compared to dry gauze dressing. The gauze dressing initially provided a moist wound environment, but gradually became desiccated due to evaporation, whereupon the fine-mesh gauze firmly bound to the wound surface, making it more painful to remove than the other moist dressings.^{5,19} This scenario also impairs the migration of epithelial cells necessary to achieve complete re-epithelization.²⁰ In an evidence-based review, Joel et al²¹ concluded that moist dressings decrease the days to complete healing as compared to non-moist dressings. Among the broad categories of non-moist and moist-dressing, no differences were found in infection rates between these two types of dressings.²¹ Other studies showed that a maintenance (foam) dressing did not significantly reduce wound healing time compared to gauze dressing.^{19,20} In a systematic review, Wiechula et al² concluded that moist wound healing products have definitive clinical advantages over non-moist products in management of split-thickness skin graft donor sites. These advantages are related to healing, comfort, and infection rates. Although, they conceded that head-to-head studies comparing products with moisture-retaining properties are needed to determine the optimum moist dressing.² Moist dressings enhance re-epithelization of partial-thickness wounds by allowing diffusion of oxygen and water vapor, while providing a barrier to the passage of fluid or wound exudate.²⁰ In a recent systematic review, Voineskos et al⁴ revealed that there is some weak evidence supporting the beneficial effect of moist dressings on wound healing in split-thickness skin graft donor sites. Due to methodological differences in the previous studies, the authors proposed that it is necessary to do parallel randomized clinical trials to confirm which is the optimal dressing.⁴ One advantage of the present study was the use of placebo cream in addition to *aloe* cream and gauze dressing, which provided reliable data to determine the beneficial effects of *aloe vera* cream on donor site wounds.

Aloe vera preparations have many biological effects including anti-diabetic, immunomodulatory, anti-inflammatory, antioxidant, and wound healing effects.²² *Aloe*

vera application was associated with a significant reduction in the wound healing time compared to the control.¹³ *Aloe* contains various carbohydrate constituents as polysaccharides. Polysaccharides are known to have properties in skin wound repair.^{22,23} Additionally, it is believed that the anti-inflammatory effect of *aloe vera* contributes to faster healing.^{14,23}

Collagen is the major protein in the extracellular matrix and provides strength and integrity to the dermis and other supporting tissues. *Aloe vera* enhances the production of collagen.^{24,25} *Aloe vera* has antimicrobial properties, which can help to prevent wound infection.²⁶ In recent clinical trials, application of aloe cream on wounds was associated with significant wound healing effects in patients with burn injuries and post-hemorrhoidectomy.^{17,18} These results showed *aloe vera* facilitates the healing process in different wound types. In this study, although the aloe cream exhibited a shorter time to wound healing compared to gauze dressing, its effect was not better than placebo cream. *Aloe* cream might be more effective at higher concentrations than the 0.5% concentration used in the present study. Both creams induced a moist wound environment as compared to gauze dressing, and maintaining a moist donor site is critical to wound healing.⁴ Winter²⁷ first described the improvement of wound healing under moist dressings in 1962, but Voineskos et al⁴ concluded that the evidence supporting that “wet dressings” is weak. In the present study, parallel wet and dry dressings confirmed that a moist environment promotes donor site wound healing. Both creams have several hydrophilic and lipophilic ingredients such as paraffin, propylene glycol, and alcohol that may be involved in keeping the wound surface moist. The cream’s simple preparation and inexpensiveness are two advantages that might further encourage commercial production.

KEYPOINTS

- Although the *aloe* cream exhibited a shorter wound healing time compared to gauze dressing, its effect was not better than the placebo cream
- *Aloe* cream might be more effective at higher concentrations than the 0.5% concentration used in the present study

Conclusion

A topical cream containing *aloe vera* and a placebo cream enhanced wound healing in split-thickness skin grafts when compared with a dry gauze dressing.

Moisture maintenance on the donor site surface may explain the observed beneficial effects.

Acknowledgement

This work was supported by a grant (grant number 752) from Tehran University of Medical Sciences, Iran.

References

1. Ferreira LM, Blanes L, Gragnani A, et al. Hemicellulose dressing versus rayon dressing in the re-epithelialization of split-thickness skin graft donor sites: a multicenter study. *J Tissue Viabil.* 2009;18(3):88-94.
2. Wiechula R. The use of moist wound-healing dressings in the management of split-thickness skin graft donor sites: a systematic review. *Int J Nurs Pract.* 2003;9(2):S9-17.
3. Hormbrey E, Pandya A, Giele H. Adhesive retention dressings are more comfortable than alginate dressings on split-skin-graft donor sites. *Br J Plast Surg.* 2003;56(5):498-503.
4. Voineskos SH, Ayeni OA, McKnight L, Thoma A. Systematic review of skin graft donor-site dressings. *Plast Reconstr Surg.* 2009;124(1):298-306.
5. Giele H. Retention dressings: a new option for donor site dressings. *Australas J Dermatol.* 1997;38(3):166.
6. Uygur F, Evinc R, Ulkur E, Celikoz B. Use of lyophilized bovine collagen for split-thickness skin graft donor site management. *Burns.* 2008;34(7):1011-1014.
7. Tan PW, Ho WC, Song C. The use of Urgotul in the treatment of partial thickness burns and split-thickness skin graft donor sites: a prospective control study. *Int Wound J.* 2009;6(4):295-300.
8. Dornseifer U, Fichter AM, Herter F, Sturtz G, Ninkovic M. The ideal split-thickness skin graft donor site dressing: rediscovery of polyurethane film. *Ann Plast Surg.* 2009;63(2):198-200.
9. Wang TH, Ma H, Yeh FL, Lin JT, Shen BH. The use of "composite dressing" for covering split-thickness skin graft donor sites. *Burns.* 2010;36(2):252-255.
10. Lohsiriwat V, Chuangsuwanich A. Comparison of the ionic silver-containing hydrofiber and paraffin gauze dressing on split-thickness skin graft donor sites. *Ann Plast Surg.* 2009;62(4):421-422.
11. Vogt PM, Hauser J, Rossbach O, et al. Polyvinyl pyrrolidone-iodine liposome hydrogel improves epithelialization by combining moisture and antiseptis. A new concept in wound therapy. *Wound Repair Regen.* 2001;9(2):116-122.
12. Hu Q, Hu Y, Xu J. Free radical-scavenging activity of Aloe vera (*Aloe barbadensis* Miller) extracts by supercritical carbon dioxide extraction. *Food Chem.* 2005;91:85-90.
13. Maenthaisong R, Chaiyakunapruk N, Niruntraporn S, Kongkaew C. The efficacy of aloe vera used for burn wound healing: a systematic review. *Burns.* 2007;33(6):713-718.
14. Rodríguez-Bigas M, Cruz NI, Suárez A. Comparative evaluation of aloe vera in the management of burn wounds in guinea pigs. *Plast Reconstr Surg.* 1988;81(3):386-389.
15. West DP, Zhu YF. Evaluation of aloe vera gel gloves in the treatment of dry skin associated with occupational exposure. *Am J Infect Control.* 2003;31(3):40-42.
16. Rosca-Casian O, Parvu M, Vlase L, Tamas M. Antifungal activity of Aloe vera leaves. *Fitoterapia.* 2007;78(3):219-222.
17. Khorasani G, Hosseini-mehr SJ, Azadbakht M, Zamani A, Mahdavi MR. Aloe versus silver sulfadiazine creams for second-degree burns: a randomized controlled study. *Surg Today.* 2009;39(7):587-591.
18. Eshghi F, Hosseini-mehr SJ, Rahmani N, et al. The effects of Aloe vera cream on posthemorrhoidectomy pain and wound healing: results of a randomized, blind, placebo-control study. *J Altern Complement Med.* 2010;16(6):647-650.
19. Persson K, Salemark L. How to dress donor sites of split thickness skin grafts: a prospective, randomised study of four dressings. *Scand J Plast Reconstr Surg Hand Surg.* 2000;34(1):55-59.
20. Weber RS, Hankins P, Limitone E, et al. Split-thickness skin graft donor site management. A randomized prospective trial comparing a hydrophilic polyurethane absorbent foam dressing with a petrolatum gauze dressing. *Arch Otolaryngol Head Neck Surg.* 1995;121(10):1145-1149.
21. Beam JW. Management of superficial to partial-thickness wounds. *J Athl Train.* 2007;42(3):422-424.
22. Hamman JH. Composition and applications of Aloe vera leaf gel. *Molecules.* 2008;13(8):1599-1616.
23. Jia Y, Zhao G, Jia J. Preliminary evaluation: the effects of Aloe ferox Miller and Aloe arborescens Miller on wound healing. *J Ethnopharmacol.* 2008;120(2):181-189.
24. Chithra P, Sajithlal GB, Chandrakasan G. Influence of Aloe vera on collagen turnover in healing of dermal wounds in rats. *Indian J Exp Biol.* 1998;36(9):896-901.
25. Chithra P, Sajithlal GB, Chandrakasan G. Influence of Aloe vera on the glycosaminoglycans in the matrix of healing dermal wounds in rats. *J Ethnopharmacol.* 1998;59:179-186.
26. Agarry O, Olaleye MT, Bello-Michael CO. Comparative antimicrobial activities of aloe vera gel and leaf. *Afr J Biotechnol.* 2005;4(12):1413-1414.
27. Spear M, Bailey A. Treatment of skin graft donor sites with a unique transparent absorbent acrylic dressing. *Plast Surg Nurs.* 2009;29(4):194-200.