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Original Article

Comparison of the effectiveness of Aloe Vera gel with 2% Nitrofurazone ointment on the healing of superficial partial-thickness burns: A randomized clinical trial study

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ABSTRACT

Background & Aim: Routine treatment of burn injuries is dressing with Nitrofurazone ointment. It has several complications, including sensitivity. Aloe Vera is a traditional treatment for wound healing. This study aimed to compare the effectiveness of Aloe Vera gel with Nitrofurazone ointment in the healing of superficial partial-thickness burns.
Methods & Materials: The present study was a split body controlled clinical trial which was carried out on 30 patients with superficial partial-thickness burns. The study was conducted in the Shafa Hospital in Kerman, Iran, in 2016. The sample was recruited from patients who had at least two burns, each burn on an alternate side of the body. On their burns, samples were allocated to two groups that received Aloe Vera gel or 2% Nitrofurazone ointment. Bates-Jensen Wound assessment tool was used to evaluate the healing of burns. Statistical analysis was conducted by SPSS-16 and using the repeated measure ANOVA.
Results: The repeated measure ANOVA showed that there was a significant change in the score of BWAT in all areas during the intervention period (p=0.001), but the trend of healing in the two groups during the intervention period was not significantly different (p=0.098).
Conclusion: Based on this study, it looks like Aloe vera gel is as effective as 2% Nitrofurazone ointment in healing wounds.

Introduction

Burn injuries are among the most common causes of hospitalization. They are responsible for 5% of hospitalization worldwide, and they have a higher burden in developing countries (1). The healing of burn wounds is critical in the recovery and rehabilitation of these patients (2). The American Burn Association (ABA) has published an educational resource that reviewed the classification and management of burn wounds. Based on the classification, superficial or epidermal burns involve only the epidermal layer of skin.

Partial-thickness burns involve the epidermis and portions of the dermis. Superficial partial-thickness burns

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characteristically from blisters within 24 hours. Blisters form between the epidermis and dermis. Superficial partial-thickness burns are painful, red, and weeping, and blanch with pressure.

One of the routine treatments of superficial partial-thickness burns is daily washing and dressing with 2% Nitrofurazone ointment (3). This ointment is widely used to treat various types of superficial wounds, including burns. However, complications such as localized and limited drug absorption in the wound, drug resistance, allergic contact dermatitis, edema, erythema, itching, and blisters have been reported (4, 5). Due to these complications, Bajaj and Gupta reported that Nitrofurazone was the most sensitizing agent in 390 patients and that 36.2% of the patients had a positive reaction due to Nitrofurazone(4). In a study conducted by Yılmaz *et al.*, contact allergic findings (erythema, bullae, pruritus) related to Nitrofurazone were found in 4 (2%) of 200 patients who had various injuries (diabetic foot, pressure sore, burn, a venous ulcer, traumatic skin wounds, skin infections, laceration, infected incision) and treated with topical Nitrofurazone cream in the plastic surgery department (6). Due to the high incidence of allergic reactions, the use of Nitrofurazone in Western countries has been largely abandoned (7).

Aloe Vera has been traditionally used for burn healing. That is a clump-forming, perennial succulent with basal rosettes of tapering thick leaves. This plant has thick, juicy, and coarse leaves. The middle of the leaves is filled with a high viscosity transparent gel (8). Aloe Vera gel contains collagen, which can enhance tissue treatment, and its anti-inflammatory properties can be effective in the process of wound healing and epithelialization (9). The anti-inflammatory effect of Aloe Vera is due to the existence of salicylic acid and arachidonic acid (10). Salicylic acid inhibits the production of bradykinin and histamine. Arachidonic acid inhibits prostaglandin production (11). Research has shown that Aloe Vera has bacteriostatic and bactericidal effects on species such as Pseudomonas aeruginosa, Escherichia coli, Salmonella typhi, and Mycobacterium. Superficial partial-thickness burns generally heal in 7 to 21 days. Treatment for this type of burn should be done with minimal skin irritation. As the Aloe Vera, in addition to its antimicrobial properties, has the effect of moisturizing and reducing irritation, it can be an excellent ingredient for superficial partial-thickness burns dressing (12).

Nazari et al. reported the cause of the effectiveness of the Aloe Vera gel is that there are certain polysaccharides in it. These polysaccharides stimulate the recovery of the skin. Glycoprotein fraction is also the major component of Aloe Vera which is involved in wound healing with cell proliferation and migration (30).

Also, many studies past shown that Aloe Vera has a compound called glucomannan. Glucomannan affects fibroblasts' growth factor receptors and stimulates the activity and proliferation of these cells. This increases the production and secretion of collagen (31). Collagen is the major protein in the extracellular matrix and provides strength and integrity to the dermis and other supporting tissues (32). Aloe Vera mucilage enhances the production amount of collagen in the wound, modifies its structure. Increasing cross-connections between collagen strands accelerates wound healing (33).

Therefore, the purpose of this study was to compare the effect of Aloe Vera gel and conventional treatment (2% Nitrofurazone ointment) on the healing of superficial partial-thickness burns.

Methods

Study design

This study was a randomized non blind split body controlled clinical trial in a 2-years period. The study population consisted of all outpatients with superficial partial thickness burns who attended to Shafa hospital burn center, Kerman, Iran.

Subjects and setting

A convenience sample of 30 patients who had inclusion criteria enrolled in the study. Inclusion criteria had superficial partial-thickness burns with one burn positioned on the one side of the body and the other positioned on the alternate side of the body, total burns between 5%- 20% of the body, each burn surface smaller than 16 cm, no sign of infection and prescribing 2% Nitrofurazone ointment by Physician, no need for hospitalization, having physician permission to use Aloe Vera Gel instead of 2% Nitrofurazone ointment, not being affiliated with underlying diseases such as diabetes and immune deficiency such as cancer, AIDS and severe skin sensitivity and skin problems, the cause of the burn was contact with heat or hot liquids, admitting to the hospital before 6 hours, no material other than drinking water was used on the wound. In this study, one of the Inclusion criteria is the similarity in total BWAT scores in both intervention and control areas.

Random allocation was done by the study statistician. The researcher prepared 30 envelopes containing 15 cards labeled R and 15 cards labeled L. Each Patient selected an envelope. If the envelope with the letter R was opened, interventions would be done on the right side of the body and vice versa. The other side of the body was treated with 2% Nitrofurazone ointment.

Wounds were washed daily with normal saline 0.9% and dressing with sterile gauze (Sterile gases had no secondary substances) in both intervention and control area a thin layer of gel and ointment was used to cover the whole wound, so about 15 to 20 grams was used based on the wound size. Dressings were changed on a daily basis (according to the routine of the hospital). The burned areas were evaluated for infection each day. Burn wound infection criteria were as detailed by the American Burn Association Consensus Conferences (including Change in color of the burnt area or surrounding skin, Purplish discoloration, mainly if swelling is also present, change in thickness of the burn (the burn suddenly extends deep into the skin), greenish discharge or pus and fever (13). Patients with signs of infection or Systemic Inflammatory Response Syndrome (SIRS) were excluded from the study. Sample recruitment and allocation are presented in figure 1.

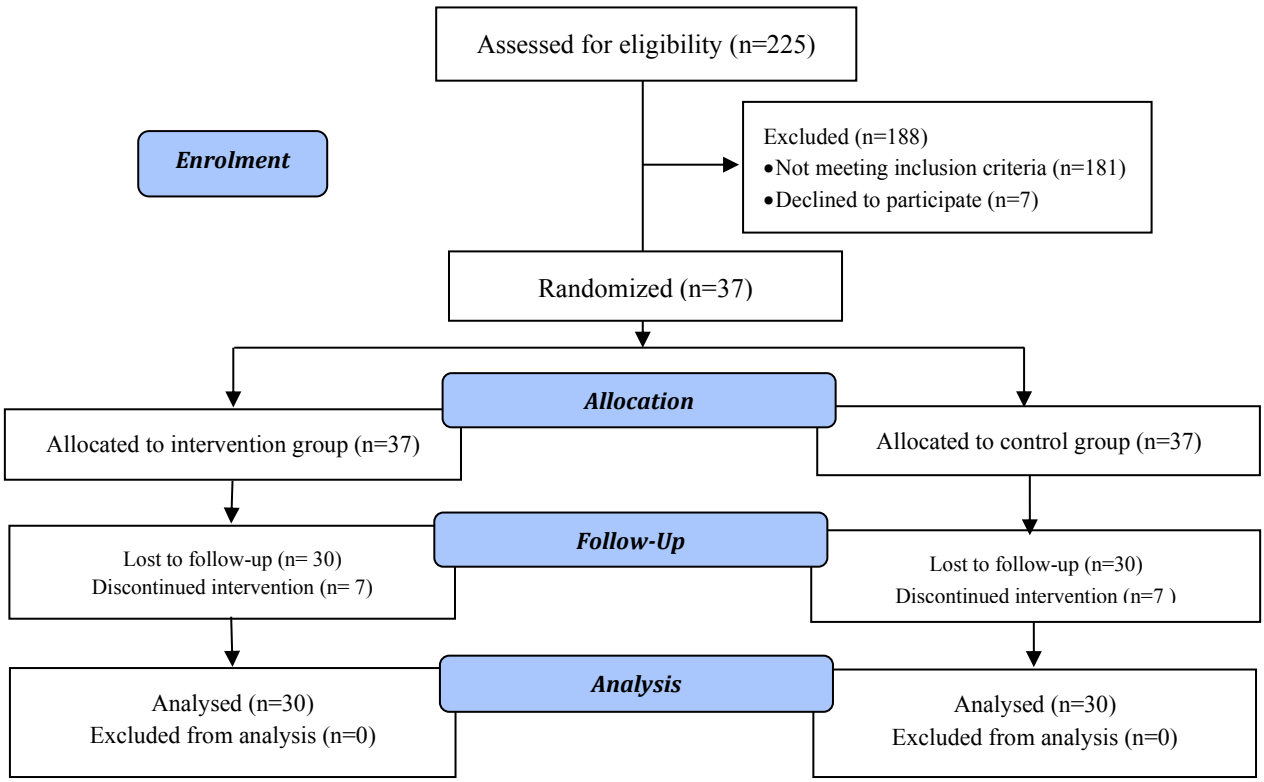

Figure 1. Consort flow diagram of the study

The Bates–Jensen Wound Assessment Tool (BWAT) was used to evaluate wound healing (14). It is a validated wound assessment tool that is used in many healthcare settings for wound assessment. BWAT is straightforward to use and allows nurses to have an objective, comprehensive assessment of wounds. It consists of 13 items to evaluate wound size, type and depth, amount of necrotic tissue, amount and characteristics of exudate, the presence of granulation tissue, epithelialization, and peri-wound skin. The items and scoring are presented in table 1. Each item is graded on a scale of 1 to 5, where a score of 1 indicates progress toward healing while a score of 5 indicates the absence of healing or wound deterioration. Cumulative BWAT scores vary from 13 to 65 (15). Two raters (The first author and another nurse) scored all wounds simultaneously, the mean of two scores considered as BWAT score. The English version of BWAT has been reported to have good reliability (Cronbach alpha=0.91 and an interrater reliability coefficient of 0.99 (16). Persian version of BWAT was used in previous studies (17), Twenty burns were assessed by two raters separately, and the interrater reliability coefficient was 0.89.

Interventions

Aloe Vera gel was extracted as 100% mucilage from the middle part of the Aloe Vera leaf and sterilized by the Iranian Institute of Medical Plants. The intervention areas dressed with the Aloe Vera gel and the Control areas dressed with 2% Nitrofurazone Ointment. The first author, who is a nurse with 5 years of work experience in a burn center did all the dressings.

Statistical procedures

The data was entered into SPSS Version 16. the Shapiro-Wilk test was used to test for normality ($p>0.05$). The change in BWAT scores within each area was tested by two-way repeated measure ANOVA.

Ethics consideration

The study protocol was approved by the Ethics Committees of the Tehran University of Medical Sciences. The trial is registered in the Iranian Registry of Clinical Trials (IRCT2014113020151N1, Registered 14 December 2014, https://www.irct.ir/trial/17874). Before participation in the study, written informed consent was obtained from each participant. All of them could withdraw from the study whenever they desired. The information on all research units was confidential.

Results

The findings of this clinical study showed the mean and standard deviation of the age of the study units were 38.23 ± 15.02 years. (53.3%) of the units were women. (56.7 %) participants were diploma and under diploma, and (43.3 %) participants had a college degree. (53.3 %) participants were single. The demographic information for participants and Frequency of burn sites have been summarized and shown in Table 1 and Table 2.

Table 1. The demographic information

	Minimum	**Maximum**	**Mean ± SD**
Age	15 years old	85 years old	39.06 ± 16.97
Gender	46.7 Men	53.3% Women	1.46 ± 0.50
Weight	46 Kg	110Kg	73.30 ± 17.56
Height	141 Cm	189 Cm	164.53 ± 12.53
Degree of education	43.3 % college degree	56.7 diploma and under diploma	2.03 ± 0.99
Marital statues	46.7 Single	53.3% Married	1.46 ± 0.50
Size wound	4--<16 sq cm	36.1--<80 sq cm	2.26 ± 0.63

Table 2. Information of burn zone

Zone of control and intervention	Forearm		Arm		Chest		Thigh		leg	
	N	%	N	%	N	%	N	%	N	%
	6	16%	5	20%	8	26%	4	13%	7	23%

The repeated measure ANOVA showed that there was a significant change in the score of BWAT in all areas during the intervention period (Time Effect). The BWAT scores did not change differently in the two groups (Group Effect). The trend of healing in the two groups during the intervention period was not significantly different (Time*Group). (Table 3). The trend of healing during the intervention period in the two groups is shown in (Figure 2).

Table 3. The comparison of BWAT scores between and within two areas

Time Area	Before intervention	First week after intervention	Second week after intervention	Third week after intervention
Aloe Vera	30.23± 3.28	27.73± 3.38	21.86± 3.13	16.80± 1.74
2%Nitrofurazone	30.51± 3.79	28.45± 3.49	23.36± 2.89	19.23± 2.11
Time Effect	F(3, 2.10)=623.787, p=0.001			
Group Effect	F(1,58)=3.778, p=0.057			
Time*Group	F(3, 2.10)= 2.333, p=0.098			

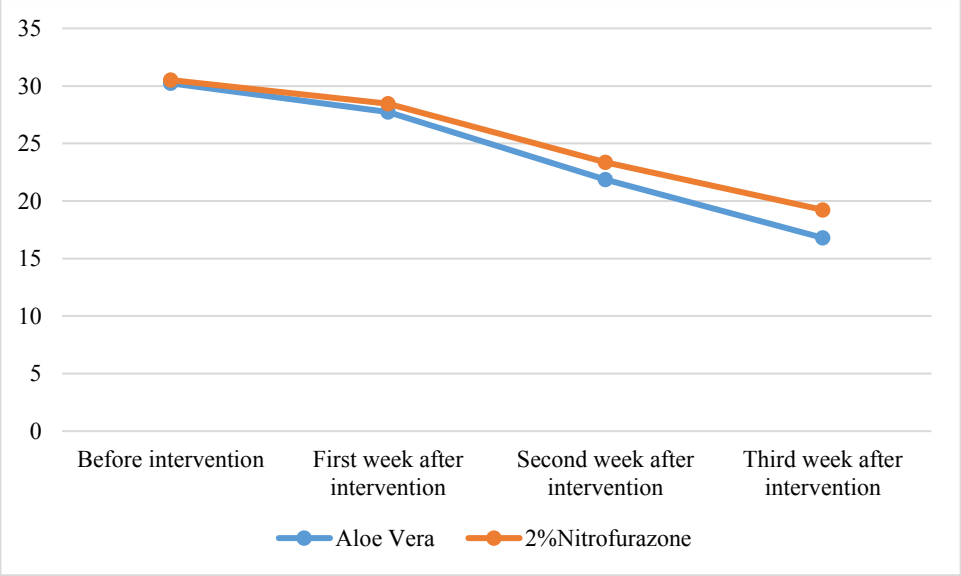

Figure 2. The comparison of BWAT scores between two areas

Discussion

According to this study, 2% Nitrofurazone and Aloe Vera gel both resulted in healing burn wounds. Also, comparing the BWAT tool's total score, the progression of wound closure in both intervention and control areas are the same. It looks like Aloe vera gel is as effective as 2% Nitrofurazon ointment in the healing of superficial partial-thickness burns, In spite of the fact that both areas of control and intervention were studied on the same person and all environmental, physical and nutritional factors- influential in the healing process- were the same.

Alongside with a large number of studies stating that Aloe Vera improve (18, 19) and accelerates (20, 21).

Collagen is the major protein in the extracellular matrix and provides strength and integrity to the dermis and other supporting tissues (22). Aloe Vera mucilage enhances the production amount of collagen in the wound, modifies its structure. Increasing cross-connections between collagen strands accelerates wound healing (23).

On the other hand, Aloe Vera dressing is classified in the category of wet dressings due to hydrocolloids. Several studies have shown that wet dressings provide an ideal environment regarding moisture and temperature for wounds (24, 25). Wet dressings can double the speed of wound healing because the wet environment allows fibroblast cells to immigrate faster to the epidermis and accelerate the recovery process (26).

As well as Aloe Vera has lysine; lysine helps with wound healing by removing toxic substances, increasing blood flow, and removing dead cells. The results of this study are consistent with the conclusion of a review study that showed that Aloe Vera gel promoted burns recovery (27) .Studies on wounds such as pressure ulcers, diabetic wounds, cesarean section, and episiotomy showed that the Aloe Vera gel was effective in wound healing and epithelialization (28-30). Comparison of the effect of Aloe Vera gel and 1% silver sulfadiazine cream on the recovery of superficial partial-thickness burns in humans and animals showed that the Aloe Vera Gel improves the wound more rapidly (17).

Conclusion

The primary outcome in this study was the recovery of burn of superficial partial-thickness burns. Our results show that the aloe vera gel was as effective as 2% Nitrofurazone ointment in recovering partial-thickness burns. So, based on this study, it looks like Aloe Vera gel is as effective as 2% Nitrofurazon ointment. Therefore, due to the systemic side effects of 2% Nitrofurazone ointment like thrombocytopenia, and allergic reactions, especially contact dermatitis and drug resistance, Aloe Vera gel can be a good herbal alternative for 2% Nitrofurazone in superficial partial-thickness burns. As researchers suggest, the lack of comparative studies between Aloe Vera and 2% Nitrofurazone necessitates further studies with a larger number of samples.

Limitation

One limitation of this study was that the outflow of samples was greater than expected. It was also not possible to carry out blinding on participants, which caused additional limitations.

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Conflict of interest

There are no conflicts of interest to declare.

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