Comparison of the effectiveness of Aloe Vera Gel with 2% Nitrofurazone ointment on the healing of superficial second-degree burns. Randomised clinical trial

Shokoh Varaei

Tehran University of Medical Sciences

Hadi Ranjbar

Iran University of Medical Sciences

Parichehr Sabaghzadeh (✉ parichehr_sabaghzadeh@yahoo.com)

<https://orcid.org/0000-0003-3760-5524>

Sanaz Bostani

Islamic Azad University of Hormozgan

Soodabhe Amirsalari

Shiraz University of Medical Sciences

Research article

Keywords: Aloe Vera, Nitrofurazone, Burns, Dressing

Posted Date: March 12th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-16854/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background Burn injuries are one of the most common sources of trauma globally that comprise a significant drain on long-term personal and healthcare cost. Large surface area burn wounds are difficult to manage and may result in significant physiologic and psychological sequelae. The aim of this study was to compare the effectiveness of Aloe Vera gel with Nitrofurazone ointment in the healing of superficial second-degree burn wounds.

Methods The present study was a split body controlled, randomized clinical trial. The sample was recruited from patients with superficial second-degree burn wound who were prescribed to treat with 2% Nitrofurazone ointment. Thirty patients with at least two burn, each burn on an alternate side of the body, entered the study – samples allocated to two groups which received Aloe Vera gel or 2% Nitrofurazone ointment on their burns. Bates-Jensen Wound assessment tool (BWAT) was used to evaluate the healing of burns. The burns were evaluated before, one, two and three weeks after the beginning of treatment.

Results The mean $\pm$ SD of BWAT scores in Aloe Vera zones were 30.32 ± 3.28 , 27.33 ± 3.38 , 21.33 ± 3.13 , 16.12 ± 2.16 respectively ($F(2, 65.07) = 440.00$, $p=0.001$). The mean $\pm$ SD of BWAT scores in Nitrofurazone ointment zones were 30.51 ± 3.79 , 28.45 ± 3.49 , 23.36 ± 2.89 , 19.23 ± 2.11 ($F(1, 52.00) = 228.00$, $p=0.001$).

Conclusions There is a significant difference in (BWAT) scores between intervention and control groups. Aloe Vera gel was as effective as Nitrofurazone ointment in the treatment of superficial second-degree burns.

Trial registration IRCT2014113020151N1. Registered 14 December 2014, <https://www.irct.ir/trial/17874>

Background

Burn injuries are among the most common causes of hospitalization (1, 2). They are responsible for 5% of hospitalization worldwide and have a higher burden in developing countries (3). About 90% of burns occur in Low and middle-income countries, where health facilities are more limited (4). Patients with burn injuries are at risk of short and long term complications (5). Delay in burn wound healing is one of these complications (6). The healing of burn wounds is very critical in the process of recovery and rehabilitation of these patients.

Burns can occur when the skin is exposed to a high degree of heat from fire or hot liquids, electricity, chemicals, or radiation. Burns are classified according to the severity of tissue damage. First-degree burns affect only epidermis and cause pain and redness. Second-degree burns extend to the dermis causing pain, redness, and blisters that may discharge. Third-degree burns include both layers of the skin and may also damage the underlying tissues including bones, muscles, and tendons. The burn site appears pale, charred, or leathery. There is no pain in the burned area because the nerve endings are

destroyed. Fourth-degree burns extend through the skin and subcutaneous tissue into the underlying muscle and bone (7).

Second-degree burns involve the epidermis and part of the dermis. They are divided into superficial and deep. These burns are very painful and the risk of infection, scar development and delay in healing is high in them (8). Deep second-degree burns may progress to third-degree burns in several days. Dressing burns with medicines that help wound healing can have an important role in reducing complications. All burns may cause complications if not properly treated (9).

One of the routine treatments of superficial second-degree burns is daily washing and dressing with Nitrofurazone (2%) ointment (10). Nitrofurazone is a topical anti-infective agent which is effective against gram-negative and gram-positive bacteria (11). 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 dermatitis, burning, edema, erythema, itching, and blisters have been reported. Due to these complications, researches are conducting to find less complicated and effective alternatives for the treatment of burns (12).

Aloe Vera 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 (12-14). Aloe Vera gel contains collagen, which can enhance the tissue granules and its anti-inflammatory properties can be effective in the process of wound healing and epithelialization (15-17). The anti-inflammatory effect of Aloe Vera is due to the existence of salicylic acid and Arachidonic acid (18). Salicylic acid inhibits the production of Bradykinin and histamine. Arachidonic acid inhibits prostaglandin production (19, 20). Research has shown that Aloe Vera has bacteriostatic and bactericidal effects on species such as *Pseudomonas Aeruginosa*, *Escherichia coli*, *Salmonella Typhi* and *Mycobacterium tuberculosis* (9). One in vitro studies has shown that Aloe Vera accelerates wound healing up to 40% (21).

Recovery of burns is a long and painful process that causes the suffering of the patient and the family and imposes substantial costs on them. Second-degree burns require 3-4 weeks to recover. Decreasing recovery time can reduce patient suffering and the cost of treatment (22). Second-degree burns are the most painful types of burns. 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 second degree burns dressing. The aim of this study was to evaluate the effectiveness of Aloe Vera mucilage in the recovery of superficial second-degree burns. We compared aloe Vera with 2% Nitrofurazone Ointment as a routine and recommended treatment for superficial second-degree burns. Study hypothesis is the Aloe vera gel accelerates recovery healing of superficial second-degree burns

Methods

This study was a randomized split body controlled clinical trial. The study population consisted of all outpatients with superficial second-degree burns who attended to Shafa hospital burn center, Kerman,

Iran. A convenience sample of 30 patients who had inclusion criteria enrolled in the study.

Inclusion criteria were having two superficial second degree 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 less than 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 disease 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.

Random allocation was done by the study statistician. He 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%. 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. Patients with signs of infection or Systemic Inflammatory Response Syndrome (SIRS) were excluded from the study. The wounds were assessed and dressed daily by the third author. Patients were followed up for three weeks afterward. At the end of each week, assessment tools (The Bates–Jensen Wound Assessment Tool) were completed for both the control and intervention areas. Sample recruitment and allocation are presented in figure 1. During the study, 7 patients were added to the research because the outflow of samples were higher than what was expected before

Aloe Vera gel was extracted as 100% mucilage from the middle part of the Aloe Vera leaf. The Aloe Vera gel was extracted and sterilized by the Iranian Institute of Medical Plants. The intervention included the use of the Aloe Vera gel in the burn area in a form that covered the whole surface of the burn. Control areas dressed with 2% Nitrofurazone Ointment. The Third author who is a nurse with 5 years of work experience in burn center did generated the random allocation sequence and enrolled participants, and assigned participants to interventions. all participant was blinded after assignment to interventions.

The Bates–Jensen Wound Assessment Tool (BWAT) was used to evaluate wound healing (23). It is a validated wound assessment tool which is used in many healthcare settings for wound assessment. BWAT is straight forward 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 (24). Items and scoring of BWAT are presented in table 1. Two raters (third 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 (25, 26). Persian version of BWAT was used in previous studies (27). Twenty burns were assessed by two raters separately, and interrater reliability coefficient was 0.89.

Table 1- Items and scoring of Bates-Jensen Wound Assessment Tool

Item	1	2	3	4	5
Size (Length * width)	<4 sq cm	4--<16 sq cm	16.1--<36 sq cm	36.1--<80 sq cm	>80 sq cm
Depth	Non-blanchable erythema on intact skin	Partial thickness skin loss involving epidermis &/or dermis	Full thickness skin loss involving damage or necrosis of subcutaneous tissue; may extend down to but not through underlying fascia; &/or mixed partial & full thickness &/or tissue layers obscured by granulation tissue	Obscured by necrosis	Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures
Edges	Indistinct, diffuse, none clearly visible	Distinct, outline clearly visible, attached, even with wound base	Well-defined, not attached to wound base	Well-defined, not attached to base, rolled under, thickened	Well-defined, fibrotic, scarred or hyperkeratotic
Undermining	None present	Undermining < 2 cm in any area	Undermining 2-4 cm involving < 50% wound margins	Undermining 2-4 cm involving > 50% wound margins	Undermining > 4 cm or Tunneling in any area
Necrotic Tissue Type	None visible	White/grey non-viable tissue &/or non-adherent yellow slough	Loosely adherent yellow slough	Adherent, soft, black eschar	Firmly adherent, hard, black eschar
Necrotic Tissue Amount	None visible	< 25% of wound bed covered	25% to 50% of wound covered	> 50% and < 75% of wound covered	75% to 100% of wound covered
Exudate Type	None	Bloody	Serosanguineous: thin, watery, pale red/pink	Serous: thin, watery, clear	Purulent: thin or thick, opaque, tan/yellow, with or without odor
Exudate Amount	None, dry wound	Scant, wound moist but no observable exudate	Small	Moderate	Large
Skin Color Surrounding Wound	Pink or normal for ethnic group	Bright red &/or blanches to touch	White or grey pallor or hypopigmented	Dark red or purple &/or non-blanchable	Black or hyper-pigmented
Peripheral Tissue Edema	No swelling or edema	Non-pitting edema extends <4 cm around wound	Non-pitting edema extends >4 cm around wound	Pitting edema extends < 4 cm around wound	Crepitus and/or pitting edema extends >4 cm around wound

Peripheral Tissue Induration	None present	Induration, < 2 cm around wound	Induration 2-4 cm extending < 50% around wound	Induration 2-4 cm extending > 50% around wound	Induration > 4 cm in any area around wound
Granulation Tissue	Skin intact or partial thickness wound	Bright, beefy red; 75% to 100% of wound filled &/or tissue overgrowth	Bright, beefy red; < 75% & > 25% of wound filled	Pink, &/or dull, dusky red &/or fills < 25% of wound	No granulation tissue present
Epithelialization	100% wound covered, surface intact	75% to <100% wound covered &/or epithelial tissue extends >0.5cm into wound bed	0% to <75% wound covered &/or epithelial tissue extends to <0.5cm into wound bed	25% to < 50% wound covered	< 25% wound covered

The data was entered into SPSS Version 16. The BWAT scores reported as mean $\pm$ SD. The Shapiro-Wilk test was used to test for normality ($p>0.05$). The change in BWAT scores within each group was tested by repeated measure ANOVA. The paired sample t-test was used to compare the BWAT scores between two zones before, one, two and three weeks after intervention. sample size was determined whit this formula:

$$\begin{aligned}
 \alpha &= 0.05 \\
 \beta &= 0.2 \\
 Z_{1-\alpha/2} &= 1.96 \\
 Z_{1-\beta} &= 1.64 \\
 \sigma_1 &= 0.524 \\
 \sigma_2 &= 0.516
 \end{aligned}$$

$$d=0.69$$

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2(\sigma_1 + \sigma_2)^2}{d^2} = \frac{(1.96 + 1.64)^2(0.524 + 0.516)^2}{0.69^2} 29.44 \approx 30$$

Results

In the end, the burns of thirty patients who entered the study were analyzed. The mean and standard deviation of the age of the study units were 38.23 ± 15.02 years. Sixteen (53.3%) of the units were women. Seventeen participants were diploma and under diploma (56.7 %) and thirteen participants had a college degree (43.3 %). Sixteen participants (53.3 %) were single, and fourteen participants were married (46.7 %). The mean $\pm$ SD of burn diameter in Aloe Vera and Nitrofurazone zones were 26.2 ± 0.63 mm and 25.8 ± 0.62 mm, respectively ($t=1.753$, $df= 28$ $p=0.09$, CI: -0.12 to 1.40). BWAT scores were not significantly different between the two methods before and one week after the intervention. The difference in BWAT scores between the two groups was significant in the second and third weeks. The BWAT scores within two groups significantly decreased over time (Table 2).

Table 2- The comparison of BWAT scores between and within two groups

Time Group	T1	T2	T3	T4	Repeated Measure ANOVA
Aloe Vera	30.32 ± 3.28	27.33 ± 3.38	21.33 ± 3.13	16.12 ± 2.16	F(2, 65.07) = 440.00, p=0.001
Nitrofurazone	30.51 ± 3.79	28.45 ± 3.49	23.36 ± 2.89	19.23 ± 2.11	F(1, 52.00) = 228.00, p=0.001
t-test	t=-0.20, df=58, p=0.41, CI= -2.02 to 1.64	t=-1.26, df=58, p=0.10, CI= -2.89 to 0.65	t=-2.61, df=58, p=0.006, CI= -3.59 to -0.46	t=-5.64, df=58, p=0.001, CI= -4.21 to -2.00	

Discussion

The results of this study showed that burns were improved on both Aloe Vera and nitrofurazone zones. The wound healing was significantly faster in zones that were dressed with Aloe Vera gel. This result is compatible with the results of previous studies.

The probable cause of the effectiveness of the Aloe Vera gel is that there are certain polysaccharides in it (28). These glycoproteins contain polysaccharides that stimulate the recovery of the skin. Aloe Vera also has a compound called glucomannan, a polysaccharide which has mannose. Glucomannan affects fibroblasts growth factor receptors and stimulates the activity and proliferation of these cells. This increases the production and secretion of collagen. Aloe Vera mucilage, in addition to increase the amount of collagen in the wound, modifies its structure. Increasing cross-connections between collagen strands accelerates wound healing (29). Aloe Vera dressing is classified in the category of wet dressings due to the presence of hydrocolloids (30). Several studies have shown that wet dressings provide an ideal environment in regards to moisture and temperature for wounds (31). Moisture increases the production of collagen and accelerates the formation of blood vessels, epithelialization and the formation of granular tissue (32). 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 (33). Aloe Vera also has lysine; lysine helps with wound healing by removing toxic substances, increasing blood flow and removing dead cells (34). The results of this study are consistent with the conclusion of a review study that showed that Aloe Vera gel accelerates burns recovery in superficial grade one burns (35). Studies on wounds such as pressure ulcers, diabetic wounds, cesarean section, and episiotomy showed that the Aloe Vera gel was effective in wound healing (36-41). Comparison of the effect of Aloe Vera gel and 1% silver sulfadiazine cream on the recovery of grade 2 burns showed that the Aloe Vera Gel improves the wound more rapidly (27). The results of another study showed that dressing with Aloe Vera gel was also effective in improving deep burn wounds (42). High rate of sample loss and the fact that desirable blinding was not achievable, are two main limitations in this study

Conclusion

Aloe Vera gel can be a good alternative for 2 % Nitrofurazone in the dressing of superficial second-degree burns. Aloe Vera accelerates wound healing and can reduce the treatment costs for patients and the health system. It can lead to the enhancement of quality of care.

Abbreviations

BWAT: The Bates–Jensen Wound Assessment Tool

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committees of the Tehran University of Medical sciences (TUMS). The trial is registered in the Iranian Registry of Clinical Trials (IRCT2014113020151N1). 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.

Acknowledgement

This article results from a master degree thesis registered at Tehran University of Medical Sciences. The authors would like to thank patients who participate in the study.

Funding

This study was funded and supported by Nursing and Midwifery Care Research Center, Tehran University of Medical sciences (TUMS); Grant no.27761. But we did not receive any financial aid regarding publication. All financial aids from the research center were to be spent on the study itself.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there is no conflict of interests.

Authors' contributions

SV and HR wrote the manuscript draft, SV and PS designed the study and conducted the data gathering, SB and SA Conducted statistical analyses. All authors reviewed the final manuscript.

Consent for publication

References

1. Lotfi M, Ghahremanian A, Aghazadeh A, Jamshidi F. The Effect of Pre-Discharge Training on the Quality of Life of Burn Patients. *J Caring Sci.* 2018;7(2):107-12. Epub 2018/07/07. doi: 10.15171/jcs.2018.017. PubMed PMID: 29977882; PubMed Central PMCID: PMC6029655.
2. Mirza Aghazadeh A, Lotfi M, Ghahramanian A, Ahadi F. Lethal Area 50 in Patients with Burn Injuries in North West, Iran. *J Caring Sci.* 2018;7(1):53-8. Epub 2018/04/11. doi: 10.15171/jcs.2018.009. PubMed PMID: 29637058; PubMed Central PMCID: PMC605889799.
3. Hosseini RS, Askarian M, Assadian O. Epidemiology of hospitalized female burns patients in a burn centre in Shiraz. *East Mediterr Health J.* 2007;13(1):113-8. Epub 2007/06/06. PubMed PMID: 17546913.
4. Peck MD. Epidemiology of burns throughout the World. Part II: intentional burns in adults. *Burns.* 2012;38(5):630-7. Epub 2012/02/14. doi: 10.1016/j.burns.2011.12.028. PubMed PMID: 22325849.
5. Deeter L, Seaton M, Carrougier GJ, McMullen K, Mandell SP, Amtmann D, et al. Hospital-acquired complications alter quality of life in adult burn survivors: Report from a burn model system. *Burns.* 2019;45(1):42-7. Epub 2018/11/28. doi: 10.1016/j.burns.2018.10.010. PubMed PMID: 30477817.
6. Muller MJ, Hollyoak MA, Moaveni Z, Brown TL, Herndon DN, Heggors JP. Retardation of wound healing by silver sulfadiazine is reversed by Aloe vera and nystatin. *Burns.* 2003;29(8):834-6. doi: 10.1016/S0305-4179(03)00198-0. PubMed PMID: WOS:000186962600013.
7. Rangaraju LP, Kunapuli G, Every D, Ayala OD, Ganapathy P, Mahadevan-Jansen A. Classification of burn injury using Raman spectroscopy and optical coherence tomography: An ex-vivo study on porcine skin. *Burns.* 2018. Epub 2018/11/06. doi: 10.1016/j.burns.2018.10.007. PubMed PMID: 30385061.
8. Prasad A, Thode HC, Jr., Sandoval S, Singer AJ. The association of patient and burn characteristics with itching and pain severity. *Burns.* 2019;45(2):348-53. Epub 2019/01/29. doi: 10.1016/j.burns.2018.06.011. PubMed PMID: 30686696.
9. Boonkaew B, Kempf M, Kimble R, Supaphol P, Cuttle L. Antimicrobial efficacy of a novel silver hydrogel dressing compared to two common silver burn wound dressings: Acticoat and PolyMem Silver((R)). *Burns.* 2014;40(1):89-96. Epub 2013/06/25. doi: 10.1016/j.burns.2013.05.011. PubMed PMID: 23790588.
10. Salehi H, Momeni M, Ebrahimi M, Fatemi MJ, Rahbar H, Ranjpoor F, et al. Comparing the effect of colactive plus ag dressing versus nitrofurazone and vaseline gauze dressing in the treatment of second-degree burns. *Ann Burns Fire Disasters.* 2018;31(3):204-8. Epub 2019/03/14. PubMed PMID: 30863254; PubMed Central PMCID: PMC6367865.
11. Yasojima EY, Ribeiro Junior RF, Pessoa TC, Cavalcante LC, Ramos SR, Serruya YA, et al. Effects of nitrofurazone on correction of abdominal wall defect treated with polypropylene mesh involved by

- fibrous tissue. *Acta Cir Bras.* 2015;30(10):686-90. Epub 2015/11/13. doi: 10.1590/S0102-865020150100000006. PubMed PMID: 26560427.
12. Bagheri T, Fatemi M, Hosseini S, Saberi M, matrix MN, 2017 u. Comparing the effects of topical application of honey and nitrofurazone ointment on the treatment of second-degree burns with limited area: a randomized. *Medical - Surgical Nursing Journal.* 2017;5(4):22-30.
 13. Nazir A, Ahsan H. Health benefits of aloe vera: A wonder plant. *International Journal of Chemical Studies.* 2017;5(6):967-9.
 14. Srikanth K, Kartikeyan S, Food AK-IJo, 2017 u. Storage studies of Aloe vera juice incorporated Peda. *researchgatenet.*
 15. Hashemi SA, Madani SA, Abediankenari S. The Review on Properties of Aloe Vera in Healing of Cutaneous Wounds. *Biomed Res Int.* 2015;2015:714216. Epub 2015/06/20. doi: 10.1155/2015/714216. PubMed PMID: 26090436; PubMed Central PMCID: PMC4452276.
 16. Oryan A, Mohammadalipour A, Moshiri A, Tabandeh MR. Topical Application of Aloe vera Accelerated Wound Healing, Modeling, and Remodeling: An Experimental Study. *Ann Plast Surg.* 2016;77(1):37-46. Epub 2014/07/09. doi: 10.1097/SAP.0000000000000239. PubMed PMID: 25003428.
 17. Radha MH, Laxmipriya NP. Evaluation of biological properties and clinical effectiveness of Aloe vera: A systematic review. *J Tradit Complement Med.* 2015;5(1):21-6. Epub 2015/07/08. doi: 10.1016/j.jtcme.2014.10.006. PubMed PMID: 26151005; PubMed Central PMCID: PMC4488101.
 18. Benson KF, Newman RA, Jensen GS. Antioxidant, anti-inflammatory, anti-apoptotic, and skin regenerative properties of an Aloe vera-based extract of *Nerium oleander* leaves (nae-8((R))). *Clin Cosmet Investig Dermatol.* 2015;8:239-48. Epub 2015/05/26. doi: 10.2147/CCID.S79871. PubMed PMID: 26005354; PubMed Central PMCID: PMC4427598.
 19. Dat AD, Poon F, Pham KB, Doust J. Aloe vera for treating acute and chronic wounds. *Cochrane Database Syst Rev.* 2012(2):CD008762. Epub 2012/02/18. doi: 10.1002/14651858.CD008762.pub2. PubMed PMID: 22336851.
 20. Paul S, Dutta S, Chaudhuri TK, Bhattacharjee S. Anti-inflammatory and protective properties of aloe vera leaf crude gel in carrageenan induced acute inflammatory rat models. *International Journal of Pharmacy and Pharmaceutical Sciences.* 2014;6:368-71.
 21. Jarrahi M, Khorasani M, M A, Taherian AA. Local effect of Aloe barbadensis Miller gel on skin incisional wound healing in Rat. *Journal of Gorgan University of Medical Sciences.* 2009;11(1):13-7.
 22. Abbaszadeh A, Mahzooni T, Emami SA, Akbari H, Fatemi MJ, Saberi M, et al. The effect of Coriander cream on healing of superficial second degree burn wound. *Tehran Univ Med J.* 2015;73(9):646-52.
 23. Sarpooshi HR, Mortazavi F, ... MV-JoB, 2016 u. The Effects of Topical Vitamin C Solution on Burn Wounds Granulation: A Randomized Clinical Trial. *jbiomcom.*
 24. Harris C, Bates-Jensen B, Parslow N, Raizman R, Singh M, Ketchen R. Bates-Jensen wound assessment tool: pictorial guide validation project. *J Wound Ostomy Continence Nurs.*

- 2010;37(3):253-9. Epub 2010/04/14. doi: 10.1097/WON.0b013e3181d73aab. PubMed PMID: 20386331.
25. Alves D, Almeida A, Silva J, ... FM-TC, 2015 u. Translation and adaptation of the Bates-Jensen wound assessment tool for the Brazilian culture. *SciELO Brasil*. 2015;24(3):826-33. doi: 10.1590/0104-07072015001990014.
 26. Karahan A, Toruner EK, Ceylan A, Abbasoglu A, Tekindal A, Buyukgonenc L. Reliability and validity of a Turkish language version of the Bates-Jensen Wound Assessment Tool. *J Wound Ostomy Continence Nurs*. 2014;41(4):340-4. Epub 2014/07/06. doi: 10.1097/WON.0000000000000036. PubMed PMID: 24988512.
 27. Ghaffar zadegan R, Alizadeh SA, Ghaffar zadegan R, Haji Agaei R, Ahmadlou M. Effect of aloe vera gel, compared to 1% silver sulfadiazine cream on second-degree burn wound healing. *Complementary Medicine Journal of faculty of Nursing Midwifery*. 2013;3(1):418-28.
 28. Najafi N, Arabi M, Shahrekord HJ. The healing power of Aloe vera mucilage: induction of insulin-like growth factor gene expression and regeneration tissue in mouse damaged skin. *Journal of Shahrekord Uuniversity of Medical Sciences*. 2014;16(2):10-21.
 29. Boudreau MD, Beland FA. An evaluation of the biological and toxicological properties of Aloe barbadensis (miller), Aloe vera. *J Environ Sci Health C Environ Carcinog Ecotoicol Rev*. 2006;24(1):103-54. Epub 2006/05/13. doi: 10.1080/10590500600614303. PubMed PMID: 16690538.
 30. Poletti S, Lucke L. Electromagnetic Stimulation Combined with Aloe vera Increases Collagen Reorganization in Burn Repair. *Journal of Pharmacy and Pharmacology*. doi: 10.17265/2328-2150/2018.07.001
 31. Yang Y, Bechtold T, Redl B, Caven B, Hu H. A novel silver-containing absorbent wound dressing based on spacer fabric. *Journal of Materials Chemistry B*. 2017;5(33):6786-93. doi: 10.1039/c7tb01286a. PubMed PMID: WOS:000408270200008.
 32. Mehrabani M, Hosseini M, Karimloo M. Comparison of Honey dressing with Hydrocolloid dressing effects on pressure ulcer healing of ICU hospitalized patients. *Journal of Health Promotion*. 2012;1(3):37-46.
 33. Seyedalshohadaee M, Rafii F, ... AH-IJo, 2012 u. Comparative Study of the Effect of Dry and Moist Dressing on Burn Wound. *ijniumsacir*.
 34. Ahmed AM, Hamid A, Soliman MF. Effect of topical aloe vera on the process of healing of full-thickness skin burn: a histological and immunohistochemical study. *Journal of Histology*. 2015;2(3):1-9. doi: 10.7243/2055-091X-2-3.
 35. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review. *Iran J Med Sci*. 2019;44(1):1-9. Epub 2019/01/23. PubMed PMID: 30666070; PubMed Central PMCID: PMC6330525.

36. Avijgan M, Kamran A, medical AA-Ijo, 2016 u. Effectiveness of Aloe vera gel in chronic ulcers in comparison with conventional treatments. *Iran J Med Sci.* 2016;41(3). PubMed Central PMCID: PMC5103537.
37. Eghdampour F, Jahdie F, Kheyrkhah M, Taghizadeh M, Naghizadeh S, Hagani H. The Impact of Aloe vera and Calendula on Perineal Healing after Episiotomy in Primiparous Women: A Randomized Clinical Trial. *J Caring Sci.* 2013;2(4):279-86. Epub 2014/10/03. doi: 10.5681/jcs.2013.033. PubMed PMID: 25276736; PubMed Central PMCID: PMC4134148.
38. Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. The effect of Aloe Vera gel on prevention of pressure ulcers in patients hospitalized in the orthopedic wards: a randomized triple-blind clinical trial. *BMC Complement Altern Med.* 2018;18(1):264. Epub 2018/10/01. doi: 10.1186/s12906-018-2326-2. PubMed PMID: 30268162; PubMed Central PMCID: PMC6162886.
39. Molazem Z, Mohseni F, Younesi M, Keshavarzi S. Aloe vera gel and cesarean wound healing; a randomized controlled clinical trial. *Glob J Health Sci.* 2014;7(1):203-9. Epub 2015/01/07. doi: 10.5539/gjhs.v7n1p203. PubMed PMID: 25560349; PubMed Central PMCID: PMC4796446.
40. Nazari S, Ezati Arasteh F, Nazari S, Shobeiri F, Shayan A, Parisa Parsa. Effect of Aloe Vera gel on perineal pain and wound healing after episiotomy among primiparous women: A randomized clinical trial. *Iranian Journal of Obstetrics, Gynecology and Infertility.* 2019;21:44-51.
41. Sabzaligol M, Safari N, Baghcjeghi N, Latifi M, Bekhradi R, Taghizadeh M, et al. The effect of Aloevera gel on prineal pain & wound healing after episiotomy. *Complementary Medicine Journal of faculty of Nursing Midwifery.* 2014;4:766-75.
42. Nasiri E, Hosseinimehr SJ, Azadbakht M, Madani SA. A review of natural products for burn healing based on the Iranian traditional medicine. *J Mazandaran Univ Med Sci.* 2014;23(110):263-80.

Figures

Figure 1

Study flowchart: recruitment and allocation to study groups

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [CONSORT2010Checklist1.doc](#)