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Effect of Aloe vera gel on wound healing process for diabetic foot ulcers: A pilot study

Efecto del gel de Aloe vera en el proceso de cicatrización de las úlceras del pie diabético: un estudio piloto

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SUMMARY

Introduction: *Patients who experience diabetic foot ulcers (DFU) should have undertaken prompt wound care. Currently, the principles of wound care have shifted to the moist principles of a wide range of treatments, advanced technology, and complementary alternative therapy. This study aimed to investigate the effects of Aloe vera gel therapy as a complementary alternative therapy to promote wound healing of DFU.*
Methods: *This study used a quantitative with a prospective design. Eight patients in the intervention group and nine in the control group were allocated based on the consecutive sampling technique. The intervention group used aloe vera gel once every two days, while for the control group, wounds were treated every day using NaCl at 0.9 %. The wound healing progress was observed for three weeks.*
Results: *The results confirmed that the mean score of the Bates Jensen Score in the intervention group decreased, which indicates that the wound healing process was improved by using the Aloe vera gel by 13.38 % (p <0.001), which was higher than in the control group.*
Conclusion: *Aloe vera gel, as a complementary alternative therapy accelerates the wound healing process in DFU. Further research with larger sample size and conducted in various regions may be beneficial to improve the evidence.*

Keywords: *Aloe vera gel, complementary alternative therapy, diabetic foot ulcers, wound status continuum.*

RESUMEN

Introducción: *Los pacientes que experimentan úlceras de pie diabético (UPD) deben haber realizado un cuidado rápido de la herida. Actualmente, los principios del cuidado de heridas se han desplazado hacia los principios húmedos de una amplia gama de tratamientos, tecnología avanzada y terapia alternativa complementaria. Este estudio tuvo como objetivo investigar los efectos de la terapia con gel de Aloe vera como una terapia alternativa complementaria para promover la cicatrización de heridas de UPD.*
Métodos: *Este estudio utilizó un diseño cuantitativo con un diseño prospectivo. Se asignaron ocho pacientes en el grupo de intervención y nueve en el grupo de control según la técnica de muestreo consecutivo. El grupo de intervención usó gel de aloe vera una vez cada dos días, mientras que para el grupo de control, las heridas se trataron todos los días con NaCl al 0,9 %. El progreso de cicatrización de heridas se observó durante tres semanas.*
Resultados: *Los resultados confirmaron que la puntuación media del Bates Jensen Score en el grupo de intervención disminuyó, lo que indica que el proceso de*

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cicatrización de heridas mejoró con el uso del gel de Aloe vera en un 13,38 % (p < 0,001), que fue mayor que en el grupo de control.
Conclusión: *El gel de Aloe vera como terapia alternativa complementaria acelera el proceso de cicatrización de heridas en UPD. La investigación adicional con un tamaño de muestra más grande y realizada en varias regiones puede ser beneficiosa para mejorar la evidencia.*

Palabras clave: *Gel de Aloe vera, terapia alternativa complementaria, úlceras del pie diabético, continuidad del estado de la herida.*

INTRODUCTION

The International Diabetes Federation (IDF) 2021 estimated those 5.7 million adults living with diabetes had diabetes complications (1). In Indonesia, a study reported that 85.7 % of people with diabetes mellitus have a high risk of having Diabetic Foot Ulcers (DFU) (2,3). DFU was reported to be 12 % (4), and the infection rate was 35.7 % (5). Thus, optimal management for DFU patients includes adequate blood glucose control and wound care (6,7).

Various wound care modalities are available, including modern wound dressing, advanced therapy, and Complementary Alternative Therapy (CAT). In addition, CAT has been introduced in wound care from animal to human studies lauding natural medicine (8) and medicinal plants (9,10). A systematic review identified 12 plants that had a healing effect and among these plants is Aloe vera (9). Today, there has been an increasing concern that Aloe vera has an advantageous effect on wound healing (11,12). Previously, the use of honey has been proven to be better than conventional therapies in the healing process (13) as well as the use of herbal medicine, which shortened the healing time (14) and had beneficial effects on the wound (15-17). However, those studies mainly used animal subjects. Therefore, Aloe vera gel's clinical effect on human subjects remains questionable.

According to the CAT, Aloe vera has some healing effects in the Deoxyribose Nucleic Acid (DNA) repair process stage, with no significant cytotoxic and mutagenic reaction to the body (15,18). Aloe vera contains a high-water content and contains various active components such as fat- and water-soluble minerals, vitamins, simple/complex polysaccharides, organic acids, enzymes, and phenolic compounds. Aloe vera gel retains moisture and integrity of the skin and accelerates the wound healing process (19). Aloe vera gel consists of amino acids and many inorganic electrolytes like iron, potassium, magnesium, chromium, copper, sodium, calcium, and zinc, which are vital parts of the wound healing process (15). Aloe vera has biological activities because it contains chemical components such as astringent, hemostatic, antidiabetic, antiulcer, antibacterial, anti-inflammatory, antioxidant, and anticancer properties. It also effectively treats gastrointestinal disorders, radiation injury, wounds, and burns (20). Aloe vera has physical, chemical, and biological properties that benefit wound healing. However, there is currently limited information regarding its effect on wound healing, particularly in DFU. Thus, the current study aimed to evaluate the effectiveness of Aloe vera gel as a CAT on wound healing progress in patients with DFU.

METHODS

Study Design and Samples

This study was a quasi-experimental design. The subjects were patients in a city outpatient health center in Indonesia. Subjects of this study were selected consecutively with the inclusion criteria including patients with diabetic foot ulcers, diabetes type 2, the depth of the Bates-Jensen wound stage 2-4 (21), age of 26-59 years, and no smoking habit. Meanwhile, the exclusion criteria from the study constituted circumstances or other diseases that interfered with the measurement or interpretation, such as heart disease, malignancies, Human Immunodeficiency Virus (HIV), chronic kidney failure, and pulmonary Tuberculosis. Using purposive sampling, the number of samples in this study was 22, divided into two groups, and each group had 11 samples. However, during the intervention of this study, several respondents dropped out due to several reasons, and only 17 samples were analysed (Figure 1).

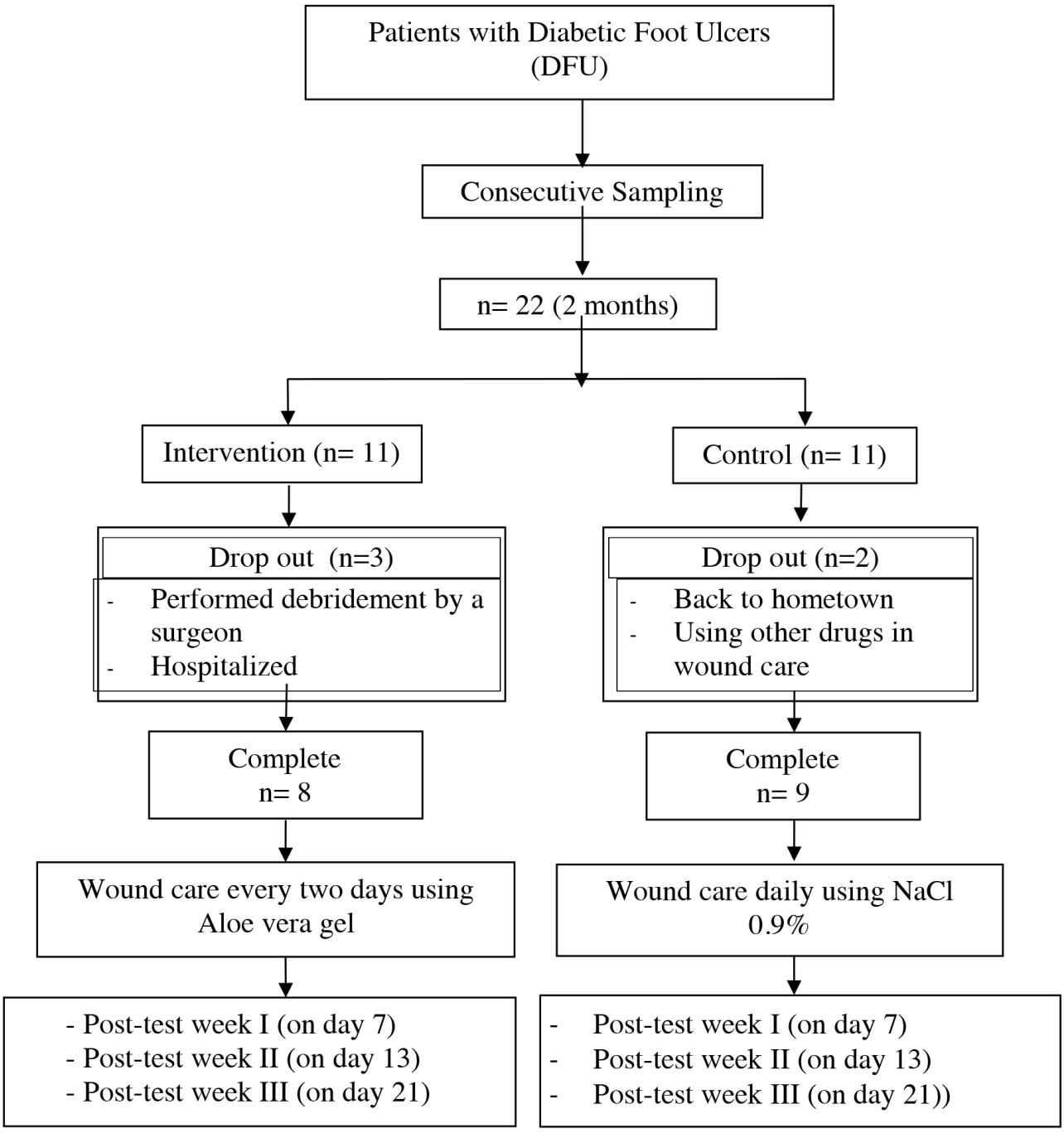

Figure 1. Consort Flowchart.

Variables and Intervention

The independent variable was Aloe vera gel (intervention group) and NaCl 0.9 % (control group), while the dependent variable was wound healing based on the Bates Jensen Wound Assessment (BJWAT) Scale (21). All participants were allocated into two groups through a consecutive sampling method, i.e., all individuals who met the selection criteria were selected until the desired number of samples was met. The Aloe vera treatment of wounds was performed once in two days for the intervention group, and the control group used standard treatment from the physician using normal saline (NaCl 0.9 %). In addition, both groups got wound care from certified home care nurses. The wound healing process uses the BJWAT, which has 13 subscales with a range of values 13-65 (21).

Instrument and Data Analysis

The instrument used in this study was the Bates Jensen Wound Assessment Scale (BJWAT), which has 13 subscales (21). Numeric data were presented in mean ± S.D., and ordinal or categorical data were reported in frequency (n). The Shapiro-Wilk test was performed to evaluate the normality of data, and homogeneity (Levene's) tests were completed before applying statistical Analyses. Repeated measures ANOVA test was used to evaluate the effect of Aloe vera gel on the wound healing process. The statistical process was conducted using statistical software.

Ethical Approval

The patients had also signed written informed consent. This study had been granted an ethical clearance from the Faculty of Medicine of Universitas Andalas review board for using CAT in performing wound care for DFU patients (IRB: 091/KEP/FK).

RESULTS

In total, there were 22 subjects initially assigned for this study for both groups. However, only eight subjects completed the treatment in the intervention groups and nine subjects in the control groups. Since a home care nurse conducted the intervention for this study, the researchers need to be granted permission from the physician and patients to continue their wound care using the Aloe vera gel. Some physicians did not approve of the patients using the Aloe vera gel. Thus, the researchers must adapt to continue the study by using a limited number of samples. The mean age of the intervention group was 53.25 ± 1 12 - 27 years old and 50.56 ± 41 – 53 years old for the control group. All subjects were non-smoking and had type 2 diabetes.

Table 1 showed that in the pre-test, week 1 and week 2 there was no significant difference between both groups for the 13 wound characteristics using the BJWAT. The difference between the two groups occurred in week 3 for necrotic tissue type, granulation, and epithelization. In general, between both groups, significant changes in eight components of the BWJAT were seen in the intervention group, while, in the control group, only four components showed significant changes. In the fourth measurement, there was a decrease in the average wound status continuum in the intervention group, as shown in the mean score of 45.63 to 42.88 in the first week, 38.00 in the second week, and 32.25 in the third week. Meanwhile, a drop in the mean value of the wound status continuum also occurred in the control group from 42.89 to 42.11 in the first week, 40.44 in the second week, and 39.67 in the third week. However, the intervention group had a more significant change than the control group because in wound care using 0.9 % NaCl changes only occurred in the amount of necrotic tissue, exudate, and granulation tissue.

Table 2 also showed the result of Repeated Measures ANOVA on all tests of Wound Continuum Status for both groups. The overall result shows that differences in all average test scores in all weeks were significant ($p < 0.05$). However, there were differences in their significance values. The intervention group had a highly significant difference ($p = 0.001$), whereas the control group obtained a lower significant p-value of 0.013. The test also showed the intervention group's significant value of $p < 0.05$. In addition, a significant difference ($p < 0.05$) was found between both group's pre-test scores for week 1 and week 3.

Table 1

The Wound Healing Process Based on BJWAT Scale in Both Groups

No	BJWAT	Pre-test			Week 1			Week 2			Week 3			p-value Friedman	
		C	I	p-value	C	I	p-value	C	I	p-value	C	I	p-value	C	I
1	Width (cm)	2	3	0.089	2	3		2	3	0.052	2	3	0.052	0.39	1
2	Depth (cm)	3	3	0.186	3	3	0.186	3	3	0.186	3	3	0.186	0.39	1
3	Edges	2	2.5	0.406	2	2.5	0.664	2	2	0.567	2	2	0.162	0.39	0.02
4	Undermining	1	1	0.719	1	1	0.719	1	1	0.396	1	1	0.396	0.39	0.39
5	Necrotic Tissue Amount	4	4	0.427	4	4	0.743	4	3	0.309	4	3	0.055	0.39	0
6	Necrotic Tissue Type	5	5	0.857	5	4	0.29	4	3	0.134	4	2	0.023*	0	0
7	Exudate Type	4	4.5	0.833	4	4	0.833	4	4	0.41	4	3	0.104	0.39	0
8	Exudate Amount	4	5	0.458	4	4	0.919	4	4	0.274	3	3	0.078	0.02	0
9	Skin Color Surrounding Wound	3	3	0.467	3	3	0.467	3	3	0.467	3	3	0.467	0.39	1
10	Peripheral Tissue Edema	3	2	0.404	3	2	0.404	3	2	0.437	3	1	0.224	0.39	0.06
11	Peripheral Tissue in duration	1	2.5	0.051	1	2	0.526	1	1	0.549	1	1	0.63	0.51	0
12	Granulation tissue	5	5	0.862	4	4	0.675	4	3	0.385	4	2.5	0.015*	0	0
13	Epithelialization	5	5	0.289	5	5	0.194	5	3.5	0.069	2	2	0.008*	0.06	0

C=Control, I=Intervention

Table 2

Comparison of Wound Measurement Continuum of Pre-Test Status by Weeks 1, 2, and 3 for Intervention and Control Groups

Group	Wound Status Continuum	Mean (S.D.)	p-value
	Pretest	45.63 (3.852)	0.001
Intervention	Week	142.88 (3.482)	
	Week	238.00 (2.204)	
	Week 3	32.25 (5.175)	
Repeated ANOVA test: analysis of post hoc <0.05 for all comparisons mean Pre-test vs Week 1 (p=0.14), Pre-test vs Week 2 (p=0.005), Pre-test vs Week 3 (p=0.005), Week 1 vs Week 2 (p=0.025), Week 2 vs Week 3 (p=0.013), Week 1 vs Week 3 (p=0.013), Week 2 vs Week 3 (p=0.019)			
Control	Pretest	42.89 (4.106)	0.013
	Week 1	42.11 (4.045)	
	Week 2	40.44 (4.640)	
	Week 3	39.67 (4.796)	
Repeated ANOVA test: analysis of post hoc p <0.05: Pre-test vs Week 1, (p=0.048), Pre-test vs week 3 (p=0.042),			

DISCUSSION

This study showed that Aloe vera gel accelerates wound healing in the third week of wound treatment, as proven by the BJWAT score. It has been impacted by changes in the wound status continuum, including necrosis tissue type, the number of necrotic tissues, exudate type, exudate amount, oedema, hardening of the margin, granulation tissue, and epithelialization. The use of Aloe vera gel in this study significantly changed the wound status continuum. There was a difference in the mean value of the wound status continuum at the pre-test weeks 1, 2, and 3. Although Aloe vera can be used to retain skin moisture, the use of Aloe vera to improve wound healing is recommended as the primary or complementary treatment alongside other methods. Several studies applying Aloe vera to wounds inhibit the migration of cells and growth factors leading to wound healing. In addition, aloe vera moistens the wound and allows optimal migration of fibroblasts and epidermal (22).

This study also found that wound care using Aloe vera gel once in two days was more effective and efficient than the care using 0.9 % NaCl once a day. During the intervention, nurses also noted that using Aloe vera gel saved more time and decreased the stress or pain experienced by the subjects in this study during wound care. In addition, a case report suggested that using aloe vera could reduce pain by blocking the synthesis of bradykinin, thromboxane synthase, and cyclooxygenase (22).

Aloe vera applied in this study could heal the wound faster than the application of conventional therapy. The changes could happen because Aloe vera contains glucomannan and gibberellins that stimulate fibroblast growth factor and proliferation to promote collagen synthesis. In addition, the active enzyme of bradykinesia and vitamins contained in Aloe vera gel can inhibit wound inflammation. Furthermore, Aloe vera gel can penetrate the skin or wounds to help heal (23). However, this study also showed that there were also changes in the wound healing of the control group. Nonetheless, some other studies showed that Aloe vera was still more effective than Saline Gas dressing and common treatment (22,23-25).

A previous study also found that wounds healed significantly in the intervention group (using Aloe vera gel) as compared to the control group (using normal saline and povidone-iodine) (26).

Even though there were significant changes in the wound healing process, this study proved there were some delays in the healing process (normally in 14 days), possibly due to several contributing factors, such as blood sugar level and nutritional status. The blood sugar might contribute to the wound healing process, as the above normal level indicates a not well-controlled condition, while well-controlled blood sugar can accelerate wound healing (27). In addition, the subjects in this study may also have inadequate nutritional intake, which can increase the risk of skin damage and slow wound healing. However, a further study that primarily measures blood sugar levels and nutritional status is needed to investigate and confirm their impact on the wound healing process. To sum up, Aloe vera gel proved to have a positive effect on improving the wound healing process since it contains glucomannan that influences the fibroblast growth factors and stimulates the production of collagen that accelerates wound improvement (28).

The main limitation of this study was the time restriction in applying the Aloe vera gel, which did not allow the researchers to show the full wound healing process. Additionally, the stage of the wound was not differentiated in the initial phase of this study. Furthermore, a limited number of subjects in this study and several contributing factors such as blood sugar level and nutritional status may also play some intervening roles that affect the research outcome, which accordingly must be considered in future studies to prove the definite and further impact of aloe vera gel on DFU patients.

CONCLUSION

This study found Aloe Vera gel can significantly accelerate the healing process of diabetic foot ulcers. In addition, wound care with Aloe Vera gel applies the principles of moisture to the wound and is also easy to apply. Therefore, the application of Aloe vera in the home care treatment for diabetic foot ulcer patients is recommended since it effectively improves wound healing and is significantly efficient for reducing labour costs and gauze in dressing.

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