Jurnal Riset Kesehatan, 11 (2), 2022, 96 - 101
DOI: 10.31983/jrk.v11i2.8883

Jurnal Riset Kesehatan

http://ejournal.poltekkes-smg.ac.id/ojs/index.php/jrk

THE EFFECTIVENESS OF MODERN DRESSING WITH A COMBINATION OF AFRICAN LEAF NANOPARTICLE HYDROGEL AND PAPUAN HONEY FOR GRADE II DIABETIC WOUND HEALING

Rolyn Frisca Djamanmona[a*] ; Oktovina Mobalen[b]

[a,b] Politeknik Kesehatan Kementerian Kesehatan Sorong ; Basuki Rahmat Street Km.11; Sorong 19486; Indonesia

Abstract

The combination of African leaf nanoparticle hydrogel (*Vernonia amygdalina*) and Papuan honey in modern dressing to heal wound in grade II diabetic patients can reduce the care day length and amputation risk for upper or lower extremity areas that are often affected and wounded in the event of hyperglycemia. Wound care is performed every 3 days for 20 days based on the physiological process in the proliferative phase of wound healing. The diabetic wound was assessed using the Bates Jensen Wound Assessment Tool (BWAT). The research was experimental with pre- and post-test control group design. The results showed that the 20-day wound care with this combination could reduce the BWAT score by 5.2, a sign of its effectiveness as compared to the control group reduction by 4.33. Conclusively, performing a modern dressing using this combination for 30-45 minutes every 3 days for 20 days was effective in accelerating the healing process of grade II diabetic wounds.

Keywords: *diabetic wound; African leaf nanoparticle hydrogel and Papuan honey; wound healing*

1. Introduction

The incidence of diabetes mellitus (DM) according to the International of Diabetic Federation (IDF) worldwide was 415 million people in 2015 and it is estimated that by 2040 it will increase to 642 million people if no preventive measures are taken(Indonesia, 2015). Indonesia is a country with a high number of people with Diabetes, In 2013, the number of people with diabetes mellitus in Indonesia amounted to 6.9% of the total Indonesian population (176,689,336), in 2018, the number of people with diabetes had increased to 8.5% of the total population of Indonesia(RI, 2018). Based on the results of basic health research in 2018, the number of cases of diabetes mellitus based on a doctor's diagnosis in the population ≥ 15 years old was highest in the Special Capital Region of Jakarta Province, namely 23.4% of the total population, while the lowest number was in East Nusa Tenggara province with a total of 0.9% of the total population (B. P. d. P. K. K. K. RI, 2018). Regarding the results of Riskesdas 2013 on the number of people with diabetes who had not been diagnosed but had signs and symptoms, the largest proportion was in East Nusa Tenggara and Central Sulawesi provinces with a percentage of 2.1% of the total population, while the largest number was in West Java province with an estimated number of 225,136 or 0.7% of the total population of West Java >14 years old (32,162,328) (RI, 2018).

Patients with diabetes mellitus are at great risk for complications of diabetic wound. Diabetic wound is an open wound on the skin surface caused by macro angiopathy, micro angiopathy and vascular insufficiency neuropathy. Typical signs of the process of diabetic ulcers on the feet start from soft tissue injury to the feet, the formation of fissures between the toes or on dry skin and callus on the skin. The number of people with diabetes mellitus with complications of diabetic wound is the most cases treated in hospital. The number of patients with diabetes mellitus suffering from

*) Corresponding Author (Rolyn Frisca Djamanmona)
E-mail: friscarolyn@gmail.com

amputation due to diabetic ulcers was around 15% to 30% (Indonesia, 2015). The mortality rate after one year of amputation was 14.8%. This number increased to 37% after three years of amputation (Merdekawati & Az, 2017).

Modern wound care with a moist concept consists of various preparations, one of which is hydrogel. Hydrogel has shown empirical evidence of greater potential for wound progress than conventional methods. Modern wound dressing in hydrogel preparations moisturize the wound area and break necrotic tissue without destroying granulation tissue. The necrotic tissue is then absorbed into the gel structure, then removed along with the wound dressing or can be called a natural autolytic debridement process. Dressing using hydrogel can be done once in 3-5 days so as to reduce the process of trauma and pain in the wound and provide an opportunity for new tissue granulation process (Kartika, 2015, 2017). In this research, the hydrogel to be used was African leaf nanoparticle (*Vernonia amygdalina*) and pure Papuan honey. *Vernonia amygdalina* has a height of ± 2-5 meters.

In South Africa, this plant is cultivated as a vegetable. Regarding the results of the research conducted by Ijeh (2011), African leaves (*Vernonia amygdalina*) contain nutrients and chemical compounds that are good for wound healing including flavonoids, saponins, tannins, polyphenols, and alkaloids (Egedigwe, Ijeh, Okafor, & Ejike, 2016; Ijeh & Ejike, 2011).The complete nutritional content in African leaves (*Vernonia amygdalina*) is very good when it is used on wound healing, including diabetic wound, which is categorized as a chronic wound. In the inflammatory phase, the content of flavonoids and tannins can function as antioxidants and saponins as antimicrobials, which is very good for killing bacteria in the wound and the content of alkaloids can function as analgesics to reduce pain in the wound. In the proliferative phase, the content of antioxidants, proteins and minerals in African leaves (*Vernonia amygdalina*) can support fibroblast cells to synthesize collagen to form new tissues. Meanwhile in the maturation phase, the content of saponins and flavonoids that function as antimicrobials is very good to prevent the occurrence of bacterial colonies(Djamanmona). Polyphenols in African leaves can function to inhibit the absorption of blood sugar in a systemic mechanism.

The pure honey contains organic acids, free amino acids and antioxidant compounds Chrysin, Pinobanskin, Vitamin C, Catalase, Pinocembrin which function as antibacterial and are good for healing Grade II diabetic wound. The catalase enzyme which functions as an antibacterial and the water content of less than 18% allow honey to attract pus around the wound area that is smeared with the natural honey. The physical and chemical properties of honey, such as acidity and osmotic effects, play a major role in killing germs. Besides, honey also contains antibiotics as antibacterial and antiseptic to protect the wound, as well as helping to overcome infection in the wound and even its anti-inflammatory properties can reduce pain and increase circulation, which contribute to the healing process. Honey also stimulates the growth of new tissue, thereby reducing the appearance of scars or seams on the skin (Sundari & Tjahjono, 2017). The antioxidant content of honey circulating in the local Indonesian market (originating from Central Java, Surabaya, Sumbawa, Papua, Jambi, Aceh, Sulawesi, and Bali), has the largest IC50 value coming from Papua at 5.45 mg / mL (Muawanah & Wardhani, 2014).

The management of diabetic ulcers has the main goal of reducing the number of bacteria and closing the wound. Basically, it consists of three main components, namely debridement, offloading and infection management. The research conducted by Prasetyo (2017) on a pre-clinical test case study for treating diabetic foot ulcers with topical hydrocolloid turmeric showed that after wound care for 21 days, the average BWAT score decreased by 15.43. It was supported by the type of hydrocolloid dressing used, which could absorb more exudates However, this research had many weaknesses because it was a case study so that it was more descriptive and subjective, and the number of research samples could not represent the population so that it could not be generalized (Prasetyo, 2017). The results of the research conducted by Purnomo (2014) showed that healing diabetes mellitus ulcers with hydrogel for 14 days could reduce BWAT scores by 13 points than using NaCl (Purnomo, Dwiningsih, & Lestari, 2014).

Wound healing is supported by a number of influencing factors including immunological status, increased blood sugar level, rehydration and wound washing, nutrition (vitamins A, C, B, zinc, mineral, protein, fat), blood albumin level, oxygen supply and vascularization, pain and corticosteroids (Kartika, 2015). In patients with diabetes mellitus, increased blood sugar level and the growth of bacteria in the wound cause

delays in wound healing. Another way is needed so that the wound area continues to receive nutrition during wound care and the number of bacterial colonies in the wound decreases, one of which is by using African leaf nanoparticle (*Vernonia amygdalina*) in hydrogel preparations combined with Papuan honey.

2. Method

This research method was conducted experimentally with a pre-test and post-test control group design. The subjects in this study were 8 respondents with grade II diabetic ulcers in the inflammatory phase in Sorong City area.

The research procedure begins with submitting an Ethical Clearance at the Poltekkes Research Ethics Commission of the Ministry of Health Sorong, then the researcher submits a research permit to the Klasaman Health Center, East Sorong Health Center and Malaisimsa Health Center, Sorong City.

After getting respondents, researchers conducted sample selection using simple random sampling. Diabetic wound patients who were selected as respondents to the study, submitted a letter of willingness to become respondents by signing informed consent. The research subjects were divided into 2 groups, namely the intervention group consisting of 5 respondents and the control group of 3 respondents.

Wound care method in the control group was treated with African leaf nanoparticle hydrogel dressing, while in the intervention group wound dressing was treated with a combination of African leaf nanoparticle hydrogel and Papuan honey. In 100 grams of African leaves, it contains 676,823 mg of flavanoids (Djamanmona & Samaran, 2022). The content of flavonoids that can prevent various diseases related to oxidative stress. The antioxidant effectiveness of flavonoids is stronger than vitamins C and E. In their function of neutralizing free radicals, flavonoids work synergistically (mutually reinforcing) with vitamin C.

In addition to having antioxidant activity, flavonoids can inhibit aldose reductase which converts glucose and galactose into polyol forms. These polyols have implications in diabetic neuropathy and in the formation of cataracts that accompany diabetes as well as galactosemia. Flavonoid compounds generally act as antioxidants, namely as free radical catchers because they contain hydroxyl groups. Flavonoids are reductors so they can act as hydrogen donors against free radicals.

This research was initiated by mixing 1:1 African leaf nanoparticle hydrogel and Papuan honey (50 gram of African leaf nanoparticle hydrogel and 50 gram of Papuan honey) into a hydrogel combination of African leaf extract and Papuan honey.

The intervention was carried out for 20 days and observed and the evaluation of the number of bacterial colonies and the wound progress was carried out 6 times, namely day 1 (pre-test before treatment and first day treatment), day 4 (post-test day 1 and second day of treatment), day 8 (post-test 2 and the third day of tratment), day 12 (post-test 3 and fourth day treatment), day 16 (post-test 4 and fifth day treatment) and day 20 (post-test 5).

The results of this study then the research data were tabulated for further analysis using Statictical Package For The Social Science (SPSS) 16.0 for window. Before the analysis was carried out, a data normality test was first carried out because the sample used was less than 50. Test the normality of the data using the Shapiro-Wilk test. The results of the normality test of the wound healing score data obtained normal distributed data ($p>0.05$) so that it was continued with the General Linear Model Repeated Measure Anova and Post Hoc Bonferroni tests to see differences in wound healing scores before and after intervention in one group and between research groups.

The multivariate analysis used in the data processing of this study is the Multivariate Analysis of Variance (Manova) to analyze the effect of providing modern wound care interventions with nano-hydrogel african leaf particles on the wound healing process. Researchers analyzed BWAT scores on post tests and startification tests to analyze the third factor (counfonding factor) against the diabetic wound healing process.

3. Result and Discussion

As seen in Table 1, the respondents were characterized based on age, gender and education. In the intervention group, the average age was 58.60 years with a minimum age of 53 years and a maximum age of 67 years, while the average age in the control group was 57.33 years with a minimum age of 55 years and a maximum age of 60 years. In both the intervention and the control groups, the respondents' ages were in the elderly range. Based on gender, male

respondents dominate among both groups. Meanwhile on the educational level, the intervention group has balanced respondents while in the control group Senior High School graduates dominate. Based on the Random Blood Sugar Test, on average the intervention group was in the range of 185.80 mgdL and the control group 166.33 mgdL.

Table 1. Characteristics of Respondents

Characteristics of Respondents	Intervention Group (n=5)		Control Group (n=3)	
	N	%	N	%
Mean±SD	58.60±5,771		57.33±2.591	
Min-Max	53-67		55-60	
Man	3	60	2	66.66
Woman	2	40	1	33.33
No School	1	20	1	33.33
Primary school	-	-	-	-
Junior high school	2	40	2	66.66
Senior high school	2	40	-	-
College	-	-	-	-
Blood Sugar During Mean±SD	185.80±12.637		166.33±11.846	
Min-Maks	168-198		159-180	

Diabetic wound healing was assessed using the Bates-Jensen Wound Assessment Tool (BWAT) instrument that was carried out 5 times in 20 days for each wound treatments, either in the intervention group using a combination of African leaf nanoparticle hydrogel and Papuan honey or in the control group using conventional wound care. The results are presented as follow:

Table 2. Wound Healing Assessment with Bates-Jensen Wound Assessment Tool (BWAT) scores

BWAT Score Measurement	Intervention Group (n=5)		Control Group (n=3)	
	Mean ±SD	Min-Max	Mean ±SD	Min-Max
Pre Test	16.80±1.304	15-18	9.80±9.121	14-19
Post Test 1	15.80±1.643	14-18	9.20±8.701	13-19
Post Test 2	14.40±1.517	13-16	8.40±7.893	12-17
Post Test 3	13.00±1.000	12-14	8.00±7.483	12-16
Post Test 4	11.60±0.548	11-12	7.20±6.686	11-14

In the intervention group, the average number of 1st day BWAT scores was 16.80 in the category of middle wound-regeneration-limit and on the 20th day it decreased to a wound-regeneration-limit of 11.60. Meanwhile in the control group 1st day BWAT scores average was 9.80 in the wound regeneration category and on the 20th day it decreased to 7.20 in the healed category.

Table 3. Analysis of BWAT Score Differences between the Time of Measurement

Variable	Type III Sum of Squares	Df	Mean Square	F	Sig.
BWAT Score of Intervention group	87.120	1	87.120	152.842	0.000
BWAT Score of control group	34.133	1	34.133	33.032	0.029

**Repeated measure anova*

Table 3 shows that from 6 wound treatments for 20 days in the intervention group and the control group, there were differences in wound healing between groups as assessed by the BWAT score.

Table 4. Analysis of BWAT values before and after the intervention

Intervention Group				Control Group			
Measurement		Mean Difference	*p*	Measurement		Mean Difference	*p*
Pre Test	Post Test 5	5.200	0.002	Pre Test	Post Test 5	4.333	1.000
Pre Test	Post Test 1	1.000	0.341	Pre Test	Post Test 1	1.0000	0.572
Post Test 1	Post Test 2	1.400	0.046	Post Test 1	Post Test 2	1.333	1.000
Post Test 2	Post Test 3	1.400	0.046	Post Test 2	Post Test 3	0.667	0.572
Post Test 3	Post Test 4	1.400	0.046	Post Test 3	Post Test 4	1.333	0.229

**Post Hoc Bonferroni*

Based on Table 4, the test results on effect per subject obtained p = 0.00, which indicates that there is no significant difference in the BWAT scores that describes the wound healing process between the measurement times in each group. The Post Hoc test in the intervention group resulted in a p-value of 0.02, which means there is a difference in the BWAT scores that describe wound healing, except for the pre-test to post-test 1 (day 1 to day 3). The twenty-day wound care with a combination of African leaf nanoparticle hydrogel and Papuan honey could reduce the BWAT score by 5.2 points, signifying that it is more effective in healing grade II diabetic wounds. While in the control group on day 1 to day 20, the value of p = 0.029 means that there was a difference in the BWAT score, which illustrated that wound healing could reduce the BWAT score of 4.333.

Diabetic wounds are chronic and can increase morbidity, mortality and reduce life quality. The causes include peripheral neuropathy, peripheral arterial disease or a combination of both (Indonesia, 2015). Acceleration to the slow healing process of diabetic wounds requires proper care and dressing.

Data normality and homogeneity tests were performed based on the results in the intervention and control groups to see the distribution of the respondents number. They obtained p>0.05, which means that the results of the first measurement of wounds in both groups were in the same condition. The wound healing process consists of 4 phases: hemostasis, inflammation, proliferation and remodeling.

In this research, after 20 days of wound care with a combination of African leaf nanoparticle hydrogel and Papuan honey, in the intervention group, the average pre BWAT measurement results were 16.80 and decreased on day 20 to 11.60 or could reduce the BWAT score of 5.2 points, meaning that the combination of African Leaf Hydrogel and Papuan honey is more effective in healing grade II diabetic wounds. Meanwhile in the control group, the average pre BWAT examination results were 9.80 and decreased on day 20 to 7.20 or decreased BWAT scores by 2.6 meaning that there was an effect of wound healing in the intervention group and control group, yet it can be seen that in the intervention group, the wound healing result was more significant by decreasing 5.2 points than the control group by 2.6 points with p value = 0.000. The results of this research are in line with the research conducted by Purnomo (2014) that hydrogels are effective for wound healing with an effect size of 3.4 (very strong)(Purnomo et al., 2014).

The wound healing process is influenced by various factors including oxygenation, infection, hormones, age, gender, stress, blood sugar levels, obesity, drugs, smoking and nutrition. The wound healing process begins with the formation of fibrin to close the wound and infiltrate inflammatory cells, particularly neutrophils. At the beginning of wound healing, neutrophils immediately clean the wound area from foreign objects, dead cells and bacteria that secrete cytokines activating local fibroblasts and keratinocytes (Mustakim, Suriadi, & Makmuriana, 2022; Suriadi, Hastuti, & Handayani, 2015).

NaCl compresses are less effective at preventing the onset of necrotic tissue, while the presence of necrotic tissue in the ulcer being a hiding place for bacterial colonies also inhibits the tissue granulation process. So that the healing process of diabetic ulcer wounds becomes prolonged. Hydrogel dressing was chosen to be used because it is suitable for grade 2 diabetic wounds, which have minimal exudation and help hydrolyzing necrotic tissue. This dressing removes dead tissue (slough and necrotic), prevents and controls infection, manages exudation, prevents and controls bleeding, prevents and controls odor, reduces pain, provides comfort, protects the wound and surrounding skin and maintains optimal temperature thereby accelerating granulation and epithelialization (Djamanmona; Suriadi et al., 2015).

In this research, many risk factors were involved in wound healing, including the average age of patients >55 years,, causing germs/bacteria to increase in the wound and poor vascularization to the wound. Poor vascularization can also cause difficulty in wound healing due to the respondent's lack of awareness about maintaining the cleanliness of the dressing and wound area. Some respondents even returned several times to health facilities with dirty dressing and even without dressing on wounds.

Selection of the right dressing in wound care is a determinant to obtain a decrease in the number of bacterial colonies and effective and efficient wound healing. Hydrogel content that functions as autolysis, antimicrobial, absorption of exudation and odor, accelerates granulation and avoids trauma is a major factor in the healing process of grade II diabetic wounds. Besides, the phytochemical content of African leaves itself is a good supporting factor including: flavonoids and polyphenols that function as antioxidants, saponins and tannins that function as antimicrobials and hypoglycemic compounds, so that when they enter the metabolic process they can lower blood glucose levels, as well as active alkaloids, which can function as an alpha glucosidase inhibitor, so that hydrogels with African leaf nanoparticles have additional advantages that are good for use in wound care.

4. Conclusion and Suggestion

Wound care with a modern dressing combination of African leaf nanoparticle hydrogel (*Vernonia amygdalina*) and Papuan Honey, which is carried out every 4 days for 30-45 minutes in 20 days, is effective in

accelerating the healing process of grade II diabetic wounds.

5. Acknowledgments

In completing this research, the research team cannot be separated from the support of various parties, including: Director and Poltekkes (Health Polytechnic) Health Institute, Ministry of Health, Sorong, as a source of research funding also Hypercholesterolemic patients who are willing to be respondents in this research, and family (husband and children). Therefore, with humility the researcher wants to express deepest appreciation and gratitude.

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