Potential of Honey Hydrogel Modern Dressing in Wound Healing of Patients with Grade II Diabetic Foot Ulcer

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Abstract

Aims: To analyze the potential of honey hydrogel modern dressing in wound healing process in patients with grade II diabetic ulcers.

Methods: The research design used a true experiment with a randomized pretest posttest control group design. This study had 36 respondents who were divided into 2 groups through simple random sampling. The intervention group was given honey hydrogel with 4 measurements. The first measurement or pretest on day 1, the second measurement or posttest 1 on day 7, the third measurement or posttest 2 on day 14, and the fourth measurement or posttest 3 on day 21. The instrument used to measure patient wound healing using the Bates-Jensen Wound Assessment Tool (BWAT).

Results: The increase in the mean wound healing score of patients who were given honey hydrogel modern dressing from a score of 42.11 on day 1 to 34.56 on day 21 with p = 0.001 while the increase in the mean wound healing score of patients who were given manufacturer hydrogel modern dressing from a score of 41.67 on day 1 to 37.17 on day 21 with p = 0.001. The effect size between the intervention group and the control group is quite strong with a value of 0.78.

Conclusion: Honey hydrogel has the potential to promote wound healing in patients with grade II diabetic ulcers. Further research is recommended to explore the use of honey hydrogel by innovating the manufacturing process to ensure consistent dosing in the treatment of grade II diabetic ulcers.

Keywords: Diabetic Foot Ulcer, Honey Hydrogel, Modern Dressing

Introduction

Diabetes mellitus (DM) is a complex chronic disease that requires continuous medical care using multi-factorial risk reduction strategies beyond glycemic control (American Diabetes Association, 2020). An increase in DM sufferers can lead to an increase in complications such as diabetic foot ulcer (DFU). In 2017, the International Diabetes Federation (IDF) reported that DFU have increased with 15-25% of people with DM experiencing DFU. As many as 23.5% of patients underwent amputations due to chronic DFU (RI Ministry of Health, 2018). Preliminary studies conducted at the Lanang Wound Care Center Children's Clinic in Semarang City, patients who experience diabetic ulcers of various grades reach 15-20 patients each day and undergo DFU treatment.

Comprehensive treatment of DFU will increase the potential for healing to reach 90%. Conventional wound care techniques are often ineffective in wound healing In addition to administering systemic antibiotics and surgical intervention, wound care is considered an important component of diabetic ulcer management (Fau et al., 2021). The results of Rohmayanti and Handayani's research found four important things in wound care, namely wound examination, types of modern dressings, how to treat wounds, and their effects on wounds (Rohmayanti & Handayani, 2017). Herbal treatment of DFU can use honey therapy, which has antibacterial, autolytic, anti-inflammatory and wound-healing properties. Honey's antibacterial properties can treat wound infections, while its anti-inflammatory properties can reduce pain, increase blood flow, and affect the healing process (Riani & Handayani, 2017).

The use of modern dressings is one of the phases of wound care that can affect the healing of DFU (Nabila, 2018). Research shows that a warm, moist environment with the right ingredients for wound healing can make patients feel comfortable and speed up wound healing. Thus, the hydrogel was chosen for modern dressings. Hydrogel is an effective barrier against microbes (Tjahjono, 2020). So it is necessary to renew the hydrogel which can further accelerate the wound healing process as it is made from natural ingredients which contain various substances which are good for diabetic ulcers.

Honey hydrogel has pharmacological activity as an antimicrobial (high sugar content, low water, H2O2, low pH), antioxidant (flavanoids), anti-inflammatory, and antiseptic (El-Kased et al., 2017). Honey hydrogel is able to retain moisture, stimulate tissue growth, angiogenesis, wound contraction, stimulate collagen synthesis, help the debridement process, and accelerate wound epithelialization (Mohd Zohdi et al., 2019). Research conducted by Zohdi, et.al., 2019 on honey hydrogel in burn wounds (animal studies) revealed that honey hydrogel showed good properties that have good transparency and the ability to absorb exudate significantly and showed an acidic pH value (pH = 4.3) compared to the control hydrogel (pH = 5.3) (Mohd Zohdi et al., 2019). In acidic wound conditions, the release of oxygen from hemoglobin will increase and help the wound healing process (Gunawan, 2017).

Honey hydrogel can overcome the problems faced by people with diabetic ulcers with several considerations, including 1) the content contained in honey hydrogel is more complete than the manufacturer's hydrogel, which only contains silver; 2) strengthening the materials used by the public who have earned the trust of the process of healing diabetic ulcers which are packaged in a modern, efficient and more useful manner; and 3) honey is a natural ingredient that is often used in the wound healing process which is easy to get and has an affordable price.

Interventions that support both externally and internally are very important to optimize the healing process of diabetic ulcers. The administration of honey hydrogel is expected to accelerate wound healing in patients with grade II diabetic

ulcers. So to purpose of this study is to analyse the potential of honey hydrogel modern dressing in wound healing process in patients with grade II diabetic ulcers.

Methods

Current research is an experimental study that requires treatment with a true experiment type with a pretest-posttest randomized control group design. The research group was divided into the intervention group with modern dressing using honey hydrogel and the control group with modern dressing using manufactured hydrogel.

The population in this study were all patients with grade II DFU at the "Klinik Anak Lanang" Wound Care Center in Semarang City, with an average population each month reaching 250-350 patients with grade II DFU with the calculation results showing that the number of samples in this study was 36 respondents, with 18 respondents in the intervention group who were given modern honey hydrogel dressings and 18 respondents in the control group who were given modern manufactured hydrogel dressings. After finding respondents who fit the selection criteria, respondents were divided into intervention and control groups using simple random sampling. Respondents chose a roll of paper containing an equal number of options from both groups.

Inclusion criteria in this study: (a) patients with grade II according to Wagner Megitt DFU who were treated at the "Klinik Anak Lanang" Wound Care Center in Semarang City, (b) patients taking anti-diabetic drugs, (c) diabetic ulcer patients who were given antibiotics, and (d) patients who came 3 times a week for 21 days for the treatment of diabetic ulcers. Meanwhile, the exclusion criteria for this study were: (a) diabetic ulcer patients were in critical condition or in shock, (b) diabetic ulcer patients were active smokers, (c) diabetic ulcer patients with comorbidities such as hypertension, CHF, CKD, and cancer, and (d)) diabetic ulcer patients who withdrew from the study.

Data collection uses the BWAT instrument (Bates-Jensen et al., 2019) to measure ulcer healing, where the wound will get better if the BWAT score decreases with a score range of 13-65. The BWAT observation sheet is seen from the line on the wound status continuum with an assessment. If the total wound score reaches 13 and above, then the wound is declared to have regenerated (wound regeneration), and if the total wound score reaches 60, then it is stated that the wound has not experienced regeneration (wound degeneration). Observations were made 4 times a week for 21 days of the DFU treatment process. Grade II DFU healing was evaluated 4 times, namely the first measurement or pretest on day 1, the second measurement or posttest 1 on day 7, the third measurement or posttest 2 on day 14, and the fourth measurement or posttest 3 on day 21.

Data from the research results before the analysis test was carried out, the data normality test was first carried out. The data normality test uses the Shapiro-Wilk because the sample is less than 50 respondents. The results of the BWAT score data are $p > 0.05$; this indicates that the data is normally distributed so that it can be continued for the General Lincar Model Repeated Measure Anova test to see the difference in BWAT scores before and after being given intervention in one group or between research groups. The researcher submitted an ethical review test to the research ethics commission of the Poltekkes Kemenkes Semarang.

Results

Characteristics of research respondents include age, gender, education, occupation, and blood glucose when the respondent. The results showed that the average age in the intervention group was 57 years old, while in the control group the average age was 58 years. The results of the study based on the gender of the male respondents in the intervention group were 11 respondents (61.1%) and 7

female respondents (38.9%), while in the control group the number of male and female respondents was the same, namely 9 people (50%). In terms of education, the highest number of respondents in the intervention group were the upper secondary level (SMA), with 9 respondents (50%), and in the control group, 7 respondents (38.9%).

Based on the results of data processing, it was found that between the intervention group and the control group the average blood glucose examination results at the time of the initial examination (pre test) on day 1 was above 210 mg/dl. Characteristics of age with p = 0.508, gender with p = 0.354, education with p = 0.509, occupation with p = 0.648, and blood glucose with p = 0.092 when respondents between study groups were homogeneous or there was no significant difference with (Table 1).

Table 1. Characteristics of Respondents

Characteristics Respondents	Intervention Group (n = 18)		Control Group (n = 18)		*p value*
	n	%	n	%	
Age					
Mean ± SD	57 ± 4,4		58± 5.1		0.508*
Min – Max	50–64		51–68		
Gender					
Man	11	61.1	9	50.0	0.354*
Woman	7	38.9	9	50.0	
Last education					
Junior high school	6	33.3	4	22.2	0.509*
Senior high school	9	50.0	7	38.9	
College	3	16.7	7	38.9	
Work					
Not Working / Retired	6	33.3	7	38.9	0.648*
Housewife	3	16.7	3	16.7	
Private	5	27.8	3	16.7	
Government employees	4	22.2	5	27.8	
Current Blood Glucose (mg/dL)					
Mean ± SD	219.78±22.9		213.67±16.8		0.092*
Min – Max	187–250		190–236		

**Descriptive Statistics *Homogeneity Test*

The results showed that the BWAT score in the intervention group and the control group experienced a significant increase in the mean score before and after treatment (Figure 1).

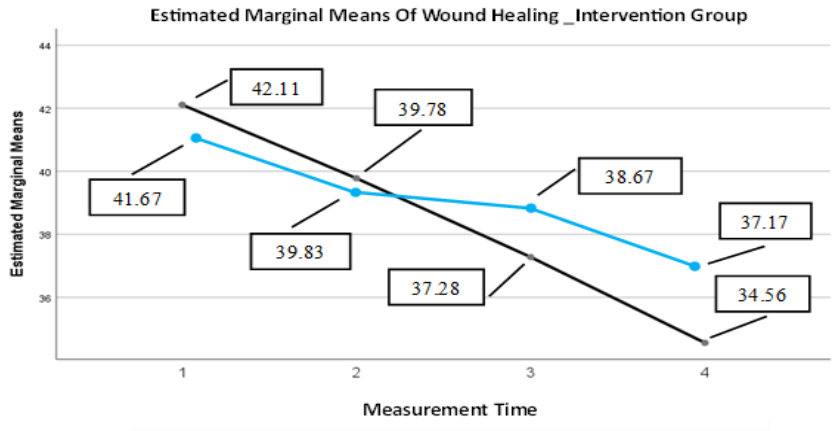

Figure 1. BWAT Scores in the Intervention and Control Groups

This study shows that administration of honey hydrogel and manufactured hydrogel can accelerate wound healing in grade II DFU patients by reducing the BWAT score and after being tested with Between-Subjects Effects ANOVA p value = 0.438, it can be concluded that there is no significant difference between the intervention group and the control group (Table 2).

Table 2. Comparative Analysis of BWAT Scores Between Groups

	Sum of Squares	**dF**	**Mean Square**	**F**	***p value***
Patient Wound Healing	7,335	1	7,335	0.615	0.438*

**Tests of Between-Subjects Effects*

The results showed that the results of the parameter estimates in the General Linear Model test in posttest 3, namely day 21, obtained a value of p = 0.024 (p <0.05) and a 95% CI value from the mean difference past zero, so that it can be concluded that there is a significant difference wound healing of patients with grade II DFU between groups on day 21. When viewed from the results of the repeated measure ANOVA (within-subjects effects) test, it was found that each group had p = 0.001, which means that there was a significant average difference in decreasing score BWAT across groups over time (Table 3).

Table 3. Differences in BWAT scores in the intervention and control groups based on the results of the pre-test and post-test on patient's wound healing

BWAT score (13 – 65)	**Intervention Group n=18 Mean±SD**	**Control Group n=18 Mean±SD**	**Difference (95% CI)**	***P value***
Day 1	42.11±3.75	41.67±3.43	-0.44 (-1.992 – 2.881)	0.713*
Day 7	39.78±3.75	39.83±3.40	0.05 (-2.480 – 2.369)	0.963*
Day 14	37.28±3.47	38.67±3.39	1.39(-3.717 – 0.939)	0.234*
Day 21	34.56±3.43	37.17±3.18	2.61 (-4.855 – 0.368)	0.024*
p value	0.001**	0.001**		

**Parameter Estimates ** Repeated Measure ANOVA*

The results showed that the effect size between the intervention group and the control group was quite strong with a value of 0.78. This research explains that honey hydrogel has a potential effect on wound healing in patients with grade II diabetic ulcers of 0.78 (Table 4).

Table 4. *Effect Size Hydrogel*Honey Against Wound Healing in Patients with Diabetic Ulcers

Variable	**Group**	**Sample**	***Cohen's Effect***
Patient Wound Healing With BWAT score	Intervention	18	0.78*
	Control	18	

**Cohen's Effect*

Discussion

Mechanism of Honey Hydrogel on Patient Wound Healing

Wound healing is the organism's response to tissue or organ damage and efforts to restore it to homeostatic conditions so as to achieve physiological stability of the tissue or organ in the skin. This is related to tissue regeneration (Primadani & Safitri, 2021). Good wound management will determine the end result of the wound healing process (Indrayati et al., 2018; Nisak, 2021). In healing DFU, things that must be done include controlling blood sugar levels on a regular basis, debridement, reducing pressure on the injured part of the body, giving antibiotics

to prevent infection, and closing the wound to keep the moisture in the lesion (Nabila, 2018; Purnama et al., 2017).

The process of healing DFU is basically the same as the process of wound healing in general. However, the process of healing DFU has a number of complications that take longer (Indrayati et al., 2018) to heal at certain points due to several influencing factors such as, diabetes related ulcer infections, high blood glucose levels, as well as wounds that contribute to chronic conditions (Husen & Basri, 2021; Widigdo et al., 2022). In addition, age, nutritional factors, and lifestyle can also affect the healing process of diabetic ulcers (Nurhanifah, 2017).

In this study the hydrogel used was honey hydrogel and manufactured hydrogel. Differences in the content of honey hydrogel and hydrogel manufacturers can affect wound healing in patients with DFU. Honey hydrogel has pharmacological activity as antimicrobial, anti-inflammatory, antioxidant and antiseptic (Rana & Ashrafuzzaman, 2021). Honey hydrogel is able to retain moisture, stimulate tissue growth, and accelerate wound epithelialization (Meo et al., 2017). Meanwhile, this manufactured hydrogel containing silver only has antibacterial, anti-inflammatory and antiseptic abilities which can only prevent further mutation of bacteria so that they can effectively kill bacteria that cause infection.

Honey hydrogel used in this study was packaged in an aerosol form, which has a liquid texture when sprayed but feels like a gel when levelled with a dose of 6 g with a sugar content of 68.53%, a water content of 14.72%, and a pH of 4.06 which is mixed with 0.4% gel material so that produced a honey hydrogel of 100 mL with a nanoparticle size of 718.2 nm. Honey hydrogel is a biomaterial with a three-dimensional hydrophilic polymer network that is able to absorb water and exudate from the atmosphere and can become a modern dressing (Mohd Zohdi et al., 2019). Honey hydrogel is able to control the moist environment helps wound healing, creates a cushioning and cooling effect on the wound area, able to stop the wound from drying out (Husada et al., 2020). Honey hydrogel is also easily removable, spreads more easily, biodegradable, non-toxic, elastic, biocompatible, non-staining water soluble and compatible with several excipients (El-Kased et al., 2017).

Manufacturer hydrogel does not have the ability as an antioxidant. Antioxidants in wound care play a role in creating collagen in the skin, forming new blood vessels, and helping the absorption of iron which can increase the strength of wound healing. In the control group, this affects wound healing, especially in the proliferative stage or the formation of new tissue, which is characterized by the formation of scar tissue in the wound with increased collagen production in the wound area.

If not used properly, honey hydrogel can cause side effects in patients with diabetic ulcers who are being treated for wounds. Side effects that can occur are in the form of a stinging sensation and tissue maceration in the wound which causes infection so that it affects healing. This happens if the osmotic activity in honey that is not managed properly can attract cell fluids, causing skin rupture due to excess exudate. However, in the study these side effects did not occur in respondents who were given the honey hydrogel modern dressing intervention.

Comparison with Previous Research

Research shows that honey hydrogel can potentially heal grade II diabetic ulcers. The study was conducted for 21 days with 4 measurements. These results indicate that the average pre-test to post-test 3 BWAT score is in the range of 42 – 37. This indicates that the wound is not in good condition or is still at the midpoint of wound regeneration. The healing process of DFU has several complications that take longer to heal at certain points due to several influencing factors such as

diabetes-related ulcer infections, high blood glucose levels, and wounds that contribute to chronic conditions (Husen & Basri, 2021). In addition, age, nutritional factors, and lifestyle can also affect the healing process of DFU (Nurhanifah, 2017).

The effect size obtained from the administration of honey hydrogel on wound healing is strong, with a value of 0.78. This research shows that performing wound care using honey hydrogel has a strong effect in accelerating wound healing in patients with grade II DFU.

Another study conducted by Rolyn in 2019 showed that African leaves could effectively accelerate the healing process of diabetic ulcers with $p < 0.05$, in which the intervention group was given wound care with hydrogel nanoparticles of African leaves and the control group was given manufactured hydrogel (Djamanmona et al., 2019). The study was conducted for 21 days with 7 measurements. The results showed that the average pre-test to post-test BWAT score was 6 in the range of 27-14. This indicates that the condition of the wound is in good condition or wound regeneration. However, the effect size of the study is low with a value of 0.35.

Wound healing with modern honey hydrogel dressing in this study was also influenced by several factors, namely the provision of interventions using honey hydrogel packaged in aerosol form to have a liquid texture when sprayed but feels like a gel when applied. At the time of the intervention, there was no determination of the appropriate dose of honey hydrogel for wound care with modern dressings because it still uses spray pressure, which has the risk of producing different pressures or doses for each intervention. In addition, human resource factors also influenced both the glucose levels at the time of responding and the objective assessment of BWAT scores by the nurses performing wound care. Thus, the average reduction in BWAT scores over time tends to have a slight difference. However, when viewed from the effect size results, the study had a fairly strong influence with a value of 0.78. This can answer the hypothesis that honey hydrogel has the potential for wound healing in patients with grade II diabetic ulcers.

Nursing Implications

Wound care includes the promotion of accelerating wound healing, preventing infection, preventing skin damage, preventing extended hospitalization, minimizing discomfort experienced by patients, minimizing the financial burden on patients and the workplace, and minimizing the workload of nurses. The nurse's role is to limit the number of tissues involved with the disease through functional changes and nursing interventions. In this theory honey hydrogel is used as a modern dressing for patients with grade II diabetic ulcers for wound healing of grade II diabetic ulcers. This honey hydrogel has gone through a process of content testing and toxicity testing so that it can be applied to the treatment of grade II diabetic ulcers.

Limitations

In this study there are still limitations, including: It has not been determined how to use the right dose of honey hydrogel for wound care with modern dressings because it still uses spray pressure which has the risk of producing different pressures or doses for each intervention. Each intervention provided has a significant effect, but this study has not conducted a cost benefit analysis or economic value.

Contribution to Global Nursing Practice

To global nursing practice, especially clinics with wound care, can use honey hydrogel that has been studied as a modern dressing option in the treatment of grade II DFU.

Conclusion

There was a significant decrease in the patient's wound healing score before and after administration of modern honey hydrogel dressings in patients with grade II diabetic ulcers. The intervention group or the control group both had significant potential for wound healing in patients with grade II diabetic ulcers, but the administration of modern honey hydrogel dressings had a better potential for wound healing in patients (34.56 ± 3.43 vs 37.17 ± 3.18) including the value of the effect size of wound healing. patient 0.78 (quite strong).

Author Contribution

All authors have accepted responsibility for the entire content of this manuscript and agree to its submission.

Conflict of Interest

The authors declare no conflict of interest.

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