The effectiveness of wound caring technique with *polyhexamethylene biguanide* and *dialkyl carbamoyl* chloride to healing process duration of diabetic foot ulcer patient

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Abstract

Background: Antimicrobial dressing on moist-based wound care is a successful wound care technique, especially for diabetes mellitus wounds. The moisture on wound can be made by closed wound care to reach a standard moisture in various wounds. The antimicrobial dressing type that can increase the wound healing is *Polyhexamethylene biguanide (PHMB)* and *Dialkyl carbamoyl chloride (DACC).* Polyhexamethylene biguanide can accelerate the tissue granulation and reduce the risk of infection. Dialkyl carbamoyl chloride is a part of moist wound healing with strong hydrophobic threat so the bacteria will be lifted and accelerate the wound healing process.
Purpose: The aim of this research is to analyze the effect of healing technique using *Polyhexamethylene biguanide* and *Dialkyl carbamoyl chloride* wound healing process on diabetic foot ulcer patients.
Methods: This research was quasi-experimental with 129 respondents. The instruments were Bates Jensen's observation sheet and data were processed by double linear regression.
Results: It was obtained an average difference between the duration of the wound healing process between PHMB and DACC therapy with a p-value of 0.0005.
Conclusions: The use of this type of DACC dressing is more effective against the duration of the healing process of diabetic foot ulcers because of the time needed for DACC to work on killing bacteria in-vitro in 30 minutes compared to other dressing.

Keywords: diabetic foot ulcer; wound healing

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Introduction

The diabetic prevalence numbers in Indonesia has increased significantly for the last five years. In 2013, the diabetic prevalence numbers in adults reached 6,9% and in 2018 increased to 8,5% (Research and Development of Ministry of Health of the Republic of Indonesia, 2018). In 2019, 463 million from total population worldwide or about 9,3% of adults in 20-79 age years old had diabetes based on global diabetes mellitus prevalence. Indonesia was in 7th highest rank for adults with diabetes mellitus in the world with over 10.7 million people in total. This number us predicted to increase and reach 16.7 million in 2045 (International Diabetes Federation., 2019). The ulcers followed by infection, gangrene, amputation, and death were a serious complication and required a higher amount of cost and longer care. Long wound healing process is caused by inappropriate wound handling in diabetic ulcer (Ekaputra, 2013). Diabetic ulcer healing duration requires about 2-3 weeks for1st stadium, 3 weeks to 2 months for 2nd stadium, ≥ 2 months for 3rd stadium, and 3 to 7 months for 4th stadium (Arisanty, 2013). Amputation is a serious consequence from Diabetic Foot Ulcer (DFU) (Decroli, 2019). *Polyhexamethylene biguanide (PHMB)* is an antiseptic

with *polyhexamethylene biguanide* which is a fatty acid derived with strong hydrophobicity (Febriani, 2018). PHMD has a strong-based bactericidal bond to negative phosphate in bacteria phospholipid membrane, destroys outer membrane from bacteria cell wall through permeability disturbance and removes bacteria cytoplasm cell by osmosis (Kurnia, Sumangkut, & Hatibie, 2017). PHMB fluid requirement is more effective and efficient compared to irrigation (p=006; p = 0.02; CI 95%) (Kristianto, 2016). DACC will bind and deactivate bacteria / microorganism. This bound is irreversible so that the bacteria / microorganism will be ruptured while the dressing is changed. The ruptured bacteria will fasten the wound healing process (Febriani, 2018). There are several factors affecting foot ulcers infection, depending on the ulcer factors (location, space, chronic or not, previous amputation, ischemia degree) and patient factors (age, kidney disorder, diabetic period, related comorbidity) (Juni, 2019). Foot ulcers care is complex and requires a multidiscipline approach related to debridement treatment, exudates purulent disposal, adequate antibiotic therapy, revascularization and wound care management (Juni, 2019). In patients with diabetic foot ulcer, 80% in Indonesia are cared for at home. It was found about 15% patients with diabetic foot ulcers, 30% with amputation risk and 32% of mortality (Sulistyowati, 2015). This research was aimed to analyze PHMB and DACC to wound healing duration in diabetic foot ulcer patients.

Materials and Methods

Design

This research was conducted at Bekasi Hospital with a letter of ethical review approval from Universitas Medika Suherman. This research applied four main principles in the ethics of nursing research: right to self-determination, anonymity and confidentiality, right to fair treatment, justice, right to protection from discomfort and harm. The research used quasi-experimental design.

Participants and Setting

The population was 129 respondents. Inclusion criteria were retinopathy ulcer feet respondents, Wagner stadium 3, get regular maintenance, and in inflammatory elongated phase. Exclusion criteria were ulcer retinopathy three feet with Wagner, no infection and cooperative.

Data Collection

The data were collected by using Bates Jensen observation sheets. The wound care applied was Antimicrobial Dressing every 2-3 days assumed from Standard Operating Procedures (SOP). The observation held was based on 3rd Wagner wound condition on 1st, 14th, 16th, 18th and 21st day to wound care schedule. On the 21st day, if the wound repair showed granulation, the researcher continued the observation until the granulation was seen.

Data Analysis

This research used bivariate analysis for the group that received special treatment the treatment of injuries using PHMB and DACC to lengthen the healing process wound with independent t-test. If the result of the test obtained p value=.05, it implies using the t-test and multivariate applied double linear regression to control the confounding possibility.

Results

The bivariate analysis using independent t test for categoric data reported no significant association in terms of dressing type (p value=.432), age (p value=.158), nutrition status (p value=.397) and significant association in terms of mobility (p value=.002), comorbidity (p value=.023), and medicine consumption (p value=.010) to the duration of wound healing process.

Included variables in the hierarchical regression analysis were decided based on p value of 0.25. In the first model, there were significant data in bivariate analysis. Bivariate selection was held after each independent and confounding variable had a bivariate analysis with the dependent variable. If the bivariate result was p-value < 0.25 those variables went to the multivariate level.

In Table 1, it was concluded that there was a variable with p-value score > 0.25 included in modeling and four variables, age, comorbidity, mobility and medicine consumption, had p-value score < 0.25. But because of the kind of dressing for having an independent mind and dressings are still included in the candidates. The same thing with the status of nutrients, which have significant roles in the healing process wound so nutrients status is still included in modeling. These six variables became the candidates and were able to be included in multivariate modeling.

The second model included effectiveness of PHMB and DACC to the duration of the wound healing process by making a model including variable and potential confounders without including interaction (interaction test was not performed).The modeling as presented in Table 2 was gained.

Table 2 shows the result from bivariate selection is that there were two variables with p-value score >0.05, dressing type, age and nutrition status, so those will be removed from modeling. The variable removed was a variable with the highest p-value score, age.

In Table 3 model 1, age, nutrition status, and mobility affected significantly to the duration of the wound healing process (p-value score < 0.05), while the dressing type and medicine consumption variables had p-value score > 0.05 so the null hypothesis was accepted which means those variables did not affect significantly the duration of the wound healing process. After identifying two variables that did not affect significantly the duration of wound healing process, the regression test was repeated by excluding the variable with highest

Table 1. Bivariate Selection Result of Research Variable

Variable	p-value
Dressing Type	0.432
Age	0.158
Nutrition Status	0.397
Comorbidity	0.023
Mobility	0.002
Medicine Consumption	0.010

Source: Primary Data

Table 2. Initial Modeling The Effectiveness of PHMB and DACC to the Duration of Wound Healing Process at Bekasi Hospital

Variable	Initial Modeling			
	Coefficient B	SE	T	p-value
Dressing Type	-0.643	2.086	-0.308	0.758
Age	0.029	0.135	0.216	0.829
Comorbidity	-5.576	2.171	-2.569	0.011
Nutrition Status	2.037	1.871	1.089	0.278
Mobility	-4.238	2.097	-2.021	0.045
Medicine Consumption	7.503	2.507	2.993	0.003

R Square: .163

Table 3. Double Linear Regression Modeling

Variable	Model 1	Model 2	Model 3	Model 4
	p-value	p-value	p-value	p-value
Dressing Type	0.758	0.798	-	0.814
Age	0.829	-	0.009	0.716
Comorbidity	0.011	0.010	0.285	0.019
Nutrition Status	0.278	0.260	0.040	-
Mobility	0.045	0.046	0.001	0.033
Medicine Consumption	0.003	0.003	0.896	0.002

Note: *Confounding

Table 4. Final Model Result Effectiveness of Antimicrobial Dressing Apply to the Duration of Wound Healing in Health Services at Bekasi Hospital

Variable	Initial Modeling			
	Coefficient B	SE	T	p-value
Dressing Type	-0.643	2.086	-0.308	0.758
Age	0.029	0.135	0.216	0.829
Comorbidity	-5.576	2.171	-2.569	0.011
Nutrition Status	2.037	1.871	1.089	0.278
Mobility	-4.238	2.097	-2.021	0.045
Medicine Consumption	7.503	2.507	2.993	0.003

R Square: .163

p-value score, the medicine consumption.

Dressing type was removed from modeling because it has p-value > 0.05 so the linear regression test was repeated. After the linear regression test was performed by removing dressing type variable, the calculation result of each variable did not change more than 10%. From the analysis result, p-value > 0.05 no longer existed so the variable searching process included in modeling was completed. Next, the final modeling was performed.

After analysis was performed, it was seen that determination coefficient (R Square) showed 0.163 score. It means, the regression modeling obtained explained 16.1% of dependent variable variant from duration of wound healing process and p-value score = 0.001 meant 5% alpha. We could declare that the regression modeling was fit to the existing data. Supported by fulfilled auto correlation assumption and homoscedasticity assumption and collinearity test, the regression equation obtained was:

Duration of Wound Healing Process = 9.17 - 0.643 dressing type + 0.029 age -5.57comorbidity+2.037nutrition status-4.238 mobility+7.503 medicine consumtion

This equation model could estimate the duration of wound healing process affected by the confounding factors after being controlled by nutrition status. The illustration of wound healing process duration is described as follows: Individuals using PHMB, at the age of 52 years, no comorbidity, good nutrition status, mobile, on average they will heal 12 days faster compared to those using DACC; Individuals using PHMB, at the age of 52 years, no comorbidity, poor nutrition status, mobile, on average they will heal 15 days longer compared to those using DACC with poor nutrition status; Individuals using DACC, at the age of 52 years, no comorbidity, good nutrition status, mobile, on average they will heal 14 days faster compared to those using PHMB with poor nutrition status; Individuals using DACC, at the age of 52 years, no comorbidity, poor nutrition status, mobile, on average they will heal 16 days faster compared to those using PHMB with poor nutrition status.

Discussion

The average value of duration of ulcer retinopathy feet in the process of healing of a wound is 13.98 days as opposed to the use of other types of dressings.

Dressing Type related to the Duration of the Wound Healing Process

DACC dressing type utilization is more effective to the duration of wound healing process in diabetic foot ulcer patients with an average score of the duration of wound healing process 7.76 days compared to PHMB dressing type utilization (Butcher, 2014). The duration of wound healing process in general can be short but the healing process in diabetic foot ulcer needs longer time in certain phases because there can be several difficulties such as wound infection and chronic condition wound. Those things extend the inflammation phase of wound healing because the inflammatory agent in a choric wound is higher than in an acute wound (Soep, 2015). Research claims that a diabetic foot wound care needs longer time and multidiscipline therapy such as to control blood sugar level and revascularization (Semadi & Irawan, 2017).

Inflammation management in wound care must also be considered as to how the inflammation process does not extend to infection. The activity to control infection might be conducted by choosing the proper wound care solution and antimicrobial dressing on the wound (Arisanty, 2013). Silver type dressings have an effect and destroy microorganisms faster than oligodynamic. The result of a research by Indrayati (2018), stated that there was a significant difference between hidrophobic (DACC) and silver with p-value score 0.01 with significance level <0.05. Eberlein (2012) claimed that PHMB and silver were both effective to reduce the pain and bacteria. PHMB as a strong base in the bactericide, binds to phosphate negatively charged on the phospholipid bacteria, destroys the outside and inside of a cell wall bacteria through the permeability of bacteria and removes the cytoplasm of a cell by means of osmosis (Kurnia, Sumangkut, & Hatibie, 2017). PHMB treatment of injuries is used to speed up or encourage granulation of tissue and reduce the risk of infection. DACC works by binding and disabling bacteria or microorganisms, so bacteria can be uplifted in the turn of the dressings, which can speed up the process of healing of a wound. DACC does not cause bacteria resistance, is not cytotoxic, is safe to be used in the long run, and does not cause allergic reaction (Febriani, 2018).

Age related to the Duration of the Wound Healing Process

Human has physiological changes that decrease drastically quicker after the age of 49. The wound healing process will be longer along with the age. The affected factors were the derivation of the elasticity amount and the reduction of the collagen regeneration process because of the cell metabolism derivation. Inelastic skin will decrease the cell regeneration capacity when the wound will and start to close so it might retard the wound healing (Bahri, 2014). The age factor is determined extremely significant to diabetic ulcer incident rate. The elderly group (45->90 years old) have a high risk to diabetic ulcer as does the late adult group (35-44 years old) (Arisanty, 2013).

The result of this research was in line with that performed by Tanujiarso and Lestar (2020) that 72.7% of diabetic ulcer patients above 50 years had longer wound because of the decrease of amount of skin elastin and the reduction of collagen regeneration process from aging. It is found that

70% of diabetic ulcers in elderly will have constraints and will take longer in the healing process because the life quality of older patients with diabetic ulcer is lower compared to the younger patients related to their better physical condition (Utami & Agrina, 2014).

Comorbidity related to the Duration of the Wound Healing Process

The wound healing is affected by comorbidity such as diabetes, heart disease, kidney disease and blood vessels disorders. The condition of the diseases aggravates the cell work in wound healing because oxygen and nutrition will be prevented reaching to the wound section. It is necessary to perform collaboration to overcome the cause and the complication during the wound healing process. The cells' heavy work might affect the circulation so the duration of wound healing process will be longer compared to normal circulation. An abnormal circulation might lead to the oxygenation reduction because of the constriction. This constriction causes the reduction of blood volume which will lead to constriction phase and the reduction of oxygen and nutrition supply for wound healing (Arisanty, 2013).

Effect of moist wound healing technique on diabetes mellitus patients with diabetic ulcer at Dhoho Ward in RSUD Prof Dr. Soekandar Mojosari showed that there were four diabetes mellitus respondents with diabetic ulcer who had other comorbidity, which is anemia with wound regression (57.1%) (Wahyuni, 2016). According to Rakhmawati, Purnamawati, and Jumaiyah (2021), circulation might be one of the most important factors that affect the wound healing pace. Inappropriate circulation might become a flow disturbance in blood vessels so the tissue will have less oxygen. In the healing context, when the tissue has less oxygen, it will lead to hypoxia. A proper circulation is highly needed to maintain an adequate duration of the wound healing process.

The result of a research performed by Rodriguez, Felix , and Woodley (2008), mentioned that circulation was related to wound healing; inappropriate circulation causes oxygen absence which affect the healing wound. Another research by Sukarmin (2016) declared that there is a relation between circulation and retardation of diabetic foot wound healing.

Nutrition Status related to the Duration of the Wound Healing Process.

The characteristic of nutrition status was counted in accordance with Body Mass Index (BMI) which is a mathematic formula declared as body weight (in kilograms) divided by body height square (in meters). The utilization of this formula might only be applied to those at the age of 19 to 85 years, with normal back spine, not an athlete nor a body builder, and not being pregnant nor breast feeding (Arisman, 2011).

The nutrition and food supply affects highly to wound healing. Poor nutrition will lengthen the duration of wound healing process and even cause an infection (Arisman, 2011). The nutrition needed and important are *amino acid, fat, carbohydrate, vitamins (C, A, B complex, D, K, E), zinc, Fe, magnesium* and water. Triwibowo (2014), declared that to hasten the duration of the gangrene wound healing process, it is necessary to fulfill the nutrition demand. Another research by Molnar, Underdown, and Clark (2014), "*Nutrition and Chronic Wounds,*" stated that every aspect of chronic wound was identical to nutrition support so it must be optimal to the patient needs.

Mobility related to the Duration of the Wound Healing Process.

Movement disorder can restrict blood flow from and to peripheral. The disturbed blood flow might be caused by a pressure or a friction with foreign objects. If it happens in capillary blood vessels it could cause a local tissue necrotic. To make the circulation function efficient, mainly in lower extremity venous, movement or mobility is necessary (Ekaputra, 2013).

According to Arisanty (2013), the bad condition of wound might be caused by blood flow disturbance. The blood flow from and to peripheral will be obstructed because of mobility disturbance. Dwi et al. (2012) declared that in 25 people (64.1%) with mobility and 14 people (35.9%) without mobility there was a relation between mobility to the duration of wound healing process in diabetic ulcer.

Medicine Consumption related to the Duration of the Wound Healing Process.

Diabetic foot ulcer is an open wound on skin surface or mucous membrane that might be invaded by germs, so it creates infection and requires an antibiotic treatment. An inappropriate antibiotic option might cause an ulcer that does not heal soon and harms the patient. The evaluation on antibiotic accuracy declared 100% indication accurate, 100% patient accurate, 42% medication accurate, and 61.9% dosage accurate (Pradipta et al., 2016). Medicine therapy has a positive effect and differs from those with antibiotic type, which affects the wound healing. As claimed by Sussman and Bates-Jensen (2012), antibiotic consumption in the long term might suppress the wound healing level. A biofilm produced by bacteria creates antibiotic resistance in ulcer and gangrene. Biofilm might prevent antibiotic penetration and detain macrophages phagocytic activity. The antiphagocytic is developed in biofilm matrix and the colony formed in biofilm matrix might facilitate a resistance to genetic material transfer horizontally and genetic expression changes (Murali et al., 2014).

Conclusions

From the bivariate analysis result, the fastest duration of wound healing process was by using DACC dressing type. The fastest was three days

to 19 days maximum. The respondents' average age was 49.62 years. It showed that all the respondents were elderly. Most of the respondents had comorbidity, proper nutrition status, mobile and consumed medicine which was 25 people (59.5%). Most of the respondents' nutrition status was good, 22 (52.4%). Most of the respondents had mobility, 28 (66.7%). Most of the respondents consumed drugs, 32 (76.2%).

There was an average difference in the duration of wound healing process between PHMB therapy and DACC. There was a relation among age, comorbidity, nutrition status, mobility and medicine consumption with the duration of wound healing process in diabetic foot ulcer patients at Bekasi Hospital. The DACC dressing type was more effective to the duration of wound healing process compared to PHMB dressing type and the most dominant variable affecting the duration of wound healing process was comorbidity and mobility after controlled for nutrition status confounding factor.

Declaration of Interest

The authors declare no conflict of interest

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