

Article

COMPARISON STUDY OF BACTERIAL PROFILE, WOUND HEALING, AND COST EFFECTIVENESS IN PRESSURE INJURY PATIENTS USING TREATMENT HONEY DRESSING AND HYDROGEL

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ABSTRACT

Background : Pressure injury is a localized soft tissue injury caused by prolonged pressure over bony prominence. Most published papers used Manuka honey as dressing, while this product is expensive. As this reason, this study will use local product honey called Nusantara honey, to prove the use of local honey has better healing process, bacterial profile, and cost effectiveness, compared to the standard dressing, hydrogel.

Method : This is a one-month experimental study conducted in patients with pressure injury that referred to our division. Parameter of the bacterial profile was taken from deep-tissue specimen. The healing process was examined with Pressure Ulcer Scale for Healing (PUSH) Tool. Cost was accumulated after all the treatment. Data was analysed with t-Test or Mann Whitney (if the distribution is not normal), with statistical significance was define as $p < 0.05$.

Result : Of 26 wounds, 12 were randomized to hydrogel and 14 to honey dressing. Characteristics were determined by sex, age, body mass index, level of consciousness, mobilization status, immobilization etiology, comorbidities, grade and location of ulcer, hemoglobin, leukocytes, and albumin level. There was clinically significant wound size reduction in honey dressing according to PUSH Tool ($p = 0.118$). The bacterial profile and reduction were similar. Honey dressing appeared to be more cost effective in terms of dressing cost ($p < 0.001$) and lower total cost.

Conclusion: The local honey dressing has better wound healing outcome, although it is not statistically significant. Its capability of decreasing pathogens is similar with hydrogel, with lower cost, particularly the dressing cost. This local honey dressing could be a good choice as wound dressing in areas where the modern dressings are not available.

Keywords: Honey; Pressure Injury; Wound Healing; Bacterial Profile; Cost

Pendahuluan: Ulkus dekubitus adalah suatu kerusakan jaringan lunak yang terlokalisasi akibat penekanan berkepanjangan di atas tonjolan tulang. Sebagian besar studi menggunakan madu Manuka sebagai perawatan luka (dressing), di mana madu tersebut mahal. Atas landasan tersebut, studi ini menggunakan madu lokal, yaitu madu Nusantara, dengan tujuan untuk membuktikan penggunaan madu lokal memiliki luaran yang lebih baik, diobservasi dari penyembuhan luka, profil bakteri, dan harga, dibandingkan dengan dressing standar, yaitu hydrogel.

Metode: Studi eksperimental selama satu bulan ini dilakukan kepada pasien ulkus dekubitus yang dikonsultasikan ke divisi kami. Parameter profil bakteri diambil melalui kultur jaringan. Proses penyembuhan luka dinilai berdasarkan Pressure Ulcer Scale for Healing (PUSH) Tool. Biaya diakumulasi dari awal sampai akhir tata laksana. Analisis data menggunakan T-test atau Mann-Whitney (jika distribusi tidak normal), dengan signifikansi didefinisikan sebagai $p < 0,05$.

Hasil: Dari 26 luka, terdapat 12 luka ditata laksana dengan hydrogel dan 14 madu. Karakteristik pasien dinilai berdasarkan jenis kelamin, usia, indeks massa tubuh, tingkat kesadaran, status mobilisasi, penyebab imobilisasi, komorbiditas, derajat dan lokasi luka, kadar hemoglobin, leukosit, dan albumin. Terdapat reduksi luas luka yang signifikan secara klinis berdasarkan PUSH Tool ($p = 0,118$). Profil bakteri dan reduksi bakteri serupa di antara kedua grup. Madu lebih efisien dalam hal biaya, terkait dengan harga dressing ($p < 0,001$) dengan total biaya lebih rendah.

Kesimpulan: Dressing madu lokal memiliki kemampuan penyembuhan luka yang lebih baik, walaupun tidak signifikan secara statistik. Kemampuan penurunan bakteri sama dengan dressing standar, dengan biaya yang lebih

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murah, terutama harga dressing. Madu lokal dapat menjadi pilihan yang baik untuk perawatan luka di mana tidak tersedia dressing modern.

Kata Kunci: Madu; Ulkus Dekubitus; Penyembuhan Luka; Profil Bakteri; Biaya

Conflicts of Interest Statement:

The author(s) listed in this manuscript declare the absence of any conflict of interest on the subject matter or materials discussed.

INTRODUCTION

Pressure injury is a localized soft tissue injury caused by prolonged pressure, commonly over bony prominence.¹ Physician are faced with ischemic condition, neuropathy, secondary bacterial infection, and immunosuppression condition in several patients, which make it more challenging in treating them.^{2,3} Pressure injury gives huge burden to the health-care system. Patients with pressure injuries were hospitalized three times longer compared to patients without pressure injuries.⁴

In the United States, 2.5 million patients are treated for pressure injury.¹ In Indonesia, a multicenter cross-sectional study conducted in four large hospital showed that prevalence of pressure injuries was 8%, with prevalence of nosocomial pressure injuries was 4,5%.⁶ In Cipto Mangunkusumo hospital, according to electrical health record data by Information System Management Unit showed increasing incidence of pressure injuries from 2016 to 2018 (112 cases in 2016, 315 cases in 2017, and 358 cases in 2018).

In support of wound healing, a standardized, accurate, and easy-to-use tool is important to measure wound healing progress. One of the most common tools is Pressure Ulcer Scale for Healing (PUSH) tool (Figure 1). It is a monitoring tool developed by NPIAP. PUSH tool components are the size, amount of drainage, and type of tissue presents.^{8,9} The components should allow the practitioner to quickly determine the ulcer is healing, remains unchanged, or is deteriorating.

Treating wound with honey was already applied for centuries. It has been used for acute and chronic wound such as pressure injury, burn, trauma, and surgical wound. There is an evidence that antimicrobial effects in honey will advantages this condition. Studies showed that honey has an antibacterial effects to inhibit or kill *Streptococcus pyogenes*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and

Clostridium oedematiens. Besides, honey also prove antifungal effects.¹⁰

Nusantara honey is Indonesian product honey that has been researched and there has been plenty published papers. It accelerates healing in cleft palate¹²⁻¹⁵, split thickness skin graft donor site^{18,19}, and wound bed preparation²¹⁻²³, a choice of dressing for wound dehiscence¹⁶, scalp defect¹⁷, and infected chronic wound²⁰. It also have antibacterial effects to *P. aeruginosa*, *Staphylococcus aureus*, and MRSA.¹¹

Pressure Ulcer Scale for Healing (PUSH)
PUSH Tool 3.0

Patient Name: _____ Patient ID#: _____
User Location: _____ Date: _____

Directions:
Observe and measure the pressure ulcer. Categorize the ulcer with respect to surface area, exudate, and type of wound tissue. Record a sub-score for each of these ulcer characteristics. Add the sub-scores to obtain the total score. A comparison of total scores measured over time provides an indication of the improvement or deterioration in pressure ulcer healing.

LENGTH x WIDTH (in cm ²)	0	1	2	3	4	5	Sub-score
	0	< 0.3	0.3 – 0.8	0.7 – 1.0	1.1 – 2.0	2.1 – 3.0	
		6	7	8	9	10	
		3.1 – 4.0	4.1 – 8.0	8.1 – 12.0	12.1 – 24.0	> 24.0	
EXUDATE AMOUNT	0	1	2	3			Sub-score
	None	Light	Moderate	Heavy			
TISSUE TYPE	0	1	2	3	4		Sub-score
	Closed	Epithelial Tissue	Granulation Tissue	Slough	Neurotic Tissue		
							TOTAL SCORE

Length x Width: Measure the greatest length (head to toe) and the greatest width (side to side) using a centimeter ruler. Multiply these two measurements (length x width) to obtain an estimate of surface area in square centimeters (cm²). **Caution:** Do not guess! Always use a centimeter ruler and always use the same method each time the ulcer is measured.

Exudate Amount: Estimate the amount of exudate (drainage) present after removal of the dressing and before applying any topical agent to the ulcer. Estimate the exudate (drainage) as none, light, moderate, or heavy.

Tissue Type: This refers to the types of tissue that are present in the wound (ulcer) bed. Score as a "4" if there is any necrotic tissue present. Score as a "3" if there is any amount of slough present and necrotic tissue is absent. Score as a "2" if the wound is clean and contains granulation tissue. A superficial wound that is re-epithelializing is scored as a "1". When the wound is closed, score as a "0".

4. **Neurotic Tissue (Eschar):** black, brown, or tan tissue that adheres firmly to the wound bed or ulcer edges and may be either firmer or softer than surrounding skin.

3. **Slough:** yellow or white tissue that adheres to the ulcer bed in strings or thick clumps, or is mucinous.

2. **Granulation Tissue:** pink or beefy red tissue with a shiny, moist, granular appearance.

1. **Epithelial Tissue:** for superficial ulcers, new pink or shiny tissue (skin) that grows in from the edges or as islands on the ulcer surface.

0. **Closed/Resurfaced:** the wound is completely covered with epithelium (new skin).

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PUSH Tool Version 3.0 3/15/08
National Pressure Ulcer Advisory Panel

Figure 1. PUSH Tool

Most published papers based on Manuka honey, while this product is available in high cost. As the reason, this study will use local product honey. This honey has both the similar chemical and physical appearance of manuka honey.²⁴ This study is conducted to prove the uses of local honey in pressure injury patients has better outcome observed by the healing process, bacterial profile, and cost effectiveness.

METHOD

This is an experimental study conducted in patients with pressure injuries that referred to our division between July – November 2021. Patients were divided into two groups. The control group was patients that were treated with hydrogel dressing. The experimental group was treated with local honey dressing. Both of the group were observed for one month. Each of the patients was judged from the aspect of bacterial profile, healing process, and cost.

The inclusion criteria were following: adult above 18 years old, patients with pressure injury stage 3, stage 4, or unstageable, and willing to take the full observations and treatment for one month. The exclusion criteria were as follows: unable to be mobilized due to the underlying diseases, allergic to honey or having history of severe symptoms after bee sting, and not willing to be the part of the study.

Before we start the study, each of the subject was asked for consent of participation. Every subjects that found malnutrition was consulted to nutritionist. Bedside debridement was done in subject with unstageable pressure injury. Subjects were divided in two groups randomly by a computer generated randomization tool to group with honey dressing or DACC hydrogel dressing. In honey group, the dressing was changed daily. In DACC hydrogel group, the dressing was changed every three to four days. Each of the subjects was treated until the end of the treatment, but only the first month of the treatment was taken for this study.

During the treatment, each of the subject was observed using PUSH Tool to monitor the healing process of the pressure injury. Each of the three components of PUSH tool was scored and summarized every week from the first time the subject was consulted. Scores were documented in monitoring paper. Each of the wound was score individually. In our study, we were adapting the PUSH Tool 3.0 introduced by NPIAP and convert it in to Indonesian language. This was to facilitate our physician to complete the form and minimize the human error due to the language barrier. Prior to data collection, there was training for all of data collectors to standardized the assessment of the wound.

Microbiological evaluation using deep-tissue biopsy specimen was collected and

transferred to the laboratory for the bacterial culture and examination. Tissue was taken for bacterial culture in the first week before the treatment given and in the last week of the study. The result was presented in a descriptive report for the types of the bacteria and numeric report for the number of bacteria involved and bacterial load.

Cost was accumulated after all the treatment done within one month. Cost that counted was dressing, consumable, and dressing change cost based on RSCM standard. The data will be presented in a numeric report. Patients that discharged before one month was given education to the caregiver regarding the dressing change. Wound was evaluated at the polyclinic every 1 week.

All data were recorded in a research form. The data were put in a table using Microsoft Excel, Microsoft Inc., USA and coded for further analysis. The descriptive analysis was presented in forms of table and narrative paragraphs. The intention to treat analysis was done in this study. The numeric data was first underwent normality test using Shapiro Wilk and box plot. After the analysis, the result of the study was analysed with t-Test (if the distribution is normal) or Mann Whitney (if the distribution is not normal), with statistical significance was define as $p < 0.05$, using SPSS v. 23 Program.

Ethical clearance of the study was given by Ethical Panel Faculty of Medicine, Universitas Indonesia and Cipto Mangunkusumo National Hospital. Subjects of the study were explained about aims of the study, the mechanisms of the study, any advantage gained by participating in the study, possible disadvantages and already signed the written consent. All medical information collected in this study is confidential.

RESULTS

Forty-three wounds in total that were assess for its eligibility, and 29 wounds met the inclusion criteria and were randomized (Figure 2). There were three patients in total loss to follow up from the two groups. The characteristics were shown in Table 1. The baseline data were similar for both groups. The most common immobilization etiology is brain tumor, followed by stroke. All of the patients were dependent to the caregiver, either it was partially or totally.

Table 1. Characteristics of Participants

Characteristic	Groups		p
	Hydrogel (n=14)	Honey (n=15)	
Sex, n (%)			
Male	11 (78,6)	9 (60,0)	0,427*
Female	3 (21,4)	6 (40,0)	
Age, n (%)			
≥ 60 years	2 (14,3)	3 (20,0)	1,000*
< 60 years	12 (85,7)	12 (80,0)	
Body mass index			
Underweight	3 (21,4)	3 (20,0)	0,273
Normal	7 (50,0)	4 (26,7)	
Overweight	2 (14,3)	7 (46,7)	
Obesity	2 (14,3)	1 (6,7)	
Level of consciousness, n (%)			
Compos mentis	5 (35,7)	10 (66,7)	0,240
Apatitis	4 (28,6)	5 (33,3)	
Delirium	1 (7,1)	0 (0,0)	
Somnolen	1 (7,1)	0 (0,0)	
Stupor	1 (7,1)	0 (0,0)	
Koma	2 (14,3)	0 (0,0)	
Mobilization			
Partially dependent	5 (35,7)	10 (66,7)	0,096
Totally dependent	9 (64,3)	5 (33,3)	
Immobilization Etiology, n (%)			
Tumor	7 (50,0)	7 (46,7)	0,680
Stroke	5 (35,7)	5 (33,3)	
Spontaneous brain haemorrhage	1 (7,1)	2 (13,3)	
Encephalopathy	0 (0,0)	1 (6,7)	
Encephalitis	1 (7,1)	0 (0,0)	
Comorbidities			
Diabetes Mellitus, n (%)	6 (42,9)	5 (33,3)	0,597
Hipertension	2 (14,3)	4 (26,7)	
Chronic kidney disease	0 (0,0)	1 (6,7)	1,000*
Systemic lupus erythematosus	0 (0,0)	0 (0,0)	
Coronary artery disease	4 (28,6)	2 (13,3)	0,390*
Acute kidney injury	1 (7,1)	2 (13,3)	
Pneumonia	9 (64,3)	6 (40,0)	0,191
History of COVID-19	2 (14,3)	3 (20,0)	
AIDS	1 (7,1)	0 (0,0)	0,483*
Lung tuberculosis	1 (7,1)	0 (0,0)	
Grade of ulcer, n (%)			
Stage 3	0 (0,0)	4 (26,7)	0,100*
Unstageable	14 (100,0)	11 (73,3)	
Location of ulcer, n (%)			
Calcaneus	1 (7,1)	3 (20,0)	0,245
Malleolus	0 (0,0)	2 (13,3)	
Sacral	12 (85,7)	10 (66,7)	
Vertebrae	1 (7,1)	0 (0,0)	
Haemoglobin level, Mean (SB)	9,67 (SB 1,93)	10,09 (SB 0,59)	0,435^
Leukocytes level, Mean (SB)	11405,71 (SB 5534,33)	11889,33 (SB 2821,05)	0,767^
Albumin level, Mean (SB)	2,45 (SB 0,35)	2,59 (SB 0,36)	0,261^

Chi Square Test; *Fisher Exact Test; ^ Independent T Test

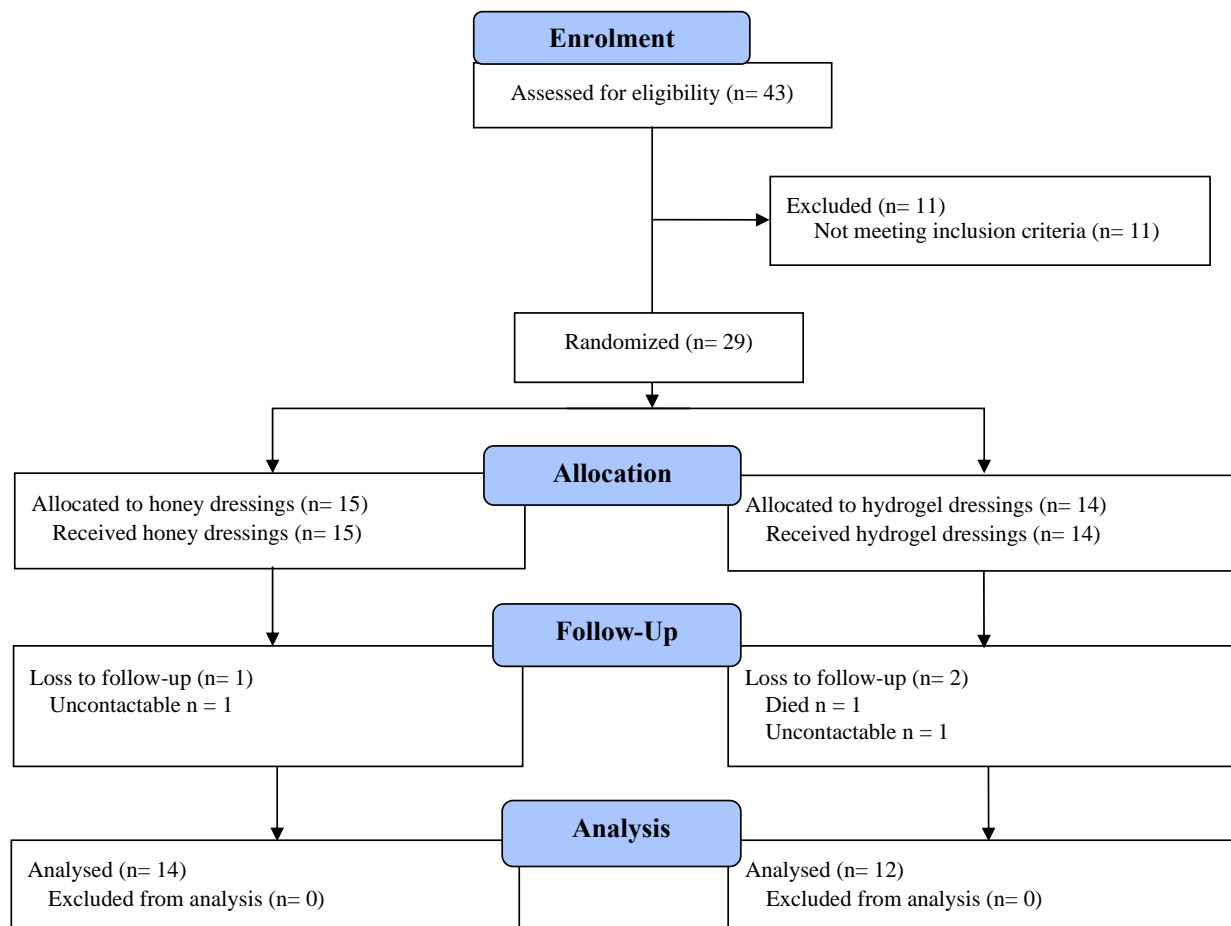


Figure 2. Flow of Participants

Wound Healing

At 4 weeks, the value difference of PUSH Tool in honey dressing group is 2 (0 – 3.25), with one sample was completely healed, compared with 0.5 (-7.5) – (2.0) in hydrogel dressing group (P = 0.118). In more detail, wound size were

calculated by multiplying the length and width of the wound. The mean reduction in honey dressing group is 5.9 cm², compared with no reduction in hydrogel dressing group. There was no significant difference between both groups (P = 0.085) as shown in Table 2-3.

Table 2. PUSH Tool

PUSH Tool	Groups		p
	Hydrogel (n=12)	Honey (n=14)	
Difference	0.5 (-7.5) – (2.0)	2 (0 – 3.25)	0.118*

*Mann Whitney Test

Table 3. Wound Size

Wound size	Groups		p
	Hydrogel (n=12)	Honey (n=14)	
Difference	0 (-7,13) - (12,0)	-5,9 (-14,0) - (-2,10)	0,085*

Values in cm²; *Mann Whitney Test

Bacterial Profile

There was downward trend on most of the pathogens from before and after the treatment (Table 4-5, Figure 3-4), except for *Klebsiella pneumoniae* and *Staphylococcus aureus ss. aureus*, although there were new pathogens on the post-

treatment period. There was also reduction on the total pathogens found before and after the treatment (Figure 5-6). Four pathogens were found consistently on the same 13 wounds before and after the treatment, with variative value of decreasing and increasing total colonies of those pathogens (Table 6).

Table 4. Types of Pathogens (pre-treatment)

Pre-treatment	Hydrogel	Group Honey	p
Pathogens:			
<i>Acinetobacter baumannii</i>	2 (9,0)	1 (4,0)	0,240
<i>E. coli</i>	4 (18,0)	9 (39,0)	
<i>Enterococcus faecium</i>	2 (9,0)	1 (4,0)	
<i>Klebsiella pneumoniae ss. pneumoniae</i>	5 (23,0)	2 (9,0)	
<i>Pseudomonas aeruginosa</i>	8 (36,0)	3 (13,0)	
<i>Staphylococcus aureus ss. aureus</i>	0 (0,0)	3 (13,0)	
<i>Staphylococcus epidermidis</i>	1 (5,0)	0 (0,0)	
<i>Streptococcus agalactiae</i>	0 (0,0)	4 (17,0)	

Table 5. Types of Pathogens (post-treatment)

Post-treatment	Hydrogel	Groups Honey	p
Pathogens:			
<i>Acinetobacter baumannii</i>	1 (6,3)	0 (0,0)	0,059
<i>Burkholderia cepacia</i>	1 (6,3)	0 (0,0)	
<i>E. coli</i>	1 (6,3)	2 (11,8)	
<i>Enterococcus faecalis</i>	0 (0,0)	1 (5,9)	
<i>Klebsiella pneumoniae ss. pneumoniae</i>	7 (43,8)	4 (23,5)	
<i>Pseudomonas aeruginosa</i>	4 (25,0)	0 (0,0)	
<i>Staphylococcus aureus ss. aureus</i>	1 (6,3)	8 (47,1)	
<i>Staphylococcus sciuri ss. Lentus</i>	0 (0,0)	1 (5,9)	
<i>Staphylococcus sciuri ss. Sciuri</i>	1 (6,3)	0 (0,0)	
<i>Streptococcus agalactiae</i>	0 (0,0)	1 (5,9)	

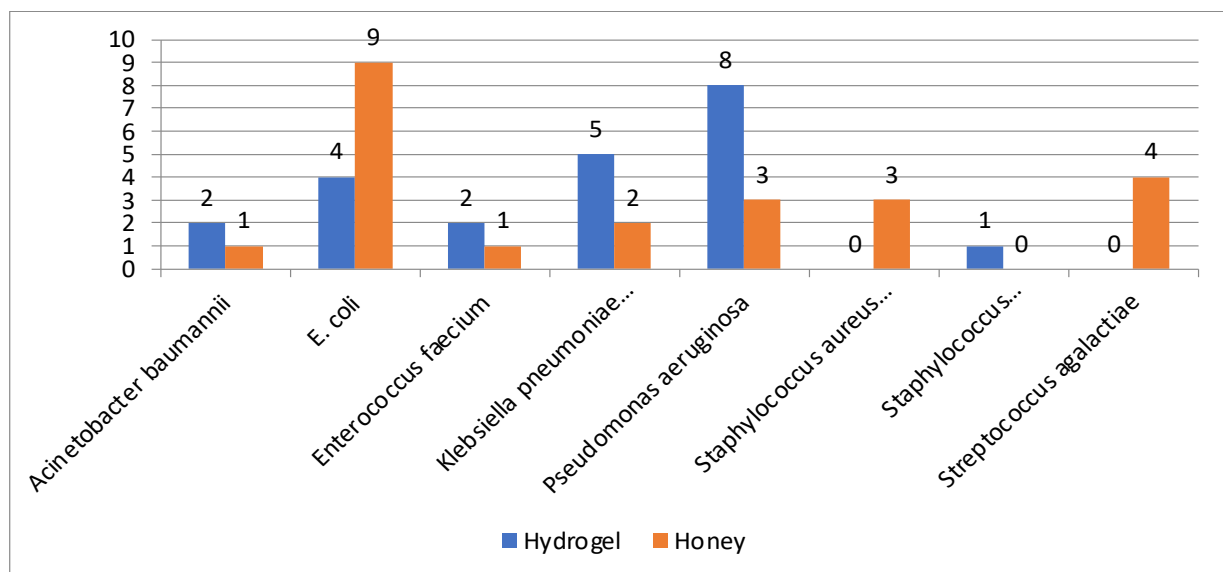


Figure 3. Diagram chart of types of Pathogens (pre-treatment)

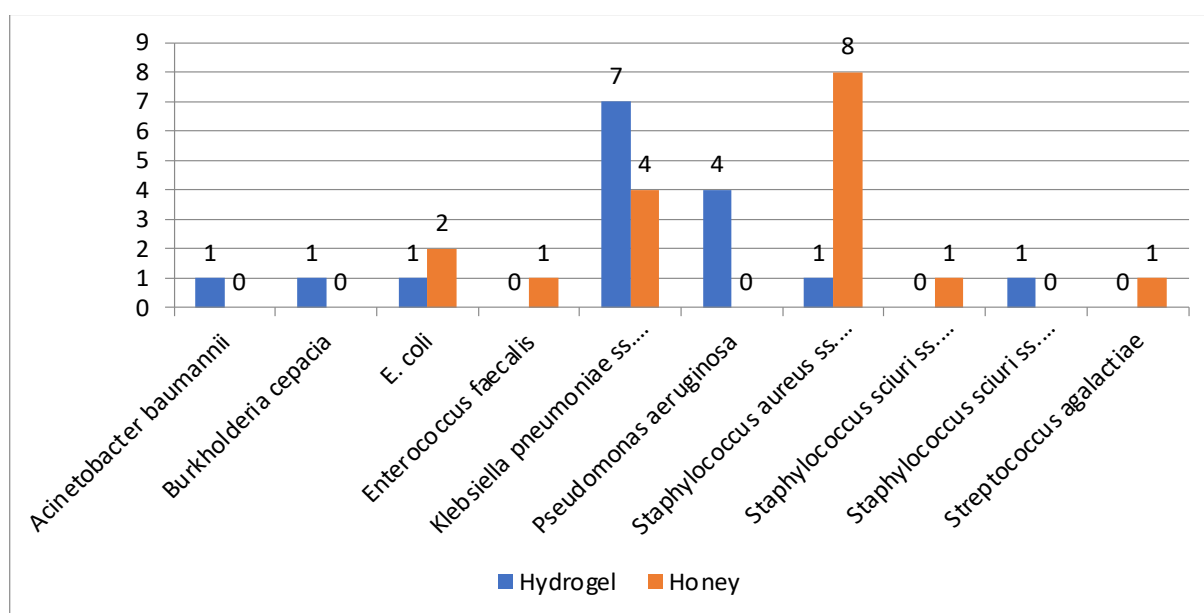


Figure 4. Diagram chart of types of Pathogens (post-treatment)

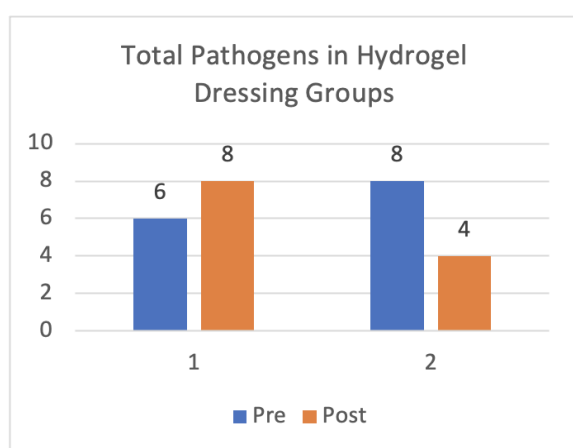


Figure 5. Diagram chart of total Pathogens in Hydrogel Dressing Groups (1: one bacterium, 2: two bacteria)

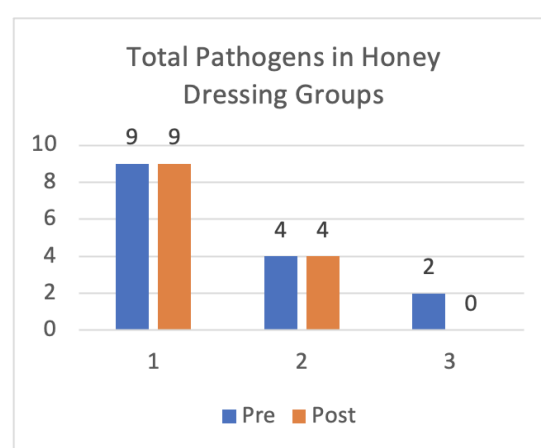


Figure 6. Diagram chart of total Pathogens in Honey Dressing Groups (1: one bacterium, 2: two bacteria, 3: three bacteria)

Table 6. Difference of Total Colony of the Same Pathogens

Difference of quantity of pathogens	Groups		p
	Hydrogel	Honey	
<i>E. coli</i>	84.000	51.000 (44.000)-(58.000)	0,665
<i>Klebsiella pneumoniae</i>	5000 (-56000)-(32500)	72.500 (63.000)-(82.000)	0,200
<i>Pseudomonas aeruginosa</i>	-18.000 (-165.750)-(95.250)	-	-
<i>Staphylococcus aureus ss. aureus</i>	-	-65.000(-112.000)-(22.000)	-

Values in CFU/ml

Cost-effectiveness

The mean total difference of cost is Rp943,906 in honey dressing group, compared to Rp1,526,113 in hydrogel dressing group, although it is not statistically significant ($p = 0.212$). There was similar cost in both groups,

except the cost for honey dressing that was lower than the hydrogel dressing ($p < 0.001$), which the mean of dressing cost in hydrogel group is Rp 580,272 (580,272-1,595,136) and the mean dressing cost in honey group is Rp 74,925 (19,980-199,800) (Table 7).

Table 7. Detail cost

Variables	Groups		P
	Hydrogel	Honey	
Dressing change cost	200,000 (125,000-200,000)	162,500 (70,000-406,250)	0.980
Dressing cost	580,272 (580,272-1,595,136)	74,925 (19,980-199,800)	<0.001
Consumables	186,425 (103,217-265,987)	182,521 (101,845-592,651)	0.527
Outpatient cost	0 (0-522,391)	172,876 (172,847-706,311)	0.252
Total cost	1,526,113 (869,198-2,181,619)	943,906 (503,292-1,555,908)	0.212

Values are mean difference in Indonesian rupiahs. *Mann Whitney Test

DISCUSSION

From the previous studies, honey shown to have benefit in improving wound healing, reduced healing time and scar formation. It also has been used on an infected wound, against some resistant bacteria.⁴⁸ In this trial there were no significant improvement shown on the PUSH Tool on both groups. One of the factors was the highest score for the biggest wound size is 10 for the size more than 24cm², made it difficult to differentiate the reduction of the wound size in this trial, that were much bigger than the maximum wound size on the PUSH Tool. For this reason, we also added the wound size data alone and compared between the two groups, to see the reduction of the wound size in more detail. The mean reduction in honey dressing group is 5.9 cm², were considered as clinically significant, as the rate of epithelialization is 2 mm/day, depending on local tissue and systemic condition.⁴⁹ However, pressure injuries were considered as chronic wound. In chronic wound, the epithelialization process was impaired, as there were hyperproliferative epidermis and presence of hyperkeratosis and parakeratosis histologically, that were deteriorate the healing process.⁵⁰ Moreover, both PUSH Tool and wound size results were lack of the depth of the wound components. Wounds may have the same or small reduction in length and width, but improvement in the depth of the wound. In this study, progressing of this component may be similarly seen in the wound base, as the wound

positively progressing from the necrotic tissue to the granulation tissue, and even epithelial tissue.

There was clinically reduction in terms of total and type of pathogens, although this was not statistically significant. This is in line with the study conducted by Yaghooobi et al which stated that honey has antibacterial effects in wound.³⁰ There were new pathogens found on the posttreatment period, which may cause by the inconsistent place of tissue sample collection, even though it is on the territory of the same wound. The results of different pathogens found in the posttreatment, compared to the pretreatment, on the same wound may cause by either the pathogens that found on the posttreatment were masked by the abundant pathogens on the pretreatment, or the pathogens in the pretreatment were already subsided by the treatment, and there were new pathogens on the wound. In consequence of the different pathogens found in the pre and posttreatment, we could only compare four types of pathogens in total of 13 wounds. This comparison also gave disparity results, vary from decreased of quantity, but there was also increasing quantity in the wound after the treatment. This may cause by the insufficient tissue upon the sample collection, due to the wound was almost fully healed, so that it could be contaminated by the normal flora of the skin. The results also showed some normal flora of the skin, such as *Staphylococcus sp*, *Streptococcus sp*, *Micrococci sp*, and *Corynebacterium sp*.⁵¹⁻⁵³ The results in this study that contained of these pathogens may be

appertained to normal flora of the skin. One of the highlighted pathogens found was *Pseudomonas aeruginosa*. *Pseudomonas aeruginosa* was known as an opportunist pathogen, commonly infected skin, eyes, and respiratory tract, that can cause more severe infection that leads to death. It is a gram-negative bacillus that was difficult to treat due to the high potential to develop resistance. *Pseudomonas aeruginosa* was the most commonly isolated bacteria in chronic wounds. It can impair epithelialization process by attached to the surface of the epithelium and formed biofilms, and also invaded the deeper structure of the skin.⁵⁴⁻⁵⁵ *Pseudomonas aeruginosa* was also found in 58.1% of the cases of skin graft loss.⁵⁶ In our study, *P. aeruginosa* was found in both groups (8 in hydrogel dressing group and 3 in honey dressing group) before the treatment and has decreased to 4 in hydrogel dressing group and not found in honey dressing group after the treatment.

The mean of total cost was lower in honey dressing group compared to the hydrogel group. One bottle of honey dressing, either 250 ml or 650 ml in size, was found to have lower cost which can be used for several times of dressing change, though the dressing change was done every day. The mean total cost was Rp943,906 in honey dressing group, compared to Rp1,526,113 in hydrogel dressing group. These had huge gap with study conducted by Brem et al, that the treatment cost ranged from \$20,000 to \$70,000 per wound.⁵⁷ We did not include the hospital inpatient cost, diagnostic and treatment cost of the underlying diseases and comorbidities, because we want to specifically compare the cost of dressing and related commodities, such as consumables, dressing change cost, and outpatient dressing change cost, alone. In our study, pressure injury itself didn't add burden to the length of stay of the patient, as the patient can be discharged if the primary diseases had resolved or improved.

The wound healing process, particularly the pressure injury, influenced by many factors. Even the best treatment of the local area of the wound won't heal the wound alone. Older age, common chronic diseases, such as cardiovascular diseases, diabetes, chronic pulmonary diseases, renal diseases, neurodegenerative disorders are the risk factors of pressure injury. Another significant complicating conditions aggravating pressure

injury are infections, anemia, malnutrition, hospitalization, incontinence, and disability. Another important factor is mobility of the patients. The laboratory values, i.e., albumin, haemoglobin, and blood glucose also have parts in pressure injury. Patients whose wounds were healed more likely to have higher haemoglobin level and mean arterial pressure.⁵⁸⁻⁵⁹ Our patients have malnutrition in 50% of hydrogel dressing group and 73.4% in honey dressing group. Although patients have been managed by nutritionist, it was not a simple task to treat, due to the comorbidities and complications of the primary disease. Type 2 diabetes was found to be the most frequent comorbid. It has known to be chronic metabolic disease that leads to serious consequences, including the wound healing. Laboratory findings showed that all patients had anemia and hypoalbuminemia. These also had portions in delayed of wound healing.

There were limitations in this study, there are many factors, not only the local site of the wound, but also the systemic factors, such as many variables of comorbidities. The wound size difference was quite different and the PUSH tool nor wound size did not take the depth of the wound into consideration. The detail of the collecting samples, although from the same site of the wound, may vary due to the extensive area of the wound. The dressing also could not be blinded, as the honey dressing had specific odor and color. More narrow study, such as particular comorbidities and wound size may be considered for further studies. The longer follow up time may be beneficial for multivariate analysis. Larger and double blinded RCT may be done in the future.

CONCLUSION

Our study has similarity in terms of the characteristics of the patients. The wound healing is better in honey dressing group, as shown by the reduction of the wound size, although it is not statistically significant. The honey dressing has capability of decreasing pathogens similar to the hydrogel dressing, with lower cost, particularly the dressing cost itself. This local honey dressing could be a good choice as wound dressing in areas where the modern dressings are not available. Larger and double blinded RCT may be done for further studies.

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