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Original Article

Kersen leaf extract gel (*Muntingia calabura* L.) to Improve the healing of perineal wounds in postpartum mothers

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A B S T R A C T

Background: Delivery processes experience 90% perineal rupture—worldwide. Previous research on test animals proved the effect of kersen leaf gel on wound healing can kill microorganisms, increase collagen, and repair wound tissue. However, no research has been found on healing perineal wounds in postpartum mothers using kersen leaf gel, so this research is necessary.

Purpose: Making and testing kersen leaf extract gel to improve perineal wound healing for postpartum women.

Method: This is a quasi-experiment with a pre-post-test with a control group design. The sample consisted of 26 postpartum women with perineal injuries grade 2, divided into two groups (Intervention and control). The intervention was given a combination of kersen leaf gel 25% with antibiotic 2x1 for seven days, and the control group was only given the antibiotic. Perineal wound healing was assessed using the REEDA score. The data analysis used the Mann-Whitney test.

Results: The results showed that the average REEDA score was lower in the intervention group than in the control group on day 3 (5.00±1.155 vs. 5.85±0.801; p=0.038), day 5 (2.31±0.650 vs. 3.23±1.013; p=0.029), and day 7 (0.23±0.439 vs. 1.15±0.987; p=0.039).

Conclusion: Kersen leaf extract gel effectively improves perineal wound healing in postpartum women.

INTRODUCTION

About 90% of deliveries result in perineal tears. There are 2.7 million perineal rupture problems in birthing mothers worldwide. The number is estimated to reach 6.3 million events in 2050, and 50% of perineal rupture events in the world occur in Asia. In Indonesia, perineal tears are felt by 75% of mothers giving birth, with a prevalence of 20-30 years of age of 63%, whereas, at the age of 31-39 years, it is 37%.[1]

Lacerations that occur during the puerperium are adjacent to the anus so that they can become a fertile place for the development of bacteria, which results in infection.[2,3] Staphylococcus aureus bacteria are often found in the results of wound bacterial culture tests in the perineum. These can cause perineal infections if perineal wounds do not get proper care and treatment.[4] According to WHO, perineal wound care includes keeping the wound clean and dry, soaking in warm water is not recommended, washing the perineal wound more than four times a day using clean water, and changing the bandages every four hours.[5]

The normal perineal wound healing process is 6 to 7 days postpartum.[6] Delays in perineal wound healing cause increased complications such as infection-related pain. Infection during the puerperium is a cause of maternal death, including in Indonesia. In Indonesia, 1,015 cases of puerperal infection were recorded, 239 (23.5%) of them died in 2016, and in 2017 there were 992 cases, 178 (17.9%) of them died.[7] Based on the Health Profile of Papua Province in 2019, there were five deaths due to puerperal infections (6.0%).[8]

Pharmacological treatment using amoxicillin has been established as the standard of care for perineal wounds, an

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antibiotic with broad spectrum.[9] However, the use of antibiotics in irrational/responsive doses can cause resistant bacteria or resistance to antibiotics if it is incomplete or inappropriate to consume antibiotics, so in 2015, WHO issued a global action plan to optimize the use of antibiotics by providing combination therapy of antibiotics with herbs to expand spectrum antibacterial, preventing resistance and minimizing toxicity.[10,11]

Non-pharmacological treatment by utilizing herbal plants in the treatment of perineal wounds in postpartum mothers has been widely carried out, including the use of aloe vera with the result that there was a significant difference in the use of aloe vera and the saline control group, wound healing occurred on the seven days. Complete healing occurred on day 10.[12] Utilization of binahong leaves with the results of perineal wound healing decoction occurs on days 6-7.[13] Utilization of green betel leaf decoction with perineal wound healing results occurs on days 4-6.[14] The use of infusion of cinnamon (Cinnamomum Verum) obtained healing results with 7-10 days for 12 respondents and healing with >10 days for three respondents.[15] The use of kersen leaves showed that the results of healing perineal wounds using kersen leaf decoction occurred on the fifth day.[16] From these studies, the fastest healing of perineal wounds occurred on day 5 when using kersen leaves compared to aloe vera, binahong leaves, green betel leaves, and cinnamon.

Kersen leaves can be used as an alternative to infection prevention. Previous research found that spray gel preparations of ethanol extract from kersen leaves can suppress the growth of Staphylococcus aureus, Staphylococcus epidermis, and Propionibacterium acnes bacteria.[17] Research using 25% kersen leaf gel preparations on rabbit perineal wounds was found to have differences in the healing time of perineal wounds on days 2 to 7.[18] Research using kersen leaf extract ointment with a concentration of 20-40% on white rat incisions showed accelerated wound healing comparable to 0.1% gentamicin.[19] Research using kersen leaf extract ointment on wound healing of hyperglycemic mice incisions showed that kersen leaf extract ointment with a concentration of 30-40% could speed up the wound healing process.[20]

From some of the results of previous studies only conducted on experimental animals and testing of antibacterial activity by looking at the Minimum Inhibitory Concentration (MIC), no research has been found on kersen leaf gel on perineal wound healing in postpartum women. So the purpose of this study was to make kersen leaf gel and test it on the healing of perineal wounds in postpartum women.

METHOD

Study Design

This is a quasi-experiment with a pre-post-test with a control group design.[21]

Settings and Respondents

This research was conducted at Kwaingga Hospital, Keerom Regency, from July to August 2022. The population of this study was all postpartum mothers who experienced grade 2 spontaneous rupture, and sutures were performed. The inclusion criteria in this study were postpartum women experiencing stage 2 spontaneous rupture and perineum suturing, primiparous and multiparous, and without complications. Exceptions to the criteria in this study were postpartum mothers who had a history of diseases such as diabetes mellitus and had a history of complications in the delivery process. The number of samples in this study was 26, randomly divided into two groups: the group given a combination of kersen leaf gel extract and amoxicillin, and the group was only given amoxicillin.[22]

Preparation of 25% Kersen Leaf Gel

Kersen leaf processing is carried out at the Jayapura Ministry of Health Poltekkes Laboratory. The initial stage of making kersen leaf gel is by making Simplicia. Kersen leaves were obtained from the Keerom Regency area. Then through a wet sorting process to drying and semi-coarse grinding, the Simplicia results were extracted using the maceration method. The kersen leaf simplicia was put into a glass jar, and then 96% ethanol was poured; stirring was carried out for three days, namely morning and evening, for 5 minutes, then the resulting liquid extract was filtered using filter paper.[18,23] The filtering results were concentrated using a rotary evaporator at a temperature of 60°C for 6 hours until it thickened according to the SOP of the Cenderawasih University Biology Laboratory.

Preparation of kersen leaf gel with a concentration referring to previous studies, namely 25% kersen leaf extract, was carried out by mixing 2.5 grams of kersen leaf extract with gel-based ingredients from 5 ml of distilled water, 0.025 grams of 1.5% carbomer, TEA, 0 methylparaben, 02% as much as 0.0001 gram then stirred until evenly distributed until homogeneous,[16] and tested for the content of phytochemical compounds. The phytochemical compounds in this study contained flavonoids marked by a change in the color of the solution to orange, saponins indicated by the presence of a frothy solution, and tannins indicated by the color of the solution turning blackish green.[24] Furthermore, using the spectrophotometric method, the average total flavonoid test was carried out at the Chemical Laboratory, Cenderawasih University. The total flavonoid content of 25% kersen leaf gel was 212.7486 mg QE/g.

The organoleptic test of kersen leaf gel was carried out on five panelists with high sensitivity; all panelists (100%) liked the semi-solid form of kersen leaf gel preparation, four panelists (80%) liked the dark green color and distinctive aroma of kersen leaf in the preparation.[25] A pH test was carried out, and the results obtained were pH 6, which means that the pH is normal for perineal wounds,[26,27] homogeneity test for the absence of particles in kersen leaf gel preparations, and has good adhesion, namely 30 seconds without being separated, a spreading power of 3.3 cm with a load of 1 gram and a spreading power of 3cm and with a load of 50 grams, skin allergy/irritation tests were conducted on 40 panelists. There were no allergic reactions such as redness, itching, or swelling.[24] Next, 13 tubes were packaged containing 5 grams of 25% kersen leaf gel, each with a Beyond Use Date (BUD) of 30 days from the time the packaging was opened.[28]

Experimental Procedure

The intervention group was given kersen leaf gel and amoxicillin 2x1 for seven days in the morning and evening/evening. Before that, personal hygiene was carried out on the perineal wound and given 30 minutes after consuming amoxicillin. In contrast, the control group was only given amoxicillin according to the recommendations that had been given, namely 2x1 for seven days in the morning and afternoon/evening.

The Variables, Instruments, and Measures

The variable measured in this study was perineal wound healing, which was observed and measured directly during the first puerperium day before receiving treatment. After treatment, subsequent assessments were carried out on days 3, 5, and 7. Assessment of wound healing using the REEDA score checklist (Redness, Edema, Ecchymosis, Discharge, and Approximation), higher values indicate a greater level of tissue trauma with a higher total score. Maximum obtained (REEDA score = 0 – 15).[29]

Data Analysis

The analysis used the Mann-Whitney test to determine the different perineal wound healing rates. The effectiveness formula was used to determine the contribution of the perineal wound healing potential in both groups.

Ethical Considerations

Ethical considerations were obtained from the Health Research Ethics Commission (KEPK) of the Health Polytechnic of the Ministry of Health Semarang No. 0612/EA/KEPK/2022.

RESULTS

Figure 1 is an example of a 25% kersen leaf gel product in 5 grams. Based on the test results using spectrophotometry, it was found that the total flavonoid content was 212.7486 mg QE/g. Table 1 shows the age characteristics of the respondents included in the age category, not at risk in both groups. Most of the respondents have normal nutritional status and perform optimal personal hygiene.

Figure 1. Kersen Leaf Gel 25%

Table 1. Characteristics of Respondents (n=26)

Characteristics	Result
Age	
20-35 years	24 (92%)
>35 years	2 (8%)
Nutritional Status (BMI)	
Normal (18.5 - 25)	20 (77%)
Abnormal (>25 or <18.5)	6 (23%)
Personal Hygiene	
Optimum (>4x)	19 (73%)
Not optimal (<3x)	7 (27%)

Table 2. The Different Perineal Wound Healing Rate

Time	Intervention	Control	p-value [a]
	Means ± SD	Means ± SD	
Baseline	10.85 ± 1.144	10.69 ± 1.109	0.688
Day 3	5.00 ± 1.155	5.85 ± 0.801	0.038
Day 5	2.31 ± 0.650	3.23 ± 1.013	0.029
Day 7	0.23 ± 0.439	1.15 ± 0.987	0.039
p-value [b]	0.001[b]	0.001[b]	

[a] Between Group, Mann Withney Test
[b] Post Hoc Wilcoxon Test

Table 2 shows a significant decrease in the average perineal wound healing on day 3, day 5, and day 7 in the intervention group compared to the control group ($p<0.05$). Based on the results of the calculation of the effectiveness formula, it can be said that the use of a combination of kersen leaf gel and amoxicillin has more potential in healing the perineal wound in postpartum women by 96.4%, while in the control group, only used the standard antibiotic amoxicillin treatment by 89.2%.

DISCUSSION

In this study, giving a combination of kersen leaf gel 25% and amoxicillin 2x1 for seven consecutive days had more potential to increase perineal wound healing by 96.4%

compared to only using standard treatment with amoxicillin antibiotics by 89.2%. This is because kersen leaf gel contains active compounds of flavonoids, saponins, and tannins, which have antibacterial properties to support the wound healing process in the inflammatory phase, the proliferation phase, and the remodeling phase.[30]

The inflammatory phase is closely related to wound healing. The inflammatory phase allows the development of leukocytes (mainly neutrophils). Neutrophils then phagocytize and kill microorganisms until they enter the fibrin framework in anticipation of new tissue formation.[31] In this phase, the content of flavonoids in kersen leaves plays a role in responding to microbial infections, which are beneficial for wound healing because they can protect wounds from free radicals and affect the speed of the inflammatory process.[24,31]

In line with previous research on testing the antibacterial activity of kersen leaf extract against Staphylococcus aureus and Escherichia coli that cause infection in perineal wounds with a total flavonoid value of 12.62% w/b, the results obtained had an antibacterial activity with a value of Minimum Inhibitory Concentration (MIC) of kersen leaf extract by 15% against Staphylococcus aureus. In comparison, the Minimum MIC value of kersen leaf extract is 25% against Escherichia coli.[32] The other research regarding the effect of applying kersen leaf extract gel20% of neutrophil cell infiltration in the gingival wound healing process of Wistar rats showed a significant decrease in neutrophil cell infiltration on days 1, 3, and 5 of wistar rats gingival wound healing with a significant value ($p<0.05$).[33]

The proliferative phase is closely related to the increase in the number of fibroblasts, the formation of collagen tissue, and granulation tissue. Saponin content in kersen leaves contributes by forming the primary collagen, which plays a role in wound healing.[34] The mechanism of saponins that have antibacterial properties can frame a complex mixture of cell layers through hydrogen bonds to penetrate cell dividers, causing cell death.[35] Adequate nutrition, age, tissue handling, hygiene, and good oxygenation deficit can affect the acceleration of wound healing.[18,36,37] In this study, most respondents were of an age that was not at risk, had normal nutritional status, and were optimal in carrying out personal hygiene. In good healing conditions, perineal epithelialization occurs in 48-72 hours, and within 10-14 days, epithelialization is complete and usually leaves only thin scar tissue.[38] The proliferative process stops after the epithelium touches each other and closes the wound. Hence, the formation of granulation tissue stops, so the remodeling phase occurs.[39]
Previous research regarding the administration of kersen leaf extract ointment was effective in increasing the process of angiogenesis in the healing of skin incision wounds of hyperglycemic mice. It can be concluded that kersen leaf extract proved to have a higher number of blood vessels than the control group. So the more blood vessels are found, the faster tissue repair, so the wound healing process is faster.[40]

Another study regarding the effect of kersen leaf extract gel (*Muntingia Calabura* L.) on the number of heat-induced traumatic ulcer fibroblasts in white rats showed that the number of fibroblasts increased from day 3 to 7, with the highest number of fibroblasts in the treatment group. Fibroblasts play an essential role in wound healing because they produce collagen. The more fibroblasts, the faster the wound healing process.[41]

The total flavonoid compound content of kersen leaf gel influenced antibacterial activity in this study. The mechanism of flavonoids as an antibacterial is to damage the structural components of bacteria by denaturing proteins in the cell membrane, which results in the inhibition of bacterial cell growth.[42] Amoxicillin antibiotics' mechanism is inhibiting the biosynthesis of the bacterial cell wall, which will multiply, causing cell damage and death of microorganisms.[43]

Combining kersen leaf gel with the antibiotic amoxicillin has synergistic properties, making it more effective in inhibiting and killing bacterial growth. In line with the global action plan issued by WHO in 2015 to optimize the use of antibiotics by providing combination therapy of antibiotics with herbs to broaden the antibacterial spectrum, prevent resistance and minimize toxicity.[10,11]

Previous studies that compared the antibacterial activity of amoxicillin against Staphylococcus aureus and Escherichia coli in vitro showed a resistance response at concentrations less than 15 mg/mL against Staphylococcus aureus and concentrations of 3 mg/mL against Escherichia Coli while the combination of Moringa leaf ethanol extract and amoxicillin antibiotic showed synergistic effect against Staphylococcus aureus. Escherichia Coli is indicated by the diameter of the inhibition zone >17 mm. This is influenced by the content of active compounds in Moringa leaf extract, namely the class of flavonoids, saponins, and tannins as antibacterial.[44]

The results of research, theory, and previous research show the effectiveness of kersen leaves which are proven to be an alternative antibacterial to prevent infection in the healing of perineal wounds in postpartum women combined with amoxicillin. The flavonoid content of kersen leaves 25% plays a role in preventing infection, with a very high total flavonoid content of 212.7486 mg QE/g. The higher the total flavonoid content, the higher the antibacterial activity.[45] So statistically as well as a clinical theory, it is proven that using kersen leaf gel can improve perineal

wound healing in postpartum women. This study has several limitations, such as uncontrolled compliance in consuming amoxicillin.

CONCLUSIONS AND RECOMMENDATION

Kersen leaf extract gel can improve perineal wound healing in postpartum women compared to standard care/treatment using antibiotics alone. Health services are expected to use Kersen leaf extract gel to accelerate healing and prevent infection in the perineal wound of postpartum mothers.

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