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Potential ointment of carica papaya leaf extract against postpartum perineal wounds healing first: experimental study in galuh wistar mice (*rattus norvegicus*)

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ABSTRACT

Background

Perineal rupture occurs in about 85% of vaginal deliveries. If the wound is not treated properly, it causes pain and infection which prevents wound healing. Perineal wound care in addition to using 10% povidone iodine, the use of papaya carica leaf herbs is more effective in accelerating healing with active compounds of flavonoids, saponins, and tannins which have the potential to be anti-inflammatory and antiseptic so as to stimulate collagen which plays a role in wound healing.

Objective

Prove the potential of Carica leaf extract ointment for the healing of the first postpartum Galuh Wistar (*rattus norvegicus*) wound perineum.

Methods

True Execution, simple random sampling, pre post control group design. The subjects of the study were galuh wistar rats after giving birth for the first time as many as 25, divided into 5 groups. The wound healing variable is measured by the REEDA scale. Evaluation is carried out every day for 7 days. Test the hypothesis using Wilcoxon, Krussall Wallis, Mann Whitney U Test.

Results

Ointment 10% papaya carica leaf extract (EDPC) has the potential to accelerate the healing of perineal wounds by achieving a score of 0, which means good wound healing, and achieve a minimum score ($p = 0.025$) on the fifth day compared to 5% EDPC ointment, 15% EDPC ointment, Betadine ointment and ointment base.

Conclusions and Recommendations

EDPC 10% ointment effectively speeds up wound healing before 7 days. It is expected that observation of perineal wounds is further enhanced by microscopic examination. Further researchers can conduct further research on the active ingredient of other Carica papaya leaf extracts that have the potential to inhibit gram-positive and gram-negative bacteria in perineal wounds.

Keywords : Ointment of Papaya Carica Leaf Extract, Wound Healing, REEDA Scale.

INTRODUCTION

Relative perineal injury occurs in almost all vaginal deliveries with reported rates of around 85% [1]. Perineal wounds can occur either spontaneously or as a result of episiotomy [2], both in primiparas and multiparas, with the highest frequency in primipara [3]. As many as 70% of perineal wounds require suturing the broken tissue to be able to reunite [4]. Long-term morbidity for women can occur in perineal wounds [5]. Some cases experience long-term complications such as perineal pain, dyspareunia, dysuria and alvi incontinence, pelvic organ prolapse, long recovery period of the puerperium and psycho-social problems [4, 6, 7].

There are 3 techniques used in the treatment of perineal wounds, namely the antiseptic technique, a dry clean technique, carried out after washing the perineum using water and soap and then drying. As well as in traditional ways with the use of natural plant ingredients [8, 9].

The use of povidone iodine antiseptic also affects the healing of perineal wounds. Povidone iodine is a bond between iodine and polynyl pyrolidone, which has a broad spectrum, has antiseptic properties (inhibits germs). Topical antiseptics povidone iodine is an effective antiseptic that does not inhibit wound healing. It is bactericidal against gram positive and negative organisms, no bacterial resistance or cross resistance, helps cure various acute and chronic wounds, anti-inflammatory properties [10]. Recent research with the results of povidone iodine enhances wound healing through TGF- β , not only increases granulation but also increases neurovascularization [11]. Other studies have shown that the duration of perineal wound healing using povidone iodine 10% is an average of 8 days [12].

Papaya Carica leaves are one of the herbs that can be an alternative choice in wound care. The compounds contained in papaya carica leaves, namely flavonoids, saponins and tannins which are efficacious as anti-inflammatory and antiseptic in inhibiting the growth of bacteria that can cause infection in wounds. Flavonoids as anti-inflammatory work by inhibiting the arachidonic acid metabolic pathway, which is an important inflammatory mediator forming prostaglandin and

releasing histamine inflammation [13, 14]. Saponins and tannins as anti-inflammatory and antiseptic work by increasing the permeability of bacterial cell membranes thereby changing the structure of membranes, denaturing membrane proteins and causing damage to bacterial cell membranes [15]. Saponins have antiseptic properties and provide a positive influence by stimulating increased collagen, which is a protein that plays a role in the process of wound healing [16]. The cavity in the area of the wound begins to be filled with granulation tissue, neurovascularization reaches its peak, the collagen fibers multiply and begin to cover the wound [17]. Tanin as an antiseptic in wound tissue, by depositing protein and having bactericidal properties against staphylococcus bacteria [18].

The choice of ointment form is expected so that there is penetration into the top layer of the skin so as to provide a healing effect. Ointment is useful for maintaining medication in an effort to prolong contact with the skin which can increase and slow the release of active substances. ointment protects or treats skin that has both acute and chronic diseases [19].

Experimental animals using galuh wistar rats will be carried out at the Animal Laboratory Unit of Diponegoro University, Semarang, because it has been known as a journal publication in Google Scholar on experimental studies, Diponegoro Medical Journal Volume 7, Number 2, May 2018, ISSN Online 2540-8844 about the Effect of Breadfruit and Honey Leaf Extract on the Microscopic Illustration of Dietylnitrisamine-induced Wistar Mice [20]. It is necessary to research using 5%, 10% and 15% papaya carica leaf extract ointment on the healing of perineal wounds in experimental animals galuh wistar (rattus norvegicus).

Study Objectives

To prove the potential of Carica leaf extract ointment for the healing of the first postpartum Galuh Wistar (rattus norvegicus) wound perineum.

METHODS

This study was an experimental laboratory with a randomized Pre Post control group design study, there was randomization in the subject group,

which used female wistar rats. This study is comparative, namely knowing the potency of 5%, 10% and 15% papaya carica leaf extract ointment for healing perineal wistar postpartum rats after giving birth first. Previously an assessment of perineal wounds of wistar rats (pretest) was carried out. After that, the treatment was given for 7 days. Evaluation of perineal wound healing after 7 days of treatment (posttest) Assessment of perineal wound healing before and after treatment using the REEDA scale.

DATA ANALYSIS

Univariate analysis was carried out with the aim of describing each variable studied separately by making

a table of mean, and standard deviation of each variable and analyzing descriptively the variables studied. To find out the time interval of the measurement, Friedman test was carried out followed by the post hoc Wilcoxon test to determine the timing of the difference. To test the differences between groups tested with kruskal-walls. Followed by the Whitney U Test posthoc test to find out which treatment group differences were the most significant among the test groups. Heterogeneous age characteristics, so it was continued by multivariate analysis to see whether there was an effect of age on REEDA scores

RESULT

Univariate Analysis

Table 1. Characteristics of Research Samples

Characteristics of the study sample	Group									
	Salep EDPC 5%		Salep EDPC 10%		Salep EDPC 15%		Basis salep		Povidon Iodine	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (month)	2,40	0,55	2,60	0,55	2,80	0,45	2,00	0,00	2,60	0,55
Weight (gr)	188,6	11,89	186,6	14,99	191,8	5,11	183,4	13,46	184,2	9,78
Number of children	6,80	2,17	6,00	3,24	6,20	3,03	6,40	2,30	5,40	1,82
Time of wound healing (days)	4,80	0,84	4,00	0,71	4,40	1,34	6,00	0,71	5,20	0,45

Based on Table 1, it is known that the characteristics of the study sample were in accordance with the inclusion criteria set by the researcher, where the study sample was between 2-

2.8 months with a weight of 183.4-191.8 grams. While the children of rats born first numbered 5-7 tails. Based on observations, the wound healing time ranges from 4-6 days.

Bivariate Analysis

Wound Healing Duration Based on REEDA Total Score

Table 2. Total REEDA score

REEDA Score measurement day to	Group				
	Salep EDPC 5%	Salep EDPC 10%	Salep EDPC 15%	Basis salep	Povidon iodine
	Mean \pm SD	Mean \pm SD	Mean \pm SD	Mean \pm SD	Mean \pm SD
1	10,00 \pm 0,00	10,00 \pm 0,00	10,00 \pm 0,00	10,00 \pm 0,00	10,00 \pm 0,00
2	8,00 \pm 2,35	6,20 \pm 2,17	7,80 \pm 2,59	9,80 \pm 0,45	8,80 \pm 0,84
3	5,00 \pm 1,41	3,40 \pm 2,70	3,80 \pm 2,83	7,80 \pm 1,64	6,40 \pm 1,52
4	1,80 \pm 1,79	0,20 \pm 0,45	1,20 \pm 1,64	5,60 \pm 1,34	4,20 \pm 1,30

5	0,20 ± 0,45	0,00 ± 0,00	0,20 ± 0,45	3,20 ± 1,92	0,80 ± 1,79
6	0,00 ± 0,00	0,00 ± 0,00	0,00 ± 0,00	0,20 ± 0,45	0,00 ± 0,00
7	0,00 ± 0,00	0,00 ± 0,00	0,00 ± 0,00	0,00 ± 0,00	0,00 ± 0,00
<i>p</i>	0,000	0,000	0,000	0,000	0,000

Friedman

Based on Table 2, it is known that there are significant differences in the first day to the

seventh day of the REEDA score in each study group ($p = 0,000$).

Table 3. Post hoc Total REEDA score

Measurement		Group	<i>p</i>
The first day	The second day	Salep EDPC 5%	0,109
		Salep EDPC 10%	0,059
		Salep EDPC 15%	0,102
		Basis salep	0,317
		Povidon iodine	0,063
The first day	The third day	Salep EDPC 5%	0,039
		Salep EDPC 10%	0,042
		Salep EDPC 15%	0,041
		Basis salep	0,038
		Povidon iodine	0,039
The first day	The fourth day	Salep EDPC 5%	0,042
		Salep EDPC 10%	0,034
		Salep EDPC 15%	0,041
		Basis salep	0,034
		Povidon iodine	0,039
The first day	Fifth day	Salep EDPC 5%	0,034
		Salep EDPC 10%	0,025
		Salep EDPC 15%	0,034
		Basis salep	0,042
		Povidon iodine	0,034
The first day	Sixth day	Salep EDPC 5%	0,025
		Salep EDPC 10%	0,025
		Salep EDPC 15%	0,025
		Basis salep	0,034
		Povidon iodine	0,025
The first day	Seventh day	Salep EDPC 5%	0,025
		Salep EDPC 10%	0,025
		Salep EDPC 15%	0,025
		Basis salep	0,025
		Povidon iodine	0,025

Post Hoc Wilcoxon

Based on the post hoc Wilcoxon results, it was found that on the second day there was no significant difference in the REEDA score in each study group ($p > 0.05$). While on the third day there was a significant difference in the REEDA score, especially in the group given the ointment base ($p =$

0.038), 5% EDPC and the group given povidone iodine ($p = 0.039$). On the sixth day, all the study groups achieved a minimum REEDA score except the group given the ointment base which achieved a REEDA score of at least on the seventh day ($p = 0.025$).

Differences in Wound Healing Duration based on REEDA Total Score

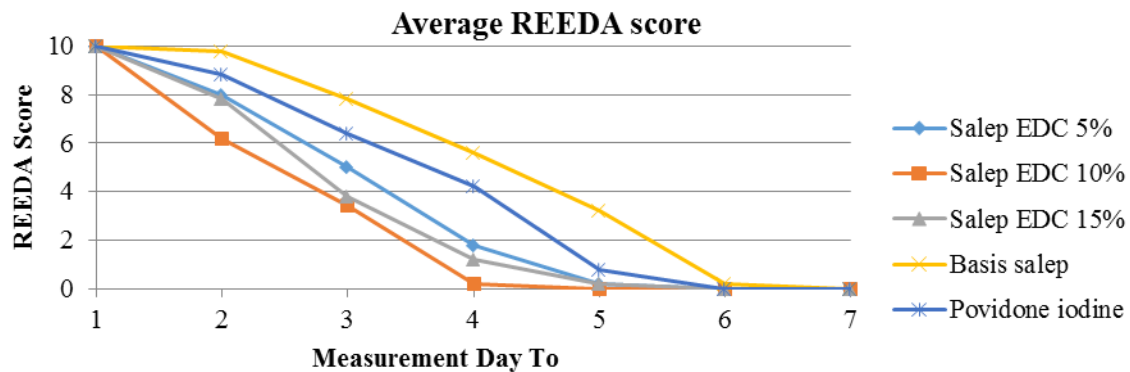


Figure 1. Comparison of the average REEDA score for each study group

Figure 1 shows that the REEDA score of each group has decreased gradually every day. However, there was a significant difference on the fourth day where the decline in the REEDA score of the group given the ointment tended to be slower compared to the other groups. While the most stable decrease in REEDA score was seen in the group given 10% EDC ointment.

DISCUSSION

In this study the wound healing was fastest in the SEDPC group 5%, 10% and 15% and the longest in the base group of ointment and betadine ointment 10%. Perineal wound care was carried out on the study sample 2 times a day, namely in the morning and evening. The treatment of the wound is cleaned and dried, then given an ointment according to each group

The purpose of wound care is a preventive effort against infection in the wound area in the vulva, perineum and in the uterus, reducing pain in the wound area, accelerating wound healing and bleeding in the perineal suture and maintaining the cleanliness of the perineum and vulva. Cleanse wounds from foreign objects or debris, drainage to facilitate the removal of exudates. In addition, perineal wound care was also given 10% betadine ointment and EDC ointment of various concentrations. The administration of papaya leaf extract is due to the compound content of papaya carica leaves, namely flavonoids, saponins and tannins which are efficacious as anti-inflammatory and antiseptic in inhibiting the growth of bacteria that can cause infection in wounds.

The research conducted by Parampasi in 2013 showed that the number of macrophages given by papaya leaf extract was more, accelerating the work of macrophages by increasing the production of interleukin in the inflammatory process. Collagen tissue that is formed becomes thicker, acts as an antiseptic by destroying germs which inhibits infection and wound healing [18].

When experiencing a wound, the body responds through several phases in the form of cellular and vascular responses that occur due to tissue damage. The inflammatory phase starts aiming to stop bleeding, clean the wound area from foreign objects and dead cells and prepare for the healing process to begin.

EDPC 10% ointment was proven to accelerate wound healing by achieving a minimum REEDA score on the fifth day. The most stable decline in REEDA score. This shows that the active ingredient of saponins, tannins and flavonoids has proven efficacy in wound healing. Flavonoids as anti-inflammatory work by inhibiting the metabolic pathway of arachidonic acid, which is an important inflammatory mediator forming prostaglandin and releasing histamine inflammation [13, 14]. Saponins and tannins as anti-inflammatory and antiseptic work by increasing the permeability of bacterial cell membranes thereby changing the structure of membranes, denaturing membrane proteins and causing damage to bacterial cell membranes [15]. Saponins have antiseptic properties and provide a positive influence by stimulating increased collagen, which is a protein that plays a role in the process of wound healing [16]. The cavity in the area of the wound begins to be filled with granulation tissue, neurovaskularization reaches its

peak, the collagen fibers multiply and begin to cover the wound [17]. Tanin as an antiseptic in wound tissue, by depositing protein and having bactericidal properties against staphylococcus bacteria [18].

CONCLUSIONS

Based on the results of research on the potential of papaya carica leaf extract ointment for healing perineal wounds after the first birth, galca wistar (rattus norvegicus) rats, it can be concluded that

carica leaf extract ointment has the potential to cure perineal and ointment wounds. perineal wound healing.

Recommendation Future

It is expected that observation of perineal wounds is further enhanced by microscopic examination. Further researchers can conduct further research on the active ingredient of other Carica papaya leaf extracts that have the potential to inhibit gram-positive and gram-negative bacteria in perineal wounds

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