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Effectiveness of honey-lidocaine and honey-povidone iodine combination cream therapy in healing second-degree perineal rupture wounds

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ABSTRACT

Background: Second-degree perineal rupture involves vaginal mucosa and perineal muscle injury, influenced by factors like primiparity, macrosomia, and prolonged labor. Wound healing follows stages of hemostasis, inflammation, proliferation, and remodeling. To accelerate the wound healing, honey has been used as an alternative due to its antimicrobial, anti-inflammatory, and antioxidant properties. This study evaluates the effectiveness of honey-lidocaine and honey-povidone iodine combinations in healing perineal wound.

Methods: A double-blind RCT was conducted at Siti Khadijah 1 Hospital (Feb–Aug 2024), involving postpartum women with second-degree perineal rupture. Participants applied one of three creams twice a day for 14 days. Healing was assessed using the REEDA scale on days 0, 1, 7, and 14. The data were analyzed using ANOVA, Kruskal-Wallis, Mann-Whitney, paired T-tests, and Wilcoxon tests ($p < 0.05$).

Results: Most participants with normal BMI were nulliparous, aged 20–35. By day 7, REEDA scores were significantly lower ($p < 0.001$) in the honey-lidocaine group. The best healing was observed by day 14.

Conclusions: Honey-lidocaine cream demonstrates faster healing than honey-povidone iodine and placebo, offering a promising postpartum wound care option.

Keywords: *perineal rupture, wound healing, honey*

1. INTRODUCTION

Second-degree perineal rupture involves injury to the vaginal mucosa and perineal muscles but spares the anal sphincter. This injury is generally influenced by several factors, such as primiparity, macrosomia, instrumental delivery, and prolonged second-stage labor [1]. The pathophysiology involves excessive mechanical stress leading to overstretching and tearing of the perineal tissues. This damage initiates an acute inflammatory response characterized by the release of cytokines and growth factors that regulate the healing process [2].

Current management strategies in wound healing focus on bioengineered skin substitutes and autologous platelet-rich plasma to enhance tissue regeneration [3]. They are a complex physiological process involving hemostasis, inflammation, proliferation, and remodeling [4]. The presence of normal skin flora, such as Staphylococcus epidermidis, modulates immune responses and prevents pathogen colonization [5]. Emerging therapies include stem-cell-based wound dressings and nitric oxide-releasing biomaterials to accelerate tissue repair [6].

Another alternative to accelerate the healing process is using a natural remedy, such as honey. Honey has been widely used as a complementary wound therapy due to its antimicrobial, anti-inflammatory, and antioxidant properties [7]. It contains flavonoids, phenolic acids, and hydrogen peroxide, which modulate bacterial colonization and oxidative stress [8]. In addition, honey promotes epithelialization, collagen synthesis, and angiogenesis, supporting its role in wound healing [7].

This study aims to evaluate the effectiveness of honey-lidocaine and honey-povidone iodine combination creams in accelerating second-degree perineal rupture healing. The study's finding is significant because it is the first to evaluate the

efficacy of honey-lidocaine versus honey-povidone iodine combinations, providing novel insights into the use of natural products like honey with anesthetic and antiseptic agents for wound healing. This study provides a more effective wound treatment strategy for postpartum women.

2. MATERIALS AND METHODS

Subject and data collection

This experimental study employed a double-blind randomized controlled trial (RCT) design. It was conducted at Siti Khadijah 1 Mother and Child Hospital from February to August 2024, involving postpartum women with second-degree perineal rupture who underwent suturing due to episiotomy or spontaneous rupture. Participants were excluded if they had a history of smoking, substance abuse, health conditions negatively affecting wound healing (such as diabetes mellitus and kidney disease), antibiotic use, or perineal hematoma. Subjects fulfilling the inclusion and exclusion criteria were randomly assigned into three groups receiving Cream Code A, B, or C. This cream was applied twice a day for 14 days. Wound healing was monitored using the REEDA scale on days 0, 1, 7, and 14. Follow-ups were conducted through direct observation, phone calls, and WhatsApp messaging. In case of allergic reactions, antihistamines were administered. Ethical approval was granted by the Research Ethics Committee of Hasanuddin University, RSPTN Hasanuddin University, and RSUP Dr. Wahidin Sudirohusodo under registration no. 545/UN4.6.4.5.31/PP36/2024.

Statistical analysis

Data in this study were analyzed using multiple statistical tests. First, univariate analysis was conducted to describe patient characteristics, usually expressed in percentage, and to calculate the wound healing scores using the mean and standard deviation. Prior to bivariate analysis, normality was assessed using the Kolmogorov-Smirnov test. Bivariate analysis was performed to examine the relationship between the two variables. Then, comparisons of means among three sample groups were conducted using ANOVA followed by Tukey's test for normally distributed data, and the Kruskal-Wallis test followed by the Mann-Whitney test for non-normally distributed data. Paired T-tests were used to compare means before and after the intervention for normally distributed data, while the Wilcoxon test was applied for non-normally distributed data. All statistical analyses were administered using the IBM SPSS 24, with a significance level set at $p < 0.05$.

3. RESULTS

The key results of this study are presented in two main parts. The first describes participants' characteristics, while the second reports the statistical findings. This study revealed that most patients with second-degree perineal rupture were aged 20–35 years and had a normal BMI. Based on parity, the injury was more common in the nulliparous group. Additionally, more than half of the subjects experienced rupture due to episiotomy. The participants' characteristics are detailed in Table 1.

Table 1. Clinical and Demography of Patients

Variable	Honey-lidocaine N (%)	Honey-povidone iodine N (%)
Age (years)		
At risk (<20 or >35)	20 (20.0)	19 (19.0)
Lower risk (20-35)	80 (80.0)	81 (810)
BMI (kg/m2)		
<23.9	71 (71.0)	73 (73.0)
≥23.9	29 (29.0)	27 (27.0)
Parity		
Nullipara	58 (58.0)	47 (47.0)
Para	42 (42.0)	53 (53.0)
Type of rupture		
Spontaneous	42 (42.0)	43 (43.0)
Episiotomy	58 (58.0)	57 (57.0)

Further, the study examined the wound healing process using the REEDA scale. Monitoring showed no significant differences on day 0 for redness, edema, ecchymosis, discharge, approximation, and total scores. However, significant differences emerged for redness on day 1 ($p = 0.047$) and day 7 ($p < 0.001$), with the lowest mean score in the honey-lidocaine group. Similarly, edema ($p = 0.007$), ecchymosis ($p = 0.003$), discharge ($p < 0.001$), approximation ($p < 0.001$), and total REEDA scores ($p < 0.001$) showed significance from day 7 onward. By day 14, all groups demonstrated effective wound healing. As shown in Table 2, the honey-lidocaine group achieved the lowest REEDA scores across all components.

Table 2. Monitoring between groups

Follow up	REEDA Scale Monitoring (Mean± SD)			p-value
	Honey-lidocaine	Honey-povidone iodine	Placebo	
Redness				
D0	0.71±0.67	0.76±0.55	0.77±0.55	0.475
D1	0.36±0.48	0.44±0.50	0.54±0.52	0.047*
D7	0.00±0.00	0.09±0.29	0.17±0.40	<0.001*
D14	0.02±0.14	0.02±0.14	0.04±0.20	0.599
Edema				
D0	1.05±0.63	1.03±0.59	1.06±0.65	0.957
D1	0.33±0.49	0.37±0.48	0.48±0.59	0.180
D7	0.01±0.10	0.02±0.14	0.10±0.33	0.007*
D14	0.00±0.00	0.01±0.10	0.01±0.10	0.606
Ecchymosis				
D0	0.59±0.53	0.63±0.50	0.61±0.55	0.826
D1	0.29±0.52	0.32±0.47	0.44±0.54	0.064
D7	0.02±0.14	0.03±0.17	0.13±0.37	0.003*
D14	0.00±0.00	0.01±0.10	0.01±0.10	0.606
Discharge				
D0	0.39±0.57	0.46±0.54	0.39±0.55	0.449
D1	0.54±0.52	0.55±0.54	0.56±0.52	0.960
D7	0.11±0.34	0.20±0.40	0.34±0.47	<0.001*
D14	0.01±0.10	0.03±0.17	0.10±0.30	0.007*
Approximation				
D0	0.34±0.48	0.33±0.47	0.39±0.49	0.637
D1	0.34±0.48	0.44±0.54	0.45±0.52	0.281
D7	0.20±0.43	0.56±0.52	0.74±0,48	<0.001*
D14	0.07±0.26	0.23±0.42	0.47±0.52	<0.001*
Total Scale				
D0	3.04±1.64	3.26±1.41	3.24±1.66	0.379
D1	1.86±1.05	2.10±0.88	2.49±1.22	<0.001*

D7	0.54±2.07	0.97±0.81	1.45±0.94	<0.001*
D14	0.08±0.37	0.28±0.49	0.64±0.69	<0.001*

*Significant

After examining the healing progression, the Mann-Whitney test was used to analyze the relationship between rupture type and REEDA scores due to non-normal distribution.

Table 3. Monitoring between spontaneous rupture and episiotomy

Subject	REEDA Scale Monitoring (Mean± SD)		p-value
	Spontaneous rupture	Episiotomy	
H0			
Honey-lidocaine	3.05 ± 1.65	3.03 ± 1.65	0.884
Honey-povidone iodine	3.23 ± 1.46	3.28 ± 1.39	0.744
Placebo	3.02 ± 1.56	3.49 ± 1.76	0.156
H1			
Honey-lidocaine	1.69 ± 0.90	1.98 ± 1.15	0.221
Honey-povidone iodine	2.07 ± 0.98	2.12 ± 0.80	0.577
Placebo	2.35 ± 1.14	2.60 ± 1.26	0.610
H7			
Honey-lidocaine	0.21 ± 0.47	0.78 ± 2.68	0.077
Honey-povidone iodine	0.81 ± 0.79	1.09 ± 0.81	0.068
Placebo	1.25 ± 0.81	1.68 ± 1.02	0.022*
H14			
Honey-lidocaine	0.00 ± 0.00	0.14 ± 0.48	0.032*
Honey-povidone iodine	0.23 ± 0.48	0.32 ± 0.51	0.338
Placebo	0.60 ± 0.69	0.70 ± 0.69	0.328

*Significant

Table 3 shows a significant difference in REEDA scores between spontaneous rupture and episiotomy in the placebo group on day 7 ($p = 0.022$). A significant difference was also found in the honey-lidocaine group on day 14, where spontaneous rupture had a lower REEDA score than episiotomy (0.0 vs 0.14; $p = 0.032$).

4. DISCUSSION

Wound healing involves hemostasis, inflammation, proliferation, and remodeling [9–11]. Collagen production started on day 3, strengthening wound integrity. Inflammatory cells release growth factors and cytokines, triggering keratinocyte and fibroblast proliferation [7,12]. These mechanisms also underlie perineal rupture healing.

In this study, the perineal rupture was most commonly observed in nulliparous women aged 20–35 with a normal BMI. Most resulted from episiotomy, which is consistent with previous findings stating that perineal trauma occurred in 53–79% of vaginal deliveries, with first- and second-degree ruptures being the most common[13,14]. Additionally, earlier studies note that nulliparity increases obstetric trauma risk [15]. Then, the rupture type (spontaneous vs. episiotomy) was also analyzed. REEDA scores were significantly lower in spontaneous rupture cases on day 7 (placebo) and day 14 (honey-lidocaine), indicating that spontaneous rupture heals faster that its counterpart.

While advanced therapy usually requires a complex process, an alternative therapy is needed to accelerate the wound healing.

Honey is one of the natural alternatives because it contains bioactive compounds, anti-inflammatory properties, and antioxidant properties [16]. As a hyperosmolar sugar solution with enzymes, amino acids, and glucose oxidase, honey aids wound healing through antibacterial and antiseptic effects. It prevents bacterial colonization, lowers pH, boosts antioxidant activity, and promotes cytokine release [17–19].

Those roles indicated the effectiveness of honey in healing wounds, which has also been reported by previous research. For example, Lavaf et al. (2018) claimed that honey cream applied twice a day for 14 days significantly improved REEDA scores by day 7, though differences were not significant by day 14 [20]. Similarly, Nikpour et al. (2019) found no significant REEDA score differences between honey, curcumin, and placebo over 10 days, though honey had a better number-needed-to-treat ratio [21]. Additionally, honey aids remodeling, minimizing scarring and contracture, and enhances MMP-9, TGF-β, and hygroscopic effects [22]. However, its effectiveness varies depending on the honey type, microbial strain, and combination agent [23].

One of the combination agents that might influence the healing process is lidocaine. In this study, indeed, a significant reduction in total REEDA scores was observed across all groups from day 1 to day 14. However, the honey-lidocaine combination cream reached nearly a score of 0 by day 14. It was the lowest REEDA score recorded, indicating faster wound healing, especially when used with bupivacaine, adrenaline, and cetrimide [24]. Individually, topical honey cream has been shown to reduce REEDA scores over 10–14 days [20,21]. Topical lidocaine has also demonstrated wound healing benefits in other studies, though not specifically assessed in perineal rupture using the REEDA scale [25,26]. Although some scholars found it might slow wound healing [25], recent studies suggest topical anesthetics, like lidocaine, induce miR-486 and miR-663 expression, promoting cell proliferation and inhibiting apoptosis, supporting its therapeutic role in wound healing [26].

Another combination to heal wounds is honey-povidone iodine. Andri et al. (2012) have studied this combination and found that consuming it twice daily for 8 days significantly increased granulation tissue formation and reduced exudate compared to povidone-iodine alone. Other studies support its effectiveness by showing reductions in redness, edema, ecchymosis, discharge, and approximation using the REEDA scale. It is even reported to be superior to silver sulfadiazine [27]. Hameed et al. (2021) found that 10% povidone-iodine was more effective than 5% in full-thickness wound healing in rabbits, enhancing granulation and neovascularization via TGF-β [28].

In this study, significant differences were observed at day 7, indicating honey-povidone's efficacy in early wound healing phases [11]. Honey-povidone iodine creams reduce inflammation by downregulating NF-kB and MAPK and suppressing pro-inflammatory cytokines, decreasing redness, edema, and ecchymosis [20,22]. It also minimized exudate by inhibiting nitric oxide [20,22] and enhanced epithelialization, granulation, and remodeling [26,27,28].

Nevertheless, several studies have reported contradictory results, such as a systematic review and meta-analysis by Ferraz Barbosa et al. (2024). Using the REEDA scale, they found no significant difference between honey and placebo in healing obstetric surgical wounds (C-section and episiotomy). However, they recognized honey's other benefits, like reducing pain levels, decreasing analgesic use, and improving patient satisfaction [29]. Luxey et al. (2024) also stated that topical local anesthetics are not recommended for postpartum pain management in women with perineal rupture or episiotomy due to a lack of evidence [30].

Despite these contrasting findings, the present study still highlights the potential of honey-lidocaine cream as an effective alternative for wound healing. This study demonstrates that honey-lidocaine cream is more effective in healing second-degree perineal rupture than honey-povidone iodine and placebo creams. While a significant reduction in REEDA scores was observed across all groups on days 1, 7, and 14, the honey-lidocaine group had the lowest score by day 14. As the first experimental study to evaluate these combination creams, the study introduces a novel approach using honey-lidocaine and honey-povidone iodine for wound healing.

5. CONCLUSIONS

This study concludes that honey-lidocaine cream has superior wound-healing effects for second-degree perineal rupture compared to honey-povidone iodine and placebo creams. However, several limitations in this study should be carefully taken into account. For example, the study did not evaluate pain intensity, patient satisfaction, and confounding factors such as hygiene, maternal knowledge, early mobilization, and assisted delivery. In fact, these variables may influence healing outcomes. Thus, further studies should address these issues. Despite limitations, these findings emphasize honey's potential when combined with anesthetic and antiseptic agents.

Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions.

S.N.Y.: Protocol development, data management, data analysis, and manuscript preparation and editing; **I.A.F.**: Protocol development, manuscript editing, and supervision; **T.I.**: Protocol development, data analysis, and manuscript editing; **F.M.:** Protocol development, data collection, and manuscript editing; **I.S.:** Protocol development and supervision. **M.F.F.:** Protocol development and supervision. **D.L.:** Protocol development and supervision. All authors made substantial contribution to the conception of the work and the interpretation of the data, revised it critically for important intellectual content and approved the final version.

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