Effect of Achillea vermicularis ointment on wound healing after episiotomy in primiparous women: a randomized clinical trial

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Research paper

Effect of *Achillea vermicularis* ointment on wound healing after episiotomy in primiparous women: a randomised clinical trial

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ABSTRACT

Introduction: Episiotomy may be followed by several maternal complications, such as postpartum infection, pain, discomfort, and prolonged wound healing. The present study was conducted to evaluate the effect of *Achillea vermicularis* on wound healing after episiotomy.

Methods: We performed a randomised clinical trial consisting of 100 participants aged on average 23.37 (± 4.96) years, who underwent an episiotomy during normal vaginal delivery from June to December 2018. The mothers were randomly allocated to the treatment or control group. Those in the treatment group used the *A. vermicularis* 3% ointment, while those in the control group received routine treatment consisting of sitz baths with betadine solution. The primary outcome was wound healing, which was assessed using the redness, edema, ecchymosis, discharge, and approximation (REEDA) scale on baseline and days 7 and 10 after the intervention.

Results: The episiotomy wound parameters did not differ significantly between groups on day 7, but there was a significant difference in redness ($P = 0.02$), discharge ($P = 0.03$), approximation of wound edges ($P = 0.03$), and wound healing ($P < 0.001$) between the two groups on day 10.

Discussion: It may be concluded that *A. vermicularis* ointment has a positive effect on wound healing after episiotomy on day 10 postpartum.

Introduction

Episiotomy is the most common perineal surgical incision in obstetric procedures (Obstetricians ACo, 2006). Post-episiotomy discomfort and its sequelae may affect maternal mental health and quality of life as well as the mother-infant relationship (Asgharikhatooni et al., 2015; Sheikhan et al., 2012). Prolonged pain is experienced by 10% of women after spontaneous vaginal delivery and 30% of women after an assisted vaginal delivery (Punasundri et al., 2006). The wound may result in several acute complications for the mother, including postpartum infection, pain, discomfort, and prolonged wound healing (Behmanesh et al., 2011; Golezar, 2016). Appropriate interventions are needed to prevent complications, minimise the duration of hospitalisation, reduce costs, enhance the mother's activity for herself and the baby, relieve her fears and concerns in regard of episiotomy, and improve her quality of life (Budhi and Raddi, 2010; Gould, 2007).

Abbreviations: ACOG, American College of Obstetricians and Gynaecologists; WHO, World Health Organisation; REEDA, redness, edema, ecchymosis, discharge, and approximation; BMI, body mass index

A. vermicularis on episiotomy wound healing.

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According to the guidelines of the American College of Obstetricians and Gynaecologists (ACOG), 'the best available data do not support the liberal or routine use of episiotomy. However, there is a role for episiotomy for maternal or fetal indications such as avoiding severe maternal lacerations or to facilitate difficult births' (Obstetricians ACo, 2006). While the World Health Organisation recommends an episiotomy rate of 10% as 'a good goal to pursue' (Organisation, 1996), the reported incidence of episiotomy is 8% in the Netherlands, 20% in the UK, 97.3% in Iran, 99% in Eastern Europe and 96% in Turkey (Asgharikhatooni et al., 2015; Eghdampour et al., 2013; Sayiner and Demirci, 2007).

Common measures in episiotomy care include the use of antiseptics (Yilmaz et al., 2010), dry-hot applications such as a lamp (Budhi and Raddi, 2010), topical ointments (Laki et al., 2019; Navi Nezhad et al., 2017), sitz baths (Oladokun et al., 2000), and ice applications (Mohamed and El-Nagger, 2012; Pore, 2014). Although the sitz bath is routinely used in postpartum care in Iran, studies have shown that some of these interventions are not useful. One study revealed no significant difference in wound healing between two groups, sitz baths as an intervention and water as a control (Oladokun et al., 2000). In another study, the Alpha ointment had no effect on episiotomy wound healing; the ingredients of this drug included the extract of *Lawsonia inermis*, the henna plant, beeswax (drug base), turpentine, and turmeric extract (Navi Nezhad et al., 2017).

The use of herbal drugs and compounds for wound healing after episiotomy has been given significant attention in recent years. The employed agents included lavender essential oil (Vakilian and Atarha, 2008), chamomile (Aradmehr et al., 2017; Azhari et al., 2014), *Hypericum perforatum* (Çobanoğlu and Şendir, 2020; Yahya et al., 2015), green tea ointment (Shahrahmani et al., 2018), frankincense ointment (Laki et al., 2019), turmeric (*Curcuma longa* L) ointment (Golmakani et al., 2008), and *Aloe vera* ointment (Eghdampour et al., 2013). One such medicinal plant is *Achillea vermicularis*.

A. vermicularis is a rich source of active substances, such as phenolic compounds, essential oils, tannins, and flavonoids, which are noteworthy secondary metabolites for the food and pharmaceutical industries (Saeidnia et al., 2011). Several investigations have demonstrated the anti-inflammatory, analgesic, antibacterial, antioxidant activities, and antifungal properties of the plant (Javidnia et al., 2004; Li et al., 2011). Also, a review study found *A. vermicularis* is used as menstrual regularity factor for wound healing, flatulence, diarrhoea, malaria, headache, cough and abdominal pain. Ae well as could affect wound healing (Dalili et al., 2022), it was hypothesised that *A. vermicularis* may have a similar effect on wound healing of episiotomy. The authors of one study investigated the effect of *Achillea millefolium* and *H. perforatum* ointments on episiotomy wound healing in primiparous women (Hajhashemi et al., 2018). However, the use of *A. vermicularis* on wound healing has not been investigated so far.

The acceleration of wound healing after episiotomy has been extensively addressed in the published literature. Maternal health after childbirth directly affects the newborn infant's quality of life. More rapid healing of episiotomy wounds may improve the quality of life during early motherhood (Araújo and de Oliveira, 2008; Kropp et al., 2005). In view of the absence of studies addressing the effects of *A. vermicularis* on the acceleration of wound healing after episiotomy, we investigated the effect of this substance versus sitz baths with betadine solution.

Materials and methods

Study design

A randomised clinical trial was conducted in women who had undergone an episiotomy during normal vaginal delivery at Yas Hospital (Tehran, Iran) from June 7, to December 21, 2018. The participants were selected through convenience sampling. The study was approved by the ethics committee of Tehran University of Medical Sciences in Iran (IR.TUMS.FNM.REC.1396.2245), and registered at the Iranian registry of clinical trials on August 10, 2017 (IRCT2017053134261N1). The enrolment of patients was started after the IRCT code had been received. At the hospital, the researcher explained the objectives of the study to the participants, assured them of data anonymity and confidentiality, and obtained their written informed consent. The participants were also informed of their right to withdraw their consent at any time. Wound healing, the primary outcome, was used to determine the sample size.

The sample size was set to a minimum of 42 women in each group, based on the study by Samadi et al. (2010). Assuming a confidence interval of 95% and a between-group mean difference of 0.6, the means (standard deviation) in the experimental and control group were 0.19 (0.5) and 0.79 (1.17), the alpha error 0.05, and the study power 80%. We assumed that 20% of the sample would be lost to follow-up. Therefore, the final sample size was 50 women in each group. The following formula was used to determine the sample size:

$$n = \frac{S1^2 \pm S2^2}{(\mu 2 - \mu 1)} f(\alpha, \beta)$$

Enrolment, randomisation, and blinding of study participants

The participants were recruited after childbirth and episiotomy repair. One hundred and thirty-eight women were assessed in regard to their eligibility. The participants were randomly allocated to the treatment or control group using a computer-generated random table of quadruple block numbers. To prevent contamination, the treatment and control groups received the allocated treatments at different times and in different rooms. Opaque-coded and sealed envelopes were used to conceal the allocation. The person in charge of allocation was unaware of the contents of the envelopes.

To ensure blinding, one person was appointed in charge of drug prescription and another was responsible for wound evaluation. Data analysis was performed by a person who was blinded to the allocation. The mothers were aware of their group allocation. Although wound healing was not a subjective patient-reported outcome, the parameters of redness, edema, ecchymosis, discharge, and approximation were evaluated by an external assessor on the (REEDA) scale. Several studies have shown that open-label placebos may affect subjective patient-reported outcomes, but do not influence wound healing (Mathur et al., 2018; Vits et al., 2015).

Study participants

To eliminate the effect of confounding factors, the following inclusion criteria were applied: primiparity, Iranian nationality, normal vaginal delivery with a grade-2 mediolateral episiotomy, living with the husband, the presence of one fetus with an anterior cephalic presentation, and a body mass index (BMI) between 19.8 and 30 kg/m^2. Exclusion criteria were diseases preventing or delaying wound healing (e.g. chronic systemic, cardiac, renal, hepatic, respiratory, coagulative, or connective tissue disease, diabetes, anaemia, cancer, and mental disease), the use of drugs affecting wound healing (such as corticosteroids, anticoagulants, immunosuppressants, antibiotics, or chemotherapy), symptomatic infection of the uterus or vulva (e.g., infectious discharge, itching, and burning), any visible malformation in the newborn (such as hydrocephaly, ascites, and bulky tumours), severe rectocele or cystocele (grade 2 or above) or a vaginal mass, a history of obstetric problems (e.g., placental abruption, polyhydramnios, oligohydramnios, and rupture of membranes more than 12 hours prior to delivery), a history of plastic surgery in the vulva or perineum, any complications during labour (a) precipitous labour: expulsion of the fetus within less than 3 hours of regular contractions; b) prolonged

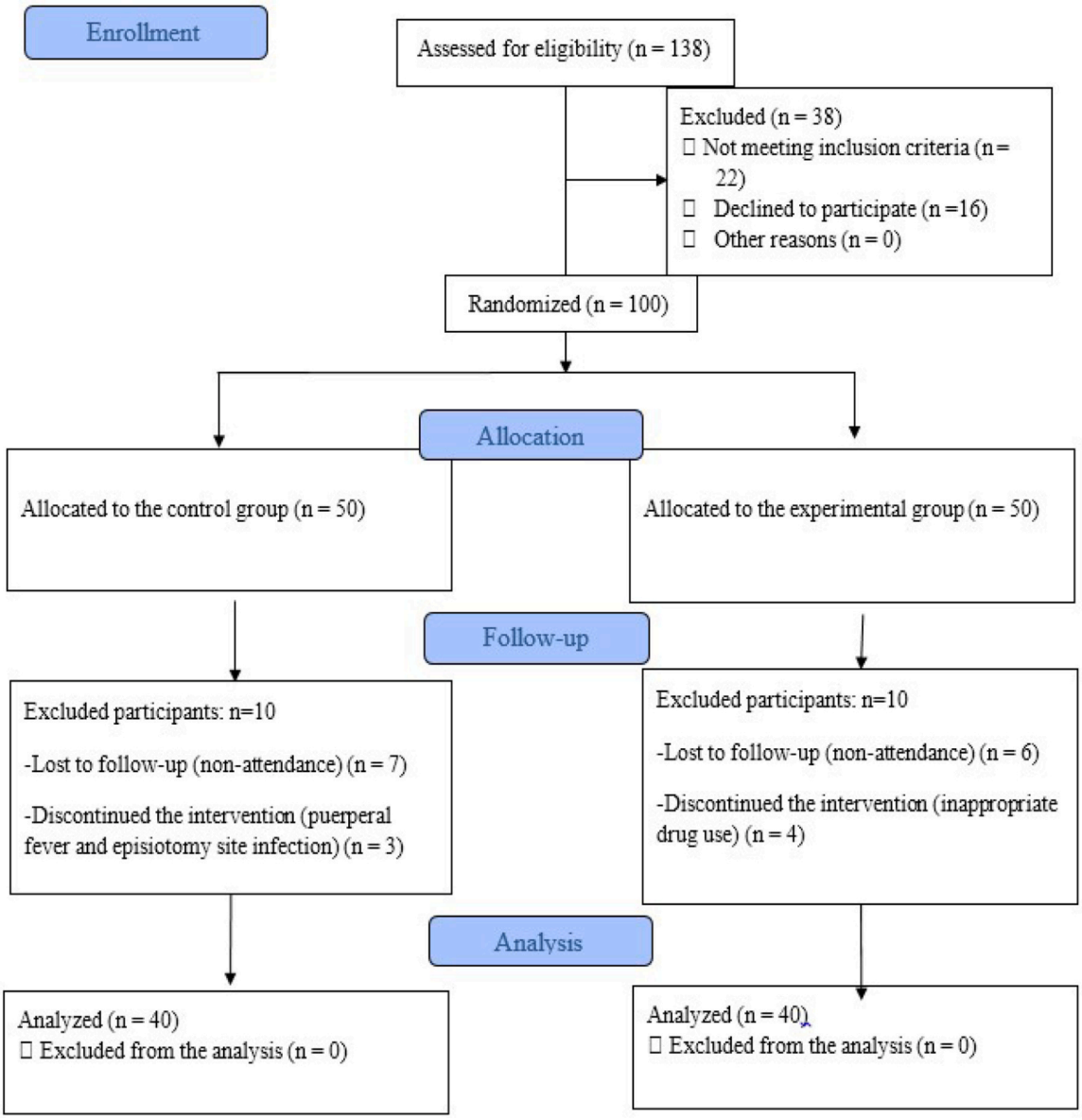

Fig. 1. CONSORT flow diagram.

labour: the first and second stages taking more than 19 hours), a prolonged second stage lasting longer than 2 hours, extension of the episiotomy site to a third- or fourth-degree tear, or the presence of any tear other than episiotomy, abnormal vaginal bleeding, shoulder dystocia requiring maneuvers other than the McRoberts maneuver, manual removal of the placenta, haematoma formation, curettage within the first 24 hours postpartum, and undesirable life events (such as serious quarrel with the husband, death of the father or mother, and substantial change in financial status). The participants were withdrawn from the study if they had sexual intercourse during the study (during the first 10 days postpartum), used the ointment irregularly (for less than eight days or 11 times), experienced an infection at the site of episiotomy, needed re-suturing of the episiotomy incision, and developed puerperal fever (temperature above 39 °C during the first 10 days postpartum, excluding the first 24 hours, measured with standard oral methods at least four times a day).

Intervention

After expulsion of the fetus and episiotomy repair in lithotomy position, we collected data concerning maternal age; education level; economic status; the newborn's head circumference; weight and height; duration of the first, second, and third stages of labour; number of sutures; perineal shaving; and meconium defecation. The researchers then instructed the mothers on wound care, perineal care, personal hygiene, and filling out the daily information sheet. Mothers in the treatment group were given a tube containing the ointment and asked them to wash and dry the perineum, and then apply a pea-sized quantity of the ointment such that it covered the entire wound surface, twice a day, 12 hours apart, for 10 days.

A. vermicularis 3% ointment was prepared from its essential oil (Azhari et al., 2014). Previous studies have assessed the effect of different percentages (7.5% and 10%) of another type of *Achillea* ointment on wound healing (Hajhashemi et al., 2018; Matić et al., 2009). As no animal or human studies have been performed with this species of the plant, we selected a moderate dose of 3%. The 3% ointment was prepared by mixing *A. vermicularis* essential oil and cold cream at the traditional pharmacy laboratory of Tehran University of Medical Sciences, Tehran, Iran. Women in the control group received routine care (sitz baths with betadine solution). They were asked to pour 10 ml of betadine into a basin of lukewarm water and sit in the bath for 20 minutes. Since cold cream does not have any effect on wound healing

Table 1
Demographic, labour, and neonatal characteristics of the two groups.

Variables		Experimental group (n = 40)	Control group (n = 40)	Statistical test and *P*-value
Age (mean ± SD)		23.67 ± 4.27	23.07 ± 5.61	U: −1.17 0.23
Body mass index (mean ± SD)		26.5 ± 2.50	26.65 ± 3.77	t[b]: −0.21 0.83
Education level	Less than a diploma	19 (47.5)	17 (42.5)	H[c]: 0.71 0.39
N (%)	Diploma	9 (22.5)	5 (12.5)	
	University	12 (30)	18 (45)	
Economic status	Good	1 (2.5)	2 (5)	H[c]: 0.058 0.77
N (%)	Moderate	32 (80)	29 (72.5)	
	Poor	7 (17.5)	9 (22.5)	
Newborn head circumference (Mean ± SD)		33.82 ± 1.31	24.0 ± 1.21	U[a]: −0.53 0.59
Newborn weight (kg) (Mean ± SD)		3.19 ± 0.37	3.21 ± 0.37	t[b]: −0.28 0.77
Newborn height (cm) (Mean ± SD)		49.35 ± 1.83	49.37 ± 1.98	U[a]: 0.049 0.96
Duration of the first stage of labour (hours) (Mean ± SD)		4.45 ± 0.81	4.52 ± 0.75	U[a]: 0.57 0.56
Duration of the second stage of labour (min) (Mean ± SD)		42.12 ± 12.60	41.48 ± 13.32	U[a]: −1.25 0.21
Duration of the third stage of labour (min) (Mean ± SD)		6.95 ± 2.43	6.87 ± 2.45	U[a]: −0.14 0.88
Number of delivery sutures (Mean ± SD)		5.77 ± 1.25	5.45 ± 1.28	U[a]: −1.44 0.14
Perineal shaving	Yes	40 (100)	39 (97.5)	X^{2d}: 1.01 0.50
	No	0	1 (2.5)	
Taking antibiotics (overall number)	1–6 days	22.33 ± 2.3	21.12 ± 3.6	U[a]: −1.56 0.11
	7–10 days	14.12 ± 2.6	15.11 ± 1.02	U[a]: −1.21 0.10
Proper hygiene	Yes	39 (97.5)	40 (100)	X^{2d}: 1.01 0.50
	No	1 (2.5)	0	
Activity level	Low	23 (57.5)	27 (67.5)	X^{2d}: 0.85 0.24
	Moderate	17 (42.5)	13 (32.5)	
Using painkillers	1–6 days	15.87 ± 3.44	15.95 ± 3.21	U[a]: −1.56 0.11
	7–10 days	7.66 ± 3.62	6.47 ± 3.41	U[a]: −1.66 0.13
Meconium defecation	Yes	4 (10)	0 (0)	X^{2d}: 4.21 0.058
	No	36 (90)	40 (100)	

P-value ≤ 0.05; Low activity level: doing less than routine housework; Moderate activity level: doing some housework.
N, number; SD, standard deviation.
[b] Independent samples *t*-test.
[c] Kruskal-Wallis test.
[a] Mann-Whitney *U* test.
[d] Chi-square test.

(Rai et al., 2019), only two treatment groups (*Achillea* ointment and sitz bath with betadine solution) were created; a cold cream-only group was not used. A card specifying the group code (treatment or control) and the date of the next visit was given to each participant. Patients of both groups were called during 10 days of follow-up and asked about their adherence to the instructions, the items on the daily information sheet, and answered any questions.

Preparation of the extract and the ointment

Plant samples were purchased from the herbal market in Tehran and approved by the herbarium department at the Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran (Code no. PMP-1305). A hydroalcoholic extract (HE) of the plant was prepared using the maceration method. The flowers of *A. vermicularis* (250 g) were powdered with a grinder and macerated three times with 70% aqueous ethanol (EtOH) (Merck, Germany), each time for 48 hours. All hydro-alcoholic extracts were combined, filtered, and concentrated to a dry substance at 40 °C using a rotary evaporator (Heidolph Laborota, Germany). *A. vermicularis* 3% cream was prepared from the HE of aerial parts (flowers) of *A. vermicularis*. *A. vermicularis* 3% ointment was prepared by mixing *A. vermicularis* and cold cream (moisturising cream 'Farabi') at the traditional pharmacy laboratory of Tehran University of Medical Sciences, Tehran, Iran. Every 100 g of the drug contained 3 g of dry extract homogenised in 10 ml of distilled water. A cream base was added to the formulation to achieve 100 g of ointment.

Microbial limit test of the Achillea ointment

The microbial control test of the product was performed at the food and drug control laboratory of Tehran University of Medical Sciences, in accordance with the World Health Organisation (WHO) protocol for herbal products. The total count of microorganisms and the microbial count of *Staphylococcus aureus* and *Pseudomonas aeruginosa,* as well as the quantity of mold were below the acceptable limits.

Total phenolic content of Achillea vermicularis ointment

The total phenolic content was measured according to the Folin-Ciocalteu method (Hajimahmoodi et al., 2013). In order to separate the extract from the cream, 15 g of the cream was extracted three times with 15 ml of methanol. The extract (200 µl) was added to 1.5 ml of the Folin-Ciocalteu reagent (diluted 10 times with double distilled water) and kept at room temperature for 5 minutes. Then, 1.5 ml sodium bicarbonate solution (70 g/l) was added to the mixture. After incubation for 90 minutes at 22 °C, the absorbance was measured at 765 nm using a UV–visible spectrophotometer (Optizen, South Korea). The total phenolic content was measured on a calibration curve obtained by measuring the absorbance of standard gallic acid solutions (25–200 µg/ml in 80% methanol). The mean total phenolic content of *A. vermicularis* cream (± SD), measured as the gallic acid equivalent per one gram of cream (standard curve equation Y = 0.0092X + 0.0212, R2 = 0.9996), was 8.54 ± 1.09 mg gallic acid equivalent per gram of cream.

Table 2
REEDA components in the two groups.

		Experimental group (n-40)	Control group (n = 40)	Statistical test[a] and *P*-value
Redness	Day 1 (4 H after delivery)	1.0 ± 0.68	0.85 ± 0.76	U: −1.03 0.29
	Day 7	0.41 ± 0.54	0.52 ± 0.59	U: −0.85 0.39
	Day 10	0.05 ± 0.22	0.22 ± 0.42	U: −2.21 0.02
	P-value[b]	0.000	0.000	
Edema	Day 1 (4 H after delivery)	1.12 ± 0.57	1.07 ± 0.79	U: −0.75 0.44
	Day 7	0.28 ± 0.45	0.4 ± 0.54	U: −0.93 0.34
	Day 10	0.05 ± 0.22	0.07 ± 0.26	U: −0.43 0.66
	P-value[b]	0.000	0.000	
Ecchymosis	Day 1 (4 H after delivery)	0.79 ± 0.61	0.62 ± 0.62	U: −1.26 0.20
	Day 7	0.02 ± 0.16	0.10 ± 0.30	U: −1.34 0.17
	Day 10	100.00 ± 0.00	0.00 ± 0.00	U: 0.00 1.00
	P-value[b]	0.000	0.000	
Discharge	Day 1 (4 H after delivery)	0.15 ± 0.36	0.15 ± 0.36	U: −0.04 0.96
	Day 7	0.20 ± 0.40	0.35 ± 0.48	U: −1.42 0.15
	Day 10	0.07 ± 0.26	0.25 ± 0.43	U: −2.06 0.03
	P-value[b]	0.257	0.113	
Approximation between the two wound edges	Day 1 (4 H after delivery)	0.25 ± 0.44	0.17 ± 0.34	U: −0.87 0.38
	Day 7	0.48 ± 0.50	0.55 ± 0.50	U: −0.00 0.57
	Day 10	0.20 ± 0.40	0.42 ± 0.50	U: −2.08 0.03
	P-value[b]	0.011	0.001	
Total scores of episiotomy wound healing	Day 1 (4 H after delivery)	3.23 ± 1.38	2.85 ± 1.64	U: −1.18 0.23
	Day 7	1.43 ± 0.91	1.90 ± 1.25	U: −1.72 0.08
	Day 10	0.41 ± 0.67	1.02 ± 0.83	U: −3.53 < 0.001
	P-value[b]	0.000	0.000	

REEDA, redness, edema, ecchymosis, discharge, and approximation.
[a] Mann-Whitney *U* test and 'Wilcoxon signed rank test'.
[b] Friedman test.

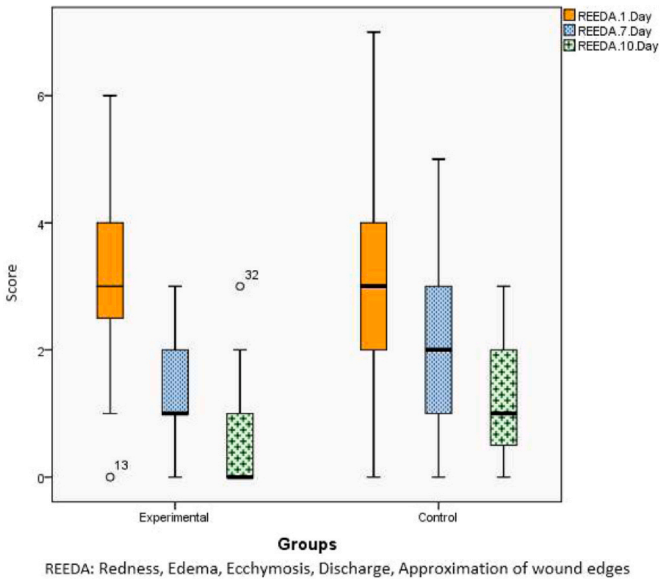

Fig. 2. Use of *Achillea vermicularis* ointment for 10 days: effect size between groups.

Outcomes, measurement and follow-up

Wound healing after episiotomy was the primary outcome of the study; any side effects of the ointment were secondary outcomes. A midwife (research assistant) performed a baseline assessment immediately before the intervention to assess the appearance of the wound (redness, edema, discharge, suture type, and approximation of wound edges). The intervention was conducted 4 hours after episiotomy repair.

The tools of data collection included the clinical examination, data entry forms (a form for the inclusion or exclusion of participants; a form for collecting labour stage and episiotomy data; a form for collecting daily information including analgesic and antibiotic use, personal hygiene, physical activity, and constipation), and the REEDA scale (redness, edema, ecchymosis, discharge, and approximation).

The REEDA scale is a standard instrument whose validity and reliability have been confirmed in several studies (Alvarenga et al., 2015; Meng and Li, 2022; Taheri et al., 2022). The scale evaluates redness, edema, ecchymosis, discharge, and the approximation of wound edges. Each item was scored between zero and three. A higher score indicated a greater level of tissue trauma. A maximum score of 15 indicated the worst perineal healing outcome. As regards approximation, a score of 0, 1, and 2 was given for complete approximation, skin separation 3 mm or less, and skin and subcutaneous fat separation, respectively. Skin, subcutaneous fat, and fascial layer separation were scored 3. With regard to discharge, a score of 0, 1, 2, and 3 was given to no discharge, serum discharge, bloody serum discharge, and bloody purulent discharge, respectively. No ecchymosis was scored 0, ecchymosis within 0.25 cm bilaterally or 0.5 cm unilaterally was scored 1, ecchymosis 0.25–1 cm bilaterally or 0.5–2 cm unilaterally was scored 2, and greater than 1 cm bilaterally or 2 cm unilaterally was scored 3. The absence of edema was given a score of 0, while edema less than 1 cm from the incision was scored 1. A score of 2 was given to edema between 1 and 2 cm from the incision, and a score of 3 was assigned to bilateral edema more than 2 cm from the incision. With regard to redness, a score of 0 was given to no redness, a score of 1 to redness within 0.25 cm of the incision bilaterally, a score of 2 to redness within 0.5 cm of the incision bilaterally, and a score of 3 to redness beyond 0.5 cm of the incision bilaterally. The summed scores of the five items yielded the total score.

Table 3
Episiotomy wound healing scores according to the two methods by linear regression.

Outcomes	Methods of analysis	*R* square	CI of the slope	CI of width from the origin
Episiotomy wound healing on the 7th day	Per-protocol	0.255	−0.09 to 0.82	−3.09 to −1.53
	Intention-to-treat		−0.09 to 0.61	−2.25 to −0.64
Episiotomy wound healing on the 10th day	Per-protocol	0.531	0.594–1.94	−3.87 to −2.81
	Intention-to-treat		−0.01 to 1.26	−3.30 to −1.62

CI, confidence interval.

A total score of 0, 1–5, 6–10, and 11–15 indicated healed, moderately healed, mildly healed, and not healed, respectively.

Follow-up visits were scheduled on days 7 and 10 postpartum. A midwife who was blinded to the treatment assessed all of the participants.

Protocol deviation

A series of measures were taken to address deviations from the protocol. A questionnaire was designed to investigate the reasons for not completing the follow-ups. The participants were asked to notify the researchers if they experienced any difficulties, complications or side effects, including drug sensitivity. The analysis included both per-protocol and intention-to-treat analyses, assuming the worst-case scenario for the missing participants of both groups in order to exclude attrition bias (20 of 100 = 20% missing patients). Regression analysis was then used to compare the results of the two methods.

Data analysis

Data were analysed using the IBM SPSS for Windows version 21 (High, 2012). Qualitative variables were described as frequency (percentage) and quantitative variables reported as mean (standard deviation). The one-sample Kolmogorov-Smirnov test was used to test for normal distribution of data, the results of which determined the choice between the parametric or non-parametric tests for comparison. Comparisons between groups were made with the Chi-square test, the Kruskal-Wallis test, the *t*-test, or the Mann-Whitney *U* test. Within-group comparisons were performed using the Friedman test. The significance level was set to *less than* 0.05.

Results

Of 138 women who were assessed for eligibility, 100 were deemed eligible for the study (50 each in the treatment and control groups). Ten women were excluded from the treatment group due to inappropriate drug use and failure to attend the follow-up visit, and 10 were excluded from the control group due to infection at the episiotomy site, puerperal fever, and failure to attend the follow-up visit. Finally, the data of 40 women each in the treatment and control groups were analysed (Fig. 1).

The mean age of the participants was 23.37 (± 4.96) years and their mean body mass index (BMI) was 26.57 kg/m^2 (± 3.18). The majority of the women were from the middle class (n = 61, 76.25%) and had a high-school degree (n = 35, 43.75%). No participant experienced constipation. The mean number of sutures was 5.61 (± 1.26). All participants used the same antibiotics and painkillers.

The distribution of demographic and obstetric parameters in the two groups before the intervention, based on the Kolmogorov-Smirnov test, showed that only BMI ($P = 0.172$) and neonatal birth weight ($P = 0.200$) followed a normal distribution. Therefore, non-parametric tests were used to analyse the data. As shown in Table 1, the two groups were homogeneous.

Redness, edema, ecchymosis, discharge, and approximation did not differ between groups on day 7 postpartum. However, there was a significant difference in redness ($P = 0.02$), discharge ($P = 0.03$), approximation ($P = 0.03$), and overall wound healing ($P < 0.001$) between groups on day 10 postpartum. The within-group analysis showed no significant difference in the domains except for discharge (Table 2).

Although the mean scores of edema and discharge were lower in the treatment group than in controls on day 7 postpartum, the difference was not significant. As the data were normally distributed, the Hodges-Lehman estimate was used to evaluate effect size, which showed significant results on day 10 postpartum. However, the median score shifted towards zero according to the scale scoring system. Figure 2 illustrates the results. As shown in Table 2 and Figure 2, the use of *A. vermicularis* for 10 days improved redness, discharge, approximation, and overall episiotomy wound healing. No participant reported any side effects.

According to the regression analysis, the results of per-protocol and intention-to-treat analysis regarding the primary outcome of the study were the same because the slope of the curve and the width of its origin overlapped for both outcomes. As a result, there were no discrepancies in the findings and attrition had no effect on the results (Table 3).

Discussion

We assessed the effects of *A. vermicularis* ointment versus the routine procedure of sitz baths with betadine solution on wound healing after episiotomy. Redness, edema, ecchymosis, discharge, and approximation did not differ significantly between groups on day 7 postpartum. However, the use of *A. vermicularis* ointment for 10 days improved wound healing, approximation, redness, and ecchymosis in the treatment group.

Hajhashemi et al. evaluated the effect of *A. millefolium* and *H. perforatum* ointments on wound healing after episiotomy, and found that *Achillea* ointment improved wound healing on days 7 and 10 and ecchymosis on day 7 postpartum (Hajhashemi et al., 2018). This is in line with the present study, which also revealed improved wound healing on day 10 postpartum. However, the present study showed no improvement in wound healing on day 7 postpartum. The reasons could be individual differences such as BMI, activity levels, and personal hygiene. Another reason for the diverse results could be the use of different *Achillea* species. We employed *A. vermicularis* while Hajhashemi et al. used *A. millefolium*. As other studies have also reported no effects of *Achillea* on day 7 but visible effects on day 10 or 14 of postpartum (Golezar, 2016; Pazandeh and Savadzadeh, 2010), it seems it would be necessary to use the drug for at least 10 days in order to achieve tissue repair and wound healing.

A clinical trial demonstrated the positive effects of *Achillea* on wound healing. The treatment of venous leg ulcers with an ointment containing 7.5% *Achillea* extract for three weeks reduced 39.64% of the total surface of all ulcers compared to a 15.1% decrease in the control group treated with a saline dressing alone. Other parameters such as granulation, epithelialization, and dermatitis were also better in the treatment group than in control group (Matić et al., 2009). Despite different anatomical locations and different treatment durations, the results were similar to our findings.

The effects of *Achillea* on wound healing could be attributed to its anti-inflammatory properties. The anti-inflammatory effect of *Achillea* is achieved by flavonoids and their impact on proteases (Benedek et al., 2007). Several compounds such as terpenes, alkaloids, tannins,

saponins, sterols, vitamins, amino acids, and fatty acids have been identified in *Achillea*, and might facilitate wound healing (Si et al., 2006). *Achillea* has antimicrobial effects on pathogens such as *S. aureus*, Escherichia coli, and Pseudomonas (Tajik and Jalali, 2009). Hajhashemi and co-workers found that *Achillea* reduced perineal pain level, redness, edema, and ecchymosis of the episiotomy wound (Hajhashemi et al., 2018).

To our knowledge, the present research is the first to analyse the effect of *A. vermicularis* on wound healing after episiotomy. One of the limitations of the study was the attrition rate of ten participants in each group. Further limitations were differences in tissue characteristics, genetic variations, and wound healing ability. Although we followed the participants by telephone, we had no means of ensuring that they consistently used the treatments as instructed. We employed rather strict inclusion and exclusion criteria to obtain eligible participants in terms of episiotomy and delivery; therefore, the findings of the study cannot be transferred to other populations. Due to the different forms of treatments, the participants as well as the researchers who assigned the participants to the experimental and control groups could not be blinded; however, the assessor was blinded.

Conclusion

A. vermicularis ointment has a positive effect on wound healing after episiotomy on day 10 postpartum. The effect of *A. vermicularis* on edema and ecchymosis was not significant on day 10 postpartum. Further studies with larger sample sizes will be needed to investigate the effects of *A. vermicularis* on wound healing and the effects of its combination with other medicinal plants.

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Ethical statement

The study was approved by the ethics committee of Tehran University of Medical Sciences in Iran (IR.TUMS.FNM.REC.1396.2245), and registered at the Iranian registry of clinical trials on 10 August 2017 (IRCT2017053134261N1). The enrolment of patients was started after the IRCT code had been received. At the hospital, the researcher explained the objectives of the study to the participants, assured them of data anonymity and confidentiality, and obtained their written informed consent.

CRediT authorship contribution statement

Azam Rahmani: Conceptualization, Supervision. **Julia Fedotova:** Writing, review & editing. **Elham Rezaei:** Formal analysis, Review. Shirin Shahbazi: Writing, review & editing. **Arezoo Fallahi:** Conceptualization, Writing the original draft. **Leila Allahqoli:** Conceptualization, Methodology. **Reza Ghanei Gheshlagh:** Writing, review & editing. **Seyedeh Narges Sadati Lamardi:** Preparation of the herbal cream. **Ibrahim Alkatout:** Writing, review & editing.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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Consent for publication

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