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Original Article

Impact of Hypericum Perforatum Ointment on Perineal Pain Intensity Following Episiotomy: a Randomized Placebo-Controlled Trial

Farzaneh Vakili[1], Mandana Mirmohammadaliie[1*], Ali Montazeri[2], Mina Farokhi[1], Mohammad Bagher Minaee[3]

[1]Department of Midwifery, Faculty of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Mental Health, Institute of Health Sciences, Tehran, Iran
[3]Department of Histology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran

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*Corresponding Author:
PhD candidate in disaster & emergency health, Email: mir mohamad1@yahoo.com

ABSTRACT

Introduction: The present study was conducted to evaluate the effects of Hypericum Perforatum ointment on perineal pain intensity following episiotomy among primiparous women.

Methods: This triple-blind clinical trial was performed on 98 eligible primiparous women referring to selected educational hospital of Tehran University of Medical Sciences for normal vaginal delivery. Block Randomization (in 1; 1 ratio) was used to categorize the participants continuously into two groups: intervention (using Hypericum Perforatum ointment) and control (using placebo ointment). Participants in each group used ointments (about 3 grams each time) on episiotomy site, twice a day and for a period of ten days. Our primary outcome was the pain intensity in different intervals following episiotomy. The data were analyzed by SPSS software (version 13) using student's t-test, Mann-Whitney U test and chi-square test.

Results: We missed 14 participants during the study and analyzed the data from 42 participants in each group. The mean of pain scores revealed no significant differences before (mean difference=-0.33; P=0.46) and four hours (mean difference=0.57; P=0.13) after ointments use, between the intervention and control groups, while these differences were significant after eight hours (mean difference=2.17; P<0.001), five days (mean difference=2.20; P<0.001) and ten days (mean difference=2.21; P<0.001) following the intervention.

Conclusion: Using Hypericum Perforatum ointment as a noninvasive, simple and effective topical formulation, can significantly reduce pain intensity of episiotomy site.

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Introduction

Episiotomy has been reported as a common procedure in vaginal deliveries[1,2] and is defined as the incision on perineum in order to provide enough space for delivery and eliminate severe perineal injuries.[3] Risk of perineal laceration and forceps delivery injuries that could lead to pelvic floor disorders, increase in absence of episiotomy.[4]

Globally, about 10-95% of pregnant women experience episiotomy incision when giving birth.[5] The prevalence of episiotomy among primiparous women in Tehran, Iran is 97.3% and mediolateral episiotomy, despite being associated with relatively more complications than the other kinds, is more prevalent.[6] During a normal vaginal delivery, perineum could be damaged (by a rupture or incision) and millions of women around the world suffer from this problem annually.[7] Asian women are at a greater risk of severe perineal injuries during vaginal delivery due to the kind of tissue and short perineum body.[5] Perineal damage can lead to a short or long term pain which is considered as a common complication of mediolateral episiotomy. As for the incidence of this surgical procedure in Iran, these two complications are quite widespread.[6] The pain occurs during daily activities and causes difficulties in newborn care, transition to motherhood and the attachment between mother and her baby.[7,1] Unfortunately, estimating the degree of pain and the associated discomforts is difficult.[7] It has been reported that 90% of postpartum women suffer from severe perineal pain which leads them to use a range of oral analgesics, nonsteroidal anti-inflammatory drugs and ice bags[8] but the pain in women who have episiotomy is more severe than women who have not received the incision.[9] Prevalence of perineal pain among Iranian women who had received episiotomy was 96.4% during the first day after delivery and 63% and 25% in tenth and forty days, respectively.[6]

In Iran, the routine protocol for perineal care after episiotomy contains povidone-iodine (Betadine) solution,[10] but there are controversies over the effectiveness of this solution in wound care. Povidone-iodine may even cause disorders in the healing process, especially at concentration of more than 10%.[11]

Evidences indicate that using complementary and alternative medicine among women of reproductive age in industrialized countries is accepted as a safe treatment that supports independence of mothers. Complementary medicine in obstetrics is widely used for the treatment of nausea-vomiting, back pain, anemia, perineal pain and postpartum depression.[12] Hypericum Perforatum (HP)

herb is used in many medical interventions.[13] Aerial parts of HP have many therapeutic properties and contains flavonoids such as hyperoside, epicatechin, and substances such as Hypericin, Hyperforin, chlorogenic acid and quercetin.[14,15] HP potency in blocking protein kinase C mediated pathways, could make it an effective treatment for migraine pain.[16] Samadi et al. showed that topical use of HP is safe, facilitates cesarean wound healing and minimizes scar formation, pain and itching.[17]

HP antidepressant effects have been widely assessed in previous studies but antinociceptive characteristics of this plant and different plant products of HP have not been completely clarified in clinical trials.[18] Also evidences on antimicrobial and antinociceptive properties of HP mostly have focused on animal subjects and human studies are limited.[19,20] Due to widespread prevalence of perineal pain after episiotomy and impact of pain on the quality of life in women, midwives support them through introducing a wide range of analgesic agents.[8]

Considering the limited studies on using HP in obstetrics and gynecology field, this study seeks to investigate the impact of HP topical ointment on perineal pain intensity following episiotomy among primiparous women.

Materials and methods

This randomized, triple blinded, parallel-group clinical trial was conducted on primiparous women referring to selected educational hospital (Baharlou hospital) of Tehran University of Medical Sciences (TUMS) in Tehran, Iran; between September 2014 and February 2015. The study protocol was approved by ethics committee of TUMS and registered at the Iranian Registry of Clinical Trial (IRCT registration number: IRCT201404085912N15).

The present study was also in compliance with Declaration of Helsinki on medical protocol and ethics. Written informed consents were obtained from 98 eligible nulliparous women referring to the delivery ward of Baharlou hospital for giving birth. Women who met the following inclusion criteria: age range of 18-35 years, admission for the first vaginal delivery, physical and mental health among mothers, normal body mass index before pregnancy (19.8-26 kg/m^2), gestational age of 37-42 weeks, singleton pregnancy, absence of amniotic membrane rupture ≥ 18 hours, cephalic vaginal delivery with normal progress of labor, receiving an episiotomy in the absence of perineal tear and instrumental (forceps/vacuum) birth, apparently healthy neonate with normal weight and spontaneous placental delivery, were enrolled in the study.

The data from participants who met following criteria were excluded from the analysis: unacceptable use of topical ointments (missing more than two consecutive or three alternative doses), episiotomy wound infection and unwillingness to continue the study or attending the examination sessions.

Our sample size for the power of 80% and confidence interval level of 95% was determined as 84 participants (α=0.05, β= 0.20). Considering any possible losses, we estimated a total of 98 women who were randomly allocated to the intervention and the control group (Figure 1).

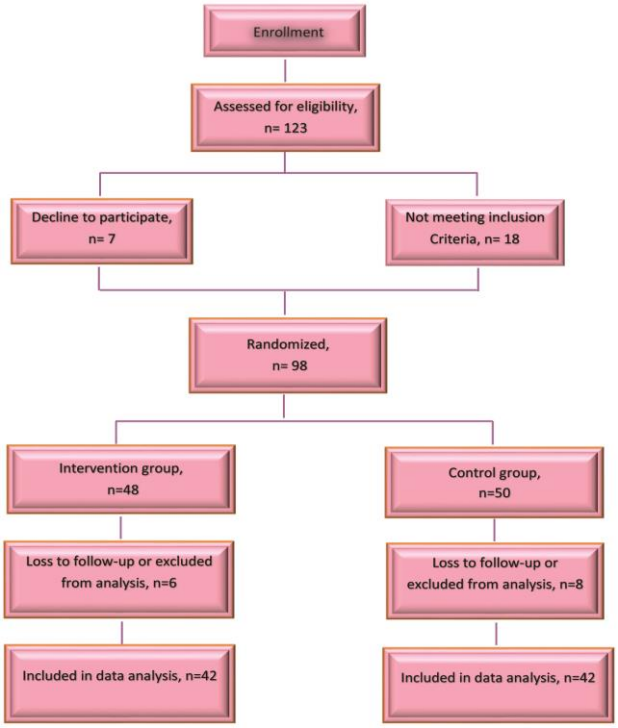

Fig 1. Consort flow chart

The labor and delivery processes were observed by the researcher to control for possible confounding variables. The amount and type of anesthetic solution before receiving incision and episiotomy repair, episiotomy type and repair methods were similar among participants. Mothers were monitored four hours after delivery and eligible women who volunteered to participate, signed written informed consent forms after receiving adequate information on the aims and process of the study. They were randomly allocated to intervention and control groups in 1; 1 ratio and based on block randomization.

We used "research randomizer" website (www.randomizer.org) for randomization. The researcher used 25 randomly numbered blocks (with the block size of 4 and different sequences of "A" and "B" groups) for allocating participants. The initial assessment of pain intensity was performed immediately before the intervention (four hours after delivery). The participants received face-to-face education about perineal care, hygiene before and after applying ointment, nutrition regimen, ointment usage instruction and recording painkillers usage at home. After answering all probable questions and eliminating worries about baby, the participants in each group started using HP or placebo ointments (about 3 grams each time) on episiotomy site, twice a day and for a period of ten days. Topical ointments were prepared and packed in identical 30 gr white tubes (with the same size and shape) by Dineh Company (Tehran, Iran) and all HP and placebo tubes were coded as "A" and "B". Hydroalcoholic extract of HP flowers was used to prepare HP ointment. Dineh

Company had the monopoly of ointments formula. It should be mentioned that the company had no participation in other steps of the study (data gathering, pain evaluations and data analysis). The research team and participants were unaware of ointments coding and Dineh Company disclosed ointments codes after statistical analysis.

The data were collected using demographic and obstetrics characteristics questionnaire, Visual Analogue Scale (VAS), painkiller and ointment usage checklist. VAS is a standard and reliable tool for measuring pain intensity in clinical situations (r=*0.90).* [21] Patients rate their pain based on this ruler from zero to ten. Zero represents "no pain"; 1-3, "mild pain"; 4-6, "moderate pain"; and 7 -10 are considered as "severe pain".[22]

Second to fifth stages of pain assessment were performed eight hours, 12 hours, five days and ten days after episiotomy. During the study period, the researcher frequently called mothers, answered their questions and recorded probable complications (associated with using topical ointments). It should be mentioned that due to ethical issues, the participants were not prohibited from taking mefenamic acid (a non-steroidal anti-inflammatory drug effective in reducing pain and vaginal bleeding).[23,24] Mefenamic acid was prescribed routinely in postpartum ward of Baharlou hospital.

We missed six participants in the intervention and eight participants in the control group during the study. In the HP group, one mother was unwilling to continue the study (due to a burning sensation during ointment usage) and five participants refused to attend the examination sessions (five and ten days after delivery) and did not return their painkiller and ointment usage checklists. In the placebo group, one mother had episiotomy site infection; two participants had unacceptable ointment usage; one mother refused to attend examination session on the fifth day and four participants refused to participate in the final examination session.

The data were analyzed using SPSS software (Statistical Package for Social Science, version 13) and chi-square test, student's t test and Mann-Whitney U test were used.

Results

During the study period we missed 14 participants and analyzed the data from 84 participants (42 mothers in each group). The majority of deliveries in HP (78.6%) and placebo (69%) groups were managed by midwives, 19% of deliveries in the intervention group and 28.6% in control group were performed by midwifery students under the professor supervision and only one delivery (2.4%) in each group was handled by an obstetrics and gynecology specialist. The time range of episiotomy repair among participants in both groups was 10-40 minutes and there was no significant difference between the two groups (P= 0.83).

Also there was no statistically significant difference between the two groups in terms of demographic features (age, Body Mass Index, education, economic and employment status), obstetrics and postpartum variables (duration of labor stages, the person who handled delivery, duration of episiotomy repair and length of incision, number of superficial stiches, time of starting daily activities after delivery and breast feeding position) and neonatal (newborn weight and head circumference) factors (Table 1). Four hours after episiotomy (before intervention) 28 participants of HP group (66.7%) and 26 participants of control group (61.9%) had severe pain (VAS 7-10) and there was no statistically significant difference between the two groups (P=0.46). The second stage of pain intensity evaluation showed that pain scores among 25 participants of intervention group (59.5%) and 26 participants of placebo group (61.9%) decreased to moderate level (VAS 4-6) four hours after intervention (8 hours after episiotomy) and there was no significant difference between the two groups (P=0.13).

Eight hours after the intervention, the level of pain score among 19 participants of HP group (45.2%) decreased to mild (VAS 1-3) while 22 participants in control group (52.4%) still had moderate pain (P<0.001).

Table 1. Demographic, obstetrics and neonatal characteristics of participants in interventio and control groups

Variable	Groups		P
	Intervention (N=42) Mean (SD)	Control (N=42) Mean (SD)	
Age (year)	24.52 (4.49)	23.02 (3.88)	0.05
Duration of episiotomy repair (min)	24.60 (5.57)	24.93 (8.30)	0.83
Body Mass Index (kg/m^2)	22.84 (1.70)	23.10 (1.98)	0.50
Episiotomy length (cm)	4.06 (0.59)	4.14 (0.60)	0.55
Duration of the first stage of labor (min)	399.86 (96.62)	424.60 (100.82)	0.25
Duration of the second stage of labor (min)	40.5 (13.40)	41.3 (13.40)	0.79
Duration of the third stage of labor (min)	10.05 (5.66)	9.95 (4.38)	0.93
Number of superficial stitches	4.57 (0.96)	4.86 (0.92)	0.17
Newborn Head circumference (cm)	34.80 (1.24)	34.61 (1.91)	0.59
Newborn Weight (g)	3206.31 (363.41)	3221.07 (423.52)	0.86
Time of starting daily activities after delivery (day)	6.90 (2.09)	7.12 (1.91)	0.62
Person who handled delivery (midwife)†	33 (78.6)	29 (69)	0.58*
Education (diploma)†	17 (40.5)	20 (47.6)	0.90*
Economic status (moderate)†	25 (59.5)	28 (66.7)	0.73*
Employment status (housewife)†	40 (95.2)	41 (97.6)	0.55*
Breastfeeding position (sitting)†	30 (71.4)	30 (71.4)	0.54*

* Chi-square- test, † N (%).

During pain evaluation in the fourth stage (five days after the intervention) only one participant (2.4%) in HP group reported severe pain, although four participants in the placebo group (9.5%) had severe pain. The majority of the participants in the intervention group (50%) reported mild pain ten days after intervention but most of the participants in the control group (61.9%) had moderate pain. Mean and standard deviation of pain intensity in HP and control groups are shown in Table 2. Using analgesic drugs among participants of the intervention group was less than that for the control group, but the difference was not statistically significant (Table 3). None of our participants reported major side effects that could be directly attributed to ointments usage. Only one participant in the HP group reported transient burning sensation at the time of ointment usage and preferred to stop participating. No other kinds of adverse effects were reported during the study period.

Table 2. Comparison of pain intensity between intervention and control groups

Pain intensity	Groups		
	Intervention (N=42) Mean (SD)	Control (N=42) Mean (SD)	P*
Before intervention	7.38 (2.02)	7.05 (2.12)	0.46
Four hours after intervention	4.95 (1.65)	5.52 (1.82)	0.13
Eight hours after intervention	3.69 (2.06)	5.86 (1.89)	<0.001
Five days after intervention	2.40 (1.75)	4.60 (2.14)	<0.001
Ten days after intervention	2.05 (1.99)	4.26 (2.31)	<0.001

* Mann-Whitney U- test

Table 3. Comparing mean number of consumed analgesics (Mefenamic acid) between intervention and control groups

Time after delivery	Groups		
	Intervention (N=42) Mean (SD)	Control (N=42) Mean (SD)	P*
Second day	1.71 (1.21)	2.07 (0.99)	0.14
Third day	1.60 (1.03)	1.69 (1.17)	0.69
Fourth day	1.40 (1.03)	1.79 (1.02)	0.09
Fifth day	1.07 (0.92)	1.33 (0.87)	0.18
Sixth day	0.79 (0.84)	0.98 (0.81)	0.29
Seventh day	0.67 (0.78)	0.95 (0.90)	0.12
Eighth day	0.74 (0.76)	0.83 (0.82)	0.58
Ninth day	0.50 (0.67)	0.79 (0.92)	0.10
Tenth day	0.57 (0.85)	0.64 (0.95)	0.72

*Mann-Whitney U test was used to compare analgesics consumption between intervention and control groups.

Discussion

This study was conducted to evaluate the effectiveness of HP ointment on the severity of perineal pain after episiotomy. The findings showed that using Hypericum ointment in comparison with placebo, significantly reduced episiotomy pain after eight hours, five and ten days following the intervention. The pain reduction in the intervention group might be due to antinociceptive properties of HP that make it a potentially good choice to be used in painful situations such as trauma, burns, rheumatism and neuralgia.[25,26] HP was traditionally used for snake bites, hemorrhoids and rheumatism treatment. Anti- inflammatory, antiviral and antibacterial properties of HP refers to Hypericin component.[27] The olive oil extract of HP brings about significant improvement on wound healing (linear and circular incision model) in rats. Also ethanolic extract of HP shows dose-dependent anti-inflammatory properties that could enrich wound healing.[28] The majority of the studies on HP extract effectiveness have focused on HP antidepressant properties which is mostly related to the Hyperforin component of the plant.[27,29] Using methanolic extract of HP in mice showed analgesic properties via central inhibitory mechanisms and probable inhibition of the prostaglandin synthesis.[26]

HP poses antinociceptive properties via conflation of two intracellular pathways: Hyperforin facilitates activation of opioid system and Hypericin has a mediating role in Protein Kinase C (PKC) blocking. Systemic injection of HP, morphine or combination of them in mice showed that the plant was able to increase antinociceptive effects of morphine in mice neuropathic pain model. Also oral administration of HP increased pain threshold and caused prolonged antinociception in mice.[30] Evaluating anti-inflammatory and antinociceptive effects of HP in rats showed that the plant significantly inhibited edema formation in comparison with the control group and antinociceptive effect of HP was also significant in the hot plate and tail electric stimulation tests in rats,[25] but there is limited evidence on the antinociceptive features of HP in human subjects.

Perineal pain after episiotomy causes eventual prescription of oral analgesics for mothers, but in order to prevent probable side-effects in mothers or infants, using an effective herbal product would be a reasonable choice. Some studies evaluated herbal medicine effectiveness in relieving pain following episiotomy. Using Equisetum Arvense (Horsetail herb) topical ointment significantly decreased episiotomy pain intensity in 108 nulliparous women and promoted wound healing in comparison with placebo, which might be related to the impact of tannins, saponins, sterols (containing β-sitosterol, campesterol and isofucosterol) and flavonoids components of Equisetum Arvense on inflammation and β-sitosterol on nociception.[31,32] Investigating the effect of Aloe Vera on post episiotomy pain and wound healing showed significant differences in the healing scores that was measured by Redness; Edema; Ecchymosis; Discharge and Approximation (REEDA) scale. Also five days after the intervention, the participants in the intervention group reported significantly lower pain scores in comparison with control group.[10] Another double-blind randomized clinical trial on 120 primiparous women showed that

using Curcumin solution three times a day had a significant effect on episiotomy wound healing in comparison with Povidone-iodine solution, but the comparison of pain scores 24 hours after the intervention showed that there was no statistically significant difference between the two groups.[33] This finding is in contrast with our results and a plausible explanation for the inconsistency could be related to different antinociceptive effects of Curcumin and Hypericum perforatum.

In our study HP ointment showed significant pain relieving properties 12 hours after episiotomy. Evaluating the effects of lavender essence sitz baths on episiotomy pain relief among Iranian primiparous women indicated significant pain reduction five days after episiotomy, although there was no significant difference between the intervention and control groups (receiving routine episiotomy care protocol) 12 hours after episiotomy[34] that might be due to the method of lavender administration.

Samadi et al., evaluated the effect of Hypericum ointment on cesarean wound healing and pain. They found that the pain score differences between the intervention, placebo and control groups were statistically significant forty days after cesarean section. [17] This finding is consistent with our results, although due to different anatomic locations of cesarean section and episiotomy incision, different nature of cesarean surgery in comparison with episiotomy, the need for a longer time span for the restoration of cesarean wound (about 6 weeks in transverse incision and more than 6 weeks in the vertical incision), and prolonged cesarean subsequent pain and greater risk of persistent pain in comparison with vaginal delivery which usually causes transient pain,[7,35,36] we are not able to compare this finding with our results properly.

In our study, the use of oral analgesic by participants (mefenamic acid) was not prohibited, because mefenamic acid was prescribed to decrease postpartum bleeding in addition to perineal pain. Our findings indicated that there was no statistically significant difference between the intervention and placebo groups in term of analgesic consumption. These findings are consistent with the results of Fardiazar et al.; they showed that the mean analgesic consumption in Lidocaine 2% gel and lubricant gel group had no statistically significant difference among women receiving episiotomy.[37]

In order to eliminate the effect of perineal pain risk factors such as neonatal birth weight more than 4 kg, nulliparity, malpositions and forceps delivery,[38] we considered all these items in the inclusion criteria so as to evaluate the severity of pain among women with similar episiotomy types (mediolateral) and parity number, which is the strength of present study.

We did not consider a specific allocation concealment strategy in our study, which is one of the main limitations in our clinical trial. Another potential limitation in pain evaluation studies refers to different pain thresholds among different people and the pain severity might be expressed more or less than the true amount. This difference might be due to individual differences, cultural factors and economic status. By recruiting participants from one educational hospital (which is mostly considered as referral hospital for the people of some specific regions) we tried to decrease the effect of cultural and economic factors.

Conclusion

Despite the widespread usage of pain killers, new studies tend to focus on natural antinociceptive products in an effort to decrease the side effects, especially during touchy situations for mothers such as postpartum period. According to the results of present study, using HP ointment as a noninvasive, simple and effective topical formulation can relieve episiotomy pain. Conducting further clinical trials with larger sample sizes and assessing the effects of HP ointment on episiotomy wound healing (redness, edema, ecchymosis, discharge, and approximation) and other painful situations is recommended to confirm the effectiveness of HP topical ointment.

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Ethical issues

None to be declared.

Conflict of interest

The authors declare no conflict of interest in this study.

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