Wound healing Benefits of Curcumin for Perineal Repair after Episiotomy: Results of an Iranian Randomized Controlled Trial

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Abstract: Pain and discomfort related to episiotomy have been reported to interfere with women's daily activities postpartum, such as sitting, walking and lifting the baby**.** To compare the effects of curcumin and Povidone-iodine solutions for episiotomy healing in primiparous women. 120 healthy primiparous women with a vaginal delivery at term were evaluated in this double-blind randomized clinical trial. Randomization was done using a table of random list numbers. Perineal healing was evaluated by research midwives blinded to random allocation at 24–48 hours and 10 days postpartum. Pain was assessed via a visual analogue scale and wound healing via the REEDA scale. Analysis was done on the intention-to-treat principle. The main outcome measure was the changes in wound healing between the two groups as measured by the REEDA Scale. Secondary outcome measures were perineal pain and wound healing 24–48 hours and 10 days after delivery. There was a greater decrease in the total scores of the REEDA in the curcumin group than in the Povidone-iodine ($P < 0.001$), however; there weren't significant differences between the groups on the VAS scores. The application of curcumin may assist in the episiotomy healing process and could be suitable replacement for Povidone-iodine.

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1. Introduction

Perineal trauma is a frequent complication to vaginal delivery, and more than 90% of primiparous women in developing countries sustain episiotomy (Morhe et al., 2004).

Episiotomy's pain and discomfort have been related to difficulties in women's daily activities in postpartum, such as sitting, walking and lifting the baby. (Albers et al., 1999). Pain related to episiotomy is identified to have a negative impact on sexual activities in the first year after childbirth (Glazener, 1997). Midwives and obstetricians increasingly face women who wish to have a caesarean section due to fear of genital tract injuries or following previous childbirth trauma (McCourt et al 2007; Wagner, 2000).

Reducing perineal trauma and associated morbidity has a high importance for childbearing women and health professionals (Homer and Dahlen ,2007). Some existing treatments for episiotomy healing aren't effective and some may prolong the healing processes (Steen et al , 2000).

Povidone-iodine is an antiseptic solution that is usually used in Iran for episiotomy healing. (Vakilian et al., 2011). Tork and Valaei (2002) demonstrated that there was no significant difference between the Povidone-iodine and water in episiotomy wound healing. Cooper et al (1991) even showed that Povidone-iodine suppresses function of fibroblasts and lymphocytes.

Alternative and complementary medicine is used widely in dermatologic surgery such as episiotomy healing. (Reddy et al., 2011). Turmeric is considered as the foundation of an herbal programmed for health. For thousands of years it has been believed to be a key balancing and detoxifying herb. The main biologically active part of Turmeric is curcumin. Curcuminoids are natural phenols that are responsible for the yellow color of turmeric. (Redfern R. 2004). Previous research suggested that curcumin has anti-inflammatory and pro-wound-healing effects

and it exerted its anti-inflammatory effects (Sidhu GS et all 1998).by increasing the mRNA transcripts of growth factor–beta 1 and fibronectin .It is notice worthy that only few number of randomiezed controlled trials have been conducted in humans to demonstrate its effective properties (White and Judkins, 2011; Reddy et al., 2011).

Therefore, this study was performed to compare the effects of curcumin and Povidone-iodine solutions for episiotomy healing in primiparous women.

2. Material and Methods

The prospective, parallel randomized clinical trial was conducted with recruitment through 2009 -2010 in the Alzahra Teaching Hospital in Tabriz, Iran. The study protocol was approved by the Ethics Committee and research center of the Tabriz University of Medical Sciences. (14.89.9 No). The trial was registered at the Iranian Registry of Clinical Trials at www.irct.ir (IRCT138810193027N1).

Eligibility and recruitment

Eligible subjects were primiparous women, without any acute and chronic disease or allergy, and had a healthy pregnancy and delivery after 37 weeks of gestation. The women also had to be able to read and speak in native language. Exclusion criteria were perineal injuries involving the anal sphincter and/or anal mucosa, postpartum hemorrhage, previous perineal surgery, obvious violence and sexual intercourse in the early postpartum period.

Written informed consent was obtained from all women who decided to participate in the study. Participants not meeting the eligibility criteria but randomized included in the analysis according to the intention-to-treat principle.

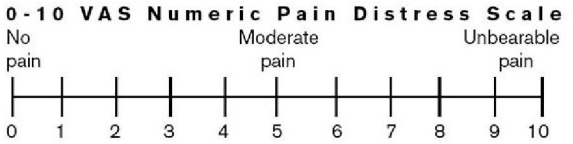
Randomization

In this study, 120 patients participated in research project .We prepared 60 Curcumin solution as well as 60 Povidone –iodine solution tubes. It is notice worthy that all 120 tubes were alike and each tube had its specific code. Therefore, researcher and patients didn't inform of the content of tubes. Participants consumed Curcumin solution categorized as an intervention group, participants who consumed the Povidone-iodine solution were as a control group (60 subjects in each arm). Therefore, each patient had a specific tube and she should consume it three times a day. It is notice worthy those women must wash their hands before using solutions in order to reach acceptable results, and every necessary information related to consuming solutions were explained to each participant individually.

Scales and Outcome of study

REEDA scale is as a descriptive scale, it can measure five components associated with healing process ,they are including :Redness ,Edema ,Ecchymosed, Discharge , Approximation ,and it is graded 0-3 .Therefore ,each category is evaluated and a number assigned for a total REEDA score ranging from 0-15.In this study ,REEDA scale was applied to represent the changes in wound healing among two solutions. Consequently, REEDA scores for curcumin and Povidone-iodine groups were 2.5 ± 0.8 and 3.7 ± 1.6 respectively.

The Visual Analogue Scale (VAS) is a subjective measure of pain. It consists of a 10cm line with two end-points representing ‘no pain’ and ‘Unbearable pain'. Patients are asked to rate their pain by placing a mark on the line corresponding to their current level of pain According to this method, score 0 (No pain), 1-3 (Mild pain), 4-7(Moderate pain), and 8-10 (Unbearable pain). Consequently, Pain was evaluated by VAS method in our research.



Blinding and compliance

Both Curcumin and Povidone-iodine solutions were packed in similar cans containing a code which was known only to the study pharmacist. The study was double-blinded and the contents were known neither to the participants, nor to the research midwives

Statistical analysis

All statistical analyses were done on an intention-to-treat basis. Data were entered twice into the software SPSS 16 software to correct for typing errors. Continuous data with normal distribution were analyzed by independent two-sample *t*-tests and without normal distribution by Mann–Whitney U test. For categorical variables the Chi-Square and Fisher’s exact tests were used. All statistical tests were two-tailed, and the significance level was set at 0.05 (α= 0.05). Values are described as the mean (standard deviation) or the median (interquartile range) if not normally distributed.

3. Results

The CONSORT diagram shows the participant flowchart through the trial (Figure 1). Three women withdrew their consent to participate. Thus, the number of intervention and Control group were 59 and 58 respectively.

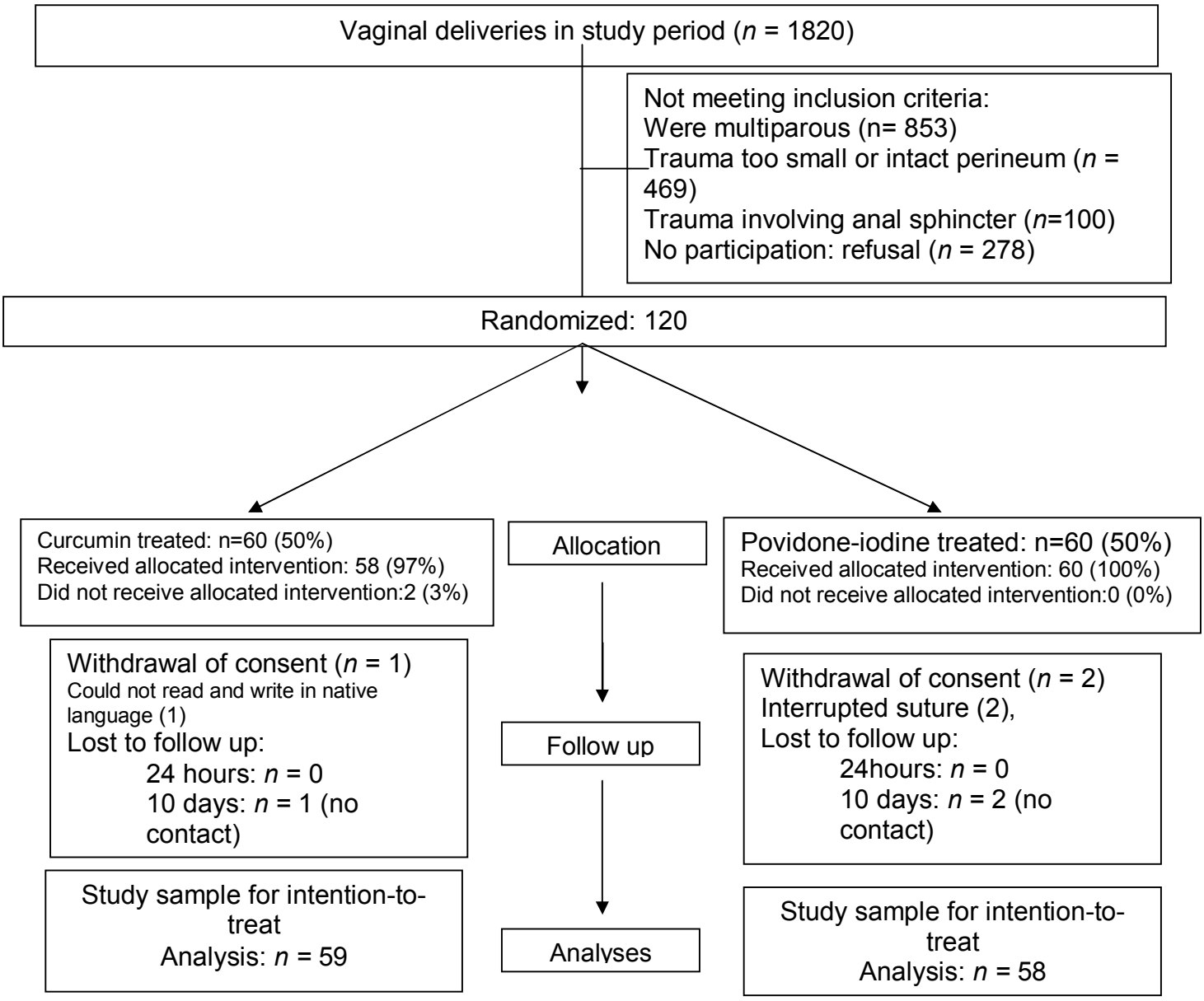


Figure 1 Consort diagram of vaginal deliveries in women during study period

Table 1 shows baseline characteristics of the curcumin and Povidone-iodine groups. The two Groups were comparable and did not differ with respect to any of the baseline demographics and delivery details variables, indicating successful randomization.

Table 2 represents the comparison of episiotomy healing evaluation in the two groups on basis of REEDA scale. As shown in table 2, at 24 hours 8 participants in the curcumin group and 0 of the Povidone-iodine group had ecchymosis. Within 0.25 cm, which was significantly different between the groups (P = 0.006). Within 10 days more participants in the curcumin group than the Povidone-iodine group had redness (P = 0.033) and edema (P = 0.027). The other REEDA parameters were not significantly different between the groups.

According to Table .3, The REEDA scores were significantly differed between the both groups at 24 hours (P = 0.032) and 10 days (P < 0.001). The VAS score differences between the two groups were statistically not significant at 24 hours (P = 0. 2) and significant in 10 days (P < 0.001); however, difference scores between 10th and first day were not statically significant.

Table 1 Characteristics of the two groups at baseline			
Variables	Curcumin group (N = 59)	Povidone - Iodine group (N = 58)	P value
Age (years)	24.2 ± 5.6	22.7 ± 4.0	0.08
Body mass index (kg/m^2)	25.8 ± 3.6	26.1 ± 3.0	0.58
Gestational age (weeks)	38.1 ± 5.1	38.6 ± 0.8	0.46
Education (diploma)	28 (47.5)	21 (36.2)	0.35
Job (housewife)	56 (94.9)	49 (84.5)	0. 61
Status of operator (supervising midwife)	20 (33.9)	11 (19)	0. 61
Note**:** Data are presented as Mean ± SD (standard deviation) and Frequency (Percentage).			

Table 2. Comparison of episiotomy healing evaluation in the two groups				
Variables		Curcumin group (N = 59)	Povidone-iodine group (N = 58)	P value
REEDA Parameters at 24 hours				
Redness				
	None	0 (0)	2 (3.4)	0.244
	0.25 cm or more	59 (100)	56 (96.6)	
Edema				
	None	6 (10.2)	2 (3.4)	0.272
	≤ 1 or more	53 (89.8)	56 (96.6)	
Ecchymosis				
	None	35 (81.4)	37 (100)	0.006
	0.25 cm or more	8 (18.6)	0 (0)	
Discharge				
	None to serum	53 (89.8)	57 (98.3)	0.114
	Serosanguinous or bloody	6 (10.2)	1 (1.7)	
Approximation				
	Closed	53 (89.8)	57 (98.3)	0.114
	Separation <= 3 mm or more	6 (10.2)	1 (1.7)	
REEDA Parameters at 10 days				
Redness				
	None	38 (64.4)	26 (44.8)	0.033
	0.25 cm or more	21 (35.6)	32 (55.2)	
Edema				
	None	50 (84.7)	39 (67.2)	0.027
	≤ 1 cm	9 (15.3)	19 (32.8)	
Ecchymosis				
	None	58 (98.3)	57 (98.3)	1
	0.25 cm or more	1 (1.7)	1 (1.7)	
Discharge				
	None to serum	49 (83.1)	45 (77.6)	0.457
	Serosanguinous or bloody	10 (16.9)	13 (22.4)	
Approximation				
	Closed	55 (93.2)	49 (84.5)	0.133
	Separation <= 3 mm or more	4 (6.8)	9 (15.5)	
Note: Data are presented as Frequency (Percentage).				

Table 3 Comparison of the two Groups at 24 hours and 10 days after deliver				
Variables		Curcumin group (N=59)	Povidone-iodine group (N=58)	P value
VAS score				
	At 24 hours	5 (4,5)	5 (4,5)	0.027

	At 10 days	0 (0,0)	1(0,1)	< 0.001
	Difference scores between 10th and first day	-4 (-5,-4)	-4 (-5,-4)	0.963
REEDA score				
	At 24 hours	5 (4,5)	5 (4,5)	0.032
	At 10 days	0 (0,1)	1 (1,2)	< 0.001
	Difference scores between 10th and first day	-4 (-5,-4)	-3 (-3,-2)	< 0.001
Note: Data are presented as Median (Interquartile Range).				

A per-protocol analysis was performed to investigate whether the noncompliance had contributed to validating a false difference between the two groups. The per-protocol analysis showed statically significant differences in the first outcome measure over again (Ps < 0.05, data not shown). There were no effects for the curcuminand Povidone-iodine groups.

4. Discussions

The main aim of this study was evaluating the role of Curcumin in wound healing in compare to Povidone-iodine .Our results showed that the curcumin solution for perineal episiotomies was more effective way to improvement of wound healing processes than the Povidone-iodine. However curcumin wasn't effective in pain relief.

Wound healing is a dynamic, interactive process concerning soluble mediators, blood cells, extracellular matrix, and parenchymal cells. Wound healing has at least three phases -inflammation, proliferation, and maturation - which overlap in time. (Singer and Clark , 1999).

Treatment with curcumin could enhance the synthesis of collagen, DNA, fibroblast, vascular densities and other important factors in wound healing. (Ghasemi Dehkordi et al (2003) demonstrated that curcumin pretreatment had a helpful effect on the irradiated wound and could be a substantial therapeutic strategy for improving radiation induced delay in wound repair in cases of radiation-induced skin injuries. Also Sidhu et al (1999) showed that curcumin accelerate wound healing in diabetic rats by increased formation of granulation tissue, faster reepithelialization and increased collagenization.

The results of a small clinical trial with 19 HIV patients found that a liquid soap of curcumin could decrease itching symptoms and infectious wound and abscess. [Hong et al., 2004). This study, as of first clinical trials conducted in humans showed that curcumin solution had wound healing effects.

Curcumin solution wasn't effective in episiotomy pain relief in this study. Vakillian et al (2011) also showed that lavender essential oil could not cause to decrease of pain. These studies may highlight the need for future trials that can employ interventions of greater strength of the clinician–patient relationship because pain relief is never about the clinician's intervention alone.

Limitations of the present study might be related to the absent of control on the nutrition and the stresses that may contribute to wound healing and pain relief. The authors believe that future trials could consider these issues.

It seems that curcumin can be used as an appropriate treatment for postpartum episiotomy wound care according to the familiarity of the mothers with complementary medicine. Consequently, the authors suggest the assessment of its application in other areas such as cesarean section and umbilical wound healing and also considering the use of curcumin solution instead of Povidone-iodine for episiotomy wound care.

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