

Tissue adhesive to repair first-degree perineal tear: a pilot randomized controlled trial

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Summary

Purpose of Investigation: This pilot study proposes to verify the feasibility of conducting a randomized controlled trial (RCT) on the use of Epiglu tissue adhesive to repair first-degree tear. **Materials and Methods:** A pilot RCT was conducted in a birth center in São Paulo, Brazil. The sample consisted of 20 women with first-degree tear. These women were randomly assigned to the experimental group (EG=10) - perineal tear repair with Epiglu or the control group (CG=10) - perineal tear repair with absorbable synthetic thread. The measured outcomes were perineal pain, perineal healing, women's satisfaction, and professional's time spent repairing the perineum. **Results:** The intensity of perineal pain was significantly lower among women in the EG than that in the CG in all stages of the study (EG range: 2.0-0.2; CG range: 2.5-0.6). Additionally, perineal healing showed significantly better REEDA scores among women in the EG than those in the CG in all stages (EG range: 0.6-0.0; CG range: 1.8-0.7). Women's satisfaction was significantly higher in the EG (100% were satisfied or very satisfied) than that in the CG (10% to 20% of them were dissatisfied or very dissatisfied). The mean time spent to repair the perineum was five minutes in the EG and 21 minutes in the CG ($p < 0.001$). **Conclusion:** This study shows that it is feasible to undertake an RCT on the use of the tissue adhesive Epiglu for first-degree perineal tear repair during normal birth.

Key Words: Natural childbirth; Perineum; Lacerations; Tissue adhesives; Cyanoacrylates; Wound healing.

Introduction

Normal birth is often associated with perineal trauma due to spontaneous tears or episiotomy [1]. Current evidence demonstrates that performing limited episiotomy is the best practice to protect the perineum from trauma [2].

Not performing routine episiotomy promotes perineal integrity but, at the same time, may increase rates of spontaneous trauma, especially first-degree (involving perineal skin and vaginal mucosa). Perineal tears can cause morbidities, pain, and dissatisfaction in women [3, 4].

Pain is higher among women with perineal tears (1.5 times more) than those without trauma [5], and other frequent morbidities are hyperemia, edema, ecchymosis, secretion, and noncoaptation of the wound, which hinder the healing process [6]. To reduce perineal pain, it is necessary to improve perineal tear assessment, repair techniques, and professionals' skills and knowledge of evidence-based recommendations [4]. Research has been carried out to show outcomes from alternative materials for repairing perineal tears, such as with cyanoacrylate-based tissue adhesive, which has been shown to be effective for perineal skin repair, with shorter repair time and less pain during and after the procedure when compared to surgical thread [7].

The octyl-2-cyanoacrylate tissue adhesive was used in a

randomized study of 102 women to compare its efficacy in the repair of first-degree spontaneous tears with conventional sutures. The results showed that the surgical glue was associated with a short repair time as well as lower use of anesthetic and low pain levels [8]. However, more studies are needed to evaluate the effectiveness of tissue adhesives as well as the most appropriate repair technique and the different types of tissue adhesives available. Thus, this pilot randomized controlled trial (RCT) aimed to determine the feasibility of conducting an RCT on the use of Epiglu tissue adhesive for repair of first-degree perineal tear. For this, the authors compared the intensity of perineal pain, the healing process, women's satisfaction, and the perineal repair time spent by professionals between Epiglu and absorbable synthetic thread.

Material and Methods

This pilot RCT was conducted at the Maternity of Itapecerica da Serra, São Paulo, Brazil. Women admitted for birth were eligible to participate in the study. The inclusion criteria were as follows: up to 6 cm of cervical dilatation, no use of steroids, no leukorrhea or signs of vulvar infection, no diabetes mellitus, no allergy to tissue adhesive or formaldehyde, no difficulties in communication, and normal birth with first-degree tear that must be repaired according to the recommendation of the professional who

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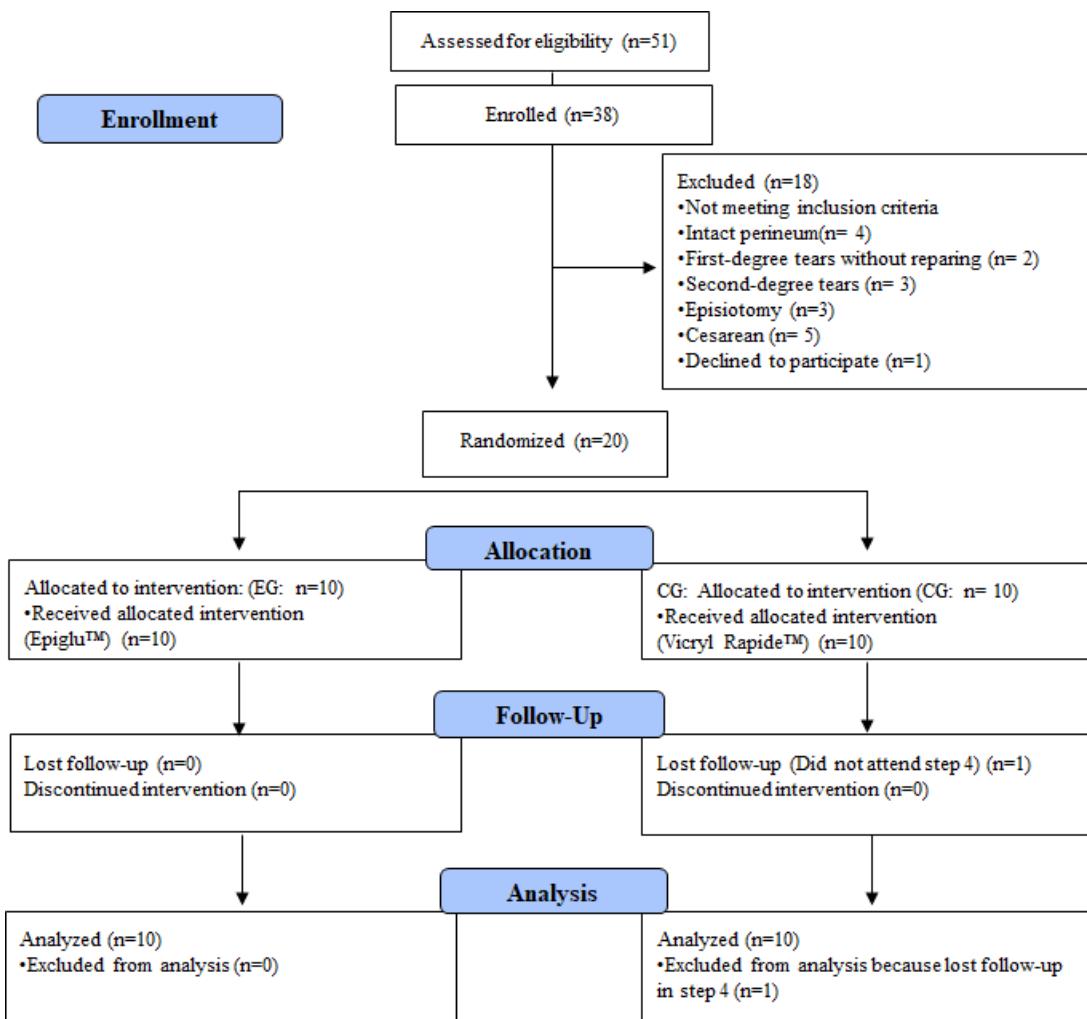


Figure 1. — Participant flowchart.

attended the birth. The sample consisted of 20 women, who were distributed into the experimental group (EG = 10) and the control group (CG = 10). In the EG, women were subjected to perineal tear repair with the tissue adhesive Epiglu single dose and in the CG, women were subjected to perineal tear repair with the fast-absorbing synthetic thread polyglactin 910 vicryl. Size 3-0, 45 cm length thread and 3/8 circular, 2.4 cm size unidirectional thread were used. Women's allocation into the EG or CG occurred randomly through a table produced by program R (version 3.4.2). Opaque envelopes that were consecutively numbered were opened only at the time of perineal repair. The primary outcome was the intensity of perineal pain after repair.

The secondary outcomes were the healing process, woman's satisfaction with perineal repair and the time spent by the professional to perform the perineal repair. The following technique was used to repair the perineal tear with Epiglu: 1) with the woman in a gynecological position, if necessary, a pad of gauze was inserted into the vagina to prevent blood leakage and keep the perineal tear dry, 2) the repair site was dried with gauze, 3) the Epiglu single dose Dosette was opened, removing the dispenser and attaching it to the upper tip of the Epiglu-Dosette, 4) the edges of the tear were approached and fixed with the index finger and thumb, 5) one or more drops of the solution were applied on the juxtaposed edges of the tear, depending on its extension, 6) the solution was spread in a thin layer using the

dispenser end, and 7) the adhesive was allowed to dry, indicating the final polymerization, which could take from 30 to 60 seconds.

The following technique was used to repair the perineal tear with Vicryl Rapide: stages 1) and 2) of the Epiglu technique were performed, 3) local anesthesia was administered with 1% lidocaine without vasoconstrictor, and 4) continuous nonlocking sutures were performed. Perineal repair was performed by the researcher in all women. Given the nature of perineal interventions and outcomes, there was no way to blind the procedures since, when examining the perineum to evaluate the healing process, it was possible to verify whether the repair was done with Vicryl Rapide or Epiglu.

The outcome evaluation was performed in four stages: up to 2 hours, from 12 to 24 hours, from 36 to 48 hours, and between 10 and 20 days after perineal repair. To evaluate the intensity of perineal pain, a 5×20 cm visual numeric scale (VNS) was used, with numbers from 0 to 10, where 0 represents no pain and 10 the worst possible pain [9]. The healing process was evaluated by means of the REEDA scale (redness, edema, ecchymosis, discharge, approximation). For each evaluated item, a score is assigned from 0 to 3 for a maximum of 15 points, which corresponds to the worst wound condition [10].

To evaluate satisfaction with perineal repair, a mirror was provided for participants to look at their perineum, and a visual ana-

Table 1. — Women's characteristics.

Characteristic	EG n=10	CG n=10	Total n=20	100%	p value ^a
Skin colour					
Brown	5	50	5	50	
White	4	40	4	40	
Black	1	10	1	10	1.000
Education level					
Incomplete elementary school	0	0	1	10	
Elementary school	5	50	6	60	
Secondary school	5	50	3	30	0.650
Occupation					
Homemaker	7	70	10	100	
Employed	3	30	-	-	0.211
Marital status					
Living with a partner	8	80	9	90	
Not living with a partner	2	20	1	10	1.000
Nutritional status					
Underweight	2	20	4	40	
Adequate	5	50	5	50	
Overweight	1	10	-	-	0.700
Obese	2	20	1	10	
Previous vaginal delivery					
No	6	60	7	70	
Yes	4	40	3	40	1.000
Previous perineal tears sutured					
No	9	90	7	70	
Yes	1	10	3	30	0.582
Intrapartum antibiotic					
No	9	90	9	90	
Yes	1	10	1	10	1.000

^aExact Fisher test.

logue scale on a 5×20 cm was presented. In this scale were drawn four faces ranging from “very dissatisfied”, “dissatisfied”, and “satisfied” to “very satisfied”. The time taken for perineal repair was recorded using a digital timer. The time started when the researcher had the repair material at hand, and it was finished when the repair was complete. Before data collection, the study was presented to the professionals to obtain their acceptance, collaboration, and integration with the research. Professionals were asked to not prescribe routine analgesics and anti-inflammatories to better evaluate the intensity of perineal pain. Nevertheless, participants were instructed to request pain medication at any time they needed. Data were collected in four different stages. Stage 1 corresponds to the outcome evaluation up to two hours after repair, Stage 2: from 12 to 24 hours, Stage 3: from 36 to 48 hours, and Stage 4: between 10 and 20 days after birth. Stages 1, 2, and 3 were performed during the maternity stay, and Stage 4 was performed at the postpartum return appointment. At all stages, data were obtained by checking medical records, interviewing the woman, and performing perineal examination.

In the inferential analysis, the Wilcoxon-Mann-Whitney test and the Linear Mixed Model (LMM) for repeated measurements were used for numerical variables. For the categorical variables, the Fisher's exact test and the Generalized Estimating Equation (GEE) were used. *P* values less than 0.05 were considered statistically significant. Analyses were performed using the statistical package Statistical Package for the Social Sciences (SPSS) (version 12.0).

This research was approved by the Research Ethics Commit-

tee of the School of Nursing of University of São Paulo and by the Municipal Council of Itapecerica da Serra and registered in the Brazilian Registry of Clinical Trials (REBEC) portal, on website: <http://www.ensaiosclinicos.gov.br/rg/RBR-2h84gt/>. Women's participation was voluntary and followed all determinations of the 466/2012 Resolution of Brazilian National Health Council, ensuring that the human rights of those involved in the research were protected. The researchers do not have associations with the manufacturers or distributors of the supplies used in this study.

Results

Data were collected from August 28th to November 12th, 2017. Fifty-one women were assessed for eligibility, 38 met the inclusion criteria, and, of these, 17 were excluded prior to randomization, and one declined to participate. The final sample was 20 women who were randomized and allocated in the EG (n = 10) and CG (n = 10). In the EG, all women were followed in the four stages; however, in the CG, there was one loss of follow-up, including a woman who did not attend the evaluation in Stage 4 (Figure 1).

Tables 1 and 2 present sociodemographic, clinical, and obstetric characteristics of women and newborns, indicating that the EG and EC were homogeneous. Both groups were also homogeneous in relation to perineal tears site

Table 2. — Women's and newborns' characteristics.

Characteristic	Group	N	Mean	SD	Min	Max	p value ^a
Age (years)	EG	10	26.6	7.3	17	39	0.158
	CG	10	21.7	5.7	16	21	
Gestational age (weeks)	EG	10	38.9	1.3	37	41	0.710
	CG	10	38.8	0.6	38	40	
BMI	EG	10	27.2	5.2	20	35	0.406
	CG	10	25.5	4.8	19	35	
Time between hospitalization and delivery (hours)	EG	10	6.2	4.4	0.4	15.0	0.880
	CG	10	6.2	5.0	0.7	17.6	
Time of amniotic membranes rupture (hours)	EG	10	6.4	6.4	0.5	16.7	0.112
	CG	10	3.9	5.2	0.2	13.0	
Newborn weight (grams)	EG	10	3250.5	324.6	2810	3760	0.226
	CG	10	3020.0	330.8	2545	3460	
Head circumference (cm)	EG	10	34.6	1.0	33	36	0.117
	CG	10	33.7	1.3	31	35	

^aWilcoxon-Mann-Whitney test

(clitoris, vestibule, labia minora, vaginal mucosa, and perineal body) ($p = 0.432$). In addition, no women had gestational diabetes or used pharmacological methods to relieve intrapartum pain or analgesics up to two hours after birth.

The women had no complications or complaints with Epiglu. Table 3 shows pain, healing, and women's satisfaction outcomes. In all stages of the study, the intensity of perineal pain was significantly lower in the EG than that in the CG. The same statistical variation was observed in perineal healing. At all stages, the REEDA score showed significantly better scores in the EG in relation to those in the CG. In the EG, the mean duration of repair was five minutes (SD = 3.6; range = 1.0-10.0) and, in the CG, it was 21 minutes (SD = 5.9; range = 12.0-30.0) ($p < 0.001$).

Discussion

The outcomes analyzed: perineal pain, healing, satisfaction with perineal repair, and time spent for repair showed results favorable to the use of the tissue adhesive. The differences obtained in the findings of this pilot study may have occurred due to chance, considering that the sample size was underpowered. However, despite the limited sample size, the results indicate adequate performance of this pilot study. One of the strengths of this study was the adherence of women, with only one declining to participate and a single loss of follow-up in stage 4 (10 to 20 days after birth), which was performed after discharge from the birth center. One limitation that is worth highlighting is the difficulty of enrollment of women during gestation.

Prenatal consultations are performed in services scattered throughout the municipality, and the study site is not the only referral service for normal deliveries. The main advantage of the present pilot study was to improve the technique of tissue adhesive application in first-degree perineal tears. The following were tested and adapted: 1) the amount of tissue adhesive applied in both single and multiple tears,

2) the precision of the different regions of the perineum, involving skin and mucosa (frenulum of clitoris, vestibule, labia minora, vaginal mucosa, fourchette, and perineal body), 3) the polymerization time, and 4) the use of the applicator. For better results, it is essential to emphasize the importance of drying the site carefully at the moment of application of the glue. The effectiveness of the tissue adhesive was compared to a gold standard repair technique (continuous nonlocked suturing technique with polyglactin 910) [11, 12], including exclusively women who had indications of tear repair (bleeding tear or with distal edges) based on the best practices and guidelines of the Brazilian Ministry of Health [1, 13, 14]. In most studies published on tissue adhesives in the perineum, the use of tissue adhesives was complementary to the suture, which was generally used for skin closure [15-19]. In the first decade of the 2000s, three other studies used tissue adhesives (Indermil and Histoacryl, both based on n-butyl-2-cyanoacrylate, and octyl-2-cyanocrylate) to close episiotomy and second-degree skin [16-18]. The other two studies cited are RCTs, with a total of 162 women. Both studies compared the intensity of perineal pain using tissue adhesive and polyglycolic acid 17 or polyglactin 910 [18]. There was reduction in pain during daily activities, and women who used tissue adhesive became pain free in a short period of time, as well as had earlier pain-free intercourse [17]. Mota *et al.* concluded that the incidence of pain in the first 30 days was similar with the use of tissue adhesive and suture. However, perineal skin closure using tissue adhesive is faster (4 minutes less; $p = 0.001$) than closure using subcuticular suture [18]. The two most recent studies are also RCTs performed in 202 women. However, these studies compared the use of octyl-2-cyanocrylate (Dermabond) and Vicryl Rapide in women with first-degree tears [8] and episiotomy [7]. Among women with first-degree tears, the cosmetic and functional results of adhesive glue use were not inferior to suturing ($p = 0.220$ and $p = 0.071$, re-

Table 3. — Pain (VNS), healing (REEDA), and women's satisfaction.

Step	n	EG		CG		Group	Step	Group x Step
		Mean (SD)	n	Mean (SD)	n			
Pain (VNS)								
1	10	0.4 (1.3)	10	2.4 (1.9)				
2	10	2.0 (2.3)	10	2.5 (2.7)				
3	10	0.8 (0.9)	10	2.5 (2.8)				
4	10	0.2 (0.6)	9	0.6 (1.1)				
Healing (REEDA)								
2	10	0.5 (1.0)	10	1.8 (1.4)				
3	10	0.6 (0.8)	10	1.2 (1.5)				
4	10	0.0	9	0.7 (1.0)				
Satisfaction (Likert-type)								
	VD	D	S	VS	VD	D	S	VS
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	10	-	-	4	6	10	-	1
		-	-	(40)	(60)		-	(10)
2	10	-	-	7	3	10	1	2
		-	-	(70)	(30)		(10)	(20)
3	10	-	-	3	7	10	-	1
		-	-	(30)	(70)		-	(10)
4	10	-	-	-	10	9	1	1
		-	-	-	(100)		(11.1)	(11.1)
							(55.6)	(22.2)

VD: very dissatisfied; D: dissatisfied; S: satisfied; VS: very satisfied; ^aLMM; ^bGEE.

spectively) at least six weeks after birth. Nevertheless, the use of adhesive glue was associated with a shorter procedure (3.29 vs. 7.88 minutes; $p < 0.001$), less need for local anesthetic (2.7% vs. 66%; $p < 0.001$), and less pain (score 1-10) than the use of sutures [8]. Among women with episiotomy, the mean time for skin closure with adhesive glue was less than that for closure with conventional skin suturing (1.16 vs. 3.52 minutes; $p < 0.05$); during and after the procedure, pain intensity was lower in the study group ($p < 0.05$) than that in the control group, and the healing time was approximately four days in the study group and approximately eight days in the control group. There was no statistically significant difference in the rate of wound complications and cosmetic results between the groups [7].

Another published study is a systematic review that included four RCTs and two quasi-RCTs, with 2,922 women with episiotomy or second-degree tear during birth [19]. The authors concluded that leaving the skin without suturing or the use of skin adhesives was more adequate in terms of pain and that more studies with a follow-up of at least six months, with a focus on long-term cosmetic results, are needed. It is important that new studies using tissue adhesive be performed and that midwives, nurse-midwives, and obstetricians be informed about the possibility of using this material. In this sense, this pilot study also served to raise professionals' awareness of the place of study. In addition to the outcomes analyzed by the cited literature, it is valid to consider the extent and depth of perineal tears in the evaluation of the effectiveness of the tissue adhesive.

It is also worth analyzing the cost-effectiveness of these products as an indication of the financial viability of their

wider use. Considering the results of this pilot study, a future RCT has been planned, and the pain scores were considered as the basis for the sample calculation.

According to the evolution of pain observed over time, the sample size needed to detect differences in the pain score is 70 women. For this calculation, the mean differences and standard deviations between the two groups were observed, and the number of participants necessary for there to be a statistically significant difference with a type I error of 5% and a test power of 95% was estimated.

Conclusion

This study shows that it is feasible to undertake an RCT on the use of the tissue adhesive Epiglu for first-degree perineal tears repair during normal birth that includes the same time of follow-up as well as the main outcomes and measures analyzed here: perineal pain and healing, satisfaction of women and time of repairing and other tears characteristics.

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