Tramadol Suppository versus Placebo for the Relief of Perineal Pain after Perineorrhaphy: A Randomized Controlled Trial in Thailand

Thanarat Srimaekarat MD*

** Department of Obstetrics and Gynecology, Trang Regional Hospital, Trang, Thailand*

Objective: *This randomized double-blinded control trial was conducted to compare the effectiveness of tramodol and placebo rectal suppository for the management of postpartum perineal pain after perineorrhaphy.*
Material and Method: *One hundred women who gave birth vaginally with episiotomy and a second- or third-degree tear, were randomly assign to receive two tablets of tramadol 50 mg or two tablets of placebo, the pill were physically similar to the real drug. Pain ratings were recorded immediately after perineorrhaphy, 30 minutes, and 1, 2, 6, 12 and 24 hours after first dose on a 10-cm visual analogue scale. Side effects and overall opinion were assessed.*
Results: *Tramadol and placebo had no statistical significances in analgesic properties, assessed by the means of pain rating at the different time intervals. There were no serious adverse events reported.*
Conclusion: *No differences were found in between Tramadol and placebo in relief perineal pain after perineorrhaphy.*

Keywords: *Tramadol, Rectal suppository, Perineal pain, Perineorrhaphy*

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Pain after episiotomy or tear of perineal tissues during childbirth is often inadequately treated and may be severe[1-3]. Research showed not less than 65% of women undergoing vaginal birth experienced perineal pain[4]. Not only did perineal pain negatively affect the physical and mental functioning of the woman, but also it might decrease the success of breastfeeding and reduced her ability to care for her child[5].

The methods of relieving perineal pain included medication and non-medication. When perineal pain was mild, the most common analgesic used was acetaminophen. Whereas, the perineal pain was more severe, other drugs had been chosen such as opioid, non-opioid, and a combination of both opioid and non-opioid analgesics. Opioid analgesics such as morphine and codeine acted centrally on the nervous system[5] and moderate to severe pain could be effectively treated[6]. Other opioids such as tramadol were widely used in the management of pain[7] and are particularly useful for moderate to severe postoperative pain control[8]. Assessing the safety of breastfeeding during maternal drug therapy required an individual risk-benefit analysis[9]. Recent research concluded that short-term maternal use of tramadol during establishment of lactation was compatible with breastfeeding[10]. Rectal route of tramadol might be another choice for management in post-episiotomy pain when the oral route was prohibited or unsuitable because some research showed that after rectal administration of the tramadol suppositories the absorption of the active ingredient was rapid enough for therapeutic levels and that the extent of the absolute bioavailability was higher than after oral administration of tramadol, possibly by reason of a reduced first-pass metabolism after rectal administration[11].

The aim of the present study was to compare tramadol and placebo rectal suppositories for relief of perineal pain following perineorrhaphy.

Material and Method

The randomized double-blinded controlled clinical trial was conducted to compare tramadol and placebo rectal suppository for the treatment of pain from perineal tear in childbirth after perineorrhaphy.

Correspondence to:
Srimaekarat T, Department of Obstetrics and Gynecology, Trang Regional Hospital, Trang 92000, Thailand.
Phone: 075-218-018, Fax: 075-218-831
E-mail: Thana_rat@hotmail.com

The present study took place at Trang Hospital, a tertiary-level teaching and referral center for Obstetric care, in Trang province, Thailand. Recruitment occurred from April to May 2010. Ethical approval for the present study was obtained from the institutional review board.

One hundred women who had completed full 37-weeks gestation, singleton, spontaneous vaginal delivery, second or third degree episiotomy tear, volunteered to participate in the present study and gave written consent. Exclusion criteria included history of allergy to investigated drug, regular use of analgesic drugs before or during pregnancy and any medical condition know to be potentially exacerbated by opioids, including hepatic and renal disease, as well as operative obstetrics. The subjects who had postpartum obstetric complications thereafter were considered to discontinue the trial.

After assessment for eligibility, the subjects were recruited and randomized to have two tablets of 50 mg tramadol (group A) or two tablets of placebo (group B) rectal suppositories. The investigated drug was placed at the rectal opening and gently pushed into the rectum. The clients and their caregivers were blinded as to group allocation.

The primary outcome for the present study was severity of pain, rated on a 10-cm visual analogue scale from 0 ("no pain") to 10 ("worst pain ever"). An initial rating was recorded before the subject took the first dose of drug, immediately after perineorrhaphy, 30 minutes, and 1, 2, 6, 12, and 24 hours after first dose. The study forms with the visual analogue scale on them were filled at the appropriate time by the postpartum nurse.

Secondary outcomes according to pain were assessed. The additional doses of analgesic drug, and its dosing, were accounted. If the clients indicated that the studied drug was inadequate and requested extra analgesia during the first 24 hours, the treatment was considered a failure.

Based on previous research performed by Dannecker et al[12], sample size calculation indicated that a sample of 35 subjects per arm was required to achieve 80% power with a type I error set at 0.05 to determine the reduction in mean pain scores at rest after episiotomy (first day post episiotomy) from 39 ± 28 mm to 20 ± 28 mm. The sample size calculation was made using Stata 9.0, Stata Corp, TX. The present research applied a sample of 50 subjects per arm.

All data analysis was performed using SPSS version 11.5. Data was expressed as mean $\pm$ standard deviation (SD) for continuous data and percentage for categorical data. Comparison of mean pain scores (SD) at difference time intervals (immediate, 30 minutes, 1, 2, 6, 12, and 24 hours after completion of perineorrhaphy) between the two groups were evaluated for the significance by unpaired t-test where appropriated for comparing between means. Chi-square test was used for categorical data. A p-value of less than 0.05 was considered significant difference.

Results

One hundred women were acceptable for enrollment in the present research. They were equally randomized allocated into two groups. Fifty women in each group were managed with either tramadol or placebo rectal suppositories. All women were tested for perineal pain level at immediate, 30 minutes, 1, 2, 6, 12, and 24 hours after completion of perineorrhaphy.

Pregnancy characteristics of tramadol and placebo group had no statistical differences, those accounted for the gestational ages of 38.40 ± 1.32 weeks and 37.92 ± 3.55 weeks, and the primigravida of 32 (64%) and 30 (60%), respectively.

Regarding the demographic features, there were no statistically significant differences in degree of vaginal tear, suture technique, and estimated blood loss between each group (Table 1). The unrequested extra analgesic drugs in tramadol and placebo groups were 39 and 32 women (p-value = 0.123), respectively. Comparison of mean pain scores at immediate and any of the time intervals after completion of perineorrhaphy between the two groups, almost all mean pain scores of tramadol management was less than mean pain scores of placebo but there were no statistical significant difference (Table 2).

Side effects, such as nausea and vomiting, nausea, constipation, headache, dizziness, dry mouth, sedation, asthenia, fatigue, sweating and rectal discomfort were not found in the research.

Discussion

The analgesic activity of tramadol administration has not been different between oral and rectal route[13]. In general, tramadol suppositories, 100 mg, showed poor pain relief in 10 of 55 subjects when compared with the acetaminophen or indomethacin suppositories for post-abortion pain relief[14].

There was no statistical difference of mean pain scores at immediate and any of the time intervals in the present study. The possible explanation is the maximum of the serum concentration curves were reached 2-6 h after rectal administration. The

Table 1. Maternal variables (means and standard deviation) and perineorrhapy variables (numbers and percents)

Variables	Tramadol group A (n = 50)	Placebo group B (n = 50)	p-value
Maternal age (year ± SD)	25.94 ± 5.69	24.44 ± 5.87	NS
Weight (kg ± SD)	64.26 ± 10.88	62.89 ± 9.96	NS
Height (cm ± SD)	157.00 ± 6.40	157.92 ± 5.99	NS
Degree of tear			
2nd degree	48 (96%)	47 (94%)	0.646
3rd degree	2 (4%)	3 (6%)	
Suture technique			
Continuous	48 (96%)	47 (94%)	0.663
Interrupted	2 (4%)	3 (6%)	
Blood loss (ml ± SD)	228.00 ± 55.49	244.96 ± 56.12	0.135

NS = no statistically significant difference

Table 2. Mean pain scores at difference interval after perineorrhaphy

Interval	Mean pain score (SD)		p-value
	Tramadol group A n = 50	Placebo group B n = 50	
Immediate	2.72 (2.26)	3.48 (2.18)	0.091
30 minutes	2.54 (1.99)	3.10 (2.31)	0.198
1 hour	2.38 (1.94)	3.08 (2.14)	0.091
2 hours	2.38 (1.51)	2.84 (1.46)	0.125
6 hours	2.16 (1.13)	2.66 (1.43)	0.056
12 hours	2.10 (1.21)	2.48 (1.47)	0.163
24 hours	2.04 (1.22)	1.72 (1.35)	0.219

multiple doses should be recommended to achieve the therapeutic effect[11].

In conclusion, no differences were found between Tramadol and placebo in relief of perineal pain after perineorrhaphy.

Potential conflict of interest

None.

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ยาทรามาดอลสอดทวารหนักเปรียบเทียบกับยาหลอกในการลดความเจ็บปวดแผลฝีเย็บภายหลังการเย็บแผลฝีเย็บ

ธนะรัตน์ ศรีเมฆารัตน์

วัตถุประสงค์: *การศึกษาควบคุมยาหลอกสุ่มอิสระปิดบังสองทางนี้เพื่อประเมินประสิทธิภาพของยาทรามาดอลสอดทางทวารหนักในการลดความเจ็บปวดแผลฝีเย็บ ภายหลังการเย็บแผลฝีเย็บ*

วัสดุและวิธีการ: *สตรีตั้งครรภ์เดี่ยวครบกำหนดจำนวน 100 ราย ที่คลอดบุตรปกติทางช่องคลอดซึ่งมีบาดแผลบริเวณฝีเย็บที่เกิดจากการตัดฝีเย็บโดยมีระดับความรุนแรงของบาดแผลระดับ 2 หรือ 3 จะถูกแบ่งออกเป็น 2 กลุ่ม แบบสุ่มอิสระปิดบังสองทางเพื่อรับยาทรามาดอลขนาด 50 มิลลิกรัม หรือยาหลอกอย่างละ 2 เม็ด สอดทางทวารหนักภายหลังการเย็บแผลฝีเย็บเสร็จทันที สตรีคลอดบุตรดังกล่าวจะได้รับการประเมินความเจ็บปวดด้วย visual analogue score ภายหลังการเย็บแผลฝีเย็บเสร็จทันที และเมื่อ 30 นาที, 1, 2, 6, 12, และ 24 ชั่วโมง พร้อมประเมินผลข้างเคียงจากยา*

ผลการศึกษา: *ยาทรามาดอลและยาหลอกไม่มีความแตกต่างทางสถิติในคุณสมบัติระงับปวด ประเมินด้วยค่าเฉลี่ยระดับคะแนนความเจ็บปวดในช่วงเวลาต่าง ๆ ไม่พบข้างเคียงรุนแรงจากยา*

สรุป: *ไม่มีความแตกต่างระหว่างยาทรามาดอลและยาหลอก ในการลดความเจ็บปวดแผลฝีเย็บภายหลังเย็บแผลฝีเย็บ*