Obstetrical and Pediatric Anesthesia

Intravenous tenoxicam reduces uterine cramps after Cesarean delivery

[Le ténoxicam intraveineux réduit les crampes utérines à la suite d'une césarienne]

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Purpose: Postpartum uterine contraction pain is a common phenomenon after Cesarean delivery. We investigated the effectiveness of tenoxicam in reducing uterine contraction pain.

Methods: We enrolled 120 consecutive non-breastfeeding women who were scheduled for elective Cesarean delivery. After the administration of spinal anesthesia with bupivacaine and intrathecal morphine 0.15 mg injection, the patients were randomly divided into two groups. Group I received placebo (normal saline) *iv* injection, and Group II received tenoxicam 40 mg *iv* injection after clamping the umbilical cord. Verbal analogue scale of wound pain and uterine contraction pain were recorded at two, four, eight,16, and 24 hr after Cesarean delivery.

Results: There was no significant difference in wound pain scores between the two groups (all scores ≤3). However, the tenoxicam group had significant lower uterine contraction pain scores and required less supplemental meperidine medication than did the placebo group (8.5% *vs* 41.4%, $P < 0.05$). The incidences of nausea or vomiting, pruritus, and bleeding were not significantly different between groups.

Conclusion: Intravenous tenoxicam 40 mg significantly reduced the intensity of uterine cramps in patients undergoing Cesarean delivery without increasing side effects.

Objectif : *La douleur des contractions utérines du postpartum est un phénomène fréquent après la césarienne. Nous avons vérifié l'efficacité du ténoxicam à réduire ces douleurs.*

Méthode : *Nous avons recruté 120 femmes qui devaient subir une césarienne non urgente et qui ne devaient pas allaiter leur bébé. Après la rachianesthésie avec de la bupivacaïne et une injection intrathécale de 0,15 mg de morphine, nous avons formé deux groupes. Les patientes du Groupe I ont reçu un placebo (soluté physiologique) iv et celles du Groupe II 40 mg iv de ténoxicam après le clampage du cordon ombilical. L'échelle verbale analogique a servi à enregistrer la douleur postopératoire liée à l'incision et aux contractions utérines à deux, quatre, huit, 16 et 24 h.*

Résultats : *Les scores de douleurs liées à l'incision n'ont pas différé d'un groupe à l'autre (tous les scores ont été ≤ 3). Par ailleurs, dans le groupe ténoxicam, les scores liées aux contractions utérines ont été plus bas et les demandes d'analgésie supplémentaire avec mépéridine moins importantes que dans le groupe placebo (8,5 % vs 41,4 %, $P < 0,05$). Nausées, vomissements, prurit ou saignements n'ont pas présenté de différence intergroupe significative.*

Conclusion : *Une dose intraveineuse de 40 mg de ténoxicam a réduit significativement l'intensité des crampes utérines sans causer d'effets secondaires à la suite d'une césarienne.*

POSTPARTUM uterine contraction pain is a very common problem and can evoke a generalized neuroendocrinal stress response producing widespread physiological effects.[1] Intrathecal injection of morphine is well established for the management of postoperative pain,[2] but it has limited effect in relieving uterine cramps.[3] However, nonsteroidal anti-inflammatory drugs (NSAIDs) cannot only provide postoperative analgesia[4–6] but also relieve the discomfort of uterine cramps after vaginal delivery.[7–10]

Tenoxicam (Tilcotil®; Roche), a long-acting NSAID, is commonly used for the treatment of rheumatoid arthritis,[11] osteoarthritis,[12,13] acute gout,[14]

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and other extra-articular diseases. The potentially beneficial effect of *iv* tenoxicam on uterine cramps after Cesarean delivery remains unknown. Therefore, we studied 120 women undergoing elective Cesarean delivery. The effectiveness of pain relief, reduction of cramps and the incidence of side effects of *iv* tenoxicam were recorded.

Methods

A prospective, double-blinded, randomized, placebo-controlled study was designed and approval was obtained from the hospital Ethical Committee. Informed consent was obtained from all patients before the study. One hundred twenty ASA I/II consecutive non-breastfeeding women who were scheduled for elective Cesarean section were studied. Patients with impaired liver or renal function, gastritis, gastric or duodenal ulcers, abnormal bleeding tendency, and known history of allergy to salicylates or NSAIDs were excluded from the study.

All patients received an infusion of Ringer's solution 1000 mL before induction of spinal anesthesia. After placement of standard monitors (electrocardiograph, automated arterial blood pressure, and pulse oximetry), spinal anesthesia was performed with a 27-gauge Whitacre needle via the L2–3 or L3–4 interspace. All patients received 1.8 mL to 2.2 mL of 0.5% hyperbaric bupivacaine (dosage adjusted according to body height) for spinal anesthesia and preservative-free morphine 0.15 mg for postoperative pain control. Sensory anesthesia (determined by pinprick) extending to the T–4 dermatome was achieved.

The patients were randomly divided into two groups. After the umbilical cord was clamped, *iv* ergonovine 0.2 mg was given. Group I received an infusion of oxytocin 10 units and placebo (normal saline) in 500 mL of Lactate Ringer's solution, and Group II received an infusion of oxytocin 10 units and tenoxicam 40 mg[15] in 500 mL of Lactate Ringer's solution. An anesthesiologist, blinded to the treatment groups, was responsible for visiting the patients to record pain scores at two, four, eight, 16 and 24 hr after Cesarean section. Patients were asked to rate the intensity of wound pain and uterine contraction pain on a 10-cm analogue scale, which ranged from 0 for no pain to 10 for the worst pain imaginable. Wound pain was defined as continuous abdominal pain, and uterine contraction pain was defined as intermittent, short lasting, cramping pain which might be unrelated to the surgical side. The postoperative supplemental analgesic regimen was standardized. *IM* meperidine 50 mg every four hours at the patient's request was prescribed. Side effects such as nausea or vomiting or both, and pruritus were managed with diphenhydramine (30 mg *im*). The surgeon evaluated uterine relaxation and decided if repeated doses of oxytocin were needed. We recorded the incidence of bleeding and bleeding was regarded as abnormal when the obstetrician decided to use additional oxytocin to increase uterine tone. Vaginal blood loss, estimated from nursing inspection of the perineal pad, was graded as small, moderate, or large.

TABLE I Clinical characteristics of patients

	Placebo group (n=59)	*Tenoxicam group (n=58)*
Age (yr)	31 ± 5	30 ± 6
Body height (cm)	158.2 ± 6.5	159.3 ± 5.7
Body weight (kg)	68.6 ± 2.4	70.7 ± 2.0
Parity: nulliparous/multiparous	16/43	21/37

Data are presented as mean ± SD. The χ^2 test was used to test associations among dichotomous parameters, and Yate's correction was used when necessary. Analysis of variance was used to compare continuous variables between groups. A P value < 0.05 was considered statistically significant.

Results

There were no significant differences between the two groups with regard to age, weight, height, and parity (Table I). Three patients (one in the placebo group and two in the tenoxicam group) were excluded because they could not make the difference between uterine contraction pain and wound pain. The results showed that the mean wound pain scores at two, four, eight, 16 and 24 hr in the tenoxicam group were not significantly different from those in the placebo group (all scores ≤3; Figure 1). However, the mean uterine contraction pain scores of the tenoxicam group at two, four, eight, 16, and 24 hr were significantly lower than those of the placebo group (Figure 2). In the 24-hr postoperative period, 8.5% of patients (5/58) in the tenoxicam group and 41.4% of patients (24/59) in the placebo group required meperidine treatment ($P < 0.05$).

The incidences and severity of nausea or vomiting, and pruritus were not higher in the tenoxicam group than in the placebo group at 24 hr after operation (Table II). Assessment of blood loss or the need for oxytocics either intra- or postoperatively was not different in patients receiving tenoxicam. The surgeon's assessment of uterine relaxation also indicated that there was no difference between the two groups.

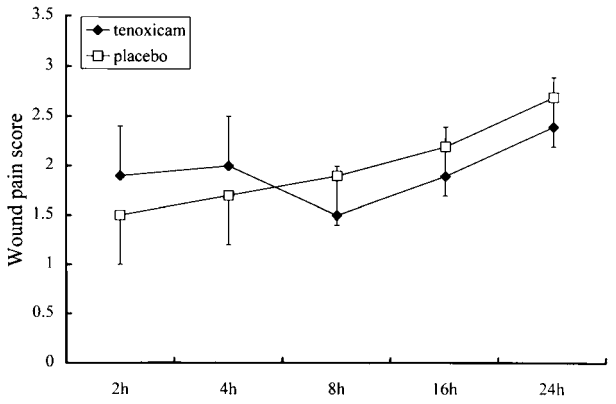

FIGURE 1 Wound pain scores in the two groups. No differences were found between tenoxicam and placebo.

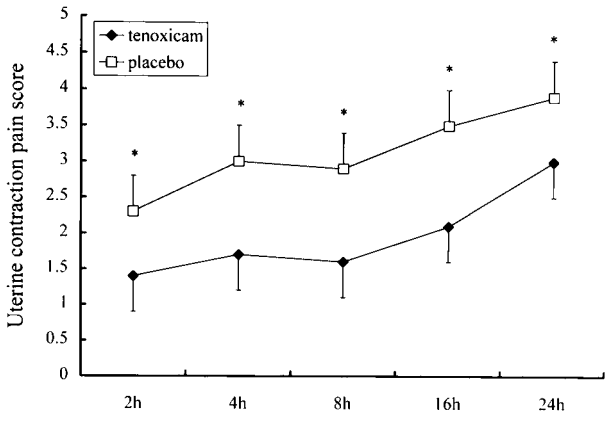

FIGURE 2 Uterine contraction pain scores in the two groups. *$P < 0.05$ tenoxicam group *vs* placebo group.

TABLE II Analgesic requirements and side-effects

	Placebo group (n=59)	*Tenoxicam group (n=58)*
Percentage that required meperidine (%)	41.4 (24/59)*	8.5 (5/58)
Nausea/vomiting	10/59 (16.9%)	12/58 (20.7%)
Pruritus	50/59 (84.7%)	47/58 (79.7%)
Bleeding	0	0

*$P < 0.05$ placebo group *vs* tenoxicam group.

Discussion

In the management of postCesarean analgesia, intrathecal morphine has remarkable efficacy in relieving incisional pain, but is ineffective for pure uterine contraction pain. This may be due to the fact that uterine contraction pain involves several chemical nociceptive mediators such as bradykinins, leukotrienes, prostaglandins, serotonin, lactic acid and substance P.[1] Its mechanism might be mediated by a second messenger-prostaglandin system[16] that can be inhibited by aspirin-type anti-inflammatory analgesics. Studies have shown that the analgesic efficacy of NSAIDs could reduce opioid consumption after Cesarean delivery.[17–19] However, wound pain and uterine contraction pain are qualitatively different. Our study demonstrates that the analgesic effect of *iv* tenoxicam can reduce the intensity of postpartum uterine contraction pain. Theoretically, tenoxicam can also reduce wound pain, but this was not the case since mean wound pain scores were not different between groups. This was probably due to the profound analgesic efficacy of intrathecal morphine (0.15 mg) in relieving incisional pain (all pain scores $\leq$ 3).

Tenoxicam, a NSAID, has a marked analgesic effect directed selectively against pain induced by inflammatory or traumatic processes.[20] It is less ulcerogenic, lacks tinnitus, dizziness, or gastro-intestinal side-effects and is tolerated better than aspirin.[20,21] Reports have shown the analgesic effect of *iv* ketoprofen and diclofenac for the treatment of pain after Cesarean delivery.[17] However, the half-life of ketoprofen is five to six hours and that of diclofenac is 1.5 hr,[22] indicating that repeated doses may be needed. Tenoxicam specifically inhibits prostaglandin synthetase and has a long plasma half-life (75 hr) allowing once daily dosage.[21] Furthermore, tenoxicam can be administered parenterally. This route is preferred to *im* and rectal routes. Oral administration may be unsuitable in the early postoperative period. In addition to inhibition of platelet aggregation and thromboxane production, NSAIDs may increase postpartum uterine bleeding[23] but no evidence of increased postoperative blood loss was found in our study.

In conclusion, tenoxicam (40 mg *iv*), a long acting NSAID that induces analgesia by inhibiting peripheral prostaglandin synthesis, reduced postpartum uterine contraction pain without adverse effects. Further studies should evaluate analgesic effects *vs* side effects of *iv* tenoxicam as a function of dosage.

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