

Comparison the Analgesic Effects of Single Dose Administration of Tramadol or Piroxicam on Postoperative Pain after Cesarean Delivery

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Abstract- A multimodal approach to postcesarean pain management may enhance analgesia and reduce side effects after surgery. We investigated postoperative pain in a double-blinded, randomized, single-dose comparison of the monoaminergic and μ -opioid agonist tramadol, 100 mg (Group T) and piroxicam 20 mg (Group P) given IM alone- single dose in 150 patients who had elective cesarean delivery. All patients were assessed at 0, 6, 12 and 24 hours post operation for pain degree (by Visual Analogue Score: VAS 1-10), nausea and vomiting. Pain degree was classified as: Painless: 0, Mild: 1-4, Moderate: 5-8, Severe: 9-10. There was no significant difference between the efficacy of tramadol and piroxicam injections ($P>0.05$). Pain intensity decreased markedly over time in both groups. Mean \pm SEM pain degrees were as follows: P=7.7 \pm 0.5, T=8.2 \pm 0.8 after 0 hours; P=5.4 \pm 0.6, T=6.1 \pm 0.5 after 6 hours; P=3.3 \pm 0.4, T=3.4 \pm 0.7 after 12 hours; P=1.1 \pm 0.4, T=1.3 \pm 0.5 after 24 hours of surgery. Side effects were similarly minimal with all treatments. It might be concluded that i.m. injections of 20 mg piroxicam (single dose therapy) could relieve postoperative pain after cesarean section as well as tramadol and it could reduce opioid analgesic requirements with less adverse side effects during the first postoperative 24 h.

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Key words: Tramadol; piroxicam; pain, postoperative; cesarean section

Introduction

Postoperative analgesia comparable with that of opioids has been demonstrated with the non-steroidal anti-inflammatory drugs (NSAIDs) (1,2). μ -Opioidergic and monoaminergic (5-hydroxytryptamine and noradrenalin) pathways and prostaglandin-dependent mechanisms are individually important in the modulation of pain (3). An opioid sparing effect has also been observed NSAIDs, as well as a reduction in opioid induced nausea, vomiting and respiratory depression. This reduction in opioid requirement and side effects may benefit the patient by producing increased postoperative analgesia and even, reduce hospital stay (4). By inhibiting the enzyme cyclooxygenase and preventing the central and peripheral synthesis of prostaglandins, NSAIDs reduce the inflammatory component of pain generation and also effectively relieve uterine contraction pain in the postpartum period and after cesarean delivery (5). They may reduce both wound and uterine cramping pain (6,7).

Prostaglandins are released from damaged tissue and directly sensitize peripheral nociceptors, and they also play a role in primary and secondary hyperalgesia (8). Piroxicam, an oxycam, is a nonselective COX inhibitor but at high concentrations, it also inhibits polymorphonuclear leukocyte migration, decreases oxygen radical production, and inhibits lymphocyte function. Its long half-life allows once-daily dosing. Piroxicam can be used for the usual rheumatic indications and post operative pain. Toxicity includes gastrointestinal symptoms (20% of patients), dizziness, tinnitus, headache, and rash (9). Piroxicam is one of the most current NSAIDs available for reducing postoperative pain in Iran and is a popular choice in this setting. Tramadol is a centrally acting analgesic with both opioid and non-opioid modes of action (10,11) and has been used for the relief of acute and chronic pain (12,13). It is an effective postoperative analgesic and can be used for a much longer time than morphine. Unfortunately, the widespread use of tramadol for

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patient-controlled analgesia (PCA) is hindered by its major adverse effects of nausea and vomiting (12-14). Many different classes of NSAIDs and routes of administration are available. However, an intramuscular preparation is favored as rectal drug administration is unpopular with many postpartum women, and in the early postoperative period oral administration may be unsuitable. The aim of this double-blinded, randomized trial was to investigate the comparative effects of single doses of tramadol (100 mg) and piroxicam (20 mg) alone in the management of postcesarean pain in women who had elective cesarean delivery.

Patients and Methods

Two-hundred patients between 18 and 40 and scheduled for elective low-risk cesarean delivery prospectively entered in this randomized, double-blinded study. Exclusion criteria included known allergy to piroxicam or tramadol, a history of peptic ulcer disease or gastrointestinal bleeding, opioid use over the past month, inability or unwillingness to give written informed consent, preeclampsia or eclampsia, significant pulmonary disease, intraoperative complications, modified surgical procedure, or deviations from the standardized anesthetic regimen. Before surgery patients were divided to one of the two following treatment groups using a computerized randomization list: T group receiving tramadol 100 mg (Biomadol®; Bakhtar Bioshimi pharmaceutical company, Kermanshah, Iran) and P group receiving piroxicam 20 mg (Darou Pakhsh Pharmaceutical Company, Tehran, Iran) as a single dose. Identical and coded placebo ampoules were prepared in Faculty of Pharmacy. Preoperative and anesthetic procedures were standardized. Patients received no opioid or NSAID premedication. After surgery, tramadol or piroxicam was given in buttock in T and P groups respectively. All patients were assessed at 0, 6, 12 and 24 hours post operation, for pain degree (by visual analogue score, VAS 1-10), nausea and vomiting. Pain degree was classified as: Painless: 0, Mild: 1-4, Moderate: 5-8, Severe: 9-10. Results are expressed as mean±SEM. The one-way analysis of variance (ANOVA) followed by the Tukey's post-test was used to analyze the data using the SPSS software (version 8.0; Chicago, IL, USA). $P < 0.05$ was the critical criterion for statistical significance.

Results

Two-hundred consecutive patients were screened for inclusion of 150 patients in this study. Exclusion reasons

were postponement of operation ($n = 15$), inadvertent intraoperative use of opioids ($n = 7$) or other analgesics ($n = 8$), vaginal delivery ($n = 5$), and other miscellaneous pre- or intraoperative reasons ($n = 15$). No patient withdrew their consent during the study. Seventy-five patients in each of the two treatment groups were therefore eligible. Details of exclusion reasons are shown in Table 1. Mean±SEM pain degrees, shown in Figure 1, are as follows: $P=7.7\pm0.5$, $T=8.2\pm0.8$ after 0 hours; $P=5.4\pm0.6$, $T=6.1\pm0.5$ after 6 hours; $P=3.3\pm0.4$, $T=3.4\pm0.7$ after 12 hours; $P=1.1\pm0.4$, $T=1.3\pm0.5$ after 24 hours of surgery. The overall drug effect was highly significant by ANOVA ($P < 0.01$). The differences between tramadol and piroxicam were not significant ($P > 0.05$). Nausea and vomiting rates were assessed in all treatment groups at each time point over the 24-h period. Nausea was reported in three patients with tramadol and two patients with piroxicam. Vomiting occurred in four patients with tramadol and two patients with piroxicam. There were no significant group differences in the incidences of nausea and vomiting.

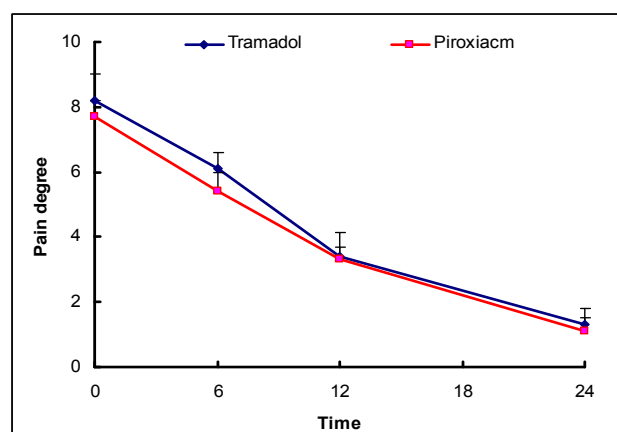


Figure 1. Pain degree in 150 patients after injection of tramadol 100 mg or piroxicam 20 mg. Values are mean ± SEM.

Table 1. Exclusion Reasons in 200 consecutive patients

Detail	N
postponement of operation	15
use of opioids	7
other analgesics	8
vaginal delivery	5
other miscellaneous pre- or intraoperative reasons	15
Total	50

Opioids or NSAIDs

Sleepiness or drowsiness in the 24 postoperative hours was reported in 35 patients with tramadol and 22 patients with piroxicam. Other slight side effects were reported in ten and twelve patients, respectively. There were no serious side effects throughout the study.

Discussion

Cesarean delivery is a major surgical procedure, after which substantial postoperative discomfort and pain can be anticipated (15). The provision of effective postoperative analgesia is of key importance to facilitate early ambulation, infant care, (including breast feeding, maternal-infant bonding) and prevention of postoperative morbidity (15). The analgesic regimen needs to meet the goals of providing safe, effective analgesia, with minimal side effects for the mother and her child. Since postsurgical pain treatment relies on the subjective nature of the patient's pain perception, new methods of pain treatment have been developed such as continuous epidural analgesia or patient-controlled analgesia. These methods have partially replaced the more traditional approach of on-demand parenteral administration of opioids (16,17). However, these new technologies are not available in many hospitals since they are expensive and require trained personnel and special equipment (18,20). Furthermore, various adverse effects of these medications have been reported (17,21,22). Cesarean sections differ from other major laparotomies because women are expected to recover expeditiously and to care for their newborns within a few hours following the operation. Therefore, women after cesarean section are reluctant to feel sleepy, drowsy or restricted by equipment that does not allow them free access to attend to their babies and these are the most common side effects of opioid analgesics (23). Various attempts have been made to improve postoperative pain relief by non-opioids to avoid adverse effects such as respiratory depression (24). Non-steroidal anti-inflammatory drugs (NSAIDs) like oxicams and diclofenac widely used in ambulatory surgery are beneficial in mild to moderate pain and have a well recognized opioid sparing role and effective when administered pre-, peri- and post-operatively (25-27). Previous studies have shown tramadol is an effective postoperative analgesic (13,14,28,29). The additive analgesic effects of opioids and NSAIDs are well documented (30,31). Opioids can reduce postoperative sensitization, especially secondary hyperalgesia and allodynia, and can also increase pain thresholds in non-operative settings (32-39). The differences between

tramadol and piroxicam were not significant ($P > 0.05$). Tramadol was tolerated similarly as well as piroxicam, and no significant increases in side effects were seen. Overall rates of gastrointestinal complaints were small. It should be noted that this study was designed to investigate analgesic and nociceptive effects, and not differences in side effects. In a previous study, diclofenac after cesarean delivery improved analgesia and had a highly significant morphine-sparing effect (40). In another study, the parenteral combination of tramadol and diclofenac resulted in more prolonged and pronounced postoperative analgesia and reduced sensory sensitization compared with the single drugs, with no increase in side effects (34). Another study shows the combination of IV ketorolac with meperidine after cesarean delivery resulted in an opioid dose-sparing effect of approximately one-third in the first 24 hours postoperatively. It did not, however, improve the quality of analgesia or influence postoperative recovery, nor did it reduce opioid-induced side effects (41). Rectal diclofenac provides effective analgesia when given after cesarean section. It also reduces the patients opioid requirements with a corresponding reduction in the opioid related side-effects (42). A single administration of 100 mg diclofenac suppository is effective in reducing post-Cesarean epidural local anesthetic/opioid requirements by 33% for the first 24 hr post-operatively (43).

Results from a study indicate that epidural tramadol 100 mg can provide adequate postoperative analgesia without respiratory depression in patients after Cesarean delivery (44). In An uncontrolled trial, the use of indomethacin rectal suppositories resulted in a significant reduction in narcotic use in the postcesarean hospital recovery period as measured in morphine equivalents (45).

Some studies failed to demonstrate significant analgesic efficacy of valdecoxib (COX-2 inhibitors) compared with placebo and morphine (46). Another study shows that prophylactic granisetron does not prevent postdelivery nausea and vomiting during elective cesarean delivery under spinal anesthesia (47). Jamal et al. concluded that intravenous acetaminophen (as a non-opioid analgesic) is a reasonable alternative to oral ibuprofen as an adjunct to morphine patient-controlled analgesia after cesarean delivery (48). Harnett et al. discussed that receiving intrathecal morphine during cesarean delivery can induce nausea and vomiting and scopolamine is an effective medication for prophylactic use in this case (49). Since cyclooxygenases are involved in the regulation of several central nervous

system processes (50), it is possible that piroxicam acts through the inhibition of one of these processes.

In conclusion, NSAIDs like piroxicam that are devoid of adverse side effect of opioids, seem appropriate for reducing the use of opioids like tramadol in management of pain in cesarean surgeries.

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Opioids or NSAIDs

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