

Comparative study of intravenous opioid consumption in the postoperative period

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Background. Intravenous patient-controlled analgesia (IV PCA) using opioids is an accepted method for delivering postoperative analgesia. The aim of this study was to compare fentanyl and tramadol with IV PCA after spinal anesthesia (SA) and general anesthesia (GA) following cesarean section (C/S).

Methods. Ninety women were randomly assigned to three groups (n=30). Group 1 was treated with IV fentanyl PCA after SA. Groups 2 and 3 were treated with IV fentanyl PCA and IV tramadol PCA after GA. Outcome measures were recorded for the first 24 h post-anesthesia.

Results. PCA use was significantly lower after SA ($P < 0.05$). Eighteen patients in the SA Group and 27 patients and 24 patients from the GA groups required additional opioid. Opioid consumption and patient satisfaction were similar for groups after GA ($P > 0.05$). 638.4 ± 179.1 μ g fentanyl was consumed by patients of Group 2, 356.3 ± 87.0 μ g fentanyl and 559.5 ± 207.0 mg tramadol was consumed by Group 1 and Group 3 respectively. There was no significant difference in the overall severity and incidence of nausea, drowsiness or pruritus.

Conclusion. Our study shows that analgesic consumption and post-operative pain scores after SA in C/S decreased, without increase in adverse reactions.

Key words: patient-controlled analgesia, fentanyl, tramadol, spinal anesthesia

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INTRODUCTION

Acute pain control can improve the quality of life in patients undergoing elective C/S (ref.¹). Laparotomy is associated with a severe pain especially in the first 6 h of the postoperative period. Opioid administration is the mainstay of pain management in these patients. To date, IV PCA, epidural PCA, infiltration analgesia or IV analgesia at intervals with different opioid regimens are the best known techniques². PCA allows patients to control their own pain as small predetermined doses of analgesic medication within the limits prescribed by their physician, resulting in pain relief and patient satisfaction^{3,4}. Fentanyl is frequently preferred because of its high lipid solubility resulting in rapid onset of analgesia, low incidence of side-effects and low risk of delayed respiratory depression⁵. Tramadol also provides effective analgesia and has a low risk of respiratory depression⁶. SA is commonly used in C/S because of its rapid onset of anesthesia and analgesia but when the SA analgesia wears off, IV PCA is an effective and safe way to maintain the postoperative analgesia.

The main goal of this randomized, prospective study was to evaluate the efficacy and side-effects of PCA with IV fentanyl or tramadol in patients undergoing C/S. Additionally we compared the GA with the SA method

on postoperative analgesic consumption during the first 24 h postoperative.

MATERIALS AND METHODS

With the local ethics committee approval, ninety patients undergoing elective C/S were enrolled in this randomized, prospective study. All patients gave informed consent. Exclusion criteria included contraindications to neuraxial anesthesia (patient refusal, coagulation defects, intracranial masses, use of acetylsalicylic acid in the last ten days, skin infection on interprice location, lumbar disc herniation, peripheral neuropathy), allergy to local anesthetics or opioids, history of chronic pain, American Society of Anesthesiologists (ASA) ≥ 3 , inability to understand how to use the PCA device, age < 18 years. Surgeries were performed by one of three surgeons. Patient monitoring included finger pulse oximetry, electrocardiogram and non-invasive blood pressure. A peripheral IV line was inserted into all patients for all needed medication and PCA was connected to patients' IV line after surgery. The patients were informed about the method of anesthesia, the use of the PCA system and standard visual analogue scale (VAS) for pain, the day before the surgery. 0 meant

“No pain” and 100 meant “Worst possible pain imagined”. The participants who accepted SA included Group 1 ($n=30$) who were treated with fentanyl IV PCA. The patients in GA groups were randomized to the fentanyl PCA (Group 2, $n=30$) or the tramadol PCA (Group 3, $n=30$) groups. All GA patients were premedicated with atropine 0.5 mg in 45 min before the surgical procedure. SA was performed through the fourth lumbar interspace using a 25 gauge Quincke needle (Excel Int, 72 mm) in a sitting position. Each participant in Group 1 received an intrathecal injection of 1.8 ml 0.5% isobaric bupivacaine with 20 μg fentanyl. GA was induced by thiopental 5 mg kg^{-1} and atracurium 0.5 mg kg^{-1} . Fentanyl 2 μg kg^{-1} was given IV and anesthesia was maintained by sevoflurane with an end-tidal concentration 1.5% in oxygen–nitrous oxide ($\text{FI}_{\text{O}_2} = 0.5$). Isotonic saline infusion was used for intraoperative fluid maintenance.

Postoperatively, patients received a PCA setting of a bolus of 20 μg fentanyl or 20 mg tramadol with a 10 min lockout interval time without basal infusion. The solution was prepared as 1 mg of fentanyl or 1000 mg of tramadol diluted in 100 ml of isotonic saline. During follow up, if the VAS score of the patient was above 30, the physician in charge gave a bolus of 2 ml solution without changing the bolus dose and lockout interval time of the PCA set. 2 ml was equal to 20 μg fentanyl in Groups 1 and 2 and 20 mg tramadol in Group 3. Respiratory rate, heart rate, systolic and diastolic blood pressure were all measured before and during surgery. Side-effects such as pruritus, nausea and vomiting were recorded: 0= no episode; 1= at least one episode. Nausea and vomiting were treated by metoclopramide 10 mg IV. Pruritus was treated with diphenhydramine 25 mg IV. All patients received paracetamol 1g IV postoperatively every six h as prophylactic analgesic.

After SA, the patients in Group 1, first began to receive analgesic medication via PCA when they started to feel pain. The patients in Group 2 received a bolus dose of 1 μg kg^{-1} fentanyl and Group 3 received 1 mg kg^{-1} tramadol immediately after the surgical procedure in the recovery room. However opioid administration for all groups was started following a value of VAS more than 30. The intensity of pain was assessed at 0, 1, 2, 4, 8, 12 and 24th h using the 100 point of VAS. Then the records of pain scores were noted.

All patients were interviewed at the end of 24th h by a blinded interviewer. They were questioned about whether they would accept the same anesthetic procedure in future. Complaints about the anesthesia technique were noted as the criteria for satisfaction.

Statistical Package for Social Sciences (SPSS) for Windows 10,0 programme was used for the statistical analysis. Group size was selected by using proportions sample size estimates (α : 0.05, β : 0.05). The power value of this study was 0.95. The values were expressed as mean \pm SD. One way ANOVA test was used for comparisons between groups for normal distributed parameters, and the Friedman test was used for nonnormally distributed parameters. The post-hoc test was Tukey-Kramer Multiple Comparisons Test. Qualitative datas were compared by using χ^2 test. A $P < 0.05$ was considered significant.

RESULTS

Ninety one patients who underwent elective C/S were enrolled in the study. 60 patients preferred GA and 31 requested local anesthesia. One patient in Group 1 was excluded from the analyses because of failure to perform the block and the participant was given an intraoperative bolus of propofol with muscle relaxant and fentanyl. Patients' age, weight, height, ASA physical status and surgery time were comparable (Table 1). There were no major anesthetic or surgical complications. Less postoperative fentanyl was required in the SA group than the GA groups. 638.4 ± 179.1 μg fentanyl was consumed by patients of Group 2, 356.3 ± 87.0 μg fentanyl and 559.5 ± 207.0 mg tramadol was consumed by Group 1 and Group 3 respectively during the first 24 h (Fig. 1). The number of patients requiring opioids in the first 24 h was significantly higher in both the GA groups than the SA group. There was no statistical difference between the GA groups. Postoperative opioid consumption, additional analgesic needs and side-effects were all similar ($P > 0.05$). 18 patients (60%) in Group 1 required additional opioid and 27 patients (90%) in Group 2 and 24 (80%) patients in Group 3 received additional opioid bolus dose during the first 24 h (Fig. 2). The patients received the bolus dose via PCA when the VAS score was above 30. Pain scores in the postoperative period were lower for the spinal group than the GA groups (Table 2). Pain scores differed significantly among groups at 1st ($P=0.008$), 2nd ($P=0.003$), 4th ($P=0.008$), 8th ($P=0.004$), 12th ($P=0.0001$) h. The values were lower in Group 1 than Groups 2 and 3. The values of Groups 2 and 3 were similar. However, there was no significant difference between groups at the 24th h ($P > 0.05$). There was a significant difference in the duration of analgesia between groups. The mean time interval to the first request for administration of analgesic in Group 1 was 5.20 h, in Group 2 3.03 h and in Group 3 2.03 h. Group 1 had significantly longer duration without analgesics ($P < 0.05$). Postoperative nausea and vomiting scores were similar ($P > 0.05$). Three patients who got spinal anesthesia complained of time-limited itching. Anti-emetics were necessary for two patients from the GA groups and for four patients from Group 1.

Twenty-eight patients from Group 1 were pleased with the spinal block technique. One patient complained about the difficulty of peroperative respiration and oxygen support via face mask was given. One patient complained about the length of motor blockade about 4 h. In total 12 patients from Groups 2 and 3 reported that they would choose SA next time. Five said that they wanted to see the surgical procedure or hear their baby's first cry. The others complained about the pain that they felt in the recovery room.

DISCUSSION

Neuraxial anesthesia has many advantages such as reducing morbidity and mortality, compared to GA for elective C/S (ref.⁷). In several clinical trials, it was con-

Table 1. Patients' demographics and duration of surgery (Values are mean \pm SD).

	Group 1	Group 2	Group 3
Age (year)	27.9 \pm 10.6	29. \pm 9.3	29 \pm 11.8
Weight (kg)	75.3 \pm 7.7	77.2 \pm 8.1	76.4 \pm 7.4
Height (cm)	163.4 \pm 4.2	163.7 \pm 4.5	162.7 \pm 4.4
Duration of surgery (min)	30.8 \pm 8.3	30.9 \pm 6.3	30.7 \pm 7.6
ASA	74% ASA1, 26% ASA2	82% ASA1, 18% ASA2	76% ASA1, 24% ASA2

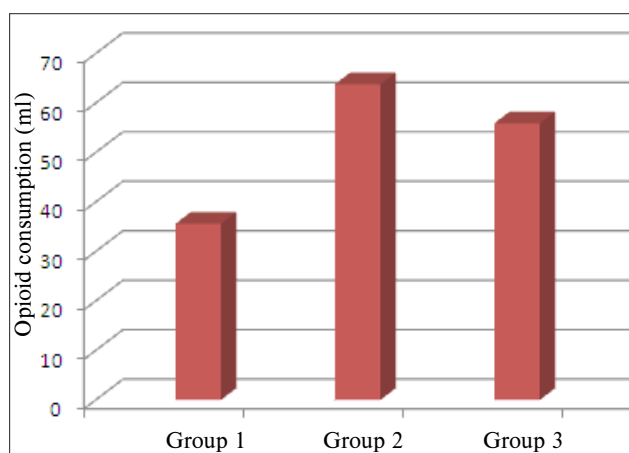
Group 1: Patients with postoperative IV fentanyl PCA following SA, Group 2: Patients with postoperative IV fentanyl PCA following GA, Group 3: Patients with postoperative IV tramadol PCA following GA.

Table 2. VAS scores of groups (Values are mean \pm SD).

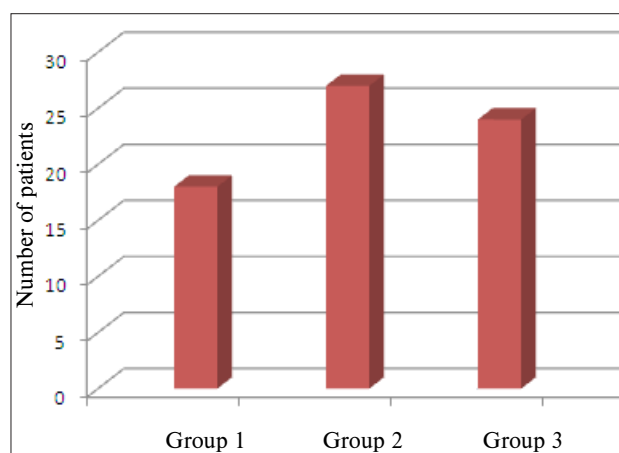
hour	Group 1	Group 2	Group 3
1 st	12.0 \pm 12.2*	31.6 \pm 14.8	32.4 \pm 11.5
2 nd	15.6 \pm 9.2*	20.3 \pm 16.5	22.1 \pm 7.9
4 th	13.0 \pm 9.8*	19.0 \pm 10.2	18.9 \pm 13.7
8 th	13.3 \pm 11.8*	24.0 \pm 13.5	23.3 \pm 11.8
12 th	12.6 \pm 10.4*	28.0 \pm 15.8	26.4 \pm 9.6
24 th	9.6 \pm 9.2	12.3 \pm 7.7	12.8 \pm 14.7

Group 1: Patients with postoperative IV fentanyl PCA following SA, Group 2: Patients with postoperative IV fentanyl PCA following GA, Group 3: Patients with postoperative IV tramadol PCA following GA.

*There is a significant difference between groups ($P < 0.05$)

**Fig. 1.** Total opioid consumption of groups (Values are mean \pm SD).

Group 1: Patients with postoperative IV fentanyl PCA following SA, Group 2: Patients with postoperative IV fentanyl PCA following GA, Group 3: Patients with postoperative IV tramadol PCA following GA.

**Fig. 2.** Additional opioid demands.

Group 1: Patients with postoperative IV fentanyl PCA following SA, Group 2: Patients with postoperative IV fentanyl PCA following GA, Group 3: Patients with postoperative IV tramadol PCA following GA.

cluded that local anesthesia provides lower postoperative pain scores than the GA technique^{8,9}. We compared both neuraxial anesthesia with GA and also the superiority of different opioids in our setting. High quality postoperative analgesia, patient satisfaction and fewer side effects result in early discharge from hospital and reduced expenditure. Therefore it is important to know which technique or opioid type is effective in the postoperative period.

Both epidural PCA and IV PCA are commonly used

in postoperative pain management. The comparison of both techniques is available in the literature¹⁰. As IV PCA is effective for individual pain relief in the postoperative period and it is generally well-tolerated, we chose IV PCA to control the postoperative pain¹¹. In the previously published retrospective study by Fassoulaki et al.¹² comparing general (n = 582), epidural (n = 423), and combined spinal anesthesia (n = 614) for C/S in patients, neuraxial anesthesia for C/S was associated with shorter duration of hospital stay than GA. In our study, patient satisfaction

was higher in the SA group but this result did not affect the time of hospital stay.

In two different randomized, prospective studies, the observers found that laparoscopic cholecystectomy under SA is associated with an extremely low level of postoperative pain, better recovery and lower cost than GA (ref.^{13,14}). Our results were similar in respect to postoperative pain scores. Although high sensorial levels after spinal anesthesia may be needed for laparoscopic cholecystectomy, T10 – T12 sensorial levels were generally sufficient for C/S. Patients' assessment of sensory levels after SA changed within the range of T4 to T12 in this trial.

In a review from the Cochrane database of systemic reviews of 16 studies and 1586 women, patient satisfaction with GA was higher¹⁵. More women preferred to have GA for subsequent procedures than epidural or spinal anesthesia. In our setting, all regional blockades were performed by anesthetists with more than eight years of clinical experience. The SA procedure was both simple and the patient satisfaction was greater.

Sudheer et al.¹⁶ compared the analgesic efficacy and side-effects of tramadol with morphine after craniotomy. Morphine produced significantly better analgesia than tramadol at all time points. As morphine is known to have a long duration of analgesia, it is a better choice for major intracranial operations. Indeed C/S is not a minor type of surgery, but we concluded that both tramadol or fentanyl provided sufficient analgesia. This also limited the incidence of side-effects.

Other studies have demonstrated that PCA tramadol is as effective as PCA morphine control following major surgery^{17,18}. In clinical trials, observers found that tramadol can also be used as an additional agent with other opioids. They also have better results than single opioid usage¹⁹. Fentanyl PCA was found safe and efficient for postoperative analgesia in children²⁰.

In conclusion, we performed a prospective, randomized comparison of general and spinal anesthesia for C/S. SA with isobaric bupivacaine provided more effective postoperative duration without analgesics than GA with propofol, atracurium, fentanyl, nitrous oxide and sevoflurane. SA with 20 µg of fentanyl and 9 mg of isobaric bupivacaine in this setting was associated with an average lower opioid consumption than the GA technique. Either general or spinal anesthesia provide satisfactory anesthesia for cesarean delivery patients. In this trial, the number of satisfied patients with SA was higher than for the GA groups. SA provided sufficient postoperative analgesia allowing the mother more comfort than with GA. We found no discrepancy between fentanyl and tramadol for the groups following GA. Both the postoperative pain scores and the incidence of side-effects were similar. These two agents can be used safely in the postoperative period. Further studies are needed to compare the postoperative pain scores and patient satisfaction following neuraxial anesthesia and GA with different opioids when

used with IV or epidural PCA techniques. These two anesthesia techniques can also be studied for different type of surgeries.

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