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ORIGINAL ARTICLE

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Analgesic effects of intrathecal tramadol in patients undergoing caesarean section: a randomised, double-blind study

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ABSTRACT
Background: Intrathecal tramadol combined with local anaesthetics has been used for postoperative analgesia following lower abdominal and perineal surgery. The present study evaluated the effect of intrathecal tramadol on spinal block characteristics and neonatal outcome after elective caesarean section.
Methods: Eighty full-term parturients scheduled for elective caesarean section were randomly divided into two groups. In the fentanyl group, patients received intrathecal 0.5% bupivacaine 10 mg with fentanyl 10 μg; in the tramadol group, patients were given the same dose of bupivacaine with tramadol 10 mg. Sensory and motor block characteristics, duration of postoperative analgesia, maternal side effects, and neonatal outcome were compared.
Results: One patient in the tramadol group and two patients in the fentanyl group were excluded from data analysis. Median [interquartile range] duration of postoperative analgesia in the tramadol and the fentanyl groups was 300 [240–360] min and 260 [233–300] min respectively ($P = 0.02$). The incidence of shivering was lower in patients who received tramadol (5%) than those who had fentanyl (32%) ($P = 0.003$). Apgar scores, umbilical cord acid–base measurement and neurologic and adaptive capacity scores were comparable between the two groups.
Conclusion: Compared to intrathecal fentanyl 10 μg, tramadol 10 mg, as an adjunct to bupivacaine for subarachnoid block for caesarean section, showed a longer duration of analgesia with a reduced incidence of shivering.

Keywords: Caesarean section; Spinal anaesthesia; Tramadol

Introduction

For women undergoing caesarean section, the addition of intrathecal opioids to bupivacaine enhances the quality and duration of intra- and postoperative analgesia.[1] However, intrathecal opioids are associated with adverse effects such as respiratory depression, nausea and vomiting.[1] Through its unique mechanism of inhibiting neuronal uptake of norephinephrine and serotonin, tramadol has many novel features, unlike other opioids that act purely on the μ-receptor.[2,3] Neurotoxicity has not been demonstrated in several animal studies when non-toxic doses of tramadol have been administered perineural or neuraxially.[4–7] Furthermore, intrathecal tramadol has been used for postoperative analgesia following various operations,[8–12] and for labour analgesia,[13] and importantly, it appears to have a safe pharmacokinetic profile in the neonate.[14] However, its effect as an adjunct to local anaesthetic for subarachnoid block for caesarean section has not been reported.

The primary objective of the present study was to compare intrathecal tramadol with fentanyl as an adjunct to hyperbaric bupivacaine, assessing sensory and motor blockade, as well as postoperative analgesia following caesarean section. Secondary objectives were to compare adverse effects, if any, in the mother and baby during the 24 h following its administration.

Methods

The study was conducted at the University Hospital of BP Koirala Institute of Health Sciences (BPKIHS), Nepal. After study approval from Institutional Ethics Committee, written informed consent was obtained from all patients after explaining the nature of the clinical study and the drugs to be used. Between March 2011

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and July 2012, full-term singleton parturients of American Society of Anesthesiologists physical status I or II, scheduled for elective caesarean section under spinal anaesthesia were enrolled in this randomized, double-blind clinical trial. Patients with cardio-respiratory problems, neurological disorders, psychiatric illness, or with allergy to opioids or local anaesthetics were excluded. During preoperative evaluation, patients were educated about the assessment of perioperative pain using the 10-cm visual analogue scale (VAS), with 0 corresponding to no pain and 10 to the worst pain imaginable.

Based on a computer-generated randomization sequence, sealed, labelled envelops were prepared and patients were assigned to two groups of 40. Group BT patients received intrathecal 0.5% hyperbaric bupivacaine 2 mL plus preservative-free tramadol hydrochloride 10 mg (Domadol®, Unichem, Ghaziabad, India) (0.2 mL); Group BF patients received intrathecal 0.5% hyperbaric bupivacaine 2 mL plus fentanyl 10 μg (0.2 mL). To facilitate blinding, a resident anaesthetist not involved in the study prepared the solutions for spinal anaesthesia.

After securing intravenous access with an 18-gauge cannula, all patients were preloaded with 10 mL/kg of lactated Ringer's over 10 min. Pulse oximetry (SpO_2), electrocardiogram and non-invasive blood pressure (NIBP) were applied and baseline values recorded. Under full aseptic precautions, spinal anaesthesia was performed using a 25-gauge pencil-point needle inserted at L3-4 or L4-5 with the patient in the left lateral position. After free flow of cerebrospinal fluid (CSF), the study solution was administered, following which patients were placed supine with a 15° left lateral tilt. Patients received supplemental oxygen at 4 L/min through a Hudson mask until delivery. Systolic blood pressure (SBP), heart rate (HR) and oxygen saturation were recorded at 5-min intervals until the completion of surgery.

Cephalad extension of the sensory blockade, determined by loss-of-touch sensation using cotton wool applied gently to the skin, was assessed bilaterally in the mid-clavicular line every minute following intrathecal injection for 10 min, every 2 min for up to 20 min and every 10 min until regression to T10. Surgical incision was allowed when loss-of-touch sensation reached T6. A modified Bromage scale[15] (0 = able to flex extended leg at hip, 1 = able to flex knee but not flex extended leg, 2 = able to move foot only, 3 = unable to move foot) was used to assess motor block every minute for 10 min after injection, then every 10 min until motor power returned to zero. The time from intrathecal injection until the sensory block reached T6; maximal sensory block height, time to regression of two spinal segments and regression to T10 from maximum block height were recorded. The onset time to maximum Bromage score and the recovery time of the motor block to a Bromage of score 0 were also documented.

Intraoperative sedation was recorded using four categories (0 = wide awake, 1 = drowsy, 2 = rousable, 3 = non-rousable).[16] Hypotension (fall in SBP >20% from baseline), and bradycardia (HR <60 beats/min) were treated with intravenous boluses of ephedrine 5 mg and atropine 0.6 mg, respectively. Nausea, vomiting, shivering, pruritus and respiratory depression (respiratory rate <10 breaths/min) were recorded for 24 h postoperatively. Intravenous ondansetron 4 mg was given for nausea or vomiting and chlorphenaramine 10 mg was used to treat pruritus. Urinary retention was not assessed as all patients had an indwelling catheter. At delivery, blood samples were collected from the umbilical artery and vein for blood gas analyses. A paediatrician who was not otherwise involved in the study evaluated the neonates using Apgar scores at 1 and 5 min and neurologic and adaptive capacity scores (NACS) at 2 and 24 h after delivery. Following surgery, parturients were questioned about the quality of their anaesthesia using a four-point scale (4 = excellent, 3 = good, 2 = satisfactory, 1 = poor).[17] The duration of postoperative analgesia was defined as the time from intrathecal injection to the time when the VAS score for pain was >0. At this point intramuscular diclofenac 75 mg was given and repeated 8-hourly. Patients received intravenous tramadol 50 mg, if pain persisted or if the VAS score for pain was >3.

Statistical analysis

Based on previous studies[9,18] the observed difference in the duration of analgesia was 198 ± 11 min. We used nMaster 2.0 sample-size calculation software (Department of Biostatistics, Christian Medical College, Bagayam, India). At the equivalence margin of 207 min (effect size = 0.854), the required sample size was 36 for each group to give 90% power at the 5% significance level. To account for dropouts, we planned to include 80 patients in the study. All analyses were performed using SPSS version 15 (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± SD, median [IQR], or number (%), where appropriate. Student's t-test and Mann–Whitney *U*-test were used for continuous and non-continuous parameters, respectively. Categorical data were analysed with Chi-square test and Fisher's exact test as appropriate. A P value <0.05 was considered as statistically significant.

Results

Of the 80 patients who consented to participate, 39 patients in Group BT and 38 patients in Group BF completed the study. One patient in each group was excluded because of spinal failure and a second patient in Group BF was withdrawn because of postpartum haemorrhage. The two study groups were similar in terms of demographic profile and surgical variables (Table 1).