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Original Research Article

A Prospective Assessment of the Analgesic Efficacy of Intrathecal 1% 2-Chloroprocaine with or Without Fentanyl in Elective Caesarean Section: A Comparative Study

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Conflict of interest: Nil

Abstract

Aim: The present study aimed to compare the analgesic efficacy and safety of intrathecal fentanyl (25 µg) as an adjuvant to low dose 1% 2-CP (30 mg) in parturient undergoing caesarean section.

Methods: The prospective comparative study was conducted in the Department of Anaesthesia, DMCH Laheriasarai Darbhanga, Bihar, India.The clinical research was done following the ethical principles for medical research involving human subjects in accordance with the Helsinki

Declaration 2013. 100 parturients with term pregnancy (≥36 weeks), belonging to the American Society of Anesthesiologists (ASA) physical status II, aged between 18 and 35 years, scheduled to undergo low-risk elective caesarean section under SAB for one year were enrolled in the study.

Results: There were no significant differences in demographic characteristics, haemodynamic parameters, onset of sensory block, onset of motor block and duration of motor block between the groups. The duration of sensory block and duration of analgesia was statistically prolonged in group B than group A (P value < 0.0001).

Conclusion: Our study concluded that intrathecal preservative-free 1% 2-chloroprocaine (30 mg) with fentanyl (25 µg) as an adjuvant result in a prolonged duration of sensory blockade and postoperative analgesia, with similar duration of motor blockade and incidence of complications when compared to preservative-free 1% 2-chloroprocaine (30 mg) without an adjuvant, in patients undergoing elective lower segment caesarean section.

Keywords: 2-chloroprocaine, caesarean section, fentanyl, spinal anaesthesia

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Introduction

Regional anaesthesia is a safer technique compared to general anaesthesia for caesarean section for both the mother and the baby. [1] Among regional anaesthetic techniques, subarachnoid block (SAB) is the preferred one for elective caesarean section, due to its advantages like it is easy to perform, economical, rapid onset, ability to provide adequate surgical anaesthesia, less neonatal depression, fewer complications and low failure rate. [2] The ideal local anaesthetic agent should

provide a rapid onset of action, faster offset of motor blockade with predictable duration, adequate postoperative pain control, low neurotoxicity potential and systemic side effects.

The changing trend of surgical practice from an inpatient to outpatient convention has urged us to modify our anesthetic drug to suit the ambulatory setting. The primary goal of ambulatory anesthesia is rapid recovery leading to early patient discharge with minimal side effects. Although low doses of long-acting local anesthetics such as bupivacaine, ropivacaine, and levobupivacaine are usually administered intrathecally, they are associated with significant delays in hospital discharge and less reliability of block efficacy, onset, and spread. [3]

Preservative free 2-chloroprocaine (2-CP) is an amino-ester local anaesthetic (LA). It has properties of faster onset, excellent sensory and motor block with quick recovery time and few adverse effects. [4] The short duration of action and poor quality of postoperative analgesia limits its use in caesarean sections. Adding adjuvant drugs to intrathecal LA improves the quality and duration of the spinal blockade and prolongs postoperative analgesia. With the addition of an adjuvant, it is possible to reduce the amount of LA and thus the incidence of side-effects.

The opioids continue to be the most commonly used adjuvants in clinical practice. [5] Among opioids, fentanyl is the most extensively used opioid in SAB, because of its potency, rapid onset, short duration of action with a reduced need for analgesia after the operation. [6,7]

Fentanyl, a short-acting lipophilic opioid stimulates μ1 and μ2 receptors, it potentiates the afferent sensory blockade and facilitates reduction in the dose of local anesthetics without intensifying the motor block or prolonging recovery, fentanyl provides good quality of intraoperative analgesia, hemodynamic stability, minimal side effects, and excellent quality of postoperative analgesia. [8]

Chloroprocaine (CP) is an aminoester local anesthetic with a very short half-life, and it was introduced and has been successfully used for spinal anesthesia since 1952, and sodium bisulfite was then added as a preservative after 1956. The drug was then abandoned in the 1980s for several reports of neurological deficits in patients receiving accidentally high doses of intrathecal CP during epidural labor analgesia, recently the preservative-free formulation has been extensively evaluated in clinical practice with a favorable profile in terms of both safety and efficacy. [9]

In recent times, post-operative outcome is considered to be positive only when it is associated with a shortened length of hospital stay. Recovery from anesthesia is much faster with chloroprocaine as compared to other short acting local anesthetics. The present study aimed to compare the analgesic efficacy and safety of intrathecal fentanyl (25 μg) as an adjuvant to low dose 1% 2-CP (30 mg) in parturient undergoing caesarean section.

Materials and Methods

The prospective comparative study was conducted in the Department of Anaesthesia, DMCH Laheriasarai Darbhanga, Bihar, India,for 1 year. The clinical research was done following the ethical principles for medical research involving human subjects in accordance with the Helsinki Declaration 2013.

Methodology

100 parturients with term pregnancy (≥36 weeks), belonging to the American Society of Anesthesiologists (ASA) physical status II, aged between 18 and 35 years, scheduled to undergo low-risk elective caesarean section under SAB for one year were enrolled in the study. Written informed consent was obtained from each parturients. The parturients who refused to

participate, having known hypersensitivity to LA, infection at the site of injection, history of bleeding disorders, parturients with pregnancy-induced hypertension, body mass index (BMI) >35 kg/m2, parturients with cardiac or renal disease, pre-existing peripheral neuropathy or neurological deficit were excluded from the study. All parturients were randomised to one of the two groups (50 each) by using a computer-generated random number table and group allocation was done with the sealed envelope method by an anaesthesiologist who was not involved in data collection.

After arrival in the operation theatre, an 18-gauge (G) intravenous cannula was secured in the non-dominant hand and the parturients was preloaded with a 10 ml/kg ringer lactate solution over

15 min. Non-invasive blood pressure (NIBP), pulse oximeter, and electrocardiogram (ECG) were applied and baseline blood pressure (BP), heart rate (HR) and oxygen saturation (SpO2) were recorded.

Spinal anaesthesia was administered in lateral position at the level of L3-4 or L4-5 interspace by using 25 G Quincke spinal needle under aseptic precaution. Parturients in group CS received intrathecal 1% preservative free 2-CP 3 ml + 0.5 ml normal saline (NS) and parturients in group

CF received intrathecal 1% preservative-free 2-CP 3 ml + 0.5 ml fentanyl (25 μg). The study drugs were prepared by an anaesthesiologist, who was not a part of the study. The anaesthesiologist administering the study drug and the patients were blinded to the group allocation. After spinal anaesthesia, the parturients were placed in the supine position with a wedge under the right buttock. The sensory and motor blockade were evaluated each minute for the first 15 min, then every 5 min till completion of the surgery.

The sensory block was assessed by pinprick sensation using hypodermic needle and pin-prick sensation over the clavicle was taken as reference point, whereas the motor block was assessed by the modified Bromage scale (0 = no paralysis, able to flex hips/knees/ankles, 1 = able to move knees, unable to raise extended legs, 2 = able to flex ankles, unable to flex knees, 3 = unable to move any part of the lower limb) at every min till adequate sensory and motor blockade for surgery was achieved. The onset of sensory block was defined as time from intrathecal drug administration to loss of pin prick sensation at T10 level, while onset of motor blockade considered from intrathecal drug administration to Bromage scores ≥2. The surgery was commenced after achieving a sensory block height of T6 level or above. Apgar score was recorded at 1, 5, 10 min after birth for all newborns. The anaesthesiologists who administered spinal anaesthesia recorded NIBP, HR,

SpO2 and VAS every 10 min in post-operative period till patient requested for first analgesic agent. The duration of analgesia was considered from the time of subarachnoid injection of drug to the time up till visual analogue scale (VAS) for pain assessment score ≥4.

The adverse events like hypotension, bradycardia, nausea, vomiting, and pruritus were recorded for first 24 h. Paracetamol 100 ml (1 gm) i.v. was administered when VAS ≥4. The occurrence of transient neurological sequelae (TNS) was assessed at days 1, 3, 7, 1 month and 6 months after surgery.

This was done by an observer anaesthesiologist by making a telephone call and asking the patients about the presence of back pain radiating to buttocks, thigh, hip and calf, inability to void, or presence of residual paraesthesia/dysaesthesia in lower limbs and buttocks. The primary outcome of the study was the duration of analgesia, while

secondary outcomes were onset of sensory block (time to achieve at T10 dermatomal level), onset of motor block, duration of sensory block, duration of motor block, time to achieve T6 and T10 dermatomal level, maximum cephalad spread, time for two-segment regression, Apgar score and any adverse effects.

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA). Kolmogrov Smirnov test was used to assess normality of quantitative variables. Numerical data like age, height, weight, BMI, duration of surgery along with spinal block characteristics were summarized as mean ± SD. Data on complications reported in each group were presented as numbers and percentages. Independent sample t-test was used to compare the baseline and spinal block characteristics between two groups. Fisher's exact test was used to compare number of complications reported between the two groups. $P < 0.05$ was considered statistically significant.

Results

Table 1: Demographic data and duration of surgery

Parameters	Group A (n=50) mean±SD	Group B (n=50) mean±SD	P
Age (years)	26.4±3.4	25.0±3.7	0.6
Height (cm)	158.2±6.0	158.4±5.0	0.8
Weight (kg)	67.3±5.7	66.4±5.0	0.1
BMI (kg/m2) X	26.4±2.8	26.2±2.7	0.1
Duration of surgery (min)	38.8±4.8	39.7±4.6	0.7

The parturients in both groups were similar with respect to demographic data and duration of surgery.

Table 2: Spinal block characteristics

	Group A (n=50)	Group B (n=50)	P from independent t-test
Mean time to achieve T10 sensory block (min)	4.36±0.96	4.18±1.15	0.80
Mean time to achieve T6 sensory block (min)	5.15±1.07	5.40±1.36	0.19
Mean time to achieve maximum cephalad spread (min)	5.95±0.87	6.24±2.09	0.25
Maximum cephalad sensory level (Median)	T6 (T4-T8)	T6 (T4-T8)	
Mean time for two segment regression (min)	58.90±6.50	58.42±8.52	0.78
Mean duration of sensory block (min)	74.16±10.33	102.1±14.61	<0.0001
Mean onset of motor block (min)	4.6±0.74	4.5±1.12	0.89
Mean duration of motor block (min)	68.2±13.66	70.6±14.46	0.40
Mean duration of analgesia (min)	78.60±10.74	116.2±26.54	<0.0001

The difference in HR, BP and SpO2 was not statistically significant in both the groups throughout the perioperative period. The time to achieve block height of T10 (onset of sensory block), time to achieve block height of T6, maximum dermatomal cephalad spread, the onset of

motor block and the duration of motor block were comparable in both the groups. The mean duration of sensory block was prolonged in group B in comparison to group A, with the difference being statistically significant (102.1 ± 14.61 versus 74.16 ± 10.33 min, P < 0.0001). The mean duration of analgesia was prolonged in group B compared to group A, with the difference being statistically significant (116.20 ± 25.54 min versus 78.60 ± 10.74 min, P < 0.0001).

Discussion

Chloroprocaine is a short acting local anesthetic that allows rapid recovery from sensory and motor function. The shorter duration of action is due to very low protein binding and rapid metabolism by pseudocholinesterase. [10] There were several concerns regarding safe use of chloroprocaine and its potential neurotoxicity due to added preservatives in the past. [11] However, studies have shown that use of preservative-free chloroprocaine provides rapid and reliable sensory and motor block in doses ranging from 30–60 mg for brief surgical procedures under sub-arachnoid block without any significant complications. [12] Addition of adjuvants to intrathecal local anesthetics improves the quality and duration of spinal blockade and also prolongs the post-operative analgesia. [13]

CP has been reintroduced recently into the market after being initially withdrawn due to concerns of neurotoxicity and is being increasingly used in day care procedures. Studies have shown that intrathecal opioids can greatly enhance analgesia of subtherapeutic doses of local anesthetics. [14,15] Fentanyl added to local anesthetic agent seems to be the most frequently used combination to enhance and increase the duration of sensory analgesia without intensifying the motor blockade or prolonging recovery from spinal anesthesia. [16]

Rapid onset of sensory block (3–5 min) and complete resolution of the sensory block in 70–150 min after intrathecal 2-CP (30–60 mg) makes it an attractive option for SAB in day care surgeries. [17-19] Use of 2-CP in low-risk caesarean section in healthy parturients has been found to reduce the length of stay in the post-anaesthesia care unit (PACU), benefit early breast feeding initiation, improve maternal satisfaction due to better and early mother-baby bonding and help in the maintenance of the new born's temperature. [20] Literature suggests a dose ranging between 30-60 mg of 2-CP for procedures lasting 60 min or less, while 10 mg is considered as no-effect dose. [21]

The LSCS can be conducted under spinal anaesthesia with either a large dose of 2-CP or a small dose of the same agent with addition of fentanyl as an adjuvant. The use of a high dose of 2-CP may be associated with prolonged duration of motor blockade, which may not be desirable. The addition of fentanyl to a smaller dose of 2-CP results in a shorter duration of the motor blockade and a longer duration of sensory block and analgesia. It is well documented that parturients require a smaller dosage of LA in SAB compared to non-pregnant patients because of mechanical factors such as changes in spine curvature, distension of epidural veins as a result of the aorto-caval compression by the gravid uterus and increased sensitivity of neurons to LA. [22] Maes et al. used 2-CP 40 mg with and without sufentanil (1 μg) in subarachnoid block for low risk caesarean section. [20]

Intrathecal LA and opioids act synergistically but on different receptors, as LA blocks afferent and efferent pathways, while opioids affect only afferent nociceptive fibers. Synergistic effect of intrathecal opioids can greatly enhance analgesia of sub-therapeutic doses of LA. [23,24] Fentanyl has a high affinity for opioid receptors; therefore, it produces a longer duration of analgesia compared to

other agents. [25] Fentanyl can depress C-fiber reflexes, whereas the opioid local anaesthetic combination results in the depression of both Aδ and C fiber mediated reflexes without efferent effect. Most authors have reported that fentanyl doses from 12.5 to 25 μg are safe and enhance spinal blockade, during caesarean and immediate postsurgical analgesia, without increasing side effects. In our study, we used 25 μg fentanyl with 2-CP. Though the time to dermatomal regression was comparable in both groups in our study, the sensory regression and duration of postoperative analgesia were significantly prolonged without intensifying the motor blockade. Many previous studies have focused on the use of intrathecal fentanyl as it provides a more intense sensory block without untoward effects. [6,7,22]

Conclusion

Our study concluded that intrathecal preservative-free 1% 2-chloroprocaine (30 mg) with fentanyl (25 μg) as an adjuvant result in a prolonged duration of sensory blockade and postoperative analgesia, with similar duration of motor blockade and incidence of complications when compared to preservative-free 1% 2-chloroprocaine (30 mg) without an adjuvant, in patients undergoing elective lower segment caesarean section. We concluded that preservative free 1% 2CP is a reliable & safe local anaesthetic agent for SAB in ambulatory day care surgery.

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