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Randomized controlled trial to determine analgesic efficacy of intrathecal 1% 2-chloroprocaine with or without fentanyl during elective caesarean section

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Abstract---Background-Preservative free 1% 2-chloroprocaine is a short acting local anaesthetic agent appropriate for day care surgical techniques. Potentiation of analgesic accomplishment of intrathecal local anesthetics by the addition of opioids is well recognized. Objectives- To investigate the effect of intrathecal fentanyl as an adjuvant to 1% 2-chloroprocaine (2-CP) in parturients undergoing elective lower segment caesarean section (LSCS). Methods: A prospective randomized double blind study was performed on 150 healthy, term parturients planned for elective LSCS, divided into two equal groups. The group C1 received 1% preservative-free 2-CP 3 ml (30 mg) + 0.5 ml normal saline and group C2 received 1% preservative-free 2-CP 3 ml (30 mg) + 0.5 ml fentanyl (25 µg) with a total volume of 3.5 ml intrathecally in both groups. The duration of sensory blockade, duration of motor blockade, maximum height of sensory block, haemodynamic parameters, quality of block, neonatal outcome, patient satisfaction and any side effects were recorded.

Results: There were no significant differences in demographic characteristics, haemodynamic parameters, onset of sensory block, and 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 C2 than group C1 (P value= 0.001). There was no statistical difference in the Apgar score of newborns in both groups. **Conclusion:** The addition of fentanyl to 1% 2-chloroprocaine intrathecally prolonged the duration of sensory block and postoperative analgesia in patients undergoing LSCS.

Keywords---2-chloroprocaine, caesarean section, fentanyl, spinal anaesthesia, local anaesthesia, intrathecal, opioids.

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.

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.[3] 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.[4] 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.[5,6]

Materials and Methods

This prospective, double-blind, randomised, comparative study was conducted after approval from the Institutional Ethical Committee and Clinical Trial Registry of India (CTRI/2022/02/051892) dated 11/03/2022. One hundred and fifty parturients with term pregnancy (≥ 36 weeks), aged between 18 and 35 years, scheduled to undergo low-risk elective caesarean section under SAB, from April 2021 to March 2022 were enrolled in the study. Written informed consent was obtained from each parturient.

Exclusion criteria

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) $>35 \text{ kg/m}^2$, parturients with cardiac or renal disease, pre-existing peripheral neuropathy or neurological deficit were excluded from the study. The sample size calculation was based on a pilot study of 10 patients in each group, with 80% power, 95% confidence interval and level of significance 0.05. The sample size (n) was calculated as 68 for each group. To cover dropouts, we enhanced the estimated sample size by 10%, which was $n = 75$ parturients in each group. Randomization- All parturients were randomized to one of the two groups C1 and C2 (75 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.

Methodology

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 C1 received intrathecal 1% preservative free 2-CP 3 ml + 0.5 ml normal saline (NS) and parturients in group C2 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 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 duration of sensory block was from the onset of sensory block till sensation was felt at the level of S2 dermatome, while duration of motor block was from time to achieve Bromage scores ≥ 2 to time to complete recovery of motor power.

Statistical Analysis

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA). 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 details and Duration of Surgery

Parameters	C1 (N=75)	C2 (N=75)	P-value
Age (years)	24.3±3.3	24.1±3.1	0.21
Height (cm)	158.4±5.8	158.3±5	0.11
Weight (kg)	68.2±5.6	66.4±4.8	0.24
BMI	27.2±2.2	26.8±2.4	0.31
Duration of surgery	38.4±4.6	38.8±4.4	0.11

As per table 1 the parturients in both groups were similar with respect to demographic data and duration of surgery. There is no significant difference in both groups of age, height, weight, BMI and duration of surgery ($p > 0.05$)

Table 2- Characteristics of Spinal Block

Parameters	C1 (N=75)	C2 (N=75)	P-value
Time to achieve sensory block (T10)	4.21±0.91	4.11±1.10	0.11
Time to achieve sensory block (T6)	5.10±1.04	5.38±1.32	0.21
Mean Duration of Sensory Block (min)	72.10±10.30	100.6±14.60	0.001*
Mean Duration of Motor Block (min)	69.6±13.54	70.2±14.20	0.11
Mean Onset of Motor block (min)	4.4±0.72	4.4±1.10	0.32
Mean Onset of Analgesia	79.58±10.62	114.2±25.52	0.001*

As per table 2 the time to achieve block height of T10 (onset of sensory block), time to achieve block height of T6, 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 C2 in comparison to group C1, with the difference being statistically significant ($P = 0.001$). The mean duration of analgesia was prolonged in group C2 compared to group C1, with the difference being statistically significant (114.20 ± 25.52 min versus 79.58 ± 10.62 min, $P = 0.001$).

Table 3- Comparison of Side Effects in two groups (N=150)

Side effects	C1 (N=75)	C2 (N=75)	P-value
Hypotension	5	4	0.21
Bradycardia	1	1	0.11
Vomiting	4	3	0.24
Shivering	8	5	0.31
Pruritus	0	4	0.11

As per table 3 the adverse effects namely hypotension, bradycardia, nausea, vomiting, pruritus, shivering, were comparable in both the groups no difference was seen ($p>0.05$). There was no statistical difference in the Apgar score of newborns in both the groups. None of the parturients reported TNS in the follow-up period.

Discussion

This prospective, double-blind, randomised, comparative study conducted among 150 cases. The principal findings of our study were that the addition of 25 µg of fentanyl to 2-CP (30 mg) for spinal anaesthesia prolonged the sensory blockade and duration of postoperative analgesia. 2-CP has a rapid onset of action, with an excellent sensory and motor block. 2-CP has a shorter duration of action due to very low protein binding and rapid metabolism by pseudocholinesterase.[3,7-9] Several older studies have highlighted the issues of safety and potential neurotoxicity with preservative of 2-CP.[10,11].

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.[12]. Literature suggests adose ranging between 30-60 mg of 2-CP for procedures lasting 60 min or less, while 10 mg is considered as no-effect dose.[12]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.[10] Maes et al. used 2-CP 40 mg with and without sufentanil (1 µg) in subarachnoid block for low risk caesarean section.[9] Since, there is no recommendation regarding the appropriate intrathecal dosage of 2-CP in parturients, we selected a lower dose (30 mg) of 2-CP keeping in mind the above mentioned concerns.

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.[5,6]. We found negligible incidences of hypotension, bradycardia, nausea, vomiting, pruritus, shivering, in our study parturients undergoing caesarean section. Also, the Apgar score of the newborns remained comparable in both groups. Though earlier studies [6,8] did not use the same concentration, volume of LA and opioid intrathecally as used in our study, their results were similar to our study.

Conclusion

1% 2-chloroprocaine (30 mg) with fentanyl (25 µg) as an adjuvant results 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.

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Conflict of Interest- None declared

Author's Contribution

Dr. A has finalized the draft and guarantor, Dr. B and C has prepared the conceptual framework, designing of draft, and data analysis, Dr. D was involved in data collection and analysis, and Dr. E has done manuscript writing and data collection.

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