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Original Research Article

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

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

Methodology: This prospective, double-blind, randomized, comparative study was conducted in Department of Anesthesia and critical care, Patna Medical college and hospital, Patna, Bihar for one year. 100 participants 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, The anaesthesiologists who administered spinal anaesthesia recorded NIBP, HR, SpO_2 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. The adverse events like hypotension, bradycardia, nausea, vomiting, and pruritus were recorded for first 24 hours. 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.

Results: The 100 participants were randomized in two groups. The participants in both groups were similar with respect to demographic data and duration of surgery. The mean duration of sensory block was prolonged in group CF in comparison to group CS, with the difference being statistically significant (101.6±14.92 versus 72.04±10.23 min, $P < 0.0001$). The mean duration of analgesia was prolonged in group CF compared to group CS, with the difference being statistically significant (114.2±25.44 min versus 79.82±10.83 min, $P < 0.0001$). The adverse effects namely hypotension, bradycardia, nausea, vomiting, pruritus, shivering, sedation and respiratory depression were comparable in both the groups. There was no statistical difference in the Apgar score of newborns in both the groups. In this study, none of the participants reported TNS in the follow-up period.

Conclusion: Our study concluded that intrathecal preservative-free 1% 2-chloroprocaine (30 mg) with fentanyl (25 µg) as an adjuvant has added advantage in prolonging the post-operative analgesia, speeding up the onset and increasing the duration of the sensory block

without affecting the recovery of motor block 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: Intrathecal, Chloroprocaine, Caesarean.

Introduction

In underdeveloped countries, caesarean section is one of the most commonly performed obstetric operations in the parturient population. It improves maternal and foetal outcomes as well as lowers the risks of spontaneous labour and vaginal delivery. Due to its easy capacity to deliver enough surgical anaesthetic, ease and simplicity of technique, quicker onset of action, and safety, Spinal anaesthesia has proven to be a safe technique and assures adequate analgesia for patients undergoing elective caesarean section.1

Regional anaesthesia is a safer technique compared to general anaesthesia for caesarean section for both the mother and the baby [2]. 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 [1]. 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.

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. Lacasse et al. showed that the unassisted ambulation time and the time of patient's hospital discharge eligibility were significantly shorter when using chloroprocaine compared to bupivacaine [3]. Adjuvants like opioids are commonly added to intrathecal local anesthetics for improving quality and duration of spinal blockade and prolonging post-operative analgesia [4]. Among opioids, fentanyl is the most extensively used opioid in sub-arachnoid block [5].

The optimal local anaesthetic should have a fast start of action, a faster offset of motor blockage with predictable duration, appropriate postoperative pain control, low neurotoxicity potential, and minimal systemic adverse effects [6]. 2-chloroprocaine (2-CP) is an amino-ester local anaesthetic (LA) available as preservative-free LA. It has a rapid onset, effective sensory and motor block, a short recovery time, and few side effects [7]. Intrathecal LA with adjuvant drugs increases the quality and duration of the spinal blockade and extends postoperative analgesia.

By using an adjuvant, it is possible to lower the amount of LA and, consequently, the occurrence of negative effects. Similar, to the parturient receiving elective LSCS, bupivacaine is the most commonly used local anaesthetic for spinal anaesthesia. Bupivacaine is a long-acting amide local anaesthetic that provides effective pain relief without having a significant effect on motor fibres [7, 8]. 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 parturients undergoing caesarean section.

Materials and Methods

This prospective, double-blind, randomized, comparative study was conducted in Department of Anesthesia and critical care, Patna Medical college and hospital, Patna, Bihar for one year. 100 participants 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,Written informed consent was obtained from each participant. The participants who refused to participate, having known hypersensitivity to LA, infection at the site of injection, history of bleeding disorders, participants with pregnancy-induced hypertension, body mass index (BMI) >35 kg/m2 , participants with cardiac or renal disease, pre-existing peripheral neuropathy or neurological deficit were excluded from the study. All participants were randomized 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 participants 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 (SpO_2) 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. Participants in group CS received intrathecal 1% preservative free 2-CP 3 ml + 0.5 ml normal saline (NS) and participants 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 participants 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, than 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, SpO_2 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. 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. 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

The 100 participants were randomized in two groups. The participants in both groups were similar with respect to demographic data and duration of surgery.

Table 1: Demographic data and duration of surgery

Parameters	Group CS (n=50)	Group CF (n=50)
Age (in years)	23.9±3.9	23.7±3.5
Height (in cm)	158.8±6.4	159.0±5.8
Weight (in Kg)	68.7±6.2	66.9±5.4
BMI (Kg/m2)	27.4±2.8	26.9±2.9
Duration of surgery (in minutes)	37.9±5.0	39.2±4.5

The difference in HR, BP and SpO_2 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.

Table 2: Spinal block characteristics

Parameters	Group CS (n=50)	Group CF (n=50)
Mean time to achieve T10 sensory block (min)	4.28±0.98	4.02±1.13
Mean time to achieve T6 sensory block (min)	5.13±1.10	5.63±1.73
Mean time to achieve maximum cephalad spread (min)	6.05±0.90	6.72±2.41
Maximum cephalad sensory level (Median)	T6 (T4-T8)	T6 (T4-T8)
Mean time for two segment regression (min)	58.02±6.76	57.92±8.27
Mean duration of sensory block (min)	72.04±10.23	101.6±14.92
Mean onset of motor block (min)	4.6±0.92	4.5±1.23
Mean duration of motor block (min)	69.9±13.82	70.7±14.34
Mean duration of analgesia (min)	79.82±10.83	114.2±25.44

The mean duration of sensory block was prolonged in group CF in comparison to group CS, with the difference being statistically significant (101.6±14.92

versus 72.04±10.23 min, P < 0.0001). The mean duration of analgesia was prolonged in group CF compared to group CS, with the difference being statistically significant (114.2±25.44 min versus 79.82±10.83 min, P < 0.0001). The adverse effects namely hypotension, bradycardia, nausea, vomiting, pruritus, shivering, sedation and respiratory depression were comparable in both the groups. There was no statistical difference in the Apgar score of newborns in both the groups. In this study, none of the participants reported TNS in the follow-up period. In patients of group CS, most common complication was shivering (14%) followed by hypotension (12%) and nausea/vomiting (10%). In patients with group CF, most common complication was shivering (10%) followed by hypotension (8%), nausea/vomiting (6%), and pruritus (6%).

Table 3: Comparison of complications

Complications	Group CS (n=50)	Group CF (n=50)
Hypotension	6 (12%)	4 (8%)
Bradycardia	2 (2%)	1 (2%)
Nausea/vomiting	5 (10%)	3 (6%)
Shivering	7 (14%)	5 (10%)
Pruritus	0 (0.00)	3 (6%)

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 [8]. There were several concerns regarding safe use of chloroprocaine and its potential neurotoxicity due to added preservatives in the past [9]. 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 [10]. Addition of adjuvants to intrathecal local anesthetics improves the quality and duration of spinal blockade and also prolongs the post-operative analgesia [4].

The mean duration of sensory block was prolonged in group CF in comparison to group CS, with the difference being statistically significant. The mean duration of analgesia was also prolonged in group CF compared to group CS, with the difference being statistically significant. Our results are in concordance with the study done by Nagar et al. in which the duration of analgesia and time to first analgesic dose was significantly prolonged in chloroprocaine with fentanyl group [11]. Our findings are also similar to those obtained with the study conducted by Madhusudhana et al. and Singariya et al. in which the time to first demand of analgesia (duration of analgesia) was significantly longer in post-operative period in the chloroprocaine with fentanyl group [12, 13].

Fentanyl as an adjuvant to local anesthetic leads to rapid onset of the sensory block when administered intrathecally due to its lipophilic nature. Mean time for onset of sensory block was statistically shorter in patients who received chloroprocaine with fentanyl. Bhaskara et al. and Suryanarayana et al. have also shown similar results in their studies [14, 15]. However, our findings are not consistent with the studies done by Nagar et al and Singariya et al [11, 13]. Vath et al. (2004) compared intrathecal injection of 40 mg 2% 2-CP with intrathecal injection of 40 mg 2% 2-CP and 20 µg fentanyl in eight healthy volunteers and demonstrated that the mean duration for ambulation in Group CF was 104±7 min and in Group CS was

95±9 min with a p value of <0.02 [5]. In a retrospective review on the discharge characteristics of spinal 2-Chloroprocaine, the time from injection to ambulation noted by Hejtmanek et al. in chloroprocaine group (median dose 40 mg and range 20–60 mg) was 107±24 min. The difference in time to eligibility for home discharge in both groups was also statistically non-significant. Our study results are consistent with chloroprocaine with fentanyl group of study conducted by Bhaskara et al [14].

We found negligible incidences of hypotension, bradycardia, nausea, vomiting, pruritus, shivering, sedation, and respiratory depression in our study parturients undergoing caesarean section. Also, the Apgar score of the newborns remained comparable in both groups. Though earlier studies [16, 17] did not use the same concentration, volume of LA and opioid intrathecally as used in our study, their results were similar to our study. In our study, we administered a small dose of a newly marketed formulation of preservative-free 1% 2-CP for spinal anaesthesia. The small dose is believed to lower the risk of neurotoxicity [18, 19,20].

Conclusion

Our study concluded that intrathecal preservative-free 1% 2-chloroprocaine (30 mg) with fentanyl (25 µg) as an adjuvant has added advantage in prolonging the post-operative analgesia, speeding up the onset and increasing the duration of the sensory block without affecting the recovery of motor block 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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