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Original Research Article

A Randomized Comparative Study of Different Doses of Chloroprocaine for Spinal Anaesthesia

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Abstract

Background: Regional anaesthesia and analgesia has the potential to provide excellent operating conditions and prolonged post-operative pain relief. The aim of the present study was to compare clinical efficacy of two doses of chloroprocaine for spinal anaesthesia.

Method: This randomized prospective observational study included total 60 adult female patients undergoing short elective gynecological procedures, who were equally divided into Group A (receiving 20mg 1% 2-Chloroprocaine) and Group B (receiving 30mg 1% 2-Chloroprocaine). Patients were observed for haemodynamic parameters, time to onset of sensory T12 Block(sec), time to onset of motor Block (Modified Bromage scale >2) (sec), time to sensory block up to T10 (sec), maximum sensory level, time to 2 dermatome regression of sensory block (min), time to resolution of motor block (Modified Bromage scale returned to 0) (min), time to first spontaneous urine voiding (min), intra operative complications, post operative neurological sequelae at 24 hrs and on 7th day.

Results: Group B had earlier time to sensory and motor blockade, longer duration ofmotor blockade than Group A. However, time to 2 dermatome regression, resolution of motor blockade andfirst spontaneous urine voiding was earlier in Group A than Group B. There were no any variations in Haemodynamic parameters and no any intraoperative complications in both groups. There were no any postoperative neurological sequelae in any patient.

Conclusion: The preservative free formulation of 2-Chloroprocaine appears to be an excellent alternative for short acting spinal anaesthesia in ambulatory surgical procedures.

Keywords: Anaesthetics, Chloroprocaine, Neuraxial Blocks, Regional Anaesthesia, Spinal Anaesthesia.

Introduction

Pain is inherent to all surgeries causing significant morbidity. Regional anaesthesia and analgesia has the potential to provide excellent operating conditions and prolonged post-operative pain relief. It is also known to reduce post-operative morbidity and mortality by its positive influence like improved blood flow with optimum tissue functionality and improved recovery thereby leading to its widespread use. As against regional anaesthesia, general anaesthesia requires administration of several analgesic drugs which trigger a number of adverse effects including nausea and vomiting respiratory depression, apnoea, muscular rigidity and bradycardia. Regional anaesthesia has the advantages of improved postoperative pain control and is more economical requiring fewer drugs. [1] Although low doses of the long acting local anaesthetics such as bupivacaine, ropivacaine and levobupivacaine are usually administered intrathecally, they are associated with significant risk of delay in hospital discharge and less reliability of block efficacy, onset and spread. [2] Short-acting local anaesthetics may therefore represent a valid alternative in these settings.

2-chloroprocaine is an amino-ester local anaesthetic with a very short half-life and a potentially favourable profile for short procedures [3], but concerns for neurotoxicity emerged two decades ago with eight cases of neurologic injury associated with the use of chloroprocaine solution containing the antioxidant sodium bisulfite. [4-6] Several studies have evaluated the neurotoxic potential of chloroprocaine and bisulfite in different experimental models, reporting conflicting results in the recent years. [7,8] Toxicological studies indicated sodium bisulfite as the likely cause of neurotoxicity, though an animal study in rat challenged this conclusion. [6] Although rigorous investigations in volunteers [9,10] and clinical reports on off-label use of chloroprocaine in daily practice [11] support the safety profile of intrathecal chloroprocaine, further data is required to better evaluate the toxicity potential of chloroprocaine. The present study was undertaken with the aim to compare clinical efficacy of two doses of chloroprocaine for spinal anaesthesia.

Material and Method

The present randomized prospective observational study was conducted in the Department of Anaesthesiology, AMC MET Medical College & Sheth L. G. Hospital after obtaining ethical clearance from the institutional review board. The study included 60 adult female patients, aged 18-49 years, with ASA grade I & II undergoing short elective gynecological procedures. Patients who had contraindications for spinal anaesthesia or hypersensitivity to chloroprocaine drug were excluded from the study. All the study patients were randomly divided into two groups of 30 each as follows:

- **Group A:** Patients received 20 mg 1% 2-Chloroprocaine.
- **Group B:** Patients received 30 mg 1% 2-Chloroprocaine.

Pre-operative evaluation was carried out in all patients with detailed history, general physical examination and routine investigations. Vital parameters were noted (Pulse, SBP, DBP, SPO_2) and systemic examination was performed and an informed written consent was obtained from each patient.

Anaesthetic Protocol:

All patients were fasted overnight 8-10 hours the night before surgery. Tab Ranitidine 150 mg was given night before the surgery. After taking patient in OT, non-invasive monitoring was started including pulse oximeter, electrocardiography (ECG) and Non Invasive Blood pressure (NIBP).

Baseline vitals of the patient were recorded. A peripheral venous access was secured on non-dominant hand with 18-gauge IV cannula. Preloading with Ringer's lactate solution was started at the rate of 8-10 ml/kg 15 min prior to subarachnoid block. No analgesics or sedative were given to any of patients preoperatively. All the patients were explained the procedure and it was kept uniform in all patients. Under strict aseptic and antiseptic precautions, subarachnoid block was performed in lateral position, between L_3-L_4 intervertebral space, with 23 Gauge Quincke's needle via midline approach. After free flow of CSF, the test drug was injected over 10-15 seconds. After completion of spinal injection, patients were placed supine and sensory and motor blocks were evaluated every 1 minute until surgical anaesthesia was achieved. After that sensory block was assessed every 3 minutes till maximum sensory block was reached. (same level of sensory block for 3 consecutive observations) Sensory block was assessed by pin prick. Motor block was assessed by using Modified Bromage scale. [12] Haemodynamic parameters: HR, SBP, DBP, SpO_2 were recorded every 1 min for first 3 min, then every 5 min up to 15 min, every 10 min interval up to 45 min. When Bromage scale more than 2 was established, lithotomy position was given. Following observations were made:

- Time to onset of sensory T12 Block: Time period from completion of drug injection to loss of pinprick sensation at the level of T12 dermatome.
- Time to onset of motor Block (Modified Bromage scale >2)
- Time to onset of sensory T10 Block: Time period from completion of drug injection to loss of pinprick sensation at the level of T10 dermatome.
- Maximum sensory level (same level for 3 consecutive observations)
- Time to 2 dermatome regression of sensory block: Time period from completion of drug injection to the time when the sensory block decrease to two dermatomes with respect to the maximum level of sensory block
- Time to 2 segment regression, resolution of motor block (Modified Bromage scale return to 0) were noted.
- Time to first spontaneous urine voiding: time period from completion of drug injection to the first time when the patient can pass urine unassisted
- The occurrence of neurological symptoms was assessed 24 hours and 7 days after surgery using a questionnaire asking patients about presence of headache, back pain, postoperative nausea and vomiting, inability to void urine or presence of residual paresthesia or dysthesia in lower limbs or buttocks commencing within 24 hours of spinal anaesthesia.

The surgical anaesthesia was considered effective when T8-T10 dermatomes were anaesthetized and Modified Bromage grade II block was achieved. Intra operative complications were noted such as hypotension, Bradycardia, Nausea and vomiting, Respiratory depression, Pruritus and Shivering. Clinically relevant hypotension (decrease in systolic arterial blood pressure >30 % of baseline) was initially treated with rapid infusion of 200 ml of crystalloid over 10 min. If that was ineffective, 6 mg mephentermine was given IV. Bradycardia (defined as a decrease in heart rate below 45 bpm) was treated with 0.6 mg atropine IV. At the end of procedure patients were shifted to postoperative ward where further monitoring of vitals was done every 30 minutes.

Results

Majority of the population in each study group belonged to 21-30 years of age, with the age ranging from 19-43 years. The mean age of the study patients was comparable between the two study groups. (Table 1)

Table 1: Age Wise Distribution of Study Population

Age (years)	Group- A		Group- B	
	Patients	Percentage	Patients	Percentage
16-20	07	23	01	04
21-25	11	37	13	43
26-30	07	23	06	20
31-35	04	13	05	17
36-40	01	04	04	13
41-45	00	00	01	03
Mean	25.4±11.90		28.4±6.63	
p- value	0.2326			

The mean weight of the patients in Group A was 48.5±5.43 kg and in Group B was 50.96±5.42 kg. More than 60% of the patients in both the groups had weight between 40-50 kg. (Figure 1)

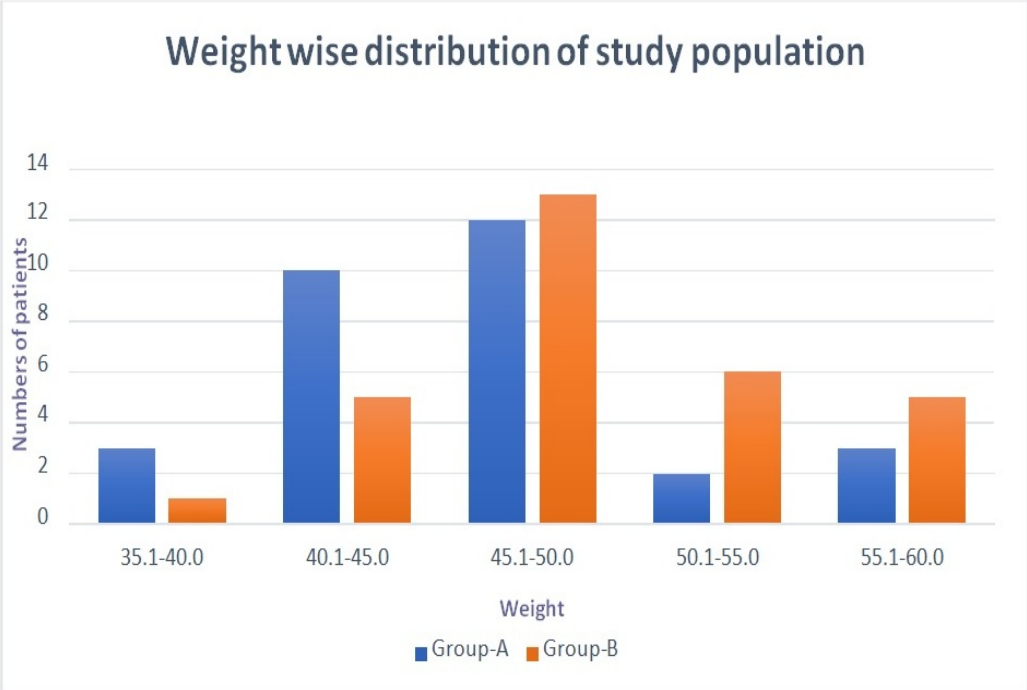

Figure 1: Weight Wise Distribution Of Study Population

The haemodynamic parameters of the patients in both the study groups remained stable and close to baseline values throughout the operation. There were no clinical & statistical differences in the haemodynamic parameters of the patients between both the groups.

Comparison of Time to onset of sensory block up to T12 & T10 level between the two groups suggested that it was earlier in Group B than Group A, which was highly significant. (Table 2)

Table 2: Comparison of Time to Onset of Sensory Block up to T12 & T10 between Two Groups

	Group- A	Group- B	P value	Inference
Sensory Onset up toT12 (sec)	154.33±6.41	129.83±22.83	< 0.0001	Highly significant
Sensory onset up to T10 (sec)	241±25.32	184.8±41.80	< 0.0001	Highly significant

The mean duration to achieve Motor block >2 with Modified Bromage scale was significantly

lesser in Group B than Group A. (Table 3)

Table 3: Comparison of Motor Block (Modified Bromage Scale >2) between Two Groups

	Group- A	Group- B	P value	Inference
Time to motor	301.07±35.04	236±26.24	<0.0001	Highly
block (Modified				significant
Bromage scale				
>2) (seconds)				

The maximum level of sensory block attained in Group A was T10 and in Group B was T8.

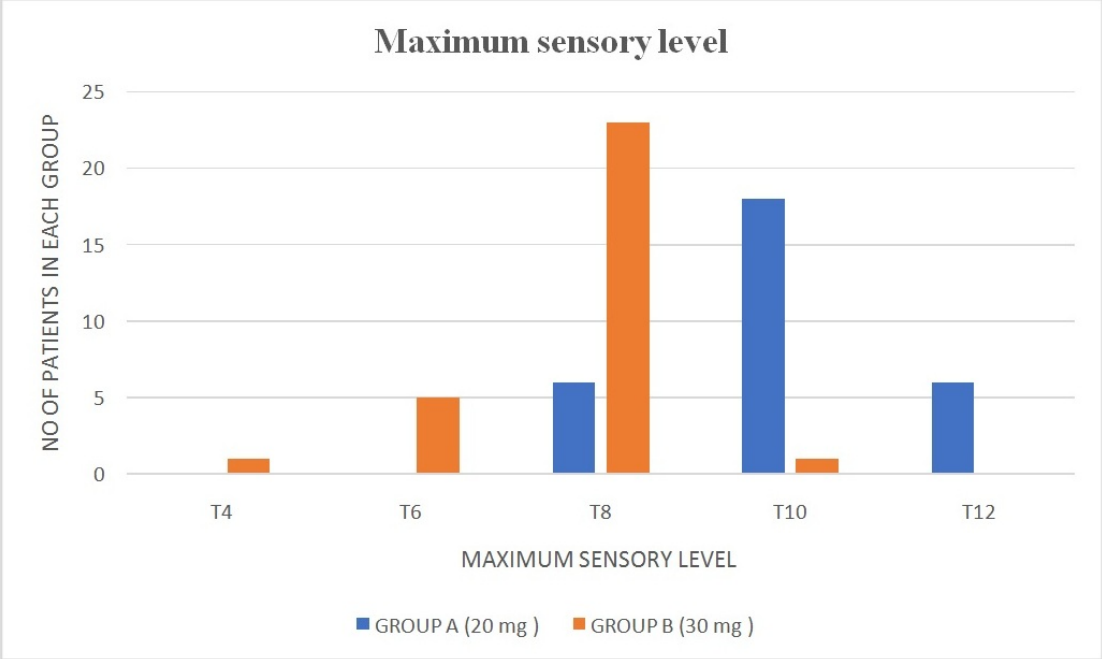

Figure 2: Maximum Sensory level attained in both the groups

Time to two dermatome regression of sensory block was compared and it was found that Group B had longer duration of two dermatome regression of sensory block than Group A, which was statistically highly significant (p<0.0001). (Table 4)

Table 4: Comparison of Time to 2 Dermatome Regression of Sensory Block Between Two Groups

	Group- A	Group- B	P value	Inference
Time to two	39.83±5.91	59.9±6.55	<0.0001	Highly
Dermatome regression				significant
of sensory block				
(minutes)				

Comparison of time to resolution of motor block between the groups showed that Group A had earlier resolution of motor block than Group B, which was statistically highly significant.(<0.0001) (Table 5)

Table 5: Comparison of Time To Resolution Of Motor Block (Modified Bromage Scale Return To 0) Between Two Groups

	Group- A	Group- B	P value	Inference
Time to resolution of	49.23±5.74	84.67±6.88	(<0.0001)	Highly
motor block (Modified				significant
Bromage scale return to 0				
(min)				

The mean Time to first spontaneous urine voiding was compared between the groups and it was found that Group A had significantly earlier first spontaneous urine voiding than Group B (<0.0001). (Table 6)

Table 6: Comparison of Time to First Spontaneous Urine Voiding between the groups

	Group- A	Group- B	P value	Inference
Time to first spontaneous urine voiding (min)	156.67±9.94	209.4±32.03	<0.0001	Highly significant

No complications or adverse effects were observed in any patient among both the groups. Also, no post operative neurological sequelae at 24 hours or within 7 days were reported by any of the patient from either group.

Discussion

Perioperativepain management lies on the shoulders of anaesthesiologists and there has been a constant struggle to bring out the best possible analgesic technique with least side effects. Spinal anaesthesia is a safe and reliable technique for surgery of lower abdomen and lower limbs. In the past, lack of ideal spinal local anaesthetic and the availability of on/off drugs like remifentanil and propofol have made general anaesthesia, the technique of choice for short procedures around 30 minutes. [13] However, short-acting local anaesthetics like 2-chloroprocaine can be used as a suitable alternative. 2-chloroprocaine belongs to an amino-ester local anaesthetic group with a very short half-life and a potent pharmacological profile for short procedures, [3] but its main concern is the neurotoxicity that was reported two decades before with eight cases of neurologic injury associated with the use of chloroprocaine solution containing the antioxidant sodium bisulfite. [4-6] However in contrast to this, clinical report on off-label intrathecal use of preservative free chloroprocaine in more than 1000 patients [3,11] as well as rigorous investigations in more than 100 volunteers and out patients [9,10,14] have not reported any case of neurological toxicity. The present study was done to compare clinical efficacy of two doses of chloroprocaine for spinal anaesthesia in 60 patients who were further divided into Group A and Group B of 30 patients each depending upon the dose of chloroprocaine administered. The results of the present study showed that both the study groups were comparable in terms of demographic data. Haemodynamic parameters remained stable in the perioperative period throughout the study in both the groups.

In the present study, time to achieve sensory T12 block in Group A was 154.33±6.41 seconds and in Group B was 129.83±22.83 seconds, Time to onset of motor (Modified Bromage scale>2) block in Group A was 301.07±35.04 seconds and in Group B was 236±26.24 seconds, and the Time to achieve sensory block up to T10 in Group A was 241±25.32 seconds and in Group B was 184.8±41.80 seconds. This suggested that surgical anaesthesia was achieved earlier in Group B, i.e, with 30 mg of Chloroprocaine as compared to Group A, i.e, 20 mg of Chlorprociane, which was clinically and

statistically highly significant. The maximum level of sensory block was T10 in Group A and T8 in Group B. Smith KN et al [10] have observed that the maximum sensory level in 30 mg without epinephrine was T8 and with epinephrine was T7, in 40 mg without epinephrine was T5 and with epinephrine was T4 and in 60 mg without epinephrine was T2 and with epinephrine were T1. This suggested that block height increases with increasing dose of spinal 2-chloroprocaine and that, the addition of epinephrine dose not significantly increase peak block height. Similar observations were made by Warren and Kopacz [15] who observed that there was no significant difference inmaximum sensory level in 2-chloroprocaine with 0.25 ml 10 % dextrose added. Davis and Kopacz [16] also observed that peak block height was similar between 2- Chloroprocaine [T8 (range T6-L2)] and 2-Chloroprocaine with clonidine [T8(range T4-T11)]. Since most of the studies showed that addition of an adjuvant does not affect the peak sensory level achieved with chloroprocaine, we did not use any adjuvant in the present study.

In the present study, time to two dermatome regression of sensory block in Group A was 39.83±5.91 minutes and in Group B was 59.9±6.55 minutes. Davis and Kopacz[16] observed that time to two dermatome regression of sensory block with 2-Chloroprocaine was 50±9 minutes and 2-Chloroprocaine with clonidine was 50± 22 minutes. Warren and Kopacz [15] observed that time to two dermatome regression of sensory block in 2-chloroprocaine was 40±10 minutes and with 0.25 ml 10 % dextroseadded was 47±8 minutes in their study.

In the present study, time to resolution of motor block in Group A was 49.23±5.74 minutes and Group B was 84.67±6.88 minutes. Warren and Kopacz [15] observed that time to complete regression of motor block in 2-chloroprocaine was 81±15 minutes and with 0.25 ml 10 % dextrose added was 80±14 minutes, suggesting that lower extremity motor blockage was not changed with added dextrose. Davis and Kopacz [16] observed that time to complete regression of motor block with 2-Chloroprocaine was 65±13 minutes and 2-Chloroprocaine with clonidine was 79±19 minutes, suggesting that lower extremity motor blockage was increased with clonidine. These studies showed that a prolonged duration can be achieved by increasing the dose of chloroprocaine and/or adding adjuvants.

In the present study, time to first spontaneous urine voiding in Group A was 156.67±9.94 minutes and in Group B it was 209.4±32 minutes. Similar observations were made by Casati A et al [14] who observed that time to first spontaneous urine voiding in 30 mg Chloroprocaine, 40 mg Chloroprocaine, 50 mg Chloroprocaine was 182 (120-267) minutes, 198 (123-271) minutes, 203 (102-394) minutes respectively. Davis and Kopacz [16] observed that time to first spontaneous urine voiding time with 2- Chloroprocaine was 99±18 minutes and 2-Chloroprocaine with clonidine was 131±15 minutes.

In the present study, no peri-operative or post-operative complications or adverse effects were seen. However, Lacasse MA et al [17] observed that hypotension occurred in 8% of patients who received 2% 2-Chloroprocaine 40 mg and 4% of patients who received 0.75% hyperbaric bupivacaine. He also observed that bradycardia (<50 beats/min) occurred in 6% of patients who received 2-Chloroprocaine and 8% who received bupivacaine. Vaghadia H et al [18] observed in their study that 10% of patients had hypotension during surgery with 40mg 2-chloroprocaine and 40mg 2% lidocaine.

In the present study, there were no post operative Neurological sequelae at 24 hours and within 7 days. Casati A et al [19] reported TNS in 33% of lidocaine patients, but not in chloroprocaine patients. Teunkens [20] compared 1% 2-chloroprocaine and lidocaine and observed

that theuse of lidocaine for observed that the use of lidocaine for spinal anaesthesia is associated with an increased risk of TNS including back and leg pain while no neurotoxicity was seen with preservative free 1% 2-Chloroprocaine. [21]

Conclusion

The right selection of local anaesthetic makes spinal anaesthesia a suitable anaesthetic technique for ultra-short outpatient procedures. If short acting local anaesthetics are involved, spinal anaesthesia could be competitive versus GA for ambulatory surgeries. This study concludes that 20 and 30 mg of plain 1% Chloroprocaine provides adequate spinal anaesthesia for short gynaecological procedure lasting ≤30 minutes. Reliable sensory and motor blockade with predictable duration and minimal side effects and no neurological sequelae can be achieved.

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