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ORIGINAL ARTICLE

A randomized double blind study to compare 1% 2-chloroprocaine and 0.5% hyperbaric bupivacaine in spinal anesthesia for infra-umbilical surgeries

Arvind Khare, MD[1], Beena Thada, MD[2], Devraj Yadav PG[3], Veena Mathur, MD[1], Maina Singh MD[4]

[1]Professor;
[2]Associate Professor;
[3]Resident Doctor;
[4]Assistant Professor

Department of Anesthesiology, Jawaharlal Nehru Medical College Medical College (JLNMC), Ajmer, Rajasthan, (India).

Correspondence: Dr. Beena Thada, MD, Associate Professor, Department of Anesthesiology, JLN Medical College and Hospital, opp. Patel Stadium, Ajmer, Rajasthan 305001 (India); Phone: 9352260425; E-mail: drbeenaverma@gmail.com

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ABSTRACT

Background: Spinal anesthesia is a reliable and safe technique for infra-umbilical surgeries. Preservative-free 2-chloroprocaine has re-emerged for use in spinal anesthesia. We compared onset and duration of sensory block with intrathecal use of 1% 2-chloroprocaine (30 mg) or 0.5% Hyperbaric Bupivacaine (15 mg) as primary objective. Secondary objectives being onset and duration of motor block, duration of analgesia, time to return of voiding function, hemodynamic parameters and side effects.

Methodology: 90 patients of age group 18-60 years, either sex, belonging to ASA physical status I/II undergoing infra-umbilical surgeries were randomly divided into two groups, 1% 2-chloroprocaine Group A (n=45) and 0.5% hyperbaric bupivacaine Group B (n=45). Each group received intrathecally either 30 mg of 2-chloroprocaine or 15 mg of hyperbaric bupivacaine 15 mg. For statistical analysis unpaired-t-test and chi-square test were used.

Results: Earlier onset and shorter duration of sensory block were observed in Group A as compared to Group B respectively ($p < 0.001$). Similarly, onset was earlier and duration of motor block, duration of analgesia and time to return of voiding function were shorter in Group A as compared to Group B respectively ($p < 0.001$). Hemodynamic parameters (HR, MAP) were comparable in both groups.

Conclusion: Intrathecal 1% 2-chloroprocaine 30 mg provides spinal anesthesia of adequate duration for infra-umbilical surgeries with the advantage of earlier onset and faster regression of spinal block resulting in earlier voiding with stable hemodynamics as compared to 0.5% hyperbaric bupivacaine 15 mg.

Keywords: Infra-umbilical surgeries, 2- chloroprocaine, Bupivacaine, Spinal Anesthesia, Sensory Block, Motor Block.

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INTRODUCTION

Majority of infra-umbilical surgeries are done under spinal anesthesia as a first technique of choice, as it is easy to administer, less expensive, blunts stress response to surgery, provides good intra and post-operative analgesia without sedation and avoid the hazards associated with general anesthesia[1] including sore throat, airway trauma and muscle pain. Unfortunately, there is no local anesthetic that provides spinal anesthesia with early onset, adequate duration and depth, early recovery and freedom from the side effects.[2,3]

Due to its early onset and shorter duration of action,

intrathecal lignocaine has been used since years as first choice of local anesthetic but its major disadvantage was transient neurologic symptoms (TNS)[4] which restricted its use in spinal anesthesia nowadays.

As an alternative to lignocaine, smaller doses of hyperbaric bupivacaine have been used but its major disadvantage was prolonged motor block and insufficient analgesia along with retention of urine post operatively which lengthen the patient stay in hospital.[5]

In 1952 an amino-ester local anesthetic 2-chloroprocaine[6] was first introduced as short acting spinal anesthetic as compared to lignocaine with less systemic toxicity. Several case reports of neurological deficits were observed in the early 1980s after inadvertent intrathecal 2-chloroprocaine injections intended for epidural delivery.[7] The antioxidant sodium bisulfite in acidic environment was thought to be the culprit in these cases.[8] So, the drug was no longer use for spinal anesthesia after that.

In recent years, 2-chloroprocaine was once again available in a preservative-free and antioxidant-free [9] form for use in subarachnoid space. It has faster onset of action, short duration of action, predictable block height and time to complete regression. Several studies such as Lacasse et al 2011[10] study, Forster et al 2011[11] study demonstrated the safe use of preservative free intrathecal 2-chloroprocaine in spinal anesthesia but still our anesthesiologists population is reluctant to use it for this purpose.

So, this study was designed to compare onset and duration of sensory block with intrathecal use of 1% 2-chloroprocaine (30 mg) or 0.5% Hyperbaric Bupivacaine (15 mg) as primary objective. Secondary objectives being onset and duration of motor block, duration of analgesia, time to return of voiding function, hemodynamic parameters and side effects.

METHODOLOGY

This randomized double-blind study was conducted on 90 patients undergoing infraumbilical surgeries (general, genitourinary, gynecologic, orthopedics) under spinal anesthesia after obtaining approval from local ethical committee of our institution and their written and informed consent were taken. This study was registered prospectively at the Clinical Trials Registry-India (CTRI/2018/11/016249). Our inclusion criteria were patients of either sex, age between 18-60 years, ASA physical status I and II, undergoing infraumbilical surgeries. Our exclusion criteria were patients with known allergy to study drugs, all well-known contraindications to spinal anesthesia, patients with any deformity, having cardiovascular, renal and neurologic diseases etc. The study population was randomly divided into two groups, 2-chloroprocaine Group A (n = 45) and hyperbaric bupivacaine Group B (n = 45) using computer generated tables of random numbers. Day before surgery a thorough pre-anesthetic evaluation of the patient was done including history, complete systemic examination and all routine blood investigation, coagulation profile, electrocardiogram and x-ray chest. All patients were kept nil per oral for a minimum period of 6 hours before the surgical procedure. After arrival of the patient in the operation theatre an intravenous cannula 20 G was inserted and crystalloid infusion was started. All routine monitors such as electrocardiography, non-invasive blood pressure and pulse oximetry were connected and baseline hemodynamic parameters were recorded. Injection midazolam 0.01 mg/kg intravenous was given to relieve anxiety as premedication. Under all aseptic precautions spinal anesthesia was performed in patient with sitting position at L_3-L_4 subarachnoid space using 25 G spinal needle. After clear and free cerebrospinal fluid flow, patients received either 3 ml (30 mg) of 1 % 2-chloroprocaine or 3 ml (15 mg) of 0.5% hyperbaric bupivacaine according to their study groups. No adjuvant medication was added to both local anesthetic. After the completion of spinal injection, the patients were immediately placed supine. The independent blinded observer evaluated the sensory and motor blocks every 2 min for 10 min, then every five min for 20 min and then every 10 min for next 30 min, and finally every 15 min until the sensory block had regressed to the S_2 dermatome. During surgery, the patient's heart rate, blood pressure, pulse oximetry were recorded at 1, 3, 5, 10, 15, 30, 60 min and every 15 min After achieving T_{10} level of sensory block surgery was started.

Sensory block was assessed in dermatomal areas of T6 to S1, S2 with a blunt 23 G hypodermic needle using following scaling system – 0 = normal sensation. 1 = loss of prick sensation (analgesia). 2 = loss of touch sensation (anesthesia). Onset of sensory block was the time from intrathecal injection to the time taken to achieve T10 dermatome level. Highest level of sensory block achieved was noted and time taken to achieve highest level of sensory block was also noted. Two segment regression and duration of sensory block (was the time taken to regress sensory block upto S1 dermatome in the heel) were also noted.

Motor block was assessed using Modified Bromage Scale 1: Complete block (unable to move feet or knee), 2: Almost complete block (able to move feet only), 3: Partial block (just able to move knees), 4: Detectable weakness of hip flexion while supine (full flexion of knees), 5: No detectable weakness of hip flexion while supine, 6: Able to perform partial knee bend. Onset of motor block and duration of motor block were recorded. VAS Numeric Pain Distress Scale

was recorded before the start of procedure and postoperatively until patient demands IM/IV analgesia.

Duration of analgesia was defined as the time from intrathecal injection to the time when VAS score recorded > 3 or when patient demands for IM/IV analgesia (rescue analgesia). Time to return of voiding function post-operatively was assessed post-operatively by asking whether patient is able to void or not.

The time to return of voiding function was assessed by asking whether patient is able to void or not. Side effects such as bradycardia (heart rate < 50 beats/min), hypotension (decrease in systolic blood pressure > 30% from the baseline), nausea, vomiting etc. were observed

Statistical analysis: Based on previous study by Casati A, Fanelli G, Danelli G, et al 2007, sample size was calculated to be 45 patients, to be randomly included in each group to demonstrate a power of 0.8 and type -1 error of 0.05. To allow for study error and attrition, 45 patients was included in each group. Data were compared by using standard qualitative and quantitative tests (e.g. unpaired student–t-test, Chi-Square, ANOVA). Using SPSS 13.0 for Windows (SPSS Inc., Chicago, IL, USA) statistical analysis was done. Categorical data are presented as number of cases recorded (percent); Continuous variables are presented as mean (standard deviation). No adjustment was made to the comparison-wise P values to account for the multiple outcome variables.

Table 2: Sensory blockade characteristics

Characteristics	2-Chloroprocaine Group A (n = 45) Mean±SD	Hyperbaric bupivacaine Group B (n = 45) Mean±SD	p-value
Onset of sensory block (min)	1.8 ± 0.3	3.2 ± 0.4	< 0.001
Highest level achieved (mean, range)	T8 (T7-T10)	T6 (T5-T7)	< 0.001
Time to achieve highest level (min)	3.4 ± 0.5	4.9 ± 0.5	< 0.001
Time for two segment regression (min)	45.8 ± 6.6	77.4 ± 7.2	< 0.001
Duration of sensory block (min)	110.9 ± 8.5	252.7 ± 35.4	< 0.001

RESULTS

120 patients were assessed for eligibility out of which 30 patients were excluded since they did not fulfill the study criteria, rest 90 patients were included in the study (Figure 1).

There was no significant difference in demographic profile, duration and type of surgery in both Group A and Group B (Table 1).

The time of onset of sensory block was earlier and two segment regression, duration of sensory block were shorter in Group A than Group B ($p < 0.001$) (Table 2).

The time of onset of motor block was earlier and

Table 1: Demographic profile, duration and type of surgery

Patients variables	2-Chloroprocaine Group A (n = 45)	Hyperbaric bupivacaine Group B (n = 45)	p-value
Age (years)	40.7 ± 14	42.9 ± 12.4	0.442
Sex (male/female)	31/14	37/8	0.141
Weight (kg)	67.9 ± 8.9	70.9 ± 7.8	0.086
ASA physical status (I/II)	37/8	39/6	
Duration of surgery (min)	52.7 ± 9.7	54.2 ± 8.0	0.429
Type of surgery			
General	32 (71.11%)	37 (82.22%)	-
Genitourinary	2 (4.44%)	4 (8.89%)	-
Gynecologic	7 (15.56%)	3 (6.67%)	-
Orthopedics	4 (8.89%)	1 (2.22%)	-

Values are expressed as Mean ± SD and n (%) ASA = American Society of Anesthesiologists P < 0.05 (significant)

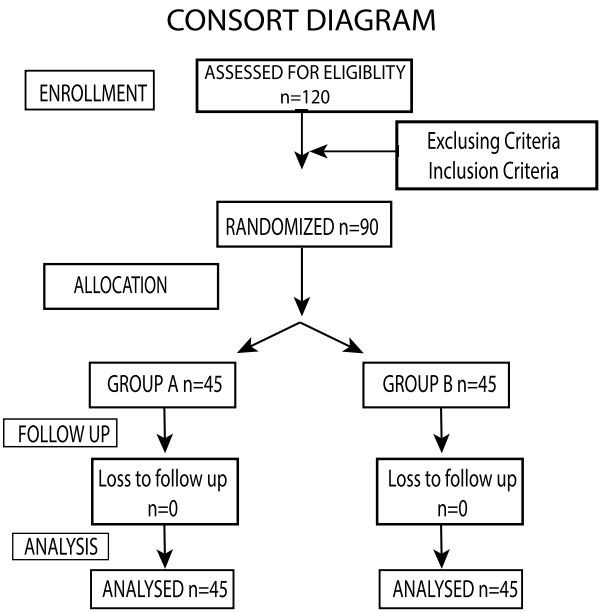

Figure 1: Consort diagram

duration of motor block and analgesia were shorter in Group A than Group B respectively ($p < 0.001$). The time to return of voiding functions was also earlier in Group A than Group B ($p < 0.001$) (Table 3).

Hemodynamic parameters (mean heart rate, mean blood pressure)

There was no significant change in mean heart rate over time in both Groups A and B ($p > 0.05$) (Figure 2).

There was decrease in mean blood pressure at baseline (0 min),1 min,3 min,5 min, in both Groups A and B which was not significant ($p > 0.05$) but at 10 min pattern of decrease in mean blood pressure was significant($p < 0.001$). Again, decrease in mean blood pressure became non-significant at 15 min, 30 min, 45 min and 60 min ($p > 0.05$) (Figure 3).

Hypotension and bradycardia were more observed in Group B than Group A. postdural puncture headache and transient neurological symptoms were not observed in any patients **(Table 4)**.

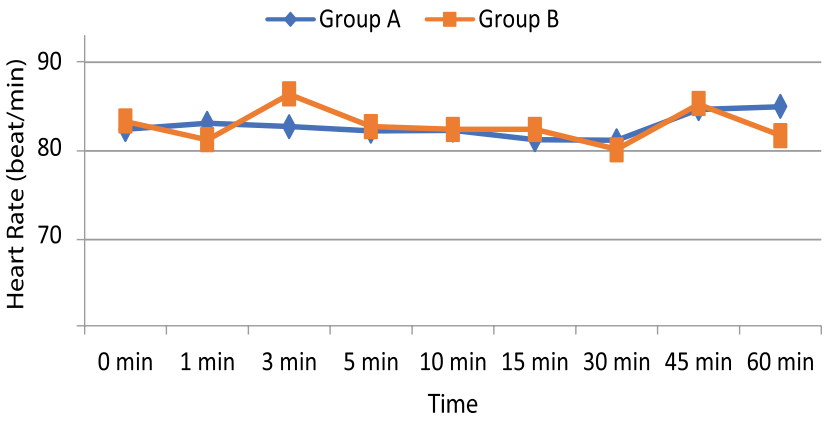

Figure 2: Comparative mean heart rates in two groups

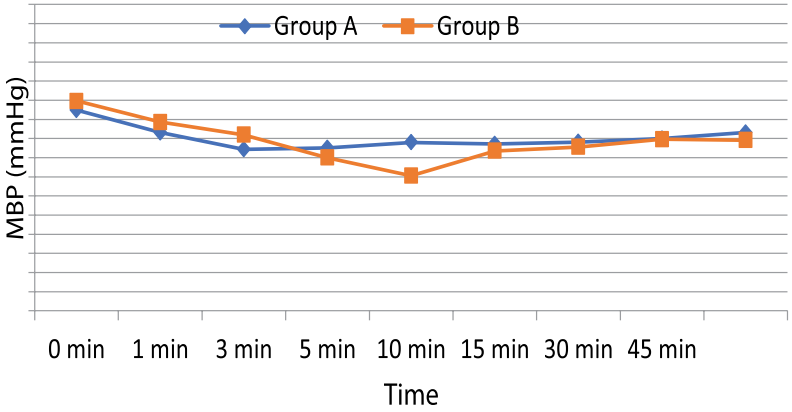

Figure 3: Comparative mean blood pressure

DISCUSSION

The aim of our study was to compare intrathecal 1% 2-chloroprocaine 3ml (30 mg) with 0.5% hyperbaric bupivacaine 3ml (15 mg) in infra-umbilical surgeries.

Amino-ester local anesthetic 2-chloroprocaine has early onset and short duration of action. Several case reports of neurological toxicity were noted in 1980, due to inadvertent intrathecal 2-chloroprocaine injections intended for epidural delivery[7] which was attributed to its preservative sodium bisulphite. 1% 2-chloroprocaine preservative free is available as 10 mg/ml solution now a days, which is approved for intrathecal use.

The time of onset and duration of

Table 3: Motor blockade characteristics, duration of analgesia and time to return of voiding functions [Mean ± SD]

Characteristics	Group A (n = 45)	Group B (n = 45)	p-value
Onset of motor block (min)	3.7 ± 0.6	4.1 ± 0.6	0.001
Duration of motor block (time to modified bromage scale 6) (min)	71.16 ± 12.3	160.7 ± 14.8	< 0.001
Duration of analgesia (VAS score > 3/rescue analgesia) (min)	127.6 ± 9.81	286.9 ± 32.01	< 0.001
Time to return of voiding functions	199.4 ± 19.2	464.9 ± .303	< 0.001

Table 4: Adverse effects

Adverse effects	Group A (n = 45)	Group B (n = 45)	p-value
Hypotension (≥30% baseline)	0	9 (20%)	0.002
Bradycardia (< 50 beats/min)	0	3 (6.7%)	0.078
Nausea	5 (11.1%)	6 (13.3%)	0.748
Vomiting	2 (4.4%)	5 (11.1%)	0.238

Values are absolute number (percent)

sensory blockade were primary objective of our study. Onset of sensory block was 1.8 ± 0.3 min versus 3.2 ± 0.4 min in Groups A and Groups B respectively with significant p value < 0.001. Thus, we observed that the onset time was significantly earlier in Group A. This finding could be attributed due to higher concentration of chloroprocaine (30 mg) used as compared to bupivacaine (15 mg).[13] This parameter was also observed by Dr. Kannan Bojaraaj et al,[14] where they found that the onset of sensory block was comparable in Group A and Group B respectively (150.42 ± 7.77 sec. and 156.5 ± 10.21 sec., p=0.77).

The time for two segment regression of sensory block was 45.8 ± 6.6 min versus 77.4 ± 7.2 min in Groups A and Groups B respectively with significant p value < 0.001. Thus, we observed that it was significantly shorter in Group A. Duration of sensory block was 110.9 ± 8.5 min versus 252.7 ± 32.1 min in Groups A and Groups B respectively with significant p value < 0. 001. Thus, we observed that the time for regression of sensory block to S2 in 2-chloroprocaine group was 2.3 times faster than hyperbaric bupivacaine. Our results coincide with Yoos and Kopacz[15] study where they observed that regression of the sensory block with 2-CP was 1.7 times faster than bupivacaine. Our results also coincide with the results shown by other researchers, where they found that duration of sensory block was shorter in Group A than Group B (p=0.001).[10,14,16,17,18]

The onset time of motor block was 3.7 ± 0.6 min versus 4.1 ± 0.6 min in Groups A and Groups B respectively with significant p value < 0.001. Thus, we observed that the onset was significantly earlier in Group A. Our results also coincide with Dr. Kannan Bojaraaj et al[14] study (5.85 ±1.46 min and 7.35±1.27 min, p=0.04). Duration of motor block was 71.16 ± 12.3 min versus 160.7 ± 14.8 min in Groups A and Groups B respectively with significant p value < 0. 001. Thus, we observed that the time for complete regression of motor block to modified Broamage scale 1 in 2-chloroprocaine group was 2.3 times faster than hyperbaric bupivacaine group. Our results were similar to some earlier studies, where it was found that duration of motor block was shorter in Group A than Group B (p < 0.05).[10,14,16,18]

Duration of analgesia was 127.6 ± 9.81 min versus 286.9 ± 32.01 min in Groups A and Groups B respectively with significant p value < 0. 001. Our results coincide with C. Camponovo et al [(17)] study (120 min and 293 min, p < 0.05). Thus, we observed that the duration of analgesia was shorter in Group A due to early regression of sensory block.

The time to return of voiding function was 199.4 ± 19.2 min versus 464.4 ± 30.3 in Groups A and Groups B respectively with significant p value < 0. 001. Thus, we observed that the time to return of voiding function was significantly earlier in Group A. Our results coincide with Yoos and Kopacz[15] Casati et al,[16] Lacasse et al,[10] Dr. Kannan Bojaraaj et al,[14] Manjulata Tandan et al[18] studies, where they found that return of voiding function was earlier in Group A than Group B (p < 0.05). Study done by Breebaart et al[19] where they compared long acting local anesthetics (levobupivacaine and ropivacaine) with shorter-acting agents (lidocaine) and observed that longer time to first voiding in patients having spinal anesthesia with long acting local anesthetics.

Based on previous studies[20-22] minimum effective dose of 2-chloroprocaine 3ml (30 mg) without additives was chosen which was compared with same volume 3 ml (15 mg) of 0.5%hyperbaric bupivacaine in our study.

Hypotension and bradycardia were more common in Group B than Group A (p > 0.05). Hypotension and bradycardia were more observed in Group B than Group A. postdural puncture headache and transient neurological symptoms were not observed in any patients as we telephonically follow-up the patient for the first 24hrs after recovery from uneventful spinal anesthesia.

CONCLUSION

Intrathecal 1% 2-chloroprocaine 30 mg provides spinal anesthesia of adequate duration for infra-umbilical surgeries with the advantage of earlier onset and faster regression of spinal block resulting in earlier voiding with stable hemodynamics as compared to 0.5% hyperbaric bupivacaine 15 mg.

Conflict of interest: None declared by the authors

Authors' contribution:

AK: Concept and design, manuscript editing and review.

BT: Literature review, manuscript editing and review.

DY: Literature search and review, concept, conduction of study work, manuscript preparation.

VM: Concept and design, literature review.

MS: Literature review.

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