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Comparison of 0.5% Hyperbaric Bupivacaine Versus 1% Chloroprocaine in Spinal Anaesthesia in an Ambulatory Setting; a Randomized Double-Blind Interventional Study

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ABSTRACT

The choice of ideal local anaesthetic agent for spinal anaesthesia is therefore crucial in the ambulatory setting. Lignocaine is associated with a high incidence of transient neurological symptoms, and bupivacaine produces sensory and motor blocks for a prolonged duration.

Aims: This study was designed to compare preservative-free 2-chloroprocaine 40 mg with hyperbaric bupivacaine 15 mg for spinal anaesthesia in an elective ambulatory setting.

Methodology: After approval from the institutional ethics committee, this prospective double-blind interventional study was conducted in 64 patients undergoing spinal anaesthesia. Informed consent was obtained and the study sample was divided into two groups. Group A-1%2-chloroprocaine(n=32), Group B-0.5% hyperbaric bupivacaine(n=32).For statistical analysis, unpaired T-test and chi-square test were used.

Results: The onset characteristics of the sensory block were similar between the groups. However, the onset of motor block, regression characteristics did show a different profile between the two groups. The time for complete regression of sensory blockade to S2 in the 2-CP group was less that of the bupivacaine group (147 min vs 252 min, respectively, p value<0.0001), a difference of 95 minutes. Similarly, the duration of the motor & sensory block was significantly shorter in the chloroprocaine group. The time for ambulation was 184 minutes in chloroprocaine group compared to 280 minutes in the bupivacaine group(p value<0.0001).

Conclusions: 40 mg of plain 1% 2-chloroprocaine proved to be comparable with 15 mg of 0.5% hyperbaric bupivacaine in terms of onset of sensory block. But showed faster recovery from anaesthesia implying superior suitability for outpatient surgeries.

Key Words: Infra-umbilical surgeries, 2-chloroprocaine, Bupivacaine, Spinal Anaesthesia, Sensory Block, Motor Block.

INTRODUCTION

Spinal anaesthesia is often addressed as one of the most desired modes of delivering anaesthesia due to its high reliability, straight forward technique, avoidance of undesirable complications of general anaesthesia, in addition to being more economical.

Infra-umbilical, perineal procedures are most commonly performed under spinal anaesthesia[1], the short duration of the procedure and high turnover of case necessitates the choice of local anaesthetic that exhibit fast onset and quick recovery profile.

Lidocaine has an attractive pharmacokinetic profile as it shows a rapid onset and allows a fast recovery of both motor and sensory block[1]. However, is associated with an increased risk of transient neurological symptoms (TNS) including back and leg pain[2,3,4]. As an alternative, attempts have been made to adapt hyperbaric bupivacaine, a long-acting local anaesthetic, Bupivacaine may provide prolonged postoperative analgesia and has a lower incidence of TNS. However, the longer duration of action may delay the recovery of motor function, cause urinary retention, and therefore ultimately may lead to delayed discharge from the hospital[5].

2-chloroprocaine is an amino-ester local anaesthetic agent

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with a short half-life and a potentially favourable for short outpatient procedures in spinal block[6,7]. 2-chloroprocaine was withdrawn from the market in the 1980s because of concern about neurotoxicity[8,9],2-chloroprocaine with a new formulation without preservatives that have no longer been associated with neurotoxicity[10,11] which was introduced into clinical practice since 2004. 2-chloroprocaine is characterized by both a very fast onset and a quick recovery time[12,13].

This study is conducted to assess and compare the onset, level and regression of sensory and motor block, postoperative ambulation, intra-operative and post-operative analgesic effect, hemodynamic stability and side effects if any after giving 1% 2-chloroprocaine (40 mg) vs 0.5% hyperbaric bupivacaine (15 mg) in spinal anaesthesia in an ambulatory setting.

SUBJECTS AND METHODS:

After obtaining approval from the institutional ethics committee (202/MC/EC/2018, Dt. 27/02/2019, SMS MC Jaipur) and acquiring a written informed consent, 64 patients were randomised into two groups(32 each) for this randomized double-blind interventional study.

Patients between ages 18 to 60 years, with an American Society of Anaesthesiologists (ASA) grade I or II, weighing between 40-80 kg, scheduled to undergo elective infra-umbilical, perineal (general, genitourinary, gynecologic) surgeries lasting for approximate 60 minutes, under subarachnoid block were included. Exclusion criteria included patients with contraindications to spinal anaesthesia, known or ascertained hypersensitivity to local anaesthetics (medications used in the trial), coagulopathies, infection at the local site of injection, history of neurological/psychiatric diseases, any spinal deformity and patient refusal. The different surgeries included were urologic surgery (transurethral resection of the prostate), general surgeries (haemorrhoidectomy, any short anorectal surgery), and gynecologic surgeries (VVF repair). The sample size was calculated as 32 subjects in each of two groups at 95% confidence & 80% power to verify the expected minimum difference of 25(±18) minutes in mean two-segment regression in both the groups[15]. So, for this study 32 subjects were taken for each of the two groups. This sample size was adequate to cover all other study variables also.

The study population were divided into two groups, 2-chloroprocaine Group A (n=32) and hyperbaric bupivacaine Group B (n=32) using the sealed envelope method. A day before surgery a thorough pre-anaesthetic 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 at least 6 hours before the surgical procedure. After the arrival of the patient in the operation theatre, an intravenous cannula of size 18G was inserted and the 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. Pre-medication in. metoclopramide 10mg IV were given. The drug was prepared in a 5ml syringe in equal volume by an anesthesiologist not involved in the study**.** The syringe used was wrapped with white paper. This trial was so planned that the anesthesiologist who had prepared and introduced anaesthetic agent was different from the anesthesiologist who observed the study participants and observed data. The patients were told that some anaesthetic agent would be given, but the type of anaesthetic agent was not disclosed to them.

Under all aseptic precautions spinal anaesthesia was performed by a blinded investigator in patient with sitting position at L3-L4 subarachnoid space using spinal needle of size 25 G. After clear and free cerebrospinal fluid flow, patients received either 4 ml (40 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 anaesthetic. After the administration of spinal injection, patient was placed in supine position with a 15° head down tilt immediately to achieve level ofblock of T5-T6. The same blinded observer evaluated the sensory (with 25g hypodermic needle) and motor blocks (as per modified bromage score) every two minutes for 15 minutes, then every five minutes for 45 minutes, and then every ten minutes for 60 minutes, and finally every 15 minutes until the sensory block regressed to the S2 dermatome. During surgery, the patient's blood pressure (systolic, diastolic and mean arterial pressure), electro- cardiogram, and pulse oximetry were recorded. Vitals were checked every 5 minutes for 30 minutes and after that every 10 minutes till the end of the surgery.

The sensory block was assessed by pin prick test bilaterally in mid-clavicular line by using 25G hypodermic needle. The level of sensory block was assessed every two minutes till the highest level of the block was achieved. The Highest level of sensory block achieved was noted and time taken to achieve highest level of sensory block was 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. During surgery, the motor block evaluation was suspended till the end of the procedure. If the patient complains of pain, fentanyl 25 to 100 mcg iv was administered. If additional sedation needed, midazolam

0.025 to 0.05 mg kg-1 iv was administered. The total dose of any given medication was recorded. If the patient still felt pain, general anaesthesia was provided and the protocol was stopped.

Intraoperatively, hemodynamic parameters (BP, HR, SPO2) were charted every 5 minutes for the first 30 minutes and then even 15 minutes until the end of surgery. Side effects like hypotension (blood pressure <30% from base line), bradycardia (heart rate < 20 % of baseline), nausea/vomiting were documented.

The pain was assessed by the visual analogue scale (VAS) postoperatively, in which patients were asked to grade their severity of pain (0 was minimal or no pain, 10 was the worst pain ever felt). Rescue analgesia in the form of intravenous infusion of injection Diclofenac was given as rescue analgesic. If VAS ≥ 3. The time for first demand for rescue analgesia (duration of analgesia) was recorded.

After the surgery, the duration of surgery was noted and the patient was shifted to the post-anaesthesia care unit where vital parameters, duration of sensory and motor blockade and any side effects of the drugs were observed. After discharge from the recovery room, the patients were transferred to the ambulatory surgical unit where the nurses responsible for the patient care undertook further management. The patient was allowed to take liquid just over an hour after they arrived in the ambulatory unit, and once they can tolerate liquids by mouth and feel a light touch on their legs. The following clinical criteria as described by Pflug[14] were used to determine the time when ambulation may safely be permitted for patients who have had a subarachnoid block:

(1) Return of pin-prick sensation in the peri-anal area (sacral 4-5)
(2) Plantar flexion of the foot (while supine) at pre-anaesthetic levels of strength
(3) Return of proprioception in the big toe.

Then patients were asked to ambulate without assistance. This was taken as the time of ambulation. The patient has monitored 24 hrs post-spinal anaesthesia for any side effects.

STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS, version 21 for Windows statistical software package (SPSS Inc., Chicago, IL, USA). The categorical data were presented as numbers (%) and were compared among the group using the Chi-square test. The quantitative data were presented as mean and standard deviation and were compared by students t-test. Probability was considered to be significant if less than 0.05.

Results: A total of 64 patients, no patients were excluded based on exclusion criteria, no block failure.

Table 1: Demographic profile and duration of surgery

	Group A	Group B	P-Value
Age (years)	38.56±11.32	40.66±14.40	0.52
Sex (M: F)	19:13	22:10	0.602
Weight (kg)	68.28±9.31	67.09±10.44	0.632
Height (cms.)	161.41±7.04	161.72±6.62	0.855
American Society of Anaesthesiologist-grade-I	23	17	0.197
American Society of Anaesthesiologist grade-II	9	15	
Duration of surgery (minutes)	35.33±4.30	38,23±4.90	0.821

Both the groups were comparable concerning age(years), sex, weight (kgs), height (cms.), ASA grade, and duration of surgery (Table 1).

The onset of sensory block (p-Value 0.800) and time to reach peak sensory block height p Value>0.05) were comparable in both the groups and not significant statistically, but the two-segment regression of sensory blockade and time for complete regression to S2(total duration of the sensory block) were significantly shorter in chloroprocaine group. (Table 2).

Table 2: Sensory blockade characteristics [Mean ± SD].

	Group A	Group B	P-value
The onset of sensory block (seconds)	143.03±10.72	142.34±11.	0.800(NS)
Time to reach peak sensory block height (minutes)	16.35±3.1	17.53±2.2	>0.05(NS)
Mean duration of surgery (minutes.)	35.33±4.30	38.23±4.9	0.821(NS)
Two segment regression of sensory block (minutes)	49.22±6.52	78.97±6.17	<0.0001(S)
Time for complete regression to s2 (total duration of the sensory block)	147.81±9.15	252.16±31.43	<0.0001(S)

The time of onset of motor block was earlier and the duration of motor block and analgesia was 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).

Table 3: Motor blockade characteristics, duration of analgesia [Mean ± SD].

	Group A	Group B	P-value
The onset of motor block(minutes.)	3.87±0.75	6.12±0.65	<0.0001(S)
Total duration of motor block (minutes)	80.91±4.86	209.88±18.07	<0.0001(S)
Duration of analgesia (VAS score > 3/rescue analgesia) (minutes)	114.31±2.15	224.66±12.05	<0.0001(S)

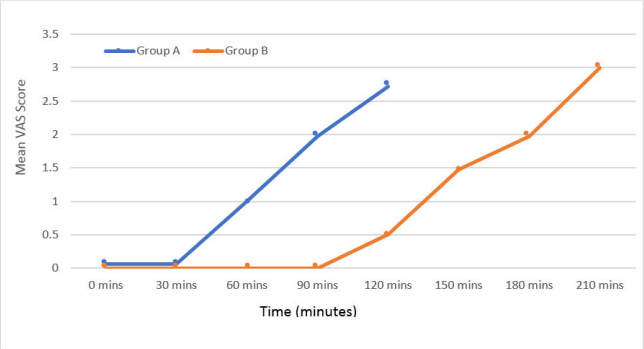

Figure 1: Shows comparison of mean VAS between the groups at different time interval in the post-anesthesia care unit.

The time for the first ambulation after spinal anaesthesia was also shorter in chloroprocaine group in comparison with bupivacaine group(Table 4).

Table 4: Criteria for safer ambulation and time for ambulation

	Group A	Group B	P-value
Time of plantar flexion of the foot (while supine) (minutes.)	71.09±6.25	188.94±56.08	<0.0001(S)
Time of return of pin-prick sensation in the perianal area (sacral4-5) (minutes.)	160.03±6.82	269.12±20.67	<0.0001(S)
Time of return of proprioception in the big toe (minutes.)	63.97±6.75	164.96±12.01	<0.0001(S)
Time to first ambulation (minutes)	184.59±6.55	280.90±22.58	<0.0001(S)

There was no significant variation in hemodynamic measurements between groups. Three subjects with bupivacaine group were treated with ephedrine 6 mg for slight nausea and two patient were treated with atropine for the incidence of bradycardia, similarly, in chloroprocaine group one patient experienced hypotension and one patient suffered from bradycardia and was treated with ephedrine and atropine respectively during the intra-operative period(Table 5).

Table 5: Side effects experienced by patients in both groups

	Group A		Group B		
	Number of patients	%	Number of patients	%	
Hypotension (>30% baseline)	1	3.12	3	9.37	P-value = 0.935 (NS)
Bradycardia/arrhythmias (<50 beats/minute)	1	3.12	2	6.25	
Nausea/ vomiting	1	3.12	1	3.12	
None	29	90.62	26	81.25	
Total	32	100.00	32	100.00	

There was no significant change in mean arterial pressure over time in both Groups A and B ($p > 0.05$) (Figure 1).

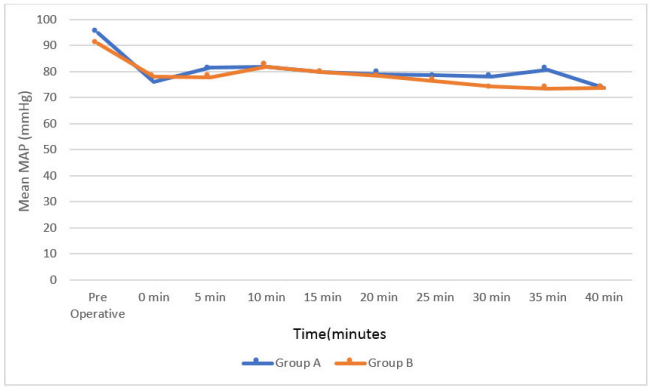

Figure 2: Intra-operative mean arterial pressure(MAP) comparison in both the groups (mm Hg)

No subjects reported any adverse symptoms, including TNS or other neurologic symptoms, either immediately after administration of spinal anaesthesia, or through the 24-hours observation period.

DISCUSSION

The study aimed to compare intrathecal 0.5% hyperbaric bupivacaine with 1% 2-chloroprocaine in infra-umbilical surgeries in an outpatient setting. The principal finding was observed that spinal anaesthesia with 2-chloroprocaine can

provide a satisfactory surgical block while permitting earlier ambulation than spinal anaesthesia with bupivacaine. This is brought about by more rapid regression of the sensory and motor block, which helped patients to ambulate faster.

The time of onset of sensory blockade in chloroprocaine and hyperbaric bupivacaine group were 143.03±10.72 seconds and 142.34±11seconds respectively. The P value< 0.800 is statistically insignificant. Thus, we observed that the difference in onset time was non-significant in both groups. This finding was also observed by Dr. Kannan Bojaraaj et al.,[18] in his study of 2- Chloroprocaine 40mg and 0.5% Bupivacaine 10mg where he observed that the onset of sensory block was comparable in group A and group B 150.42 ± 7.77 seconds and 156.5 ± 10.21 seconds respectively(P value=0.77).

The time of onset of motor block was 3.87±0.75 minutes and 6.12±0.65 minutes in group A and group B respectively with the P-value of <0.001 which was statistically significant. Our results also coincide with the study by C. Camponovo et al.[21] patient received 50 mg of plain 1% 2-chloroprocaine vs. 10 mg of 0.5% plain bupivacaine, he observed time to motor block was 5 minutes and 6 minutes (P-value 0.0337). Our results were similar to some earlier studies, where it was found that the duration of motor block was shorter in Group A than Group B ($p < 0.05$)[18.20].

Maximum cephalad spread was T7 (T5-T9) (mean, range) in all the groups. The P-value is 0.517 which was comparable between all groups. Our observations were consistent with the results of some previous studies[15,16.19,20].

The mean time to reach peak block sensory height in group A was 16.35±3.1 minutes, and in the group, B was 17.53±2.2 minutes. The difference was statistically insignificant between both the groups (P value>0.05). Our result also coincides with the previous study by Marie-Andre ´e Lacasse et al.[15] who observed Spinal anaesthesia with 2% preservative-free 2-chloroprocaine 40 mg or 0.75% hyperbaric bupivacaine 7.5 mg. Time to reach peak block height (minutes) were 15 (8)minutes with 2-chloroprocaine and 18 (11)minutes with bupivacaine(P value=0.15). Similar results were also observed by Dr.ManjulataTandan et al[19] in her study.

The mean time for two-segment regression of sensory block was 49.22 ± 6.52 minutes versus 78.97 ± 6.17 minutes in groups A and groups B respectively with statistically significant P value< 0.001. Thus, we observed that difference in the mean time for two-segment regression was significantly shorter in group A. Our results were similar to the previous study by Jessica R. Yoos et al.[16], who compared chloroprocaine 40 mg vs bupivacaine 7.5 mg; the two-segment regression was 45±20 minutes vs 74±20 minutes(P value=0.01)[15,19,20].

The time for complete regression to S2 (Time for the full recovery of the sensory block) in group A was 147.81±9.15 minutes and in the group, B was 252.16±31.43 minutes. The difference was statistically significant between the group's P-value<0.0001. Our observations were consistent with the results of some previous studies in a similar study by Marie-AndreLacasse et al.[15] who stated that spinal anaesthesia achieved with 2% preservative-free 2-chloroprocaine 40 mg or 0.75% hyperbaric bupivacaine 7.5 mg, the time for resolution of sensory block up to S2 were146±38 minutes vs 329±82 minutes(P-value < 0.001). Our observations were also consistent with the results of some previous study[19,20,21].

The mean duration of motor block was 80.91±4.86 minutes in group A and 209.88±18.07 minutes in group B. The difference was statistically significant between both the groups (P value<0.001). Thus, we observed that the mean duration of motor blocking 2-chloroprocaine group was faster than hyperbaric bupivacaine group. Our results were similar to some earlier studies, in a study done by Marie-Andre Lacasse et al.[15] in their study spinal anaesthesia was achieved with 2% preservative-free 2-chloroprocaine 40 mg or 0.75% hyperbaric bupivacaine 7.5 mg, the duration of motor block was 76±25 minutes vs 119±93 minutes(P-value = 0.005). Our results also coincide with the results shown by other researchers, where they found that the duration of motor block was shorter in Group A than Group B[18.19,20].

The mean time of first rescue analgesic requirement in group A was 114.31±2.15 minutes, and in the group, B was 224.66±12.05 minutes. The difference was statistically significant with a P value<0.001. Our results coincide with the previous study by Camponovo et al[21] in which he compared50 mg of plain 1% 2-chloroprocaine v/s 10 mg of 0.5% plain bupivacaine, his observation showed that the time for first rescue analgesia were 120 minutes and 293.5 minutes respectively (P value< 0.05). Thus, we observed that the duration of analgesia was shorter in chloroprocaine group due to early regression of sensory block[20].

After the sub-arachnoid block, we used the following three criteria as described by Pflug et al.[10]for safer ambulation.

The mean time of plantar flexion of the foot (while supine) (minutes.) In the group, A was 71.09±6.25 minutes, and in the group, B was 188.94±56.08 minutes. The difference was statistically significant between both the groups. (P-value = <0.005).

The mean time of the return of pin-prick sensation in the peri-anal area (sacral 4-5) (minutes.) In the group, A was 160.03 ±6.82 minutes, and in the group, B was 269.12±20.67 minutes. The difference was statistically significant between the groups. (P-value: <0.001).

The mean time of the return of proprioception in the big toe (minutes) in group A was 63.97 ±6.75 minutes and in the group, B was 164.96±12.01 minutes. The difference was statistically significant between the two groups. (P-value:

<0.001).

Udonquak MM et al.[22] also used plantar flexion of the foot (while supine) and return of proprioception in the big toe for early ambulation in their study, they compared pethidine 1mg/Kg with 2.5 ml 0.5% bupivacaine in spinal anaesthesia. He observed the meantime to plantar-flexion was 193.85±39.56 minutes, and the meantime to the recovery of proprioception in big toe was 172.50±42.70 minutes in bupivacaine group. Our study results were nearly similar to their study results for bupivacaine group

The mean time for ambulation was 184.59 ±6.55minutes in group A, and in the group, B was 280.90±22.58 minutes. The difference was statistically significant between both the groups (P value<0.001). Our observations were consistent with the results of some previous studies. In a similar study by Marie-Andre Lacasse et al.[15] where spinal anaesthesia was achieved with 2% preservative-free 2-chloroprocaine 40 mg or 0.75%, hyperbaric bupivacaine 7.5 mg Time to ambulation was 225±56 minutes vs 265±65 minutes (P-value =0.001). Our results were also consistent with the results of the previous studies[17,18,19,21].

In our study, after recovery from sensory and motor block and satisfying all three criteria for safer ambulation, patients were asked to ambulate only when they were physically and mentally satisfied to stand and walk on their own. This was the reason for the time difference between the fulfilment of safer ambulation criteria and time of ambulation.

Hypotension and bradycardia were more common in Group B than Group A. Post-Dural puncture headache and transient neurological symptoms were not observed in any patients as we followed-up the patient for the first 24hrs after recovery from uneventful spinal anaesthesia.

LIMITATIONS OF OUR STUDY

First, in the majority of the available studies, patients are discharged once a recovery from the motor block has been obtained, and ambulation is possible. In our study patient were discharged according to surgical condition. One of the biggest limitations of our study is that it was not perfectly double-blinded. Since the block in the 2-chloroprocaine group regressed earlier and faster, the blinded observer could guess the group to which the patient had been assigned. An additional limitation of our study was determining the precision of the sensory level of the block within two dermatomal levels by a pinprick. This imprecision was minimized by having the same blinded observer responsible for collecting all data during the entire study.

CONCLUSION

A study suggests that for spinal anaesthesia in patients undergoing infra-umbilical day-care surgeries chloroprocaine is a good alternative for bupivacaine, as chloroprocaine has faster regression of sensory and motor block and enables early ambulation because of its short duration of action.

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