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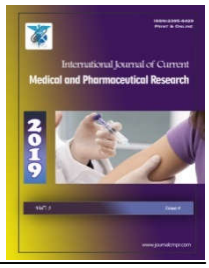

Research Article

COMPARATIVE EVALUATION BETWEEN BUPIVACAINE AND 2-CHLOROPROCAINE FOR SPINAL ANAESTHESIA IN AMBULATORY SURGERIES: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Spinal anesthesiais one popular modality of regional anesthesia. It is popular owing to its safety, simplicity and low cost. Different local anesthetics can be used in spinal anesthesia. Choice depends on duration of anesthesia required, patient profile and postoperative discharge criteria. Bupivaciane heavy has been a popular local anesthetic for the purpose. We have compared bupivacaine and chlorprocaine, 2 local anesthetics based on various parameters.

INTRODUCTION

Spinal anaesthesia is often addressed as one of the most desired modes of delivering anaesthesia due to its high reliability, straightforward technique, avoidance of undesirable complications of general anaesthesia, in addition to being more economical. Quest for search of an ideal spinal anaesthetic possessing qualities of rapid onset, minimal complications and rapid recovery to enable faster ambulation and discharge, has been long underway. 5% Lidocaine, owing to its rapid onset and potency, was widely used to achieve subarachnoid block for ambulatory procedures in the past. However, reports of neurologic deficits associated with spinally administered lidocaine generated concern regarding the potential toxicity of this agent.[1] Additionally, the recognition that transient neurologic symptoms (TNS) often occurred following spinal administration of lidocaine, prompted more enthusiasm to search for better alternatives.[2]

Bupivacaine has been employed commonly for sub arachnoid block. However, with the emerging trends and inclination towards ambulatory surgeries favouring early discharge, the long duration of action of this drug does not make it a popular choice for the same.[3]

Chloroprocaine, an amide local anaesthetic has a profile resembling that of lidocaine in terms of onset and duration. Doses varying between 30 to 60 mg produce therapeutic effects similar to lidocaine.[4]However, neurologic injury had been identified in about 8 cases who were given a chloroprocaine solution contained sodium bisulfite as the preservative via epidural route, limiting the use of this drug in clinical practice. Thorough analysis of the cases eventually revealed the cause of the injury to be an accidental injection of large volume of anaesthetic aimed for epidural route into the intrathecal space. Some experiments carried out by Gissen *et al*. demonstrated irreversible block by 3 % chloroprocaine containing 0.2% sodium bisulfite at a pH 3, but increasing the pH of the solution to 7.3 led to a complete recovery.[5] This pointed to the hypothesis that that liberation of sulphur dioxide was the probable etiology of injury. Therefore, a chloroprocaine solution devoid of preservative is now available for intrathecal use commercially.

Our study aimed at comparing the efficacy of intrathecally administered 12.5 mg of 0.5% hyperbaric bupivacaine to 40 mg of 1% isobaric preservative-free chloroprocaine.

MATERIALS AND METHODS

After obtaining approval from thelocal ethic committee and procuring a written informed consent, 120 patients were randomised into two groups to undergo this prospective, double -blinded, analytical trial.

Patients between ages 18 years and 60 years, with an American Society of Anesthesiologists (ASA) physical status I or II, weighing between 40-90 kg, scheduled to undergo elective ambulatory lower abdominal or lower limb surgeries lasting for < 60 minutes, under sub arachnoid block were included.

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Exclusion criteria included patients with contraindications to spinal anesthesia, patients with an ASA physical status more than II, known or ascertained hypersensitivity to local anaesthetics (medications used in the trial), coagulopathies, infection at local site of injection, history of neurological/psychiatric diseases and patient refusal.
The different surgeries included were urologic surgeries such as cystoscopy, transurethral bladder tumour resection, circumcision, hydrocelectomy), general surgeries (haemorrhoidectomy, any short anorectal surgery), and gynecologic surgeries (hysteroscopy, cystocele repair, dilatation, and curettage).

Each subject was allotted an enrolment number based on the alphabetical sequence of the letters of his/her surname. An observer then blinded to this format assigned each patient a number that corresponded to their enrolment order (the first patient received the number 1; the second patient received the number 2, and so on). Next, an unblinded anaesthesiologist, using a computer dependent randomized list where each number was linked to a local anaesthetic, either 2-Chlorprocaineor bupivacaine, divided the patients into two groups. The same anaesthesiologist then performed the spinal anesthesia in both the groups using the allotted local anaesthetic to that patient. The effect and final outcome of the drug administration was assessed by another anaesthetist blinded to the local anaesthetic administered. Hence, the patient, observer who recruited these patients and anaesthetist assessing the effect of the drugs were blinded.

The day before surgery, all patients underwent thorough pre-anaesthetic check-up, which included routine history, general as well as systemic examination. Necessary investigations were obtained in indicated cases. The patients were made familiar with Visual Analogue Scale (VAS) to grade the severity of postoperative pain. Patients were kept nil by mouth for solids for at least 6 hours and clear fluids for 2 hours.

On the day of surgery, standard monitoring in terms of non-invasive blood pressure (BP), heart rate (HR) and pulse oximetry (spO_2) were instituted. A wide bore intravenous line was secured an infusion of Normal Saline (0.9%) was initiated in both the groups. Premedication in the form of i.v midazolam (0.02mg/kg) was given if needed. Depending on the result of the computer based randomisation process, the patients were planned to receive one of the following two local anaesthetic(40 mg of 1% 2-chloroprocaine plain solution to Group C, or 12.5 mg of hyperbaric 0.5% bupivacaine in Group B). The patient was positioned in left lateral position. Under aseptic precautions, skin over the back was cleaned with povidone-iodine solution and draped. A skin wheal using 2% lidocaine was raised at L3-L4 level by the same anaesthesiologist in both the groups. Lumbar puncture was performed with a 25 G or 27 G Quincke's needle using the midline approach. Following successful localisation of the subarachnoid space, the patient was administered the drug depending upon the group he/she was randomly allotted to.

A number of parameters were evaluated and noted by an anaesthetist who was blinded to the type of local anaesthetic given. Sensory block was evaluated by assessing the peak level dermatome (assessed by loss of pinprick sensation starting at the L2 dermatome and graded according to Gromley and Hill 1996: Normal sensation-0, Blunted sensation-1, No sensation-2 with grade 2 being considered as the onset of sensory block).Motor block was assessed by using the modified Bromage scale (no motor block = 0; hip blocked = 1; hip and knee blocked = 2; hip, knee and ankle blocked = 3).Readiness for surgery was defined as a sensory level of T10 and a motor block of Bromage grade 2. The time to reach sensory block of T10 (t1) and motor block of Bromage 2 (t2), time taken to reach peak sensory level of block(t3), and then every 30 minutes until complete regression of sensory block to S2 (t4) and motor block to Bromage grade 0 (t5) was noted.If the level of anaesthesia was inadequate, the regimen was switched to general anaesthesia and excluded from the study.

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 likehypotension (blood pressure <30% from base line), bradycardia (heart rate < 20 % of baseline), nausea/vomiting were documented.

At the completion of surgery, the duration of surgery was noted and the patient was shifted to the PACU where vital parameters, duration of sensory and motor blockade and any side effects of the drugs were observed for 12 hours. 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 tramadol 2 mg/kg was given if VAS $\geq$ 3. The time for first demand for rescue analgesia (duration of analgesia) was recorded.

Statistical Analysis

The primary outcome was the time taken to achieve a sensory level of T10. The secondary outcome was the time to complete regression to S2 (complete resolution of sensory effect). The clinical end point of analysis was time to unassisted ambulation. The sample sizewas calculated based on a pilot study which suggested 54 subjects per group (alpha = 0.05, power =80%). Therefore, 120 subjects in total were considered adequate for this study.

Demographic characteristics were evaluated according to qualitative or quantitative data. Comparison of block regression over time was made using a two-way analysis of variance for repeated measures. Incidence data (incidence of hypotension, bradycardia, postoperative nausea and vomiting (PONV), and postoperative complications) were compared using Chi square test. Student's t test was used to compare the other variables, including the primary outcome (time to reach peak sensory level) and secondary outcomes (time for complete regression of the sensory and motor blocks, time for first rescue analgesia). P value <0.05 was considered as statistically significant.

RESULTS

124 patients were enrolled for this study of which 4 were excluded due to withdrawal of consent. The patients shared similar demographic characteristics (Table 1).

Sensory block reached the T10 dermatome after a mean of seven and a half minutes in group B whereas the time in group C was a mean of six minutes. The peak block height was T6 in group C and T8 in group B and the time taken to reach the same was almost similar (14 minutes for group C and 17 minutes for group B) (Table 2). The duration of block markedly differed in both the groups. Time to complete regression of block to S2 was faster with chloroprocaine (138

minutes vs 356 minutes, p <0.001).The duration of motor blockade displayed similar differences between the two groups (73 minutes for chloroprocaine vs 124 minutes for bupivacaine). The time for first dose of rescue analgesia in the form of intravenous tramadol (2mg/kg) was faster with chloroprocaine (110 minutes) than bupivacaine (214 minutes) (Table 2). The incidence of intraoperative hypotension was higher with bupivacaine (10%). Similarly, only 1 patient in group C developed bradycardia as against 5 patients in group B. Nausea/Vomiting were similar in both groups. 4 patients in group B had insufficient levels of anaesthesia requiring conversion to general anaesthesia and were excluded from our study. There were no cases of transient neurological symptoms reported in a follow up of 24 hours in either group.

Table 1 Demographic characteristics and duration of surgeries in both groups

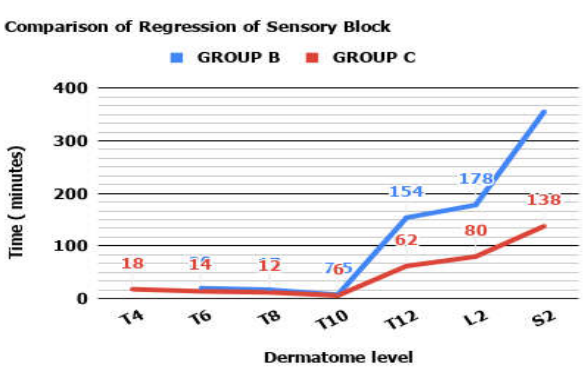
VARIABLES	GROUP B (n= 60)	GROUP C (n = 60)
AGE (years)	43 ± 8	47 ± 6
SEX (Male/Female)	26/34	38/22
WEIGHT (kg)	42.5 ± 15.1	50.1 ± 12.4
HEIGHT (cm)	162 ± 8	164 ± 7
ASA PHYSICAL STATUS (I/II)	24/36	40/20
LENGTH OF SURGERY (minutes)	48.2 ± 5.4	38.2 ± 10.1

Table 2 Analysis of sensory and motor blockade

VARIABLES	GROUP B	GROUP C
Time to Sensory Block of T10 (t1, minutes)	7.5 ± 1	6 ± 2
Time to onset of Motor Block (Bromage 2) (t2, minutes)	6 ± 2	5 ± 3
Time to reach peak Sensory Block(t3, minutes)	T8: 17	T6: 14
Duration of Sensory Block (t4, minutes)	356 ± 8	138 ± 6
Duration of Motor Block(t5, minutes)	124 ± 7	73 ± 5
Postoperative VAS Score (12 hours)	2 ± 1	3 ± 1
Time for first Rescue Analgesia(t6, minutes)	214 ± 8	110 ± 7
Time to unassisted ambulation (t7, minutes)	221 ± 7	265 ± 8

Table 3 Incidence of complications associated with drugs administered

COMPLICATION	GROUP B	GROUP C
Nausea/Vomiting	1 (1.6%)	0 (0%)
Bradycardia	5 (8.3%)	1 (1.6%)
Hypotension	6 (10%)	2 (3.3%)
Insufficient Anaesthesia	4 (6.6%)	0 (0%)



Graph 1 Differences in time to regression of sensory block to S2

DISCUSSION

Our study implies that anaesthesia sufficient to perform lower abdominal and limb ambulatory surgeries (lasting less than 60 minutes) can be provided by 40 mg of 1% chloroprocaine. Both chloroprocaine and bupivacaine demonstrated similar pharmacological profiles in terms of time to reach readiness for surgery (T10 sensory level) with the former offering a 1.5 minutes shorter latency period. On the other hand, comparing motor blockade, the time to onset of motor blockade as gauged by a Bromage of 2 was 1 minute longer with bupivacaine. Peak sensory block was achieved in 14 minutes with chloroprocaine and 17 minutes with bupivacaine.

The regression of sensory block to S2 occurred almost 2.5 times faster with chloroprocaine (amounting to 138 minutes) when compared to bupivacaine (356 minutes). When considering motor blockade, the duration was 73 minutes with chloroprocaine and 124 minutes with bupivacaine. Chloroprocaine demonstrated superiority in terms of time to complete ambulation allowing the same in an average time of 44 minutes lesser as against bupivacaine. The shorter duration leading to faster recovery from intrathecal anaesthesia displayed by chloroprocaine tends to give it a clinical advantage in ambulatory surgeries.

Our findings were similar to previous literature. In a previous study conducted by Lacasse *et al* comparing these 2 drugs, discharge ready times were 277 and 353min for 2% 2-chloroprocaine and 0.75% bupivacaine, respectively. Additionally, the time for regression of the sensory block to S2, as 2-CP was 2.3 times faster than bupivacaine in their study.[6]

Previous studies of 2-CP suggested that 40 mg would be the minimum dose required to achieve a reliable and sufficient sensory and motor block for short duration surgeries. Ben-David *et al*. showed that hyperbaric bupivacaine 7.5 mg was sufficient to provide satisfactory anesthesia for arthroscopic knee surgery. Hence, the dose of local anaesthetic administered in our study was clinically equivalent and efficacious.[7]

Following completion of surgery, patients were transferred to the post anaesthesia care unit for routine observation. Time for first rescue analgesia was 110 minutes for 2 chloroprocaine and 214 minutes for bupivacaine. Our findings were consistent with the study conducted by Campnova *et al*. The first analgesic requirement in their study was shorter with chloroprocaine (120 minutes) than with bupivacaine (293 minutes).[8]The earlier demand for analgesics with chloroprocaine certainly can be outweighed by faster time to ambulation and complete recovery of sensory function.

In terms of intraoperative hemodynamic perturbations, in group B, 8.3% of patients experienced bradycardia and 10% of patients developed hypotension requiring pharmacological intervention. In contrast in group C, 1.1% of patients developed bradycardia and 3% patients developed clinically significant hypotension.

Our study was limited by a few factors. We did not follow up the patients beyond the period of their discharge from the hospital through follow up phone calls to evaluate any neurologic toxicity or other adverse effects. (Even though none of the patients had any complaints pertaining to anaesthesia during their surgical outpatient department follow up). Urinary

retention after spinal anaesthesia for lower limb procedures has an overall incidence of around 3.8%.We did not assess the time taken to void and the incidence of urinary retention in both groups post operatively.

We believe that the speedier recovery from spinal anaesthesia with the utilization of 2 chloroprocaine could provide a potential advantage of cost savings by facilitating earlier discharge without compromising the quality of patient care.

To conclude, 40 mg of plain 1% 2-chloroprocaine proved to be comparable with 12.5 mg of 0.5% hyperbaric bupivacaine in terms of onset of sensory block to T10 in patients undergoing spinal anaesthesia for short procedures. Furthermore, 1% 2-chloroprocaine showed faster recovery from anaesthesia implying superior suitability for outpatient surgeries.

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