Original Research Paper

Volume-8 | Issue-6 | June-2018 | PRINT ISSN No 2249-555X

Anesthesiology

HYPERBARIC BUPIVACAINE AND 2-CHLOROPROCAINE FOR SPINAL ANESTHESIA IN OUTPATIENT PROCEDURES : A COMPARATIVE STUDY.

Dr.Manjulata Tandan*	Department Of Anaesthesia And Critical Care, Late Shree Lakhiram Agrawal Memorial Hospital Raigarh (C.G.)*corresponding Author
Dr.A.M. lakra	Department Of Anaesthesia And Critical Care, Late Shree Lakhiram Agrawal Memorial Hospital Raigarh (C.G.)
Dr.sandeep Bhagat	Department of Anaesthesia And Critical Care, Late Shree Lakhiram Agrawal Memorial Hospital Raigarh (C.G.)
Dr. S.K.Dwivedi	Department of Anaesthesia And Critical Care, Late Shree Lakhiram Agrawal Memorial Hospital Raigarh (C.G.)

ABSTRACT

Background:Its always been wandered for the ideal local anesthetic agent for spinal anesthesia in outpatient procedures As Lignocaine is associated with a high incidence of transient neurological symptoms, and bupivacaine produces sensory and motor blocks of long duration. Being a short-acting agent of increasing popularity in recent years ; preservative- free 2-chloroprocaine (2-CP) seems to be a promising alternativeto them. This study was designed to compare 2-CP with bupivacaine for spinal anesthesia in an elective outpatient surgeries.

Method:After obtaining institutional ethical committee approval and caregivers written informed consent 50 patients of age group 18-60 years of ASA grade I & II of either sex undergoing urologic surgeries (i.e.cystoscopy, circumcision, anorectal surgeries i.e. fissure in ano fistula and hemorrhoides, varicocelectomy, and hydrocelectomy) and gynecologic surgeries i.e. (hysteroscopy, vulvar or vaginal biopsy, cystocele repair, dilatation, and curettage) were included in this comparative study. After getting a detailed history, general and systemic examination and necessary investigations patients were randomly allocated into two groups. In Group B patients received spinal anesthesia with 0.75% hyperbaric bupivacaine 7.5 mg (n = 25) and Group C received 2% preservative-free 2-CP 40 mg (n =25). The primary endpoint for the study was the time reaching the patients ability to get discharged . Secondly our study included the duration of sensory and motor blockades, the length of stay in PACU, the time until ambulation and micturition.

Results:The average time for patients discharge was 245 min in the 2-CP group and 340 min in the bupivacaine group, a difference of 95 min (95% confidence interval [CI]: 40 to 112 min; $P < 0.001$). The average time for complete regression of the sensory block was 130 min in the 2-CP group and 290 min in the bupivacaine group, a difference of 160 min (95% CI: 159 to 212 min; $P < 0.001$). Times for ambulation and micturition were also significantly lower in the 2-CP group.

Conclusion:Spinal 2-chloroprocaine provides adequate duration and depth of surgical anesthesia for short procedures with the advantages of faster block resolution and earlier hospital discharge compared with spinal bupivacaine.

KEYWORDS : Outpatient surgeries, Bupivacaine, Spinal Anesthesia, Lignocaine, 2- chlorprocaine, Motor Block, Sensory Block

INTRODUCTION

Nowadays many procedures are performed in an outpatient settings, and many of them are conducted under spinal anesthesia. Unfortunately, no local anesthetic can provide a block with rapid onset, predictable duration, good effectiveness and reliability, fast recovery, and lack of side effects. Spinal anesthesia is a reliable and a safe technique for procedures of the lower abdomen and extremities.Though, some of its characteristics may limit its use for ambulatory surgery i.e. delayed ambulation, risk of urinary retention, and pain after block regression. The current availability of short-acting local anesthetics has renewed interest for this technique in context to short- and ultra-short procedures. Chloroprocaine (CP) is an amino-ester local anesthetic with a very short half-life. It was introduced and has been successfully used for spinal anesthesia since 1952. Sodium bisulfite was then added as a preservative after 1956. The drug was then abandoned in the 1980s for several reports of neurological deficits in patients receiving accidentally high doses of intrathecal CP during epidural labor analgesia. Animal studies have proven the safety of the preservative-free formulation, which has been extensively evaluated in volunteer studies as well as in clinical practice with a favorable profile in terms of both safety and efficacy. In comparison with bupivacaine, 2-chloroprocaine (2-CP) has faster offset times to end of anesthesia, unassisted ambulation, and discharge from hospital. These findings suggests that 2-CP may be a suitable alternative to low doses of long-acting local anesthetics in ambulatory surgery. Its safety profile also suggests that 2-CP could be a valid substitute for intrathecal short- and intermediate-acting local anesthetics, such as lignococaine and mepivacaine – often causes transient neurological symptoms. In this context, literature suggests a dose ranging between 30 and 60 mg of 2-CP for procedures lasting 60 minutes or less, while 10 mg is considered the no-effect dose.Our study was designed to compare 2-CP with bupivacaine for spinal anesthesia in elective ambulatory surgeries. We hypothesized that 2-CP can provide spinal anesthesia with a shorter recovery profile than bupivacaine, permitting earlier discharge from hospital after ambulatory surgery.

Methods

After receiving approval from the ethical committee a written informed consent was obtained from each patient. All patients were informed about the cases of neurotoxicity in the 1980s that were related to the use of 2-CP (the preparation with a low pH and with sodium bisulfite as an antioxidant). A total of 50 patients were enrolled in this randomized double-blind study.

INCLUSION CRITERIA

1. Patients age 18yrs and above and below 60 years.
2. ASA grade I & II .Z
3. Patients with either sex.
4. Urologic surgeries (cystoscopy, circumcision, anorectal surgeries like fissure in ano fistula and hemorrhoides, varicocelectomy, and hydrocelectomy), general surgeries (hemorrhoidectomy, rectal biopsy, or any short anorectal surgery), and gynecologic surgeries (hysteroscopy, vulvar or vaginal biopsy, cystocele repair, dilatation, and curettage). were included in this comparative study.

EXCLUSION CRITERIA

Patients with contraindication to spinal anaesthesia i.e.

1. Having cardiovascular diseases
2. With a known history of allergy to study drugs
3. With Bleeding diathesis
4. With Local and systemic infection,
5. With Psychiatric illness,

6. With Chronic headache and backache in the past and
8. Patients on anticoagulant therapy with (international normalized ratio > 1.3, platelets < 75,000)
9. with neurologic disease (multiple sclerosis, symptomatic lumbar herniated disc, spinal stenosis), were excluded from the study.

After a detailed history, general and systemic examination and necessary investigations patients were randomly allocated into two groups. In Group B patients received spinal anesthesia with 0.75% hyperbaric bupivacaine 7.5 mg (n = 25) and Group C received 2% preservative-free 2-CP 40 mg (n =25). The primary endpoint for the study was the time reaching the patients ability to get discharged . Secondly our study included the duration of sensory and motor blockades, the length of stay in PACU, the time until ambulation and micturition.

(international normalized ratio > 1.3, platelets < 75,000, use of anticoagulant drugs), neurologic disease (multiple sclerosis, symptomatic lumbar herniated disc, spinal stenosis),

The same blinded observer recruited all patients and 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). Afterwards, an unblinded anesthesiologist, the anesthesia provider, consulted a computer-generated randomized list where each number was linked to a local anesthetic, either 2-CP or bupivacaine, for each patient. The anesthesiologist then performed the spinal anesthesia using the local anesthetic randomly assigned to that patient. Both the patients and the observer who recruited the patients and collected the data were blinded.

All patients were kept NBM for at least 4-6hrs before the procedure. After arrival in the operation theatre, an 18 G peripheral intravenous catheter was inserted into the patient's forearm, and approximately 10 mL/kg of crystalloids were infused. Standard monitoring was used i.e. NIBP, ECG (4 leads), and SpO2. I/V midazolam 0.025 to 0.05 mg/kg was given for sedation before or immediately after giving spinal.

Spinal anesthesia was given under under all asceptic conditions after local infiltration of the skin with 1% lidocaine. With the patient in the sitting position, the subarachnoid space was entered at the L2-3, L3-4, or L4-5 interspace via the midline approach using a 25 or 27G Sprotte spinal needle. According to their randomization, patients received an intrathecal injection of either 0.75% hyperbaric bupivacaine 7.5 mg (1 mL) (n = 25) or a preservative and bisulfite-free formulation of 2% 2-CP 40 mg (2 mL)(n = 25).

After the completion of the spinal anaesthesia , the patients were immediately placed supine. The independent blinded observer evaluated the sensory and motor blocks by pin prick method on every three minutes for 15 min, then every five minutes for 30 min and finally every 15 min until the sensory block had regressed to the S2 dermatome. During surgery, the patient's blood pressure (systolic and diastolic), electrocardiogram, and pulse oximetry were recorded.
The sensory block was assessed in a caudal to cephalad directionby pin prick method and The degree of motor block was assessed by using the

Modified Bromage scale:
Grade 0 = no block, full straight leg raise possible
Grade 1 – inability to elevate extended leg (able to flex knee)
Grade 2 – inability to flex knee (able to move foot only)
Grade 3 – inability to flex ankle
Grade 4 – complete motor paralysis
Readiness for surgery was defined as loss of pin prick sensation ≥ T10.

During surgery, evaluation of the motor block was suspended until the end of the procedure. If additional sedation was needed, midazolam 0.025 to 0.05 mg/kg *iv* was administered. The total dose of any given medication was recorded.

The occurrence of clinically relevant hypotension (defined as a decrease in systolic arterial blood pressure ≥ 25% from baseline values) was treated with mephentermine. Clinically relevant bradycardia (defined as heart rate < 60 beats/min) was treated with atropine . The total dose of mephentermine or atropine needed was recorded.

Postoperative analgesia consisted of diclofenac 75mg *iv* if needed, Ondansetron 4 mg *iv* was given for nausea. The cumulative doses of these medications were recorded. Patients were discharged from the postanesthesia care unit (PACU) when they had attained all of the following criteria: a minimum 60-min stay, stable vital signs, signs of regression of the motor block (Bromage 0 to 2), no analgesia within the previous 20 min, and normal consciousness.

After discharge from the PACU, the patients were transferred to the ambulatory surgical unit where the nurses responsible for patient care undertook them. The patients were given a light snack just over an hour after their arrival in the ambulatory surgical unit, and once they could tolerate liquids by mouth and feel a light touch to their legs, they were asked to ambulate without assistance. Success at walking was followed by an attempt to void. Discharge from hospital was possible when the patients attained following criteria: complete regression of the block to light touch, ability to void, ability to walk, stable vital signs, no nausea, pain controlled with oral medication and ability to tolerate liquids per orally. The primary outcome of this study, i.e., the time to eligibility for discharge from hospital, was measured from the time spinal anesthesia was performed to the time the patient attained all of the discharge criteria.

The following data were recorded: peak block height and time to reach peak block height, time two segments regression , time for regression to L1, and time for complete regression. For the motor block, the Bromage score at the end of the surgery and the time to reach a score of 0/3 were also recorded. In addition, time to reach readiness for surgery, length of surgery, length of stay in the PACU, time to void, time to ambulate, and time to reach discharge readiness criteria were also recorded.

Patients were contacted by telephone 24 hr and seven days following surgery to assess potential complications related to the spinal anesthesia. A standardized questionnaire was used to check for the presence of headache, paresthesia or dysesthesia in the lower limbs, lower back pain, nausea or vomiting, and difficulty voiding. Also, during the first follow-up call, the patient's satisfaction with the anesthesia provided was assessed using a scale from 0 to 10 (0 = total dissatisfaction; 10 = total satisfaction).

Statistical analysis
In a pilot study of 50 patients having spinal anesthesia using hyperbaric bupivacaine 7.5 mg for urologic, gynecologic, and general procedures, the mean time to eligibility for discharge was 340 min. The sample size was based on a two-sided test with an alpha of 0.05 and a power of 90%. To obtain a 60-min reduction, a minimum of 25 patients per group was required.

An integer was assigned to each dermatomal level (i.e., T1 = 1, T2 = 2, T3 = 3, T4 = 4, etc.) for statistical analysis of dermatomal height. To calculate the regression time of the block, the dermatomal height of the sensory block was compared for each patient in each group for each time interval. Comparison of block regression over time was made using a two-way analysis of variance for repeated measures. Incidence of hypotension, bradycardia, pain requiring analgesia, postoperative nausea and vomiting (PONV), and postoperative complications were compared using Chi square test (when the expected values in any of the cells of a contingency table were < 5). Student's t test was used to compare the other variables, including the primary outcome (time to eligibility for discharge) and secondary outcomes (time for complete regression of the sensory and motor blocks, length of stay in the PACU, and time to ambulation and micturition).

Statistical analysis was performed using SPSS 13.0 for Windows (SPSS inc., Chicago, IL, USA). Continuous variables are presented as mean (standard deviation); categorical data are presented as number of cases recorded (percent). No adjustment was made to the comparison-wise P values to account for the multiple outcome variables.

Results
The patients were similar in terms of baseline demographics and the type and length of surgery (Table 1). The average time to discharge readiness was 245 min in the 2-CP group and 340 min in the bupivacaine group, a difference of 95 min (95% confidence interval [CI]: 40 to 112 min; P < 0.001).

Table 1

	2-Chloroprocaine (n = 25)	Bupivacaine (n = 25)
Age (yr)	45	46
Sex (male/female)	22/28	20/30
Weight (kg)	65	63
Height (cm)	165 (8)	165
ASA physical status (I/II)	19/32	23/29
Length of surgery (min)	20.2	25.5
Type of surgery		
Genitourinary	6	4
General	11	12
Gynecologic	2	2
Anorectal surgeries	6	7

The onset characteristics of the block were similar between the groups, as was the time required to achieve readiness for surgery, the peak block height, and the time to reach peak block height. In both groups, the sensory block reached the T10 dermatome after a mean of six minutes, and the peak block height was T7 (Table 2). However, regression characteristics did show a different profile between the two groups. Regression of the block to L1 was almost 50% faster in the 2-CP group than in the bupivacaine group (82 min vs 160 min, respectively, a difference of 79 min; 95% CI: 61 to 97; P < 0.001). The time for complete regression to S2 in the 2-CP group was less than half that of the bupivacaine group (146 min vs 329 min, respectively, a difference of 185 min; 95% CI: 159 to 212; P < 0.001) (Figure). Similarly, the duration of the motor block was significantly shorter in the 2-CP group (Table 2). Successful spinal anesthesia was attained in all patients, which was defined as the ability to complete the surgery without the need for general anesthesia.

Table 2

	2-Chloroprocaine (n = 25)	Bupivacaine (n = 25)	Pvalue	Difference between groups (95% CI)
Primary outcome				
Time to eligibility for discharge from hospital (min)	245	340	< 0.001	75.9 (39.9 to 112.0)
Secondary outcomes				
Sensory				
Time to readiness for surgery (min)				
Mean (standard deviation)	4	4	0.50	−0.4 (−1.7 to 0.8)
Range	2 to 10	2 to 8		
Peak block height (mean, range)	T7 (T1 to T10)	T7 (T1 to T11)	1.00	T7 (T6 to T8)
Time to peak block height (min)	12	15	0.15	2.8 (−1.1 to 6.7)
Time for two-segment regression (min)	45	70	< 0.001	25.4 (14.2 to 36.6)
Time for regression to L1 (min)	75	155	< 0.001	78.8 (60.7 to 96.8)
Time for complete regression to S2 (min)	140	320	< 0.001	185.4 (158.5 to 212.4)
Motor				
Duration of the motor block (min) (time to Bromage = 0)	70	115	0.005	43.3 (16.4 to 70.2)
Discharge				
Length of stay in PACU (min)	64	65	0.66	1.3 (−4.6 to 7.2)
Time to ambulation (min)	220	245	0.001	40.0 (16.3 to 63.7)
Time to micturition (min)	260	330	0.001	67.7 (27.3 to 108.1)
Interval from first try to successful voiding (min)	6	20	0.02	20.6 (3.8 to 37.4)

Length of stay in the PACU was similar in both groups. However, in terms of discharge criteria, the time to ambulation, micturition, and eligibility for discharge were all significantly shorter in the 2-CP group (Table 2).

During surgery, the incidence of hypotension, bradycardia, pain requiring analgesia, and the total dose of fentanyl given were similar between groups (Table 3). In the PACU, the incidence of hypotension, bradycardia, and PONV were also similar between groups. However, patients in the 2-CP group experienced more pain in the PACU, with a 19% difference in the incidence of pain between groups (P = 0.007). Patients in the 2-CP group also received more fentanyl in the PACU than the bupivacaine group (a mean of 25 µg vs a mean of 4 µg, respectively, a difference of 21.4 µg; 95% CI: −36.3 to −6.6; P = 0.01) (Table 3).

Table 3
Hemodynamic changes and supplemental analgesia required during spinal anesthesia

During surgery				
Hypotension (≥ 25% baseline)	2 (5%)	3 (8%)	0.40	
Bradycardia (< 50 beats·min−1)	2 (6%)	4 (1%)	0.70	
Pain requiring analgesia	15 (19%)	5 (9%)	0.16	
In the PACU				
Hypotension (≥ 25% baseline)	1 (6%)	2 (2%)	0.31	
Bradycardia (< 50 beats·min−1)	0 (0%)	1 (4%)	0.15	
PONV	1(4%)	2 (4%)	1.00	
Satisfaction (/10)	9.2	9.1	0.59	−0.2 (−0.7 to 0.4)

Values are absolute number of cases recorded (percent). Differences between groups are mean (95% confidence interval [CI]). Total dose of fentanyl is mean dose per patient (standard deviation). PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting

The incidences of complications recorded during the follow-up phone calls (postdural puncture headache, transient neurological symptoms, and back pain) were all similar between groups (Table 4). One case of possible TNS was described in each group.

Discussion

The purpose of our study was to compare 2-CP with bupivacaine for spinal anesthesia in an outpatient setting. Our chief finding was giving 2-CP in spinal anesthesia can provide a satisfactory surgical block while permitting an earlier discharge from hospital than spinal bupivacaine due to more rapid regression of the sensory and motor block in 2-chlorprocaine, which helps patients ambulate and void faster.

The most significant advantage is the time for regression of the sensory block to S2, as 2-CP was 2.3 times faster than bupivacaine. The primary outcome of this study i.e., the time to eligibility for discharge from hospital, was measured from the time spinal anesthesia was performed to the moment the patient attained all of the discharge

criteria. As to this outcome, a significant difference of 75 min was observed in favour of the 2-CP group due to faster regression of the block, resulting in earlier ambulation and earlier voiding. Delayed discharge due to urinary retention was particularly problematic in the bupivacaine group. Even with good block regression and successful ambulation, many patients who received bupivacaine experienced a longer delay between their first attempt and their eventual successful complete voiding. This delay may be explained by the need for a regression of the sensory block to at least the S3 dermatome in order to obtain normal detrusor function. Breebaart et al. Although our study was not designed to measure health care costs. As health care costs are determined,by the length of hospital stay, achieving faster discharge from hospital through the utilization of 2-CP for spinal anesthesia could provide potential cost savings without compromising the quality of patient care as being a new medical institution we may face lack of manpower due to few faculty members attending the same 400 inpatients with these ambulatory patients additionally.

The doses of local anesthetics used in this study can be considered clinically equivalent Ben-David et al. showed that spinal hyperbaric bupivacaine 7.5 mg provided satisfactory anesthesia and rapid recovery for ambulatory arthroscopic knee surgery, but that further dilution resulted in failed blocks. Prior studies of 2-CP suggested that 40 mg would be the minimum dose required to achieve the rapid onset of a reliable sensory and motor block of sufficient duration.

After surgery, all of our patients were transferred to the PACU for routine observation, where they remained for a mean of 64to 65min. Although there was no difference between the groups in our study, there may be an opportunity to institute changes that could optimize the time spent in the PACU, e.g., permitting patients to be discharged earlier when they are stable and when the block has shown signs of regression. According to our results, this milestone would be achieved sooner in patients with 2-CP spinal anesthesia.

The patients in the 2-CP group experienced more pain in the PACU because their spinal anesthesia regressed more rapidly. Consequently, patients in the 2-CP group were treated with opioids earlier by nurses who were more familiar with pain control modalities. Thus, patients receiving 2-CP could be assured of optimal post-block pain control prior to being transferred to the ambulatory unit.

One of the biggest limitations of our study is that it was not perfectly double-blinded. Since the block in the 2-CP group regressed earlier and faster, the blinded observer could guess the group to which the patient had been assigned. Although this limitation was identified prior to the enrolment of the first patient, no better alternative to the protocol was determined. An additional limitation of our study was determining the precision of the sensory level of the block within two dermatomal levels by pin prick . This imprecision was minimized by having the same blinded observer responsible for collecting all data during the entire study. Our study could also be criticized for not using opioids to supplement the local anesthetics, as is common clinical practice.

Conclusion

Intrathecal 2-CP 40 mg produces a satisfactory surgical block for procedures lasting < 60 min. When compared with hyperbaric spinal bupivacaine 7.5 mg, it resulted in a significantly faster regression of the block, shorter time to ambulation and micturition, and earlier discharge from hospital. In future our predication will be confirmed that choosing 2-CP for spinal anesthesia in an ambulatory surgery setting may free the PACU and ambulatory surgical unit resources with a corresponding decrease in total perioperative costs.

References

1. Foldes FF, McNall PG. 2-Chloroprocaine: a new local anesthetic agent. Anesthesiology 1952; 13: 287-96. 12.
2. Anonymous. Chloroprocaine hydrochloride. J Am Med Assoc 1957; 163: 38-9.
3. Ansbro FP, Blundell AE, Bodell B, Pillion JW. Nesacaine (2-chloroprocaine): its relative nontoxicity as demonstrated by in vivo studies. Anesth Analg 1960; 39: 7-12.
4. Krumperman LW, Meschter SC, Close EL, Wester MR, Erickson JC, Strenge HJ. Transdural diffusion of 2-chloroprocaine hydrochloride in man. Anesth Analg 1960; 39: 55-8. 15.
5. Barsa J, Batra M, Fink BR, Sumi SM. A comparative in vivo study of local neurotoxicity of lidocaine, bupivacaine, 2-chloroprocaine, and a mixture of 2-chloroprocaine and bupivacaine. Anesth Analg 1982; 61: 961-7.
6. Riggi SJ. Chloroprocaine: neurotoxicity and formulations in perspective. Anesth Analg 1982; 61: 715-7.
7. Covino BG. Potential neurotoxicity of local anaesthetic agents. Can Anaesth Soc J 1983; 30: 111-6.
8. Rosen MA, Baysinger CL, Shnider SM, et al. Evaluation of neurotoxicity after subarachnoid injection of large volumes of local anesthetic solutions. Anesth Analg 1983; 62: 802-8.
9. Ready LB, Plumer MH, Haschke RH, Austin E, Sumi SM. Neurotoxicity of intrathecal local anesthetics in rabbits. Anesthesiology 1985; 63: 364-70.
10. Myers RR, Kalichman MW, Reisner LS, Powell HC. Neurotoxicity of local anesthetics: altered perineurial permeability, edema, and nerve fiber injury. Anesthesiology 1986; 64: 29-35.
11. Kalichman MW, Moorhouse DF, Powell HC, Myers RR. Relative neural toxicity of local anesthetics. J Neuropathol Exp Neurol 1993; 52: 234-40.
12. Schneider M, Ettlin T, Kaufmann M, et al. Transient neurologic toxicity after hyperbaric subarachnoid anesthesia with 5% lidocaine. Anesth Analg 1993; 76: 1154-7.
13.. Hampl KF, Schneider MC, Umenhofer W, Drewe J. Transient neurologic symptoms after spinal anesthesia. Anesth Analg 1995; 81: 1148-53.
14. Pollock JE, Neal JM, Stephenson CA, Wiley CE. Prospective study of the incidence of transient radicular irritation in patients undergoing spinal anesthesia. Anesthesiology 1996; 84: 1361-7.
15. Liu SS, Ware PD, Allen HW, Neal JM, Pollock JE. Dose-response characteristics of spinal bupivacaine in volunteers: clinical implications for ambulatory anesthesia. Anesthesiology 1996; 85: 729-36. 9.