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Comparison of 2-Chloroprocaine, bupivacaine, and lidocaine for spinal anesthesia in infraumbilical day-case surgeries

Dr. Ram Nivas[1], Dr. Neelam Meena[2*], Dr. Ram Parsad[3], Dr. RK Solanki[4] Dr Vandana Sharma[5]
[1, 3] senior resident department of anaesthesia and critical care, drsnmc Jodhpur, Rajasthan, India
[4] senior professor anaesthesia, department of anaesthesia and critical care, drsnmc Jodhpur, Rajasthan, India
[2] associate professor, department of anaesthesia and critical care dr snmc Jodhpur, Rajasthan, India
[5] assistant professor anaesthesia and critical care dr snmc Jodhpur, Rajasthan, India
Corresponding author: Dr. Neelam Meena

Abstract
Introduction: Spinal anesthesia is a safe and reliable technique for surgery of the lower abdomen and lower limbs. The choice of the correct local anaesthetic for spinal anesthesia is crucial in the ambulatory setting, ideal anaesthetic should allow rapid onset and offset of its own effect for fast patient discharge with minimal side effects.
Materials and Methods: Patients received one of the following into the subarachnoid block*:* Group C: 40mg 1% preservative free plain 2-chloroprocaine or Group L: 40mg of 1% plain lidocaine or Group BU: 7.5mg of 0.5% plain bupivacaine. To assess onset, level, regression of sensory block by dermatome level, motor block by Modified Bromage Score, time to complete recovery from sensory and motor block, time until first ambulation.
Result: Time to full recovery of sensory block (min) in group C, L and BU was 152.54±20.33, 203.51±36.77 and 413.77±99.49. Mean Duration of motor block (min) in group C, L and BU was 96.82±16.09, 115.4±17.87 and 201.54±64.68. Mean time of First ambulation (min) in group C, L and BU was 171.54±41.53, 211.45±20.14 and 287.91±39.06.
Conclusion: Patients undergoing spinal anaesthesia for infraumbilical day-case surgery, chloroprocaine had shortest time to onset and time until complete recovery of sensory and motor block when compared lidocaine. Voiding, ambulation, discharge times were shorter for chloroprocaine compared with bupivacaine, but not in comparison with lidocaine.

Keywords: chloroprocaine, lidocaine, bupivacaine, infraumbilical day-case surgery, subarachnoid block

Introduction

In the last years, the number of surgical procedures performed on an ambulatory basis has increased worldwide [3]; between 50% and 70% of all surgeries are currently performed as outpatient procedures in North America alone [4].

Spinal anesthesia is a safe and reliable technique for surgery of the lower abdomen and lower limbs [5, 6]. Nevertheless, some of its characteristics may limit its use for ambulatory surgery, including delayed ambulation, risk of urinary retention, and pain after block regression [7]. The choice of the correct local anaesthetic for spinal anesthesia is therefore crucial in the ambulatory setting: the ideal anesthetic should allow rapid onset and offset of its own effect for fast patient discharge with minimal side effects [8].

In the past, the lack of the ideal spinal local anesthetic and the availability of fast acting drugs such as remifentanil and propofol have made general anaesthesia the preferred choice for short outpatient procedures [9, 10]. Although low doses of long-acting local anesthetics such as bupivacaine, ropivacaine, and levobupivacaine are usually administered intrathecally, they are associated with significant risk of delays in hospital discharge and less reliability of block efficacy, onset, and spread [12].

An increasing number of day-case surgical patient is challenging the presently used methods of anaesthesia. Reliable surgical anaesthesia should be fast, with rapid recovery and minimal side effects. To produce reliable spinal anaesthesia with a reasonable recovery time, it is essential to understand the factors affecting the spread of spinal block and to choose the optimal drug and adequate dose for specific surgical procedures [13].

Lidocaine has an attractive pharmacokinetic profile as it shows a rapid onset and allows a fast recovery of both motor and sensory block (130-170minutes) [14]. However, when compared with other local anaesthetics, the use of lidocaine for spinal anaesthesia is associated with an increased risk of transient neurological symptoms (TNS) including back and leg pain [15, 17].

2-chlororprocaine is an amino-ester local anesthetic with a very short half-life and a potentially favourable evolution of spinal block for short outpatient procedures [22, 23]. Over the last few years, 2-chloroprocaine has regained popularity. While 2-chloroprocaine was withdrawn from the market in the 1980s because of concerns about neurotoxicity [24, 25], a new formulation without preservatives that has no longer been associated with neurotoxicity [26, 27] was introduced into clinical practice in 2004.2-chloroprocaine is characterized by both a very fast onset (5-10minutes) and a quick recovery time (70-150minutes) [28, 29]

Aims and Objectives

To assess onset, level, regression and time to complete recovery of sensory block by dermatome level **,**motor block by Modified Bromage Score. To watch for hemodynamics and respiration including Blood pressure (BP), Pulse rate

(PR) and Respiratory rate (RR), to assess time to rescue analgesia ,time until first mobilization (ambulation),time until first voiding intraoperative and postoperative complications

Material and Methods

Source of Data

This study was carried out in the department of Anaesthesiology, Dr. S. N. MEDICAL COLLEGE and associated group of hospitals on patients undergoing infraumbilical surgeries. A written and informed consent was taken from the patient.

Methods of Collection of Data

Inclusion Criteria

1. Patients belonging to age group 18 -60 years.
2. ASA grade 1 and 2 patients and body mass index between 20 and 35 kg/m^2.
3. Patients undergoing elective inguinal, perineal and lower limb day-case surgeries.

Exclusion Criteria

1. Patients refusal
2. Patients with history of bleeding disorders or patients on anticoagulants
3. Patients with infection at the site of injection
4. Patients with allergy to local anaesthetics
5. Patients with cardiac disease, heart blocks, dysarrythmias.
6. ASA grade 3 & 4 patients
7. Anatomical abnormality at the regional site
8. Pregnant women.

Sample Size Calculation

The sample size of 35 per group was determined by power analysis; due to the preliminary study results of decrease in insertion time measurements, when delta was assumed to be 1.25 and SD as 1.8, with 80% power and $\alpha = 0.05$, the sample size (n) was calculated to be minimum 35 for each group. Considering a 20% drop-out rate.

All statistical analyses were performed by using SPSS 22.0 software package (SPSS Inc., Chicago, IL, USA). *T* test for independent samples was used to compare three groups for data with normal distribution and Mann Whitney *U* test was used for comparing data with non-normal distribution. Yates continuity correction test *(Chi square test), Fisher's exact test and Fisher Freeman Halton test were used for comparison of qualitative data. All data were summarized as mean ± SD for continuous variables, numbers and percentages for categorical variables. A $p < 0.05$ was accepted as statistically significant

Randomization

The patients were randomly allocated into one of the three predefined groups 35 in each group by computer generated method.

Groups

105 patients were divided into 3 groups with 35 patients in each and total drug volume was 4.5ml.

Group C (chloroprocaine) - Patient in the chloroprocaine group receive 40mg (4.5ml) 1% preservative free plain 2-chloroprocaine intrathecally (4ml 2-chloroprocaine±0.5ml NS).

Group L (lidocaine) - Patient in the lidocaine group was receive 40mg(4.5ml) of 1% plain lidocaine intrathecally (4ml lidocaine ± 0.5ml NS).

Group BU (bupivacaine) - Patient in the bupivacaine group was receive 7.5mg (1.5ml) of. 5% plain bupivacaine as intrathecal anaesthetic. (1.5ml bupivacaine ± 3.5 ml NS).

Double Blinding

The drug was prepared in a 5ml syringe in equal volume by anaesthesiologist not involved in the study. The anaesthesiologist who prepares the drug solutions were different from the person who administers the block and the anaesthesiologist who monitor the quality and duration of block and the haemodynamics post-operatively.

Methodology

During preoperative visits, patients detailed history, general physical examination and systemic examination was carried out. Basic Patient's all routine investigations were checked out as mentioned above. Patients were explained in detail about the anaesthesia procedure and drug. All patients were premedicated with Inj. Midazolam 0.03mg/kg given 5 minutes before procedure to reduce the anxiety. On arrival in the operating room, an intravenous infusion was started in all patients with 500ml Ringer's solution. All patients were monitored with automated NIBP, pulse oximetry and electrocardiogram. Spinal needle used was 25 gauge quincke needles and was introduced at L3-4 or L4-5 interspinous space. The patient was turned supine, and surgery was started once a T10 sensory block was reach. Oxygen was administrated via a mask if the pulse oximetry reading decreased below 90%. boluses of intravenous (i.v.) mephentermine 6mg was given as needed to treat clinically relevant hypotension (defined as a decrease in systolic blood pressure >30% from baseline values) and i.v. atropine was given if the heart rate fell below 50 beat/min. Sensory testing was performed using a loss of cold sensation downward from the midclavicular line, starting at T2, using arm with unblocked C5-C6 dermatomes as reference point and dermatomal levels were tested every 3 minutes until the level had stabilized for four consecutive tests. Testing was then conducted every 10 minutes until the point of two segment regression of the block. Further testing was performed at 20 minutes intervals until the recovery of S2 dermatome. Data related to the highest dermatomal level of sensory blockade, the time to reach this level from the time of injection, modified Bromage scale of motor blockade at the time of reaching peak sensory level, time to two segment regression, time to S2 sensory regression, side effects if any was collected. All times were recorded from injection of the spinal anesthetic. Request time for postoperative pain relief was also recorded, and tramadol 100mg was given at VAS score 4, same dose was given when VAS score was more than 4.

Evaluation of block-

- Block start time)needle insertion (was recorded .
- Time to achieve total motor blockade, sensory blockade and duration of surgical procedure was also recorded.

Sensory block

Sensory block was evaluated by the loss of cold sensation downward from the midclavicular line, starting at T2, using the arm with unblocked C5-C6 dermatomes as reference point .

Cold Sensation Test

Table 1

0	=	No block
1	=	Analgesia (touch sensation)
2	=	Anaesthesia (no sensation)

Motor block

Total duration of motor block was calculated from the time of onset of motor blockade to the recovery from blockade by using Modified Bromage Score.

Modified Bromage Score

Table 1

Score	Criteria
1	Complete block (unable to move feet or knees)
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

Time taken to reach Modified Bromage 1 was recorded.

The outcome of the study was the time until complete recovery of sensory block (defined as the return of cold sensation down to the level of S5), time until recovery of the motor block (defined as reaching bromage scale =6),voiding time, ambulation time (defined as time until the first mobilization), the incidence of hypotension/ bradycardia (defined as above), rate of conversion to general anaesthesia, need for and dose of supplementary analgesics administered intra operatively and post operatively, discharge time and incidence of TNS.

Transient neurological symptoms were defined as lower back pain radiating from the gluteal region to the lower extremities [3]. The study was stopped if TNS incidence was significantly higher than 5% in all groups combined or in 1 of the 3 group separately. The incidence of TNS was recorded at discharge and 24 hour post operatively (by contacting patient via phone). In case of TNS, the patient was contacted daily until problem was resolved.

Observations and Results

Demographic profile

Table 2

		Group C	Group L	Group BU	P value
Age (yrs)		40.68±11.75	39.88±13.23	37.42±13.04	Group C vs Group L=0.790 Group L vs Group BU=0.436 Group C vs Group BU= 0.274
Sex	Male	29	32	32	P value 0.428
	Female	6	3	3	
Weight (kg)		66.02±9.19	61.62±12.71	66.34±8.23	Group C vs Group L = 0.101 Group L vs Group BU= 0.070 Group C vs Group BU= 0.880
Height (cm)		169.28±9.15	166.54±9.62	166.6±9.08	Group C vs Group L = 0.226 Group L vs Group BU= 0.674 Group C vs Group BU= 0.094
ASA	I	27	29	28	P value 0.836

Time to start surgery/ onset of T10 sensory blockade

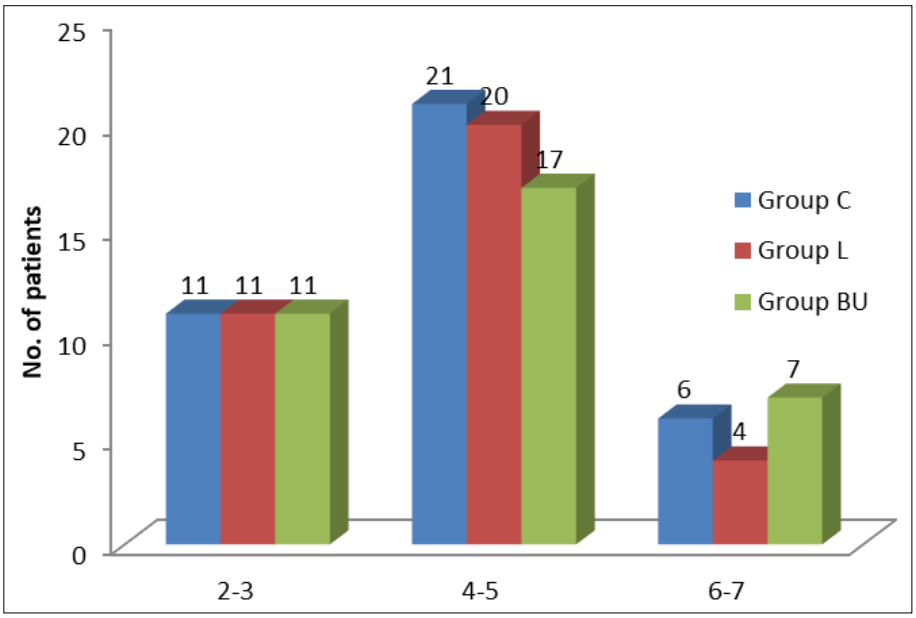

Fig 1: Onset T10 sensory blockade

The mean time to onset of T10 sensory blockade / Time to start surgery (in min) in group c was 3.85±1.06, in group L was 4.17±1.12 and in group BU was 4.2±1.30. The difference was statistically insignificant between the three groups (p value, Group C vs Group L = 0.233, Group L vs Group BU = 0.922, Group C vs Group BU= 0.231).

Haemodynamic parameter

Haemodynamic parameter comparable at all times in all the groups and the difference was not found to be statistically significant (p >0.05).

Table 3

Parameters	Group C (Mean±SD)	Group L (Mean±SD)	Group BU (Mean±SD)	p value		
				Group C vs Group L	Group L vs Group BU	Group C vs Group BU
Time for max cephaled spread (min)	17.51±3.94	18.28±4.12	20.94±4.42	0.426	0.011	0.001
Time to maximum motor block(min)	17.11±3.88	18.54±4.30	20.11±4.13	0.149	0.123	0.002
Two segment regression of sensory block(min)	49.97±2.98	56.14±3.98	83.34±9.66	<0.0001	<0.0001	<0.0001
Time to full recovery of sensory block (min)	152.54±20.33	203.51±36.77	413.77±99.49	<0.0001	<0.0001	<0.0001
Duration of motor block (min)	96.82±16.09	115.4±17.87	201.54±64.68	<0.0001	<0.0001	<0.0001
First analgesic requirement(min)	100.45±20.41	118.57±21.16	152.85±21.87	0.0005	<0.0001	<0.0001
First micturation (min)	184.11±6.18	201.62±31.70	242±26.98	0.002	<0.0001	<0.0001
First ambulation (min)	171.54±41.53	211.45±20.14	287.91±39.06	<0.0001	<0.0001	<0.0001

Time to full recovery of sensory block (min

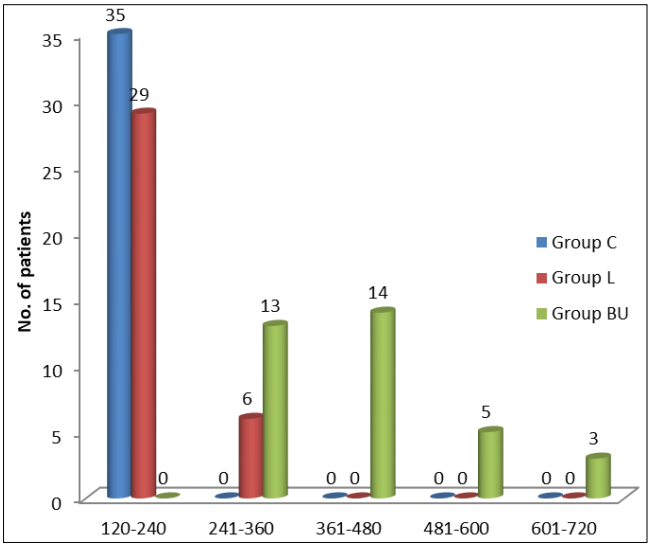

Fig 2: Time to full recovery of sensory block (min)

Modified bromage scale

The difference was statistically significant between the Group C vs Group L at 6, 9, 12, 24, 70, 80, 90, 120 minute, Group L vs Group BU at 9, 12, 15, 80, 90,120, 150, 180 minute and Group C vs Group BU at 6, 70, 80, 90, 120 minute.

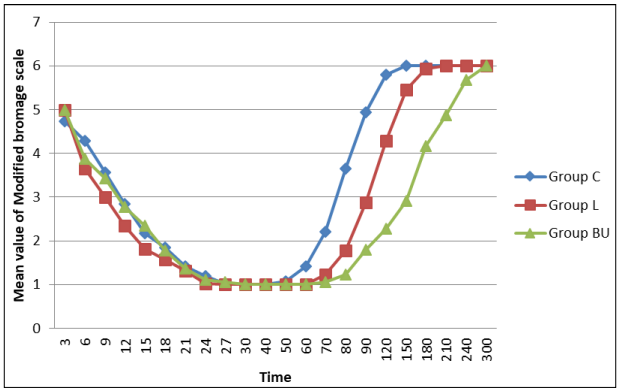

Fig 11

Discussion

Haemodynamic parameters

The results of our study show that there were minimal variations in preoperative, intraoperative as well as postoperative mean heart rate, blood pressure and oxygen saturation in the three groups, which were statistically insignificant. Our results were in agreement with most of the previous similar studies [33, 34, 36, 37]. They also didn't find any significant difference in haemodynamic parameters between the groups.

Time to start surgery/ Onset of T10 sensory blockade

In our study, the mean time to onset of T10 sensory blockade (in min) in group C was 3.85±1.06, in group L was 4.17±1.12 and in group BU was 4.2±1.30. The difference was statistically insignificant between the three groups (p value, Group C vs Group L = 0.233, Group L vs Group BU = 0.922, Group C vs Group BU= 0.231). Our observations were consistent with the results of some previous studies [33, 34, 36].

Maximum cephaled spread (dermatome)-

Number of patients of maximum cephaled spread to T5-T9 in all groups. The P value was comparable between all groups. Our observations were consistent with the results of some previous studies [34, 36, 37, 39]

Time for max cephaled spread (min)

The difference was statistically significant between the Group L vs Group BU and Group C vs Group BU (p value: Group L vs Group BU= 0.011, Group C vs Group BU= 0.001). The difference was statistically insignificant between Group C vs Group L (p value: Group C vs Group L = 0.4260 [37, 41]

Two segment regression of sensory block (min)

The mean time for two segment regression of sensory block (min) in group C was 49.97±2.98, in group L was 56.14±3.98 and in group BU was 83.34±9.66. The difference was statistically significant between the Group C vs Group L, Group L vs Group BU and Group C vs Group BU. (p value : Group C vs Group L = <0.0001,Group L vs Group BU= <0.0001, Group C vs Group BU= <0.0001) [35, 37]

Time to full recovery of sensory block (min)

Time to full recovery of sensory block (min) in group c was 152.54±20.33, in group L was 203.51±36.77 and in group

BU was 413.77±99.49. The difference was statistically significant between the Group C vs Group L, Group L vs Group BU and Group C vs Group BU. (p value : Group C vs Group L = <0.0001,Group L vs Group BU= <0.0001, Group C vs Group BU= <0.0001). Interquartile range (Q1-Q3)
Group C 135-169min, Group L 178-224min, Group BU 343-432min
Our observations were consistent with the results of some previous studies [33, 35, 37, 39]

Time for max motor block (min)
The mean time for max motor block (min) in group c was 17.11±3.88, in group L was 18.54±4.30 and in group BU was 20.11±4.13. The difference was statistically significant between the Group C vs Group BU. The difference was statistically insignificant between Group C vs Group L and Group L vs Group BU. (p value: Group C vs Group BU= 0.002, Group C vs Group L = 0.149 Group L vs Group BU= 0.123). Our observations were consistent with the results of some previous studies [36, 39].

Duration of motor block (min)
The mean Duration of motor block (min) in group C was 96.82±16.09, in group L was 115.4±17.87 and in group BU was 201.54±64.68. The difference was statistically significant between the Group C vs Group L, Group L vs Group BU and Group C vs Group BU. (p value : Group C vs Group L = <0.0001,Group L vs Group BU= <0.0001, Group C vs Group BU= <0.0001).
Interquartile range (Q1-Q3) Group C 85-113min, Group L 99-126min, Group BU 168-247min. Our observations were consistent with the results of some previous studies [33, 34]

Time to first analgesic requirement (min)
The mean time of first analgesic requirement (min) in group C was 100.45±20.41, in group L was 118.57±21.16 and in group BU was 152.85±21.87. The difference was statistically significant between the Group C vs Group L, Group L vs Group BU and Group C vs Group BU. (p value : Group C vs Group L = 0.0005, Group L vs Group BU= <0.0001, Group C vs Group BU= <0.0001). Our observations were consistent with the results of some previous studies.39

Time to First micturation (min)
The mean time of first micturation (min) in group c was 184.11±6.18, in group L was 201.62±31.70 and in group BU was 242±26.98. The difference was statistically significant between the Group C vs Group L, Group L vs Group BU and Group C vs Group BU. (p value: Group C vs Group L = 0.002, Group L vs Group BU= <0.0001, Group C vs Group BU= <0.0001). Our observations were consistent with the results of some previous studies [33, 35, 37]

Time to First ambulation (min)
The mean time of First ambulation (min) in group C was 171.54±41.53, in group L was 211.45±20.14 and in group BU was 287.91±39.06. The difference was statistically significant between the Group C vs Group L, Group L vs Group BU and Group C vs Group BU. (p value: Group C vs Group L = <0.0001, Group L vs Group BU= <0.0001, Group C vs Group BU= <0.0001). Interquartile range (Q1-Q3) Group C 125-184min, Group L 193-227min, Group BU 253-311min. Our observations were consistent with the results of some previous studies [33, 39]

Adverse effect
Telephone follow-up identified one possible case of TNS in each group, defined as pain and/or dysesthesia occurring in the legs and/or buttocks in the first 24 hr after recovery from an uneventful spinal anesthetia, we did not detect a single patient suffering from TNS in neither group. While this finding confirms recent reports on the lack of neurotoxicity of the preservative-free chloroprocaine formulations [26], it is in striking contrastto the literature reporting a mean incidence of TNS of 17% (0%–33%) for lidocaine [15, 44. 45] We are unable to elucidate the exact reasons why in our study lidocaine did not cause TNS but suggest that the routine use of paracetamol and/or NSAIDS might have probably masked possible symptoms of TNS in our patients.

Conclusion
In patients undergoing spinal anesthesia for infraumbilical day-case surgeries, chloroprocaine 40 mg had the faster onset of maximal spinal block, shortest time to two segment regression and complete recovery of sensory block, when compared with lidocaine 40 mg and bupivacaine 7.5 mg. Chloroprocaine 40 mg had the faster onset of maximal motor block compare to and bupivacaine 7.5 mg but not in comparison with lidocaine. chloroprocaine 40 mg had shortest time to complete recovery of motor block, when compared with lidocaine 40 mg and bupivacaine 7.5 mg. Voiding, ambulation, were shorter for chloroprocaine 40 mg, when compared with lidocaine 40 mg and bupivacaine 7.5 mg. The use of rescue medication for postoperative pain was significantly earlier for chloroprocaine 40 mg compared with lidocaine and bupivacaine. There were no differences in onset of sensory block to T10, time to start surgery, level of maximal cephaled spread, duration of surgery, haemodynamic parameter, adverse events or the incidence of TNS and demographic parameters (age, sex, weight, height, ASA) between the 3 groups.
This suggests that for spinal anesthesia in patients undergoing infraumbilical day-case surgeries chloroprocaine is a good alternative for bupivacaine. In our setting in which the incidence of TNS was zero, chloroprocaine had no clinically relevant superiority compared with lidocaine.

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