Original Article

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Efficacy of Different Doses of 1% of 2-Chloroprocaine in Spinal Anaesthesia for below Umbilicus Surgery: A Randomised Clinical Trial

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ABSTRACT

Introduction: A 2-chloroprocaine is a short acting amino-ester group of local anaesthetic drug used in spinal anaesthesia. The dose of 30 mg of 1% 2-chloroprocaine can also be used for below umbilicus surgery.

Aim: To compare the efficacy of two doses of 1% of 2-chloroprocaine in spinal anaesthesia for below umbilicus surgery.

Materials and Methods: This prospective randomised clinical trial was conducted from December 2019 to April 2020, on 32 patients who were allocated into two groups. Group A received 30 mg of 1% of 2-chloroprocaine and group B received 40 mg of 1% of 2-chloroprocaine for spinal anaesthesia. Onset of motor and sensory block, peak block height and haemodynamic parameters were noted in the intraoperative period. Recovery from spinal anaesthesia was noted and transient neurologic symptoms were also noted after 24 hours and seven days after surgery. Mean and standard deviations were calculated from the collected data and Statistical Package for Social Sciences (SPSS) version 20.0 was used for the analysis.

Results: A total of 32 subjects (aged 20-60 years) were divided into group A (n=16; mean age: 31.56±10.05 years) and group B (n=16; mean age: 34.19±11.72 years). Time taken for the onset of sensory and motor block was similar in both the groups. The peak height reached was T8-T10 in group A and T6-T10 in group B. During recovery period, time taken for regression of sensory block were similar between the groups. Complete recovery from motor block took 75.69±10.78 minutes in group A and 93.53±8.96 minutes in group B which was statistically significant ($p<0.001$). Time taken for mobilisation without support was 113.85±25.50 minutes in group A and 119.87±13.42 minutes in group B ($p=0.4115$). There were no Transient Neurological Symptoms (TNS) in both the groups. All the patients were haemodynamically stable.

Conclusion: Both doses of 2-chloroprocaine can be used in day care surgery due to its short duration of action.

Keywords: Ambulatory surgery, Local anaesthetics, Regional anaesthesia

INTRODUCTION

A 2-Chloroprocaine is an amino-ester group of local anaesthetic with fast onset time and short duration of action [1,2]. It has a higher pKa (8.7) compared to other local anaesthetic like lignocaine, bupivacaine and ropivacaine leading to faster onset of action. It has low lipophilicity and low protein binding capacity making it one of the local anaesthetics with shortest duration of action [3,4]. Spinal anaesthesia is not used in day care surgery due to certain limitations such as delayed motor recovery and ambulation and risk of urinary retention. But in the last few years, due to availability of preservative free short acting drugs like 2-chloroprocaine and 2% lignocaine, spinal anaesthesia is gaining popularity in the day care surgery [1].

The dose of chloroprocaine required to achieve a subarachnoid block of adequate sensory and motor blockade is assumed to be 30 mg and above [4]. Kopacz DJ; studied the minimum effective dose for spinal anaesthesia of 10 mg and 20 mg, but these doses did not provide adequate sensory and motor blockade for the proposed procedure[5]. The dose of 20 mg has been used for perianal surgeries but may not be adequate for below umbilicus surgeries. In another study done by Casati A et al., dose required to produce effective motor and sensory blockade for procedures lasting less than one hour were around 40 mg and above [3]. There are very few articles on the dose of spinal anaesthesia required to provide a sensory block of T10. Large volume of any local anaesthetics for spinal anaesthesia will lead to high spinal block with haemodynamic changes which is not required for short duration procedures.

The aim of the study was to find the efficacy of different doses of chloroprocaine (30 mg and 40 mg) for below umbilicus surgery of less than one hour duration. The primary outcome of the study was to find the onset time, duration of block, height of sensory block and level of block achieved. The secondary outcomes were offset time, haemodynamic stability and time to mobilisation and micturition.

MATERIALS AND METHODS

This randomised clinical trial was conducted in KS Hegde Medical Academy Hospital, Karnataka, India from December 2019 to April 2020. This study was conducted after Institutional Ethical Committee clearance (NU/CEC/2019/0230) and (CTRI/2019/12/022203). Study allotment was done as per Consolidated Standards of Reporting Trials (CONSORT) flow diagram [Table/Fig-1].

Sample size calculation: Based on the study by Casati A et al., sample size was calculated using standard deviation formula [3]:

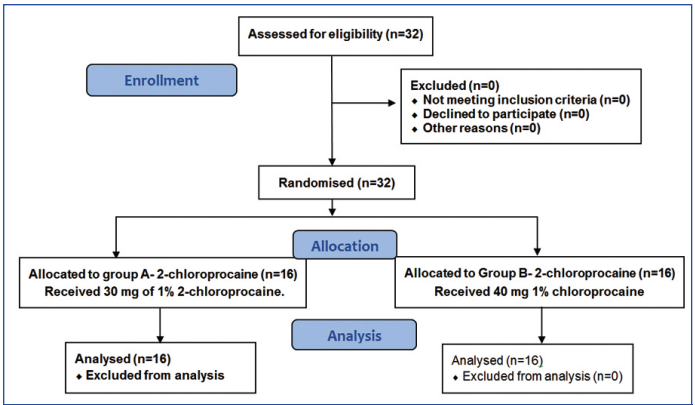
$$n=\frac{\sigma^2 (Z_{(1-\alpha/2)}+Z_{\beta})}{e^2}$$

σ=time (20 min) α=5% β=20% e=10 power=80%

Final sample size n=32

Inclusion criteria: Patients undergoing below umbilicus surgery of less than 60 minutes, American Society of Anaesthesiologist Physical Status (ASA PS) I and II, aged between 20-60 years of both genders, with Body Mass Index (BMI) <35 kg/m^2 were included in the study.

Exclusion criteria: Emergency surgery, pregnancy, patients with contraindications for spinal anaesthesia and patients with allergic reactions to the drug were excluded from the study.



[Table/Fig-1]: CONSORT diagram of the study.

Procedure

Patients were allocated into two groups randomly by computer generated randomisation method. Pre-anaesthetic check-up was done on the previous day of the surgery and written informed consent was taken from all the patients enrolled for the study. On the day of surgery, Nil Per Oral (NPO) status was confirmed and patients were shifted to the operating room and standard monitors like 5-lead electrocardiogram, non invasive blood pressure and pulse oximetry connected. All patients received ringer lactate solution as intravenous fluid started at 8 mL/kg. Trained anaesthesiologist performed spinal anaesthesia in the lateral decubitus position at L2-L3 interspinous space using 25-gauge Quincke Babcock needle. Group A received 30 mg of 1% 2-chloroprocaine and group B received 40 mg of 1% 2-chloroprocaine. The observer who was blinded for the dose of the drug, recorded the sensory block level, motor blockade and haemodynamic parameters. The haemodynamic parameters and the level of sensory and motor block were checked every minute for the first 10 minutes.

The onset of sensory block was defined as loss of sensation at L1 dermatome and the sensory level was assessed with pin prick. The maximum height of the block reached at ten minutes of spinal anaesthesia was also noted. Bromage score of 3 was considered as adequate motor block for surgery. The level of block was checked every 10 minutes till complete recovery from the block, which was defined as recovery of sensation to L1 level. Postoperative assessment included total duration of block (sensory and motor), time required to ambulate and micturition time. All the patients were followed-up for one week to assess Trigeminal Nerve Stimulation (TNS). Duration of sensory block was noted till regression of sensory block to below L1 as tested by pin prick.

Regression of motor block was assessed using Bromage score with score zero considered to be complete regression of motor block. Once patients recovered from motor and sensory block, patients were mobilised without support and time to first micturition after spinal anaesthesia was documented. Patients were considered fit for discharge once they were able to walk without support. Intraoperative hypotension was defined as fall in Systolic Blood Pressure (SBP) by 30% from the baseline which was treated with intravenous fluid boluses and ephedrine 6 mg.

STATISTICAL ANALYSIS

Continuous data was analysed using mean and standard deviation. Association between variables were tested by using unpaired t-test and $p<0.05$ was considered to be statistically significant. Statistical software Statistical Package for Social Sciences (SPSS) version 20.0 was used to analyse the research data collected.

RESULTS

The socio-demographic characteristics like age, sex, Body Mass Index (BMI) and ASA physical status were comparable between the groups [Table/Fig-2]. The characteristics of motor and sensory block between the two groups were similar and p-value was not significant [Table/Fig-3]. Peak height attained in Group A (30 mg) were T8-7 (43.75%) and T10-9 (56.25%) and in Group B (40 mg) were T6-5 (31.25%),T8-6 (37.5%) and T10-5 (31.25%).

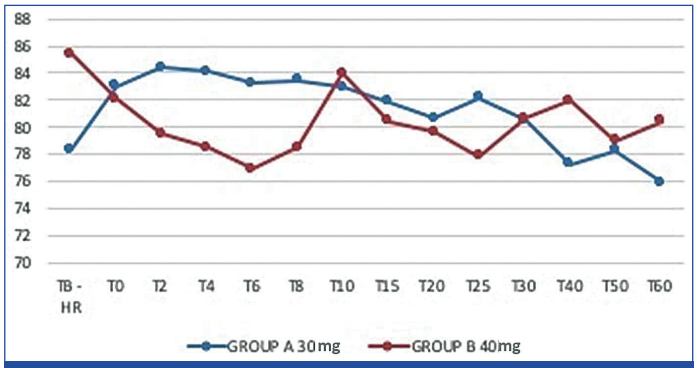
Parameters	Group A (30 mg)	Group B (40 mg)	p-value
Age (years)	31.56±10.05	34.19±11.72	0.502
BMI (kg/m^2)	22.06±1.47	21.38±1.88	0.263
ASA I (%)/II (%)	12 (75)/4 (25)	11 (68.75)/5 (31.25)	0.694
Male/female (%)	9 (56.2)/7 (43.8)	7 (43.8)/9 (56.2)	0.724

[Table/Fig-2]: Demographic parameters.

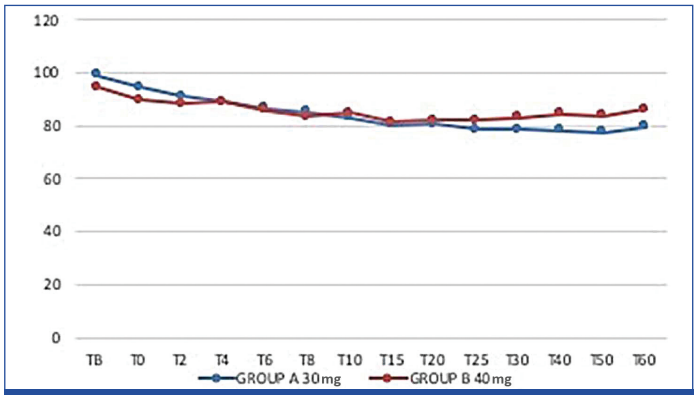
Parameters	Group A (30 mg)	Group B (40 mg)	p-value
Onset of sensory block (sec)	184.58±30.78	175.00±43.05	0.474
Peak block height reached at 10 minutes	T8-T10	T6-T10	-
Time taken to reach Bromage score 3(sec)	223.33±38.21	219.88±84.04	0.896

[Table/Fig-3]: Characteristics of motor and sensory block.

There was no significant difference in heart rate between the group [Table/Fig-4]. The blood pressure recorded were also similar in both the group and was not statistically significant [Table/Fig-5,6]. There was no fluctuation in blood pressure from the beginning till the end of the surgery suggesting all the patients in the study group were haemodynamically stable.

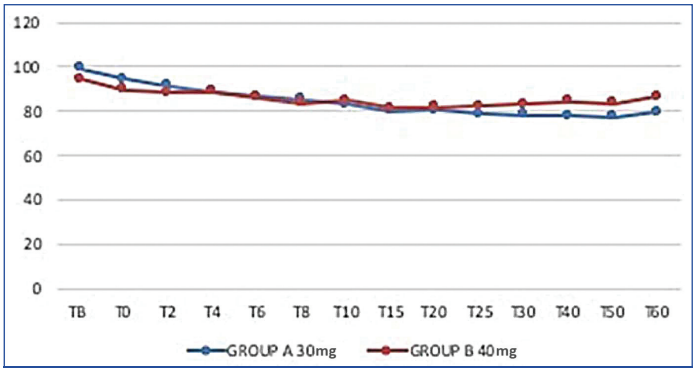


[Table/Fig-4]: Comparative analysis of heart rate in both group A and group B at different times.



[Table/Fig-5]: Comparison of Systolic Blood Pressure (SBP) between the two groups: x-axis showing time interval at which SBP was recorded and y-axis showing SBP. (p>0.05)

Time taken for completion of surgery were similar in both groups. Time taken for recovery from motor block was 75.69±10.78 minutes in group A and 93.53±8.96 minutes in group B which was statistically significant with p-value of <0.001. Time taken to micturition in the chloroprocaine 30 mg group was faster compared to 40 mg group which was statistically significant (p<0.001) [Table/Fig-7]. Level of



[Table/Fig-6]: Comparison of mean arterial pressure (MAP) between the two groups. X-axis showing time interval at which MAP is recorded and y-axis shows MAP. (p>0.05)

Parameters	Group A (30 mg)	Group B (40 mg)	p-value
Time taken for completion of surgery (min)	36.54±11.065	36.40±11.382	0.972
Time taken for regression of sensory block below L1 (min)	57.54+8.33	62.47+9.84	0.136
Time taken to achieve Bromage of 0 (min)	75.69±10.78	93.53±8.96	**<0.001**
Time taken to micturition(min)	97.64±13.98	121 .31±11.280	**<0.001**
Time taken to mobilisation (min)	113.85±25.50	119.87±13.426	0.4115
Transient neurologic symptoms after 24 hours and after 7 days	Nil	Nil	---

[Table/Fig-7]: Recovery parameters.
p-value <0.05 considered significant

sensory and motor block was similar in both groups for surgery proving 30 mg was also adequate for below umbilicus surgery lasting less than 60 minutes.

All the patients were assessed for any transient neurologic deficit during the first 24 hours and were followed-up for seven days for any symptoms of TNS. Patients were asked to report to hospital if there were any features of TNS; there were none.

DISCUSSION

Short acting local anaesthetic drugs are available in spinal anaesthesia but not very commonly used due to the side-effects like neurological deficits, TNS. Chloroprocaine, an ester group of local anaesthetics with short duration of action and faster recovery [6,7]. Few reports highlighting its association with TNS caused its withdrawal from clinical practice [8,9]. But later animal studies revealed sodium metabisulphite, a preservative added to chloroprocaine to increase its shelf life caused the adverse effect [1,2]. In the 21st century, there was resurgence of 2-chloroprocaine. By eliminating sodium metabisulphite, it was established that this drug could be safely instilled as a local anaesthetic agent into the subarachnoid space. Nevertheless, the fear and ambivalence still exists among the practicing anaesthesiologists. Chloroprocaine has faster onset time with short duration of action [9]. These patients can also be ambulated and discharged early from postoperative care unit. In this randomised controlled study, the authors compared the efficacy of chloroprocaine 30 mg and 40 mg in spinal anaesthesia for below umbilicus surgery. Both the doses were adequate for below umbilicus surgery of short duration.

The dose of 2-chloroprocaine for spinal anaesthesia ranges between 30-60 mg for below umbilicus surgery [2,3,5,9-12]. In the study by Goldblum E and Atchabahian A, the dose suggested was 30 mg chloroprocaine for below umbilicus surgery [2]. Taking this into consideration the dose chosen was 30 and 40 mg for below umbilicus surgery of less than 60 minutes.

In the study by Casati A et al., chloroprocaine of 30 mg, 40 mg and 50 mg was studied. The time taken for readiness to surgery was similar in all the three groups. The maximum level of sensory block was T9 in all the three groups. The intraoperative analgesic supplementation was around 50% in chloroprocaine-30 mg group, 33% in chloroprocaine-40 mg group and 13% of patients in chloroprocaine-50 mg group. The time of onset of block and level of sensory block were similar in the present study [3]. In the present study, none of the patients required intraoperative analgesia or sedation in both the groups. This shows that 30 mg and 40 mg dose of 1% of 2-chloroprocaine was adequate for below umbilicus surgery.

Chloroprocaine was compared with other local anaesthetics like bupivacaine, lignocaine, procaine and atricaine for the onset of block. In most of the studies, chloroprocaine had similar or faster onset of action but the offset time was faster in the chloroprocaine group [1]. In this study, as different doses of chloroprocaine was compared the onset of action was similar in both the groups. In the study, by Kouri ME and Kopacz DJ, 2-chloroprocaine was compared with lidocaine. The time of onset of the block and peak block height were similar in both groups. Chloroprocaine required shorter time for complete regression of sensory block and had faster voiding of urine [13]. In Camponovo C study, 50 mg of plain 1% 2-chloroprocaine was compared with 10 mg of 0.5% plain bupivacaine in terms of sensory block onset time. They noted that both chloroprocaine and bupivacaine had similar onset of sensory block but chloroprocaine had faster recovery than bupivacaine [14]. Chloroprocaine and atricaine has been used in day-case knee arthroscopy under spinal anaesthesia. Both local anaesthetics provided a rapid onset of spinal anaesthesia and were satisfactory for day-case knee arthroscopy. Recovery from the motor and sensory block was faster with chloroprocaine [15].

The secondary outcome of the present study was to assess haemodynamic parameters. All the patients were haemodynamically stable and did not require any vasopressor or sympathomimetic drugs in the intraoperative and postoperative period. In the study by Herndon CL et al., compared chloroprocaine spinal anaesthesia with a longer acting bupivacaine for perioperative outcomes in patients undergoing fast-track total hip arthroplasty. It was found that chloroprocaine use was associated with less intraoperative hypotension and faster recovery compared to bupivacaine [16]. This suggests that with these doses of chloroprocaine, there is haemodynamic stability.

Chloroprocaine has pKa greater than lignocaine and bupivacaine, hence, it has a faster onset of action in both spinal and epidural anaesthesia. There is also low systemic toxicity due to rapid metabolism by pseudocholinesterase [9]. Thus, the risk of toxicity is less with chloroprocaine. Time taken for regression of sensory block to below L1 were also similar to the study done by Casati A et al., with 60 (41-98) minutes in the 30 mg group and 85 (46-141) minutes in the 40 mg group. The difference in the time taken to regression from motor block was statistically significant which showed 40 mg dose had slower regression of motor blockade [3]. Patients can be mobilised early and can be discharged on the same day.

There was a significant difference in the recovery from motor block after spinal anaesthesia. It was faster in the 30 mg chloroprocaine group compared to the 40 mg group. Patients were assessed for TNS, 24 hours after spinal anaesthesia and till the 7th postoperative day and were not seen with both the groups. In the study by Casati A et al., TNS were reported in 1% lignocaine patients but was not seen in chloroprocaine patients [3]. In a retrospective analysis of spinal anaesthesia using chloroprocaine and lignocaine showed no transient neurologic symptoms in any of the patients [1]. It has not been noted after use of chloroprocaine in spinal anaesthesia. It suggests these patients can be discharged on the same day of the surgery.

Limitation(s)

This study was conducted on a small group of population. Any adjuvants like opiod were not added for proper observation in duration of action of the spinal anaesthesia, that is chloroprocaine.

CONCLUSION(S)

In conclusion, 30 mg and 40 mg of 2-chloroprocaine had similar pharmacological and clinical profile. After analysis of the results in the study population, it was noted that both groups had adequate level of block for required duration of time. There were no reports of any neurological symptoms in the preservative free chloroprocaine and can be safely used in subarachnoid space and it can be included in procedures which does not require a motor and sensory block for a long duration. Chloroprocaine can be an ideal choice of local anaesthetic for short duration procedures.

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