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A comparative study to evaluate the efficacy of intrathecal 1% chloroprocaine with clonidine versus 1% chloroprocaine for infraumbilical surgeries

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Abstract

Background: Bupivacaine, the commonly used local anesthetic agent in spinal anaesthesia having duration of sensory and motor blockade of 90 to 200minutes limits its use for short duration ambulatory surgery with delayed ambulation and risk of urinary retention. But 2-Chloroprocaine (2-CP) has duration of action of 70 to 150 minutes. With Clonidine, an α2-adrenergic agonist, as an adjuvant has been shown to prolong both the sensory and motor blockade when combined with spinal Bupivacaine. In our study, we compared the effectiveness of intrathecal 1% 2-Chloroprocaine with clonidine vs. intrathecal 1% 2- Chloroprocaine for infraumbilical surgeries in terms of their onset of blocks, duration and offset of blocks along with the hemodynamic variations.
Methods: A prospective and omised controlled double blind study was conducted in 60 ASA I and ASA II patients in the age group 18-60 years, posted for elective infraumbilical surgeries under subarachnoid block. They were randomised into 2 groups of 30 patients each and Group CC (n=30) received intrathecal 3.0 ml of 1% 2-CP with 30 mcg Clonidine and Group CS (n=30) received intrathecal 3.0 ml of 1% 2-CP with 0.2ml Normal Saline. Hemodynamic parameters, onset of sensory blockade, time for highest sensory and motor blockade, total duration of sensory an motor blockade, two dermatome regression time, time for rescue analgesic, time for ambulation and first micturition, sedation score were recorded. Side effects werenoted.
Results: Demographic data as well as operating data were comparable between the 2 groups. Group CC showed faster offset and prolonged sensory and motor blocks compared to Group CS. Time for ambulation and micturition were less in Group CS compared to Group CC. No side effects were note din both the groups.
Conclusion: Addition of clonidine to Intrathecal isobaric 2-chloroprocaine decreases the onset time for sensory and motor blockade, produces higher level of sensory blockade, prolongs postoperative analgesia, prolongs sensory blockade and motor blockade, prolongs ambulation and voiding time and has less haemodynamic changes which could be easily managed. Hence it may be proposed for day care surgeries.

Keywords: Intrathecal, Chloroprocaine, clonidine, infraumbilical surgeries; ambulatory surgery

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Introduction

Spinal anesthesia with local anesthetic is most commonly used for surgery of the lower abdomen, lower limbs and for cesarean sections. Nevertheless, some of its characteristics may limits its use for ambulatory surgery, including delayed ambulation, risk of urinary retention, and pain after block regression [1].

Bupivacaine, the commonly used local anaesthetic agent in spinal anaesthesia having a duration of sensory and motor blockade of 90 to 200 minutes, limits its use for ambulatory surgery due to delayed ambulation and risk of urinary retention [2]. And usage of Lidocaine was associated with symptoms of transient neurologic syndrome (TNS) [3-4]. 2-Chloroprocaine (2-CP) is an amino ester local anaesthetic, has a duration of action of 70 to 150 minutes [5]. In comparison with Bupivacaine, 2-CP showed faster recovery from anesthesia, unassisted ambulation and early discharge from hospital [6-7]. These findings suggestions that 2-CP can be a suitable alternative for ambulatory surgery [8].

The addition of adjuncts improves the quality of spinal anesthesia. Clonidine, an α-2-adrenergic agonist, has been shown to prolong both the sensory and motor blockade when combined with spinal Bupivacaine and Ropivacaine [9-10]. Intrathecal clonidine used in doses larger than 100 mcg has been associated with hypotension, bradycardia and sedation. However, doses as small as 15 to 30 mcg have been shown to improve the quality of Ropivacaine and Bupivacaine Spinal Anesthesia, without producing the systemic effects [9-10].

This study is designed to evaluate the efficacy of intrathecal 1% 2-CP with small-dose of Clonidine on the duration of spinal anesthesia, whether independently alter sensory or motor blockade, on time for ambulation and voiding in comparison with intrathecal 1% 2-CP in patients undergoing infraumbilical surgeries, as there are limited studies available comparing these drugs.

Objectives

1. To compare the onset and duration of sensory brick and motor block and hemodynamic changes between intrathecal 2-CP with Normal Saline versus 2-CP with Clonidine as an adjuvant.
2. To compare the initiation of ambulation and onset of voiding with 2-CP with Normal Saline versus 2-CP with Clonidine as an adjuvant.
3. To evaluate the safety profile of the drug.

Methodology

After approval from institutional ethics committee, this prospective randomized double blind study was conducted from November 2017 to May 2019. Those patients who gave written informed consent of either sex in the age group of 18-60 years with ASA physical status I and II with BMI 21-24 and who were posted for infraumbilical surgeries expected tubeless than 45 minutes (after discussing with the operating surgeon) were included in the study. Patients with allergy to local anesthetics and clonidine, Contraindications to spinal anaesthesia like raised intracranial tension, progressive neurodegenerative disorder, CNS infections, local infections, Spine deformities and patients with uncontrolled diabetes mellitus, hypertension, recent myocardial infarction, Pregnancy, Psychiatric disorder, hypovolemic shock, Bleeding diathesis and coagulopathy and emergency surgeries were excluded from the study.

Then patients were divided into two groups of 30 patients each by using the computer generated randomization table (http://www.randomizer.org). Allocation concealment done by sealed envelope method into 2 study groups. The study drug was given by anaesthetist not involved in the study. Patients and observer was not aware of the study drug.

- Group CC (n=30): Intrathecal 3.0ml of 1% 2-CP with 30mcg Clonidine.
- Group CS (n=30): Intrathecal 3.0ml of 1% 2-CP with 0.2ml Normal Saline.

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Preoperative evaluation of the patient was done on the day before surgery. After explaining the procedure, written and informed consent was obtained. All patients was kept nil per orally for 8 hours. Tab Ranitidine 150mg was given night before the day of surgery. On arrival to the operation room, intravenous access was secured and patients were preloaded with 10ml/kg of Ringer Lactate over 15 minutes. Non Invasive Blood Pressure, Pulse Oximetry and Electrocardiogram (ECG) were connected. The baseline Systolic, Diastolic and Mean arterial blood pressures (SBP, DBP and MAP), Heart Rate (HR) and Oxygen Saturation (SpO_2) was recorded.
Under strict aseptic precautions Subarachnoid Block was performed using 25G/26G quincke Babcock spinal needle in the L3-L4 Babcock spinal needle in the position. The loaded drug (Total volume 3.2ml) was injected over 10-15 seconds. The time at which injection is completed was considered zero time of the study and all measurements were recorded from this point. Following Subarachnoid Block, patients were made to lie supine.

Assessment of sensory blockade: Sensory testing was assessed by loss of temperature sensation to cold swab for onset and dermatomal levels was tested every minute interval for first 5 minutes and then every 5 minutes for the next 60 minutes, then at 10 minutes intervals until complete resolution of sensory anesthesia. Time of onset, maximum level of sensory block, time for two segment sensory regression and duration of sensory block was recorded. Recovery time for sensory blockade was the time taken to reach L5/ S1 dermatome from the maximum level.
Motor block was assessed at every 1 minute interval for first 5 minutes, then at every 5 minutes until the resolution of the motor block using a modified Bromage scale.
Haemodynamic variables was recorded at every 1 minute interval for first 5minutes, then at every 5 minutes for next 60 minutes and then at every 10 minutesthereafterupto120minutes.
The Ramsay sedation score was used to assess the level of sedation at every 5 minute interval for the first 60 minutes, then at every 10 minutes intervals upto 120 minutes.
After the surgery, patients were shifted to the post anesthesiac are unit (PACU) where the hemodynamic variables were monitored and they remained under monitoring until there was complete recovery of sensory and motor blockade. Once recovery of the S2 dermatome occurred, the subjects were attempted to ambulate with your assistance and instructed to avoid.
The incidence of any adverse effects such as hypotension, bradycardia, shivering, drowsiness, nausea and vomiting, respiratory de pression was recorded.

Efficacy parameters

- Time of onset of sensory block.
- Time for maximum level of sensory block.
- Highest level of sensory block.
- Time for complete resolution of sensory block.
- Duration of sensory block.
- Time of onset of motor block.
- Duration of motor block.
- Time for Ambulation.
- Two segment regression.
- Voiding time.
- Side effects.

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Calculation of sample size in comparative study was done using formula

$$N(\text{sample size}) = \frac{2(SD)^2(Z\alpha + Z1-\beta)^2}{d2}$$

α-Type I error =
1.96β–Type
IIerror=0.84
d = Mean1-Mean2=76-65=14
SD = Standard deviation = $\frac{SD1+SD2=19+13=16}{2 \quad 2}$

Assuming a decrease in duration of regression of sensory block of at least 20% with 2-chloroprocaine and with the significance at 0.05 and 80% power, we found 26 and considering dropout cases, we require 30 subjects in each group. Reference from Davis BR, Kopacz DJ. Spinal 2-Chloroprocaine: The effect of added Clonidine. Anesth Analg. 2005;100(2):559–565 (Duration of motor block 76±19min versus 65±13min) [11].

Data was entered into Microsoft excel data sheet and was analyzed using IBM SPSS 22 version software. Student test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups, Inter group analysis) on metric parameters. Levene's test for homogeneity of variance has been performed to assess the homogeneity of variance. Mann Whitney U test has been used to find the significance between two groups for parameters on non-interval scale. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results

All the patients included in the study received the assigned intervention and were followed up till the end of study. There were no exclusions or drop outs. Patient demographic characteristics were comparable in both the groups. Number of patients belonging to ASA class I and II were uniformly distributed between the groups. There was no significant difference in mean duration of surgery between the groups. (Table 1).

The mean time of onset for sensory blockade in group CS was 5.57±0.97mins and in group CC was 3.83±0.65 mins. There was a statistically highly significant difference between group CS and group CC($p < 0.001$). The mean time taken for attaining the highest level of sensory blockade was7.90±0.80 mins in group CS and 5.37±0.89 mins in group CC, which was statistically highly significant ($p<0.001$). The mean time taken for regression of sensory block by two segments was 47.67±8.98 min sin group CS and 67.33±9.07 min sin group CC, which was significant ($p<0.001$). The mean duration of sensory block was 80.33±11.29 mins in group CS and 159.67±10.66 mins in group CC and was statistically significant (<0.001). The mean duration of analgesia was 98.67±11.37minsin group and 178.0±14.0 mins in group CC, which was a significant ($p<0.001$). The mean time taken for the onset of motor blockade was 6.53±0.78 min sin group CS and 5.37±0.89 min sin group CC and was statistically highly significant. The mean duration of motor blockade was 49.0±8.33 mins in group CS and 83.67±10.66 mins in group CC which was statistically significant ($p<0.001$). (Table 2)

The mean time for voiding was 97.0±12.08 mins in group CS and 165.33±13.31 min sin group CC which was statistically significant. The mean time for ambulation was 97.0±12.08 mins in group CS and 165.33±13.31 mins in group CC which was significant ($p<0.001$). Mean Ramsay Sedations core sin Group CC were not significantly higher compared to group. (Table 3)

In group CS the basal value of mean heart rate was 83.70±12.73bpm and decrease in mean heart rate maximum of 11.16bpm from basal value at 45th min (13.8% decrease from basal value). In the group CC the basal value of mean heart rate was 78.37±8.40bp man decrease in mean heart rate which was maximum of 15.90 bpm from basal value at 45th min (19.46% decrease from basal value). The mean

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heart rate from basal to 50th minute recording was statistically not significant between the groups. (Fig 1)

In the group CS the basal value of mean SBP was 128.77±11.62mmHg and observed a fall in mean SBP which was maximum of 22.07 mmHg from mean basal SBP at 30th min (17.13% fall from basal SBP). In the group CC the basal value of mean SBP was 125.43±13.17mmHg and fall in mean SBP which was maximum of 27.43mmHg from mean basal SBP at 30th min (21.87% fall from basal SBP). The mean SBP at 40th, 45th, 50th minute recording was statistically moderately significant between group CS and group CC. (fig 2)

In the group CS the basal value of mean DBP was 79.533±7.842mmHg and fall in mean DBP which was maximum of 11.86 mmHg from mean basal SBP at 30th min (8.88% fall from basal SBP). In the group CC the basal value of mean SBP was 81.433±9.835 mmHg and fall in mean SBP which was maximum of 21.40mmHg from mean basal DBP at 25th min (17.42% fall from basal SBP). The mean DBP at 20th and 40th minute recording was statistically significant between group CS and group CC. (fig 3)

In the group CS the basal value of mean MAP was 95.94±7.53mmHg and a fall in mean DBP which was maximum of 14.80 mmHg from mean basal MBP at 30th min (14.18% fall from basal SBP). In the group CC the basal value of mean MAP was 94.33±12.95mmHg and fall in mean MBP which was maximum of 20.90mmHg from mean basal MAP at 45th min (19.13% fall from basal SBP). The mean MAP at 45th minute recording was statistically significant between group CS and group CC. (fig 4)

In Group CS incident of bradycardia was 1 and 2 in Group CC. In Group CS incident of hypotension was 1 and 2 in Group CC. It was not statistically significant.

Table 1: Comparison of demographic parameters, ASA grade and duration of surgery

Parameter	Group CS	Group CC	P Value
Age	**34.05±9.54**	**32.93±8.91**	
Female: Male	15:15	18:12	
BMI (KGM2)	22.25±0.85	22.39±0.77	
ASA 1: ASA2	17:13	14:16	
Duration of Surgery	41.0±6.07	41.17±6.52	0.553

Table 2: Comparison of onset and duration of sensory and motor block

Parameters	Group CS	Group CC	P Value
Sensory Block Onset (MIN)	**5.57±0.97**	**3.83±0.65**	<0.001
Time for Maximum Sensory Level (MIN)	7.90±0.80	5.37±0.89	<0.001
2 Segment Sensory Regression (MIN)	47.67±8.98	67.33±9.07	<0.001
Duration of Analgesia (MIN)	98.67±11.37	178.0±14.0	<0.001
Motor Block Onset (MIN)	6.53±0.78	5.37±0.89	<0.001
Duration of Motor Block	49.0±8.33	83.67±10.66	<0.001

Table 3: Comparison of mean time for voiding and Mean Time for ambulation

Parameters	Group CS	Group CC	P Value
Mean time for voiding (min)	97.0±12.08	165.33±13.31	<0.001
Mean Time for ambulation (MIN)	97.0±12.08	165.33±13.31	<0.001

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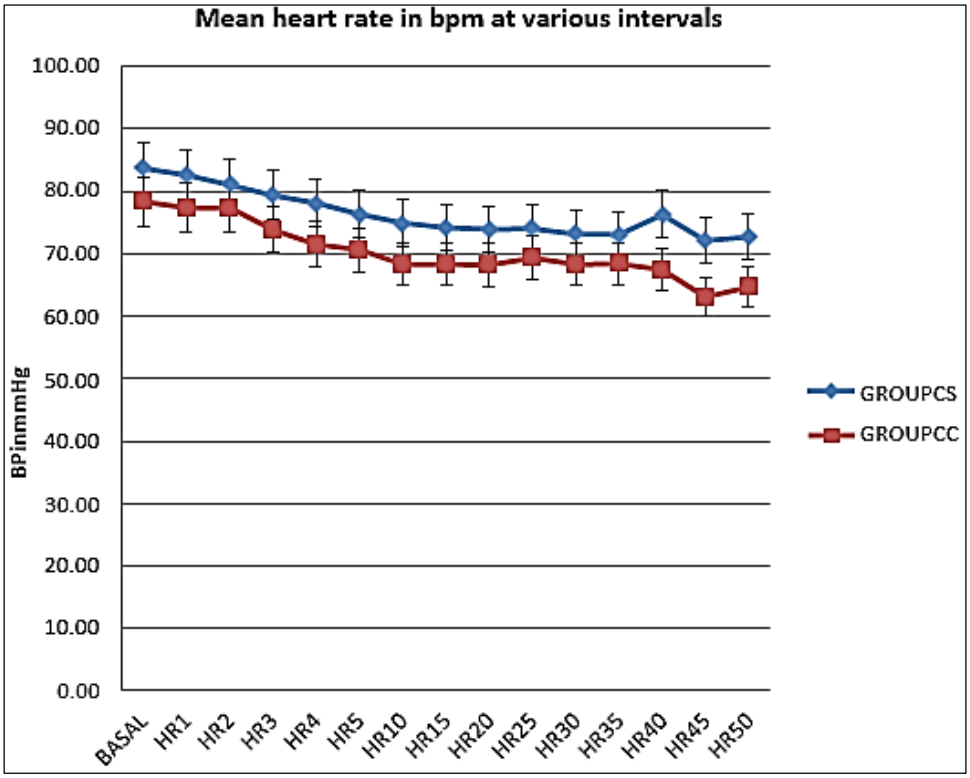

Fig 1: Mean heart rate in bpm

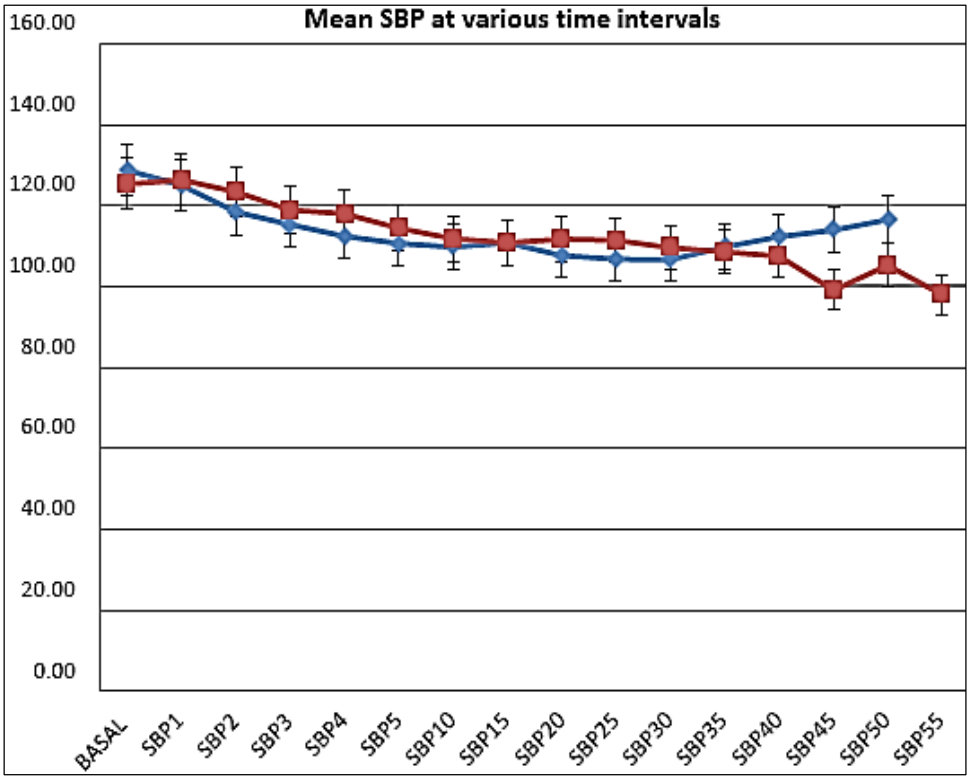

Fig 2: Mean SPB at various time interval sin mm Hg

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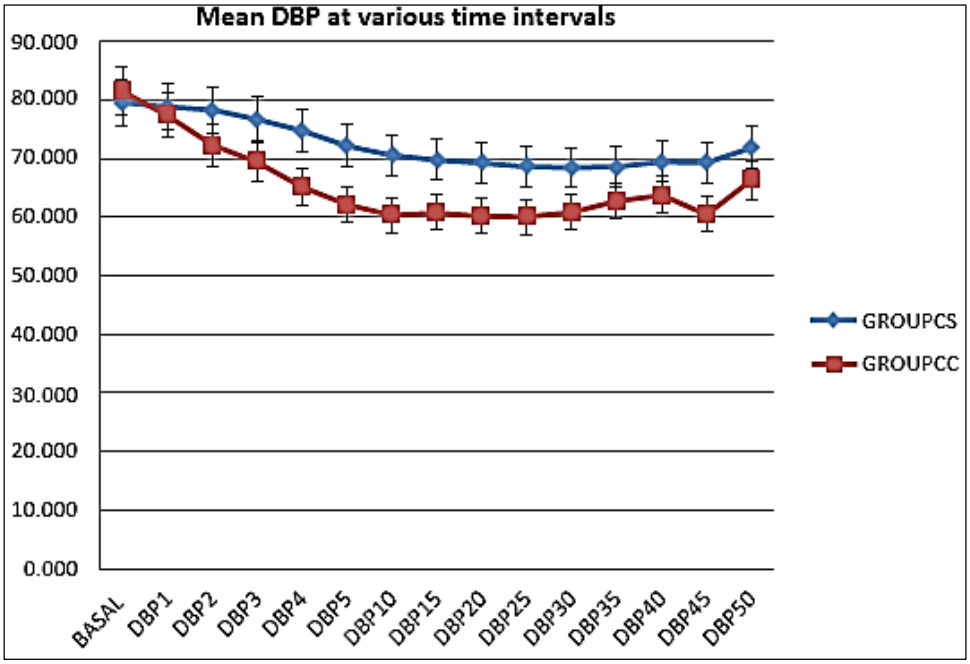

Fig 3: Mean DBP at various time intervals in mmHg

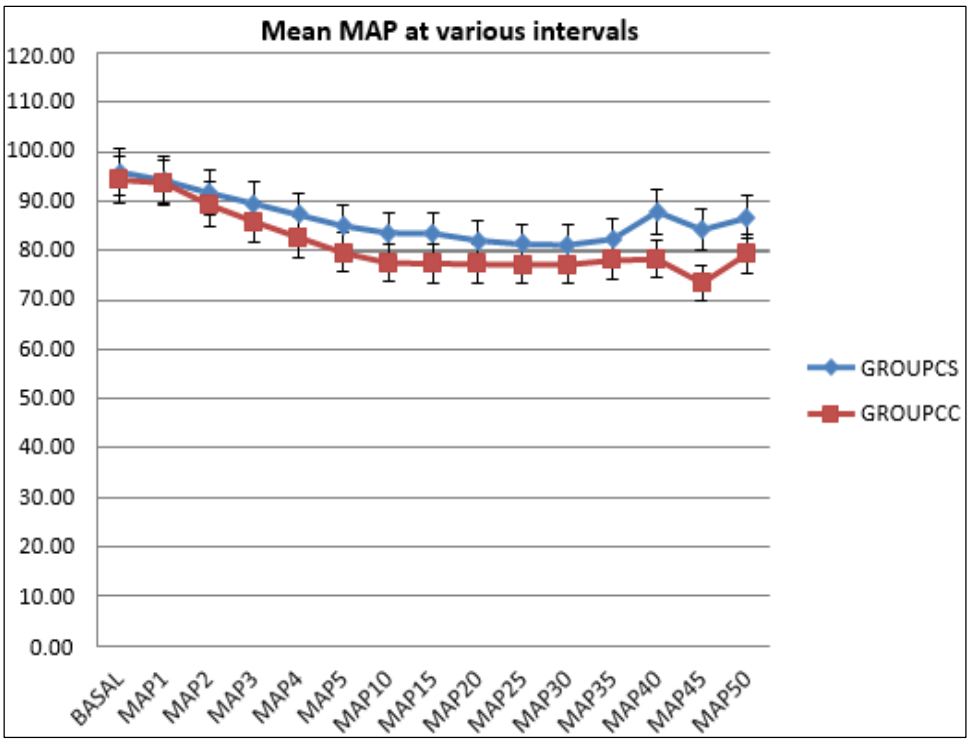

Fig 4: Mean MAP at various time intervals in mmHg

Discussion

This study hypothesized that intrathecal 2- chloroprocaine in combination with clonidine has faster onset and prolonged duration of sensory and motor block when compared to intrathecal 2-chloroprocaine with insignificant hemodynamic changes and side effects such that the drug may be proposed for day care surgeries. Various authors have used different doses of 2-Chloroprocaine for intrathecal blockade starting from 10mg to 40mg along with adjuvants. Sell and Pitkanen [12] tested four different doses of spinal 2-CP (35, 40, 45 and 50 mg) in a cohort of 64 patients scheduled for elective lower extremity procedures.

The regression of sensory block and time to discharge were faster in the lower dose groups (35 and 40 mg), although the higher level of block and time to complete block regression were comparable in all four groups. Kopacz [13] tested 10 mg and 20 mg of 2-CP in 8 volunteers and compared the results with previous data obtained for 30 to 60 mg in the same human model.Theyfoundthat10-mgdoseproduces only brief and inconsistent sensory anesthesia and consider edit as a no-effect dose. Similarly, the 20 mg dose did not reliably produce dense motor block, even though it was able to produce a cephalad level of sensory anesthesia of at least 1 in all subjects. Dose 30-mg produced adequate sensory anesthesia for brief surgical procedures with less motor block. Hence we choose dose of 2-Chloroprocaine of 30mg (3ml) for our study for intrathecal administration.

Kouri and Kopacz [14] (2004) compared intrathecal injection of 40mg 2% lidocaine with 40mg 2% 2-CPi weight healthy volunteers and demonstrated that hemodynamic changes were mild and did not vary significantly between groups. No vasoactive drugs were required. Sethi BS [15] *et al*. in their study observed lowest mean MAP (70 mmHg) in clonidine group (1 µg/kg, mean weight 57.93±4.75 kg) which is less than that in our study (76.05±2.54mmHg). Strebel S [16] *et al*. found out the maximum decrease in MAP was 25%±14%, 26%±12% and 25±13%, who received clonidine at 37.5µg, 75µg and 150 µg respectively. Our study was consistent with Sethi BS *et al*. and Strebel S *et al*., as we observed significant difference in mean value of SBP, DBP and MAP in our study. Our study results were not comparable with Davis *et al*. and this might be due to the usage of 30 µg of clonidine compared to 15µg of clonidine used in their study.

Davis and Kopacz [11] (2004) showed maximum level of sensory block in Group CS was T8 (T6-T12) and in Group CC it was T6 (T4-T11). Our study is consistent with this study. Yoos and Kopacz [8] (2006) showed maximum level of sensory block in Group 2-CP 40mg was T7 (T3-T10). Our study was consistent with this study in Group CS.

Davis and Kopacz [11] (2004) showed two dermatome regression time in Group CS 50±9 min and in Group CC it was 50±22 min. Our study was consistent with this study in CS group and has prolonged time for two segment regression of sensory blockade in Group CC. Lacasse [7] *et al*. (2011) showed two dermatome regression time with 40 mg 2-CP of 50±18min. Our study was consistent with this study in time for two segment regression of sensory blockade in Group CS.

Davis and Kopacz [11] (2004) showed Mean duration of sensory block in Group CS 99±18min and in Group CC it was 131±15 min. Mean duration of analgesia in Group CS99±18min and in Group CC it was 131±15 min. Mean duration of motor block in Group CS65±13min and in Group CC it was79±19 min. mean duration for ambulation in Group CS99±18min and in Group CC it was 131±15 min. Our study was consistent with this study in CS group and had prolonged time for Mean duration of sensory block, analgesia, motor block and prolonged time for ambulation in Group CC. Cassati *et al*. [17] (2006) showed Mean duration of sensory block with 40 mg 2-CPof 85 (46–141) min. Our study was consistent with this study in time for Mean duration of sensory block in Group CS. Gonterand Kopacz [18] (2005) showed Mean duration of motor block with 30mg 2-CP of 54±23min. Our study was consistent with this study in time for Mean duration of motor block in Group CS. Warrenand Kopacz [19] (2007) showed mean duration for ambulation with 40mg 2-CP of 96±7 min and Mean duration for voiding with 40 mg 2-CP of 101±7 min. Our study was consistent with this study in time for ambulation in Group CS and had prolonged time for voiding in Group CC. Davis and Kopacz [11] (2004) showed Mean duration for voiding in Group CS99±18min and in Group CC it was 131±15 min. Our study was consistent with this study in CS group.

Conclusion

From the present study it can be concluded that intrathecal clonidine in the dose of 30 µg along with 3 ml (30mg) isobaric 1% 2-Chloroprocaine, in patients undergoing elective infraumbilical surgeries, decreases the onset time for sensory blockade and motor blockade, Produces higher level of sensory blockade, prolonged sensory and motor blockade, postoperative analgesia and prolonged ambulation and voiding time.

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