Original Research Article

Comparison of anesthetic effects of intrathecal 1% 2-chloroprocaine versus 0.5% ropivacaine with fentanyl in urological surgeries: A randomized double-blind, interventional study

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Received: 24-11-2021 / Revised: 16-12-2021 / Accepted: 08-01-2022

Abstract

Introduction: Spinal anaesthesia has got inherent advantages like intense motor and sensory blockade,reliability and avoids side effects of multiple drugs. Ropivacaine is safer long acting local anesthetic having greater sensorimotor differentiation. 2-Chloroprocaine (CP) is an amino-ester local anesthetic with a very short half-life; have favorable profile for short procedures. Addition of fentanyl to the local anesthetics for intrathecal injection improve the quality and duration of sensory anesthesia without prolonging motor recovery. **Aim:** To investigate the anesthetic effect of ropivacaine and chloroprocaine with fentanyl intrathecally for day care urological surgeries, to assess the characteristics of sensorimotor block, mean time to first postoperative rescue analgesia, and adverse effects if any. **Methods:** This prospective randomized, double blind, interventional study included 30 patients of ASA grades I & II undergoing urological surgeries under spinal anesthesia with intrathecal 3 ml of 1% 2-chloroprocaine with 12.5µg of fentanyl (GroupC) or 1.5 ml of 0.5% ropivacaine with fentanyl 12.5µg (Group R). **Results:** Mean time to achieve sensory block at T10 level was significantly short with CP (Group C 1.875 ± 0.47, Group R 2.51±0.54 min, (p value <0.001). Mean onset time of the motor block was short with CP (Group C 2.51 ± 0.73 min, Group R 4.74 ±1.08 min, p-value <0.001). Mean duration of sensory and motor block were significantly shorter in Group C compared to Group R (104.4 ± 10.89 min vs 154.16 ± 10.58 min) and (92.96 ± 12.02 min vs 143.66 ± 10.92 min) respectively. Mean time to two segment sensory regression was longer with Ropivacaine (Group R 118.2 ± 12.48 and Group C 79.73 ± 12.48 min). Difference in Modified Bromage score was significant at 1, 2, 3 and 4 hour postoperatively among two groups with p-value <0.05 showing early regression of motor blockage in Group C in comparison to Group R. **Conclusion:** Intrathecal chloroprocaine is a good alternative to long acting local anesthetic ropivacaine for short duration urological surgeries, it facilitates early ambulating with minimum side effects. Furthermore, fentanyl as an adjuvant to both ropivacaine and chloroprocaine enhances the duration of analgesia and stabilizes hemodynamic variables.

Keywords: Day care anesthesia, urological day care surgery, ambulatory surgery, spinal anesthesia, chloroprocaine , ropivacaine.

Introduction

Spinal anesthesia, the most common anesthetic technique used for urological surgeries, is often associated with delayed ambulation, increased risk of urinary retention. In this era of fastly changing trends of surgical practice to day care surgery, we need to switch to ambulatory anesthesia so that early patient discharge with minimal side effects becomes a reality.

Various long acting anesthetics such as bupivacaine, levobupivacaine and ropivacaine are being used intrathecally, which even in low doses these are associated with longer hospital stay and discharge.

Ropivacaine, a long acting local anesthetic, has lower lipid solubility than bupivacaine, which is responsible for its lower penetration into myelinated motor fibers and thus lesser motor blockade with greater sensory-motor differentiation[1]. It produces prolonged sensory block, therefore may be a useful agent in ambulatory settings[2].

2-Chloroprocaine (2-CP), recently gaining popularity after the concerns over its neurotoxic potential have been resolved with availability of preservative free solutions. It's an amino-ester local anesthetic with a very short half-life and this shows a favorable profile for short procedures[3].

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With a reduced dose of 35-40 mg there is faster motor recovery along with faster onset (5-10 minutes) & quick recovery time (70-150 minutes) subsequently leading to early ambulation[4].The addition of intrathecal opioids is a well known practice as opioids act synergistically with local anesthetics (LA) to potentiate sensory block without affective sympathetic blockade. Intrathecal opioids decrease the dose of LA, enhance anesthesia, hemodynamic stability and provide prolonged postoperative analgesia without increasing adverse effects[5]. Fentanyl is a potent lipid soluble synthetic µ-opioid agonist, it potentiates the afferent sensory blockade without affecting motor block.We designed this study to investigate the anesthetic effect of ropivacaine and chloroprocaine with fentanyl intrathecally for day care surgeries, to assess the characteristics of sensori-motor block, mean time to first postoperative rescue analgesia, and adverse effects if any.The aim of this study is to determine which combination is providing longer duration of analgesia and shorter duration of motor blockade to provide early ambulation with least side effects and can be used in day care ambulatory surgeries.

Methods and materials

The study was conducted at a tertiary care center after obtaining permission from the Institution Ethics Committee (ref no. 456 /MC/EC/2021, Dated April 01,2021) and written informed consent from patients. The trial was registered with CTRI and issued registration number CTRI/2021/11/037980. This prospective, randomized double blind interventional study included 60 patients belonging to ASA grade I & II, age between 18 and 55 yrs, weighing

between 50 and 75 kg and height ranging from 150 and 180 cm undergoing elective urological surgeries under spinal anesthesia were considered for enrollment in two groups. A sample size of 60 subjects was calculated at 95% confidence & 80% power to verify the expected minimum difference of 64 (±17.44) minutes in mean time duration of motor block in both the groups (as per the seed article). This sample size was adequate to cover all other study variables. Patients with skin infection at a local site, severe hypovolemia, severe MS, blood coagulopathies, raised intracranial pressure, allergic to drugs used for study and failure of spinal anesthesia, cases in which general anesthesia was required were excluded. Randomization into two groups of thirty patients each was done by using a computer-generated random number table and the allocated group number of each patient was kept in a sealed opaque envelope. Patients in Group C (n=30) received intrathecal 3 ml of 1% 2-chloroprocaine and 12.5µg of fentanyl and Group R (n=30) received intrathecal 1.5 ml of 0.5% ropivacaine and fentanyl 12.5µg. Total volume was kept constant 3.25ml in each group by adding normal saline.All patients were thoroughly examined pre-operatively which included history, physical examination, and all routine investigations. The procedure was explained to patients and an informed written consent for spinal anesthesia and surgery was taken and the concept of 10 point visual analogue scale (VAS) was explained to the patient during pre anesthetic check up.On the day of surgery, patient was taken to the OT, fasting status was confirmed, monitors were attached, baseline heart rate (HR), systolic blood pressure(SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation (SpO2) and electrocardiogram were recorded. Ramsay sedation score was used for assessing sedation, baseline sedation score noted. A good IV line was secured with 18G cannula. Preloading was done by administering 10ml/kg Ringer lactate solution preoperatively over 15 min. Under all aseptic precautions, spinal anesthesia was performed at the $L_3 – L_4$ intervertebral space, with the patient in sitting position. A volume of 3.25ml of the study drug was injected over 30 seconds through a 25-gauge spinal Quincke's needle. Patients received medications by spinal route depending on the group allocated by randomization.

The patient and anaesthesiologist was involved in drug preparation, block administration and the one who recorded the data were blinded to the study drugs.After administering the block, the patient was placed in the supine position immediately to achieve a desired level of block. Oxygen (4L/min) was administered.The onset of sensory block was defined as the time from the intrathecal injection of the study drug to the time taken to achieve the highest level of sensory block. This was assessed every 2 minutes by pinprick test bilaterally in the midclavicular line by using 22 G needle until the highest level of the block was achieved and stabilized for four consecutive tests.Regression of the sensory block was defined as the time taken for the sensory block to regress upto 2 segments of dermatome from the highest level achieved. Onset of motor block was defined as the time from intrathecal injection of the study drug to the time taken to achieve complete motor block by using Modified Bromage Scale. Duration of the motor block was assessed by recording the time elapsed from the lowest to the maximum Bromage score. Pain was assessed by Visual Analogue scale was assessed intraoperatively as well as postoperatively, ranging between 0 and 10 (0 = no pain, 10 = most severe pain). Total duration of analgesia was time taken from intrathecal drug administration to patient's first demand of rescue analgesia (On VAS >3). Patients received rescue analgesic Inj. Diclofenac 75mg on VAS score of 3. Intraoperative and postoperative sedation level was measured by using Ramsay sedation score. Hypotension was defined as a systolic arterial blood pressure (SBP) < 90 mm of Hg or a decrease in SBP by 20% or more from baseline values and was treated by incremental doses of mephentermine 6 mg IV and IV fluid as required. Bradycardia was defined as a fall in heart rate below 55 beats per minute and was treated with incremental doses of atropine 0.3 – 0.6 mg IV. Respiratory depression was defined as a respiratory rate of less than 8 breaths per minute and/or oxygen saturation less than 90% in room air. The incidence of adverse effects such as nausea, vomiting, headache, bradycardia, respiratory depression, and hypotension were also recorded.

Statistical analysis

Statistical analysis was done using Epi info version 7.2.1.0 statistical software. Nominal/categorical variables were summarized as frequency and percentage and were analyzed using Chi square test as applicable. Continuous variables were summarized as mean and standard deviation and were analyzed using independent sample student t tests. Hemodynamic variables were summarized as mean and variance and were analyzed using ANOVA test. A p value < 0.05 was taken as statistically significant.

Results

Both groups were comparable for demographic variables such as age, gender, weight, height, ASA grades and mean duration of surgery(Table 1).Onset of the sensory block in Group C was faster (1.875 ± 0.47 min) as compared to the Group R (2.51 ± 0.54) min) with the p value <0.001. Mean onset time of motor block was longer in the Group R (4.74 ± 1.08 min), in comparison to the Group C (2.51 ± 0.73min) with p value <0.001. The difference between the mean duration of sensory block of Group C and Group R (104.4 ± 10.89 min and 154.16 ± 10.58 min respectively) with p value: <0.001 (Table 2).

Difference in mean duration of motor block in Group C and Group R was (92.96 ±12.02 min and 143.66 ±10.92 min. respectively) with p value: <0.001. It was statistically significant (Table 2).On comparing the mean time to two-segment sensory regression between the two study groups, we observed that Group R (118.2 ± 12.48 min) took more time than Group C (79.73 ±12.48 min). It was found to be statistically significant. Mean time to first dose of analgesia was significantly shorter (111.63 ± 14.06) min) in Group C while it was (157.53 ±11.22 min) in Group B(Table 2).Intraoperative variations in heart rate at various time points-1,2,3,4,5,10,15, 20,25,30 ,40,50,60,70 mins during surgery was comparable (Figure 1). Mean SBP and DBP were significantly lower at 25 mins and 30 mins with p value < 0.05 in the Group R.. The mean values for MAP were significantly low at 4, 25, 30 and 40 mins with p value <0.05 in Group R(Figure 2). The mean saturation was comparable among both groups during the intraoperative period. Postoperatively, mean HR, SBP and mean oxygen saturation were comparable at 1, 2, 3, 4 hours while there was statistically significant reduction in mean DBP and MAP was noted in Group R at 4 hours.VAS Scores were comparable at 1 and 4 hrs among both the groups (p value 0.279 and 0.15 respectively). But it was significantly lower in Group R at 2nd and 3rd hour postoperatively (p value 0.007 and 0.014 respectively).Modified Bromage Score was significantly different at 1,2,3 and 4 hour postoperatively among two groups with p value < 0.001 at all time intervals, showing the early regression of motor blockage in Group C in comparison to Group R. Mean Ramsay Sedation Score was comparable at 1,2,3 and 4 hour postoperatively among two groups.In Group C, incidences of hypotension and nausea were more as compared to Group B. But, none of these achieve statistical significance. None of the other adverse effects were noted in both groups.

Table 1: Demographic distribution among two groups

	MEAN±SD	MEAN±SD	P Value
	GROUP C	GROUP R	

Age (years)	38.36 ± 13.56	37.7 ± 15.01	0.85(NS)
Weight (Kg)	65.66 ± 7.63	63.1 ± 6.96	0.178(NS)
Height (cm)	165.96 ± 4.85	164.3 ± 3.83	0.145(NS)
Duration of surgery (min)	45.66 ± 16.22	55.16 ± 21.67	0.06(NS)
ASA Grade I	20 (66.6%)	23 (76.6%)	0.390(NS)

Table 2: Comparison of block characteristics among two groups

	MEAN±SD	MEAN±SD	P Value
	GROUP C	GROUP R	
Mean time to sensory block(min)	1.875 ± 0.47	2.51 ± 0.54	<0.001
Mean time to motor block (min)	2.51 ± 0.73	4.74 ± 1.08	<0.001
Mean duration of sensory block(min)	104.4 ± 10.89	154.16 ± 10.58	<0.001
Mean duration of motor block(min)	92.96 ± 12.02	143.66 ± 10.92	<0.001
Mean time to two-segment sensory regression (min)	79.73 ± 12.48	118.2 ± 12.48	<0.001
Mean time to first dose of analgesia	111.63 ± 14.06	157.53 ± 11.22	<0.001

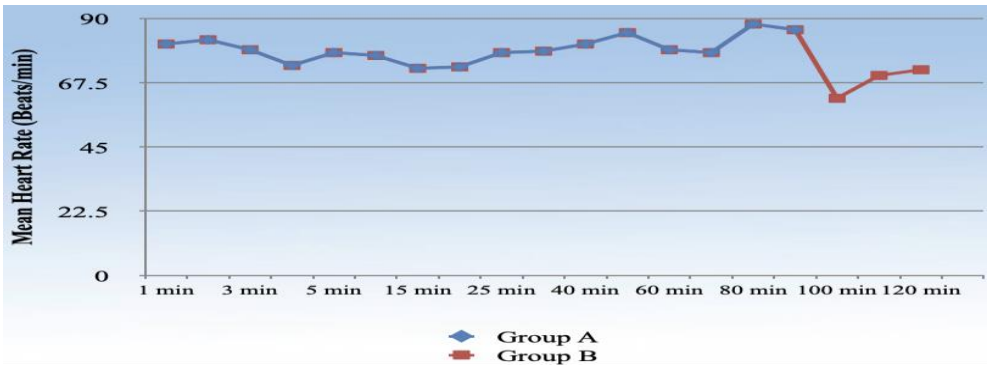

Figure 1: Trends of mean heart rate

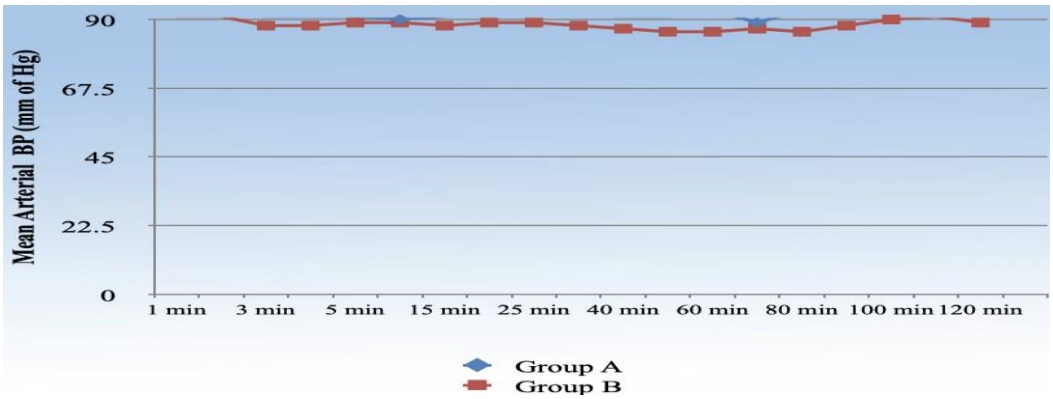

Figure 2: Trends of mean arterial pressure

Discussion

Chloroprocaine has been used successfully for spinal anesthesia since 1952, and sodium bisulfite was then added as a preservative after 1956. It was then abandoned in 1980s after several reports of neurological deficit in patients, recently the preservative free formulation has been extensively evaluated in clinical practice with a

favorable profile in terms of both safety and efficacy[6].Ropivacaine is a S-enantiomer, amide local anesthetic, with low lipid solubility, which blocks nerve fibers involved in pain transmission Aδ and C fibers to a greater degree than those controlling motor functions Aβ fibers. Prasad G et al[7] demonstrated that intrathecal ropivacaine in a dose of 18.75 and 22.5 mg were observed to be equally effective in providing satisfactory analgesia.

Studies have shown that intrathecal opioids as an adjuvant to low dose local anesthetics, produces a synergistic effect by acting directly on the opioid receptors in the spinal cord[8,9,10] and provides increased the duration of analgesia and provided hemodynamic stability with no major complication.In our study, both the groups were comparable with respect to age, sex, weight, and height, ASA physical status and duration and types of surgery. The mean onset time of sensory block at T 10 in group C was significantly shorter (1.87 ± 0.47 min) in comparison to group R (2.51 ± 0.54 min) with a P value of <0.001. Similar results were observed in various other studies[11,12]. Camponovo C et al[13] compared 1% 2-CP in doses of 50 mg with 0.5% bupivacaine (10 mg), they reported mean onset time to the sensory block was 5 mg for 2-CP, this difference in time may be attributed to use of fentanyl as an adjuvant in our study.

Mean onset time of motor block (Group C- 2.51 ±0.73min, Group R 4.74±1.08min, P <0.001.) was significantly shorter in the Group C. Our results are in accordance with other studies[14,15] Khare et al[16] reported faster onset of the motor block (3.7 ± 0.6 min) for chloroprocaine Group. In our study,time to maximum motor block (Group C- 92.96 ± 12.02 min, Group R- 143.66 ± 10.92 min, P <0.001) was significantly shorter in the Group C. Our results are similar to other studies[17,18] Sangariya G et al[19] observed in their study that mean duration of motor block of chloroprocaine with fentanyl was 70.4±14.44 min, which is comparable with our study.

The mean duration of the sensory block (Group C-104.4 ± 10.89 min, Group R-154.16 ± 10.58 min, P<0.001) was significantly longer in the Group R. Similar results were observed in other studies . In our study , we observed that at 5 minutes of spinal anesthesia , the maximum level of motor block was achieved by Group C (Modified Bromage 1 level by 27 patients, Modified Bromage 2 level by 3 patients) and in Group R (Modified Bromage 1 level by 30,). A higher number of individuals achieved complete motor block in Group R as compared to Group C. Similarly. McNamee et al[20] in a study on 104 patients concluded that in the ropivacaine group all patients achieved modified bromage score 1 levels**.** .Mean VAS score was comparable among two study groups (Group C - 0.2±0.48), (Group R -0.16±0.46), (P - 0.785) at 5 minutes after administering spinal anesthesia. The mean VAS Score was less in Group R at 1h, 2h, 3h, 4h time interval postoperatively, it achieved significance only at 2nd and 3rd hour postoperatively. This implies that Group C patients required an earlier and frequent rescue analgesic doses as compared to Group R . Dany et al[21] obtained similar results when compared analgesic effect of 4ml of 0.5% Ropivacaine and 4ml of 1% Chloroprocaine in 90 patients in day care perineal surgeries. VAS scores were lower in Group R at 1,2,3,4,5 and 6 hours, with statistically significant values at 1,2,4 and 6 hours. Similar findings were observed in other studies[12,19].

Mean time to two-segment sensory regression in (Group C - 79.73±10.9 min, Group R- 118.2±12.48 min, P <0.001) which shows that sensory blockade was significantly longer in Group R than the Group C. Our results are in accordance with other studies[12,14,19]. Yoos et al[22] also demonstrated a 1.7 times faster regression of the sensory block with 2-CP (a difference of 78 min) in comparison to low dose bupivacaine. Mean time to first dose of analgesia was (Group C 111.63±14.06 min, Group R -157.53±11.22 min, P <0.001) significantly longer in the Group R. These findings are compatible with various studies[19,23,24].In our study, variations in intra operative mean HR and mean oxygen saturation was comparable. Difference in the intra operative mean SBP and DBP was significant at 25 mins and 30 mins with p value < 0.05 while difference in MAP among two groups were statistically significant at 4, 25, 30 and 40 mins with p value <0.05. Similar results were shown by Herndon et al[25]; they observed significantly less hypotension in the chloroprocaine group as compared to bupivacaine (59.5% vs 83.8% ; p-value 0.04). Our results are consistent with other studies[26,27].

More participants in Group C experienced hypotension and nausea as compared to Group R. But, these differences were statistically not significant. No other postoperative side effects were reported in both groups. These results are in correlation with studies[12,18,27]. The mean Modified Bromage Score was significant at 1,2,3 and 4 hour postoperatively (P < 0.05) which signifies that the regression of motor blockade was significantly earlier in Group C in comparison to Group R. Thus patients receiving chloroprocaine were discharged earlier than the patients receiving ropivacaine. Siddaiah J et al[28] found that the time to reach Modified Bromage score of 0 during the postoperative period for the chloroprocaine group was 67.16 ± 21.73 min, which is similar to our results.The mean Ramsay Sedation Score at 1,2,3 and 4 hours postoperatively was comparable between two groups, which is consistent with the study done by Breebaart MB et al[29].

Limitations

As we are focussing more on day care surgeries, we should have also assessed time to ambulation, time to micturition and time to discharge.

Conclusion

Intrathecal chloroprocaine can be used as an alternative to long acting local anesthetics such as ropivacaine for urological surgeries requiring short duration and early ambulation with minimum side effects. As we observed in this study that the intrathecal 1% 2-chloroprocaine with fentanyl provides adequate motor blockade and analgesia for day care urological surgeries while 0.5 % ropivacaine with fentanyl provides a greater duration of sensory and motor blockade than chloroprocaine. Furthermore, fentanyl as an adjuvant to both ropivacaine and chloroprocaine enhances the duration of analgesia and stabilizes hemodynamic variables.

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Conflict of Interest: Nil Source of support: Nil