Original Research Article

Comparison of chloroprocaine and chloroprocaine with clonidine in spinal anaesthesia: A prospective study, double-blind randomised trial

Aslam K M[1], Asif P Mammutty[2], Daber Pareed[3], Sunny Alex[4*], Vijish Venugopal[5]

[1]Senior Resident, Department of Anaesthesiology, KMCT Medical College, Calicut, Kerala India
[2]Assistant Professor, Department of Anaesthesiology, KMCT Medical College, Calicut, Kerala, India
[3]Assistant Professor, Department of Anaesthesiology, KMCT Medical College, Calicut, Kerala, India
[4]Professor, Department of Anaesthesiology, KMCT Medical College, Calicut, Kerala, India
[5]Professor, Department of Anaesthesiology, KMCT Medical College, Calicut, Kerala, India

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Abstract

Background and Aims: Clonidine improves quality of spinal anaesthesia as an adjuvant with bupivacaine and ropivacaine, but has not been studied much in combination with preservative-free 2-chloroprocaine, hence this study. **Methods**: This prospective randomised control trial was conducted in 60 adult male patients of age 18-60 years undergoing urological surgeries of short duration (<40 minutes). Patients were randomly assigned into two groups: Group A (n=30), patients who received intrathecal injection of 2-chloroprocaine and Group B (n=30), patients who received intrathecal injection of 2-chloroprocaine with 30µg of clonidine. The primary aim of our study was to compare isobaric 1% 2-chloroprocaine and 1% 2-chloroprocaine with 30µg of clonidine in terms of onset and duration of motor block, onset and duration of sensory block, time for 2 segment regression of sensory block and peak block height. Statistical analysis was done using SPSS version 20.0. Quantitative data was analysed by student's 't' test and qualitative data by Chi-square test. **Results:** Onset of sensory blockade was faster and peak block height was higher for Group B. There was no statistically significant difference in the onset of motor blockade and time of 2 segment regression between the two groups. The total duration of sensory and motor block was longer in Group B compared to Group A and mean time for first request of analgesic was longer in Group B compared to Group A. There was no statistically significant difference in the heart rate and mean arterial pressure between the groups at various time intervals. There was no incidence of hypotension, bradycardia or post spinal head ache in the two groups. **Conclusion:** Addition of 30µg of Clonidine to 4ml of 1% Chloroprocaine intrathecally enhances onset and duration of sensory and motor blockade in urological surgeries of short duration without significant difference in the hemodynamic parameters and side effects compared to Chloroprocaine alone.

Key words: Chloroprocaine, Clonidine, Spinal anesthesia, Adjuvant

Introduction

Spinal anaesthesiaprovide intense sensory, motor and sympathetic blockade with smaller doses of local anaesthetics[1]. Chloroprocaine is amino-ester local anesthetic with very short half-life. Preservative freeChloroprocainewas not associated with neurotoxicity[2,3]. Chloroprocaine is characterized by very fast onset and quick recovery time[4]. Clonidine, $^{\alpha}{}_{2}$ -adrenergic agonist, is used as adjuvant to intrathecal local anesthetics with potent analgesia, free of opioid-related side effects and increase both sensory and motor blockade of local anesthetics[5]. Aim of study was to evaluate whether adding small-dose clonidine, changes duration of spinal anesthesia, independently alters sensory or motor blockade, or has no effect on subarachnoid Chloroprocaine

Materials and methods

This prospective randomised control study was conducted in 60 male patients of age 18-60 admitted at KMCT Medical college, Calicut, undergoing urological surgeries, after obtaining ethical committee approval and written informed consent, from October 2018 to June 2019. Statistical analysis was done using SPSS version 20.0. Quantitative data will be analysed by student's 't' test and qualitative data will be analysed by Chi-square test. All values were expressed as mean ± standard deviation.

*Correspondence
Dr. Sunny Alex
Professor, Department of Anaesthesiology, KMCT Medical College, Calicut, Kerala, India
E-mail: sunnex76@hotmail.com

P <0.05 was considered statistically significant. In our study, male patients of age18-60 years of American society of anaesthesiologist grade I and II undergoing urological surgeries scheduled for short duration (less than 40 min) requiring ≥ T_{10} level of sensory block were included. Those with absolute contraindications to spinal anaesthesia, ASA physical status III / V, allergy or intolerance to local anaesthetics or para-aminobenzoic acid and atypical plasma cholinesterase were excluded. On the morning of surgery patients will be randomly allocated into two groups by computer generated random number table:

Group A (n=30): patients who received intrathecal injection of 2-chloroprocaine.

Group B (n=30): patients who received intrathecal injection of 2-chloroprocaine with 30µ of clonidine.

The study was designed to compare the quality and duration of spinal anaesthesia with 2-chloroprocaine and 2-chloroprocaine with clonidine, with respect to onset and duration of motor block, sensory block, time for 2 segment regression of sensory block, intra operative hemodynamic parameters at various time intervals, time for first request of analgesic and side effects if any.

All patients received oral premedication with Ranitidine 150 mg the night before surgery and on the morning of surgery along with Tab. Ondansetron 4mg. All necessary equipments and drugs necessary for resuscitation were kept ready in the operation theatre. All the patient fasted for at least 6 hours before the procedure. On arrival at the operation theatre, electrocardiogram (ECG), pulse oximeter, and non invasive blood pressure monitors were attached. The baseline blood pressure and heart rate were recorded. Intravenous line was secured and patients were preloaded with normal saline solution 10ml/kg

before the initiation of procedure. Before the commencement of anaesthesia patients were instructed on the methods of sensory or motor assessment. The co-guide loaded the respective drug under strict aseptic precautions based on group allocation and handed the syringe to the anaesthesiologist performing the block so that he/she is blinded to the drug. Spinal anaesthesia was performed under aseptic precautions in sitting position with 25G Quincke‟s needle at L3-L4 interspace by the attending anaesthesiologist who was not involved in the study. Once free flow of clear cerebrospinal fluid was obtained, according to randomization, patients received an intrathecal injection of 4ml of preservative free 2-chloroprocaine with 0.2ml of sterile water or 4 ml of preservative free 2-chloroprocaine with 0.2ml(30µg) of clonidine. It was given over 15-20 seconds and the time noted when the drug was given. The patients were then placed in supine position. Then the chief investigator who was blinded to the drugs given, did the observations and patient assessments. When complete motor blockade and sensory block up to T10 dermatome was achieved, patient was placed in the lithotomy position and the surgeon was allowed to proceed. Characteristics of sensory and motor block, hemodynamic parameters, time for first request of analgesic and adverse outcomes, if any, were studied.

Results

The two groups were homogenous with respect to age, weight, height, ASA status and duration of surgery/anaesthesia. Mean time taken for onset of sensory blockade was 5.20 minutes for GroupA and 4.00 minutes for GroupB with standard deviation of 1.34 min and 1.43 min respectively. The difference was statistically significant with p value 0.002. Peak block height was T8 [T6-T10] for Group A and T6[T5-T9] for Group B with Chi square value of 17.8. The difference was statistically significant with p value 0.004. Mean time taken for 2 segment regression of sensory blockade was 48.83 minutes for Group A and 51.16 minutes for Group B with standard deviation of 4.29 and 5.20 respectively. The difference was statistically insignificant with p value 0.06. Mean duration of sensory blockade was 58.00 minutes for Group A and 77.83 minutes for Group B with standard deviation of 5.01 and 8.47 respectively. P value was found to be <0.001i.estatistically highly significant (p< 0.05). Mean time taken for onset of motor blockade was 6.50 minutes for Group A and 5.00 minutes for Group B with standard deviation of 1.94 and 1.81 respectively. P value was found to be 0.003 which is statistically significant. Mean duration of motor blockade was 67.00 minutes for Group A and 89.66 minutes for Group B with standard deviation of 6.89 and 6.14 respectively. P value was found to be <0.001 i.e. statistically significant (p< 0.05). First request of analgesic is 208.00±22.19 minutes in Group A and 284±33.17 minutes in Group B. The difference between them was statistically highly significant as the p value is <0.001. Student's t test used to compare the mean value of heart rate and mean arterial pressures between the two groups at different time intervals showed that there is no statistically significant difference in mean heart rate between the 2 groups. Hypotension, bradycardia, post spinal headache and transient neurological symptoms were not reported in either group.

Discussion

In our study, comparison of mean time of onset of sensory blockade between Group A (chloroprocaine group) and Group B (chloroprocaine with clonidine group) showed that mean time taken for onset of sensory blockade was faster for Group B (4 minutes) as compared to group A (5.20 minutes) and it was statistically significant and with p value of 0.002 (Table I).

Table I: Comparison of mean time of onset of sensory blockade

Groups	Mean	SD	t value	P value
A	5.20	1.34	3.33	0.002
B	4.00	1.43		

Manuraj V. S. et al[6]. compared bupivacaine and bupivacaine with clonidine under spinal anesthesia in patient for total abdominal hysterectomy. The mean time for onset of sensory block in group B [0.5% hyperbaric bupivacaine 4 ml] was 137.60 seconds and in group C[0.5% hyperbaric bupivacaine 3. 5 ml + 50µg clonidine] was 112.22 seconds (p<0.001) which supports our results, as addition of clonidine to intrathecal local anaestheticwill make onset of sensoryblockade shorter than local anesthetic alone.

In our study, peak block height achieved was T8 (T6-T10) for Group A and T6(T5-T9) for Group B (Table II).

Table II: Comparison of highest level of sensory block

Groups	T5	T6	T7	T8	T9	T10	Chi square value	P value
A	0	1(3.3)	7(23.3)	12(40)	8(26.7)	2(6.7)	17.8	0.004
B	1 (3.3)	11(36.7)	10(33.3)	6(20)	2(6.7)	0		

But in the study by Brad R. Davis et al[7]. it was T8 (T6 to L2) for chloroprocaine group and T8 (T4 to T11) for chloroprocaine with clonidine group.

The difference may be due to difference in dosage of chloroprocaine and clonidine used and smaller sample size in the study (8 volunteers) compared to our study(60 patients). In our study we used 40 milligrams of chloroprocaine and 30 micrograms of clonidine while they used 30 milligrams of chloroprocaine and 15 micrograms of clonidine.In the study by Julie S. Vath et al[8]. peak height achieved was T9 (L1-T4) for chloroprocaine group and was T5 (T3-7) for chloroprocaine with fentanyl group. So this study supports our results, as addition of an adjuvant to intrathecal chloroprocaine will make peak block height higher than chloroprocaine alone.

In our study, comparison of mean value of time (in minutes) for 2 segment regression of sensory blockade between Group A (chloroprocaine group) and Group B (chloroprocaine with clonidine group) showed that mean time taken for 2 segment regression of sensory blockade was 48.83 minutes for Group A and 51.16 minutes for Group B with standard deviation of 4.29 and 5.20 respectively (Table III).

Table III: Mean time for 2 segment regression of sensory blockade

Groups	Mean	SD	t value	P value
A	48.83	4.29	1.89	0.06
B	51.16	5.20		

The difference was statistically insignificant with p value 0.06 which was similar to the study by Brad R. Davis et al[7]. and Julie S.Vath et al[8]. Lacasse et al[9]. conducted a double-blind randomised control trial which compared hyperbaric bupivacaine 7.5 mg to chloroprocaine 40 mg. Time for two segment regression of sensory blockade for chloroprocaine was 50±18 min vs 75±37 min for bupivacaine group, which was statistically significant.

In our study, the mean duration of sensory blockade was 58.00 minutes for Group A and 77.83 minutes for Group B with standard deviationof 5.01 and 8.47 respectively. P value was found to be <0.001 i.e. statistically highly significant (Table IV).

Table IV: Duration of sensory blockade between Group A and Group B (Time for regression to L1)

Groups	Mean	SD	t value	P value
A	58.00	5.01	11.28	<0.001
B	77.83	8.47		

In the study done by Brad R. Davis et al, time for regression to L1 was 51±23 for chloroprocaine group and was 76±11 for chloroprocaine with clonidine group with P value of 0.0021 which was statistically significant which supports our results. Julie S. Vath et al. study showed that time for regression to L1 was 53±19 for chloroprocaine group and 77±7 for chloroprocaine with fentanyl group with P value of 0.02 which was statistically significant which supports our observation that addition of an adjuvant to intrathecal chloroprocainewill make duration of sensoryblockade more than chloroprocaine alone. The study done by Kristin N. Smith et al[10]. also showed that there is significant difference in "Time for regression to L1" between plainChloroprocaine and Chloroprocaine with epinephrine as adjuvant.

In our study, comparison of mean time of onset of motor blockade was 6.50 minutes for Group A and 5 minutes for Group B with standard deviation of 1.94 and 1.81 respectively (Table V).

Table V: Mean time of onset of motor blockade between Group A and Group B (Time to achieve maximum motor block)

Groups	Mean	SD	t value	P value
A	6.5	1.94	3.08	0.003
B	5.00	1.81		

P value was found to be 0.003, which is statisticallysignificant.

In study by Manuraj V. S. et al., the mean time for onset of motor block in group B [0.5% hyperbaric bupivacaine 4 ml] was 231.80 seconds and in group C[0.5% hyperbaric bupivacaine 3. 5 ml + 50µg clonidine] was 165.1 seconds(p<0.001) which supports our observation that, addition of adjuvant to local anaesthetic will make onset of motorblockade faster.Mean duration of motor blockade in Group A and Group B was 67 minutes and 89.66 minutes respectively with standard deviation of 6.89 and 6.14 respectively (Table VI).

Table VI: Mean duration of motor blockade between Group A and Group B

Groups	Mean	SD	t value	P value
A	67.00	6.89	13.43	<0.001
B	89.66	6.14		

Results of Brad R. Davis et al., Julie S.Vath et al. and Kristin N. Smith supports our observation that addition of adjuvantwill make duration of motorblockade more than local anaesthetic alone. The mean time forfirst request of analgesic was 208.00±22.19 minutes in Group A and 284±33.17 minutes in Group B which was was statistically highly significant as the p value is<0.001. This was consistent with the findings of Manuraj V. S. et al. There were no statistically significant differences between the mean heart rate and mean arterial pressures at various timeintervals, which was the same observation in the other studies also.The study patients of Kristin N. Smith et al. showed nonspecific flu-like symptoms, radiating back pain in 2 patients, non-radiating low back ache in 4 patients after 2-Chloroprocaine and epinephrine and non-radiating low back pain in 1 patient after 2-Chloroprocaine intrathecal injection. None of the patients in both groups of our study showed any adverse effects.

Conclusion

We conclude that addition of 30 micrograms of clonidine to 4ml of 1% chloroprocaineintrathecally enhances onset of sensory and motor blockade in urological surgeries. It also prolongs the duration of sensory blockade, motor blockade and time for first request of analgesia. Hemodynamic parameters where comparable between the groups. There was no incidence of side effects like post spinal headache, transient neurological symptoms, bradycardia and hypotension observed in both groups.

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