Original Article

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Clonidine as an Adjuvant to Intrathecal Bupivacaine for Infraumbilical Surgery

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Abstract

Background: Clonidine is a partial α2 adrenoreceptor agonist which has been shown to interact synergistically with local anesthetics. The present study was aimed to evaluate and compare the effect of 75 mcg of clonidine added to 3 ml of 0.5% bupivacaine, with respect to duration of sensory block and motor block, hemodynamic parameters, and associated side effects. **Subjects and Methods:** Patients scheduled to undergo infraumbilical surgery during the study period were randomly allocated to receive either 3 ml 0.5% bupivacaine and 0.5 ml 0.9% normal saline or 3 ml 0.5% bupivacaine and 0.5 ml 75 mcg injection clonidine. Various intraoperative parameters were noted and compared between the control and clonidine group. **Results:** Baseline characteristics of the patients were similar in both the study groups. Onset of motor block was significantly shorter in the clonidine group (378.55 ± 23.92 seconds vs 350.26 ± 21.22 seconds; p value < 0.001), duration of motor block and time for two segment regression was significantly higher in the clonidine group (158 ± 8.2 minutes vs 186.14 ± 9.15 minutes; p value < 0.001 and 78.97 ± 7.18 minutes vs 102.70 ± 5.61 minutes; p value <0.001 respectively). The hemodynamic parameters and side effect profile was found to be similar among patients in both the study groups. **Conclusion:** 75 mcg clonidine used as an adjunct with 3 ml of 0.5% bupivacaine for spinal anaesthesia in patients undergoing infraumbilical surgeries provides better sensory and motor blockade.

Keywords: Alpha2 adrenoreceptor agonist, clonidine, intrathecal anesthesia, spinal anesthesia.

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Introduction

Local anesthetics are the commonest agents used for spinal anesthesia, but their relatively short duration of action may lead to early analgesic intervention in the postoperative period. A number of adjuvants to local anesthetics have been used intrathecally to prolong the intraoperative as well as postoperative analgesia. Intrathecal α2 agonists are used as adjuvant drugs to local anesthetics. They potentiate the effect of local anesthetics and allow a decrease in the required doses of anesthetic agents. Clonidine is a partial α2 adrenoreceptor agonist used intrathecally and is thought to prolong the duration of surgical anesthesia. It shares similar analgesic pathways to local anesthetics and has also been shown to interact synergistically with local anesthetics. The present study was aimed to evaluate and compare the effect of 75 mcg of clonidine added to 3 ml of 0.5% bupivacaine, with respect to duration of sensory block and motor block, hemodynamic parameters, and associated side effects.

Subjects and Methods

Study Design and Sampling

In this prospective randomized clinical study, patients belonging to American Society of Anesthesiologists grade I and II posted for elective surgeries below umbilicus under spinal anaesthesia were included. During the study period, such patients aged 18 to 65 years, weighing 40 to 80 kilograms with normal cardiac, renal and hepatic functions were included in the study. We excluded patients who underwent surgeries under general anaesthesia, with bleeding tendencies, congestive heart failure, heart block and renal failure and those with history of psychiatric illness or allergies. The study was approved by the institutional ethics committee. The patients were explained the purpose of the study and a separate informed consent was obtained before being included in the study.

Anaesthetic protocol

A detailed pre-anaesthetic evaluation was done. Patients were kept nil per oral for 8 hours the day before the surgery. All patients received tablet Ranitidine 150 mg as a premedication. On the morning of surgery, patients were randomly allocated to receive either 3 ml 0.5% bupivacaine and 0.5 ml 0.9% normal saline or 3 ml 0.5% bupivacaine and 0.5 ml 75 mcg injection clonidine. Upon arrival, 18G intravenous line was established and patients were loaded with 500 ml of crystalloid solution. Patients were positioned in left lateral position and under strict aseptic precaution,

back was prepared with 5% povidone iodine solution and area draped. L3-L4 intervertebral space was identified, skin infiltrated with 2 ml 0.5% lignocaine and lumbar puncture was performed using midline approach with 23G Quincke's spinal needle. Patients were administered the mixture according to the study group after ensuring free flow of CSF.

Outcome parameters

Time of onset of sensory block and maximum level achieved was assessed by pin-prick method and attainment of complete motor block was assessed using Bromage scale. Sensory level was monitored at 15 minutes interval until they regressed two segments below as assessed by pin prick method. Duration of analgesia was taken as the time taken for two segemtn regression of sensory analgesia as assessed by pin prick method. Duration of motor block was considered at time interval between completion of injection of local anaesthesia to subarachnoid to patients' ability to rise the extended leg as assessed by Bromage scale. Non-invasive monitoring of blood pressure, pulse oximetry, electrocardiography and respiratory was done. No sedation was given intra-operatively so that frequent communication and reassurance could be achieved. Patients' blood pressure, pulse and oxygen saturation were noted every minute for first 5 minutes, every ten minutes thereafter for 30 minutes and hourly after that. A fall in mean arterial pressure (MAP) to more than 30% from the baseline value was treated with mephentermine. Fall in heart rate to more than 20% of baseline value was considered significant and treated of less than 50 beats per minute (bpm) with injection atropine. Post-operatively, patients were assessed for side effects like nausea and vomiting, headache, hypotension and bradycardia. Urinary retention could not be assessed as some patients were electively catheterized during the study period.

Data Collection and Data Analysis

Patient related data were collected using a semi-structured case report form. Demographic and anthropometric information of the patients was obtained from the medical records of the hospital. Data were analysed in SPSS version 23 (IBM, New York). Quantitative data were described as mean and standard deviation and qualitative data as frequencies. Means of various quantitative variables were compared between the two study groups using student's t test and frequencies of qualitative variables were compared using chi-square, p value less than 0.05 was taken as statistically significant.

Results

In the present study, 68 patients were included, which were randomly assigned to either the control group or the clonidine group. [Table 1] describes and compares the baseline characteristics of the patients included. Mean age, height, weight and gender distribution were similar in both the study groups. Comparison of anaesthesia related parameters have been described and compared in [Table 2]. We observed no statistical difference in the onset of sensory block between the control and the clonidine group, though it was lower in the clonidine group (148.29 ± 14.09 seconds vs 143.14 ± 12.61 seconds; p value = 0.11). Onset of motor block was significantly shorter in the clonidine group (378.55 ± 23.92 seconds vs 350.26 ± 21.22 seconds; p value < 0.001). Duration of motor block was observed to be significantly higher in the clonidine group (158 ± 8.2 minutes vs 186.14 ± 9.15 minutes; p value < 0.001). Lastly, time for two segment regression was significantly higher in the clonidine group as compared to the control group (78.97 ± 7.18 minutes vs 102.70 ± 5.61 minutes; p value <0.001). The hemodynamic parameters were observed and compared between the two study groups and illustrated in Figure 1. Heart rate, blood pressure and oxygen saturation were noted every minute for first 5 minutes, every ten minutes thereafter for 30 minutes and hourly after that. Mean heart rate was found to be significantly lower in the clonidine group at 10 minutes mark (69.88 ± 9.88 bpm vs 75.02 ± 10.74 bpm; p value <0.05), which continued for next three hours. Mean pulse remained between 69.6 to 85 bpm throughout the period of observation. Mean arterial pressure was significantly lower in the clonidine group at 2 minute mark (84.47 ± 6.69 mm Hg vs 91.76 ± 7.7 mm Hg; p value < 0.001), which continued for next 2 hours, after which the blood pressure became similar in the two study groups. Oxygen saturation was significantly lower in the clonidine group almost throughout the observation period, never falling below 99.00%. Overall, we noted no statistical difference in the proportion of patients experiencing sedation, hypotension and bradycardia in the clonidine group as compared to control group [Table 3]. Hypotension was transient and easily treated with rapid administration of intravenous fluids and 12 to 24 mg of mephentermine. Bradycardia responded to 0.6 mg of intravenous atropine. None of the patients complained of neurological symptoms.

Table 1: Comparing baseline characteristics of patients included in the study

Variable	Control group (n=34)	Clonidine group (n=34)	p value
Mean age (in years)	42.64 ± 8.9	40.20 ± 9.08	0.26
Mean height (in cm)	159.91 ± 6.00	160.79 ± 6.08	0.54
Mean weight (in kg)	60.76 ± 5.63	61.82 ± 6.38	0.47
Gender distribution			
Females	15	17	0.62
Males	19	17	

Table 2: Comparing parameters related to sensory and motor blockade

Variable	Control group (n=34)	Clonidine group (n=34)	p value
Onset of sensory block (in seconds)	148.29 ± 14.09	143.14 ± 12.61	0.11
Onset of motor block (in seconds)	378.55 ± 23.92	350.26 ± 21.22	<0.001
Motor duration (in minutes)	158 ± 8.2	186.14 ± 9.15	<0.001
Time for two segment regression (in minutes)	78.97 ± 7.18	102.70 ± 5.61	<0.001

Table 3: Comparing the adverse effects noted in the two study groups

Variable	Control group (n=34)	Clonidine group (n=34)	p value
Nausea and vomiting	02	03	0.14
Sedation	00	02	0.15
Hypotension	05	07	0.10
Bradycardia	02	03	0.21

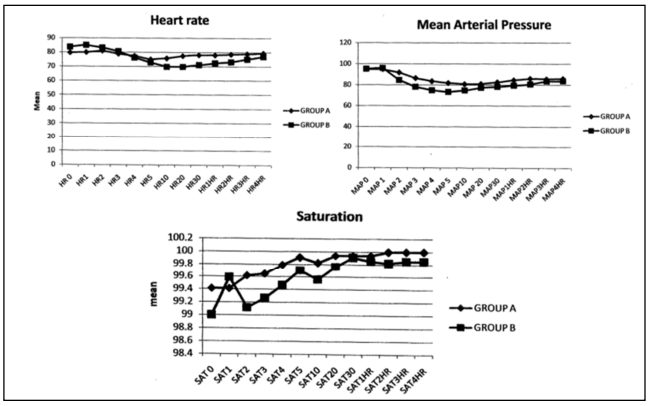

Figure 1: Line diagram illustrating variations in mean heart rate, mean arterial pressure and oxygen saturation over a period of observation (Group A = Control group, Group B = Clonidine group)

Discussion

Clonidine is a selective partial agonist for α2 adrenoreceptors. Its analgesic effect is mediated spinally through activation of post-synaptic α2 receptors in substantia gelatinosa of the spinal cord. It is known to increase both sensory and motor blocks of local anesthetics by 30–50%. The present study was conducted to assess the analgesic and sedative effects of intrathecal clonidine in patients undergoing infraumbilical surgeries. Baseline demographic and anthropometric parameters were comparable between the two study groups and the test drug was randomized so as to remove observer's bias. We observed a decrease in the onset sensory block with the use of 75 mcg injection clonidine, which was statistically not significant and a significant increase in 2 segment regression time. Similar increase in 2 segment regression with clonidine has been described by other studies as well. Furthermore, a meta-analysis found evidence of a significant dose-response (crude regression coefficient: 1.6; 95% CI 0.5-2.8; P = 0.006). The authors found that for each increase in 10 µg of intrathecal clonidine, the time to 2 segment regressions was prolonged by a little less than 2 minutes. This result remained significant after adjustment for type and baricity of local anesthetics. Even higher increase in regression of sensory block to the S1 segment was observed with dexmedetomidine, with a mean time of 231.50 minutes, as compared to the clonidine group with a mean time of 209.23 minutes in a study by Zhang et al.

We observed that the onset of motor block was significantly reduced and duration of motor block significantly increased in the clonidine group as compared to the control group. Dobrydnjov et al added 0, 15, or 30 mcg clonidine to 6 mg of intrathecal hyperbaric bupivacaine for inguinal hernia repair and found increase in duration of motor block (146, 155, and 182 min, respectively) as in our study. The authors suggested that intrathecal clonidine when combined with local anesthetic significantly potentiates the intensity and duration of motor blockade possibly due to the fact that α2 adrenoreceptor agonists induce cellular modification in the ventral horn of the spinal cord and facilitate the local anesthetic action, and prolongation in sensory block can be due to vasoconstrictive effect of clonidine. However, increasing dose of clonidine may not increase the intensity and duration of motor block as shown by De Kock et al, who observed that increasing the dose of clonidine from 15 to 45 mcg with 8 mg of ropivacaine did not result in much difference in the motor block parameters.

Furthermore, we observed that mean heart rate, mean arterial pressure and oxygen saturation were statistically lower in the clonidine group for a period of observation, but none of them were clinically significant. Similar observations have been made previously as well. However, Singh et al observed no significant difference in hemodynamic parameters of patients receiving 50 µg and 75 mcg of clonidine intrathecally undergoing cesarean section. Similarly, Nazareth et al also reported stable hemodynamic parameters in the groups receiving intrathecal clonidine and fentanyl combination.

Conclusion

Our results demonstrate that 75 mcg clonidine, when used as an adjunct with 3 ml of 0.5% bupivacaine for spinal anaesthesia in patients undergoing infraumbilical surgeries, led to a significant decrease in onset of motor block and a significant increase in duration of motor and sensory block. Side effects like hypotension and bradycardia were noted but were easily treated and did not affect the clinical outcome of the patients.

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