ORIGINAL ARTICLE

Effect of Oral Clonidine on Epidural Anaesthesia in Hip Replacement Surgery

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Abstract

Background: Analgesia, sedation, hemodynamic stability, and improved postoperative outcomes are important for orthopedic surgery. Researchers have found clonidine, a centrally acting partial α2 adrenoceptor agonist serves this well. This study was conducted to find out the effect of oral clonidine on epidural anesthesia in hip replacement surgery.

Methods: This open-level, randomized control trial (RCT) was conducted at the Department of Anesthesia, Analgesia, and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. A total of 60 patients were included in the trial; 30 in the Intervention (clonidine) group and another 30 in the control group (placebo). Sensory block, motor block, visual analog scale (VAS), and vital parameters were assessed. Ethical approval was taken from the institutional review board (IRB) of BSMMU and informed written consent was taken from each participant.

Results: The onset of sensory blockade was significantly quick (intervention group vs control group:15.8±1.3 min vs 19.4±2.0 min) and analgesia sustained significantly for a prolonged period (p-value: 0.003) higher in the intervention group (256.1±18.7 min) than the control group (192.9±16.1 min). After 5 and 10 minutes of intervention; significantly (p-value: 0.001) lower systolic blood pressure was observed in the intervention group. And in 15 and 45 minutes, diastolic blood pressure was significantly (p-value: 0.013, 0.001; respectively) higher in the intervention group.

Conclusion: Oral clonidine gave early onset and prolonged duration of sensory blocking, analgesia without major hemodynamic instability, and post-operative side effects.

Keywords: Clonidine, Epidural anaesthesia, Hip-replacement surgery

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Introduction

Hip replacement is a prevalent procedure in Orthopedic surgery [1]. The increasing demand for hip replacement surgeries in recent years has triggered the creation of new and innovative anesthetic techniques and analgesic pathways to support the best possible outcomes[2]. Duration of the surgery, age, and comorbidities of the patients guide the anesthetist in considering proper anesthetic and analgesic techniques in such patients. However, in hip replacement surgeries, regional anesthetic, and analgesic techniques have gained popularity due to their effectiveness, long-lasting and focused pain control, and reduced need for systemic analgesics[3], reduced unanticipated admissions due to uncontrolled pain[3], shorter hospital stay [4,5,] higher patient satisfaction[6,7]. On the other hand, the use of regional anesthesia for orthopedic procedures mitigates some of the complications associated with general anesthesia such as nausea, vomiting, airway trauma, hypoxia, respiratory depression, and the risk of pulmonary aspiration[8,9]. Nowadays, Epidural or spinal anesthesia has been shown to improve perioperative outcomes, especially for orthopedic patients[10].

The goal of surgery is to speed up recovery so that patients can get back to their normal lives as soon as possible. Patients should also be more stable hemodynamically and need fewer painkillers that last longer. Opioid premedication can cause respiratory depression and post-operative nausea and vomiting[11]. Benzodiazepines cause sedation but it has no analgesic property[12]. On the other hand, clonidine has sedation and analgesic properties and obtunds post-operative nausea and vomiting[13]. Clonidine, an α-2 agonist with some α1 adrenergic properties has been used as an adjuvant to local anesthetics in various regional anesthesia techniques to prolong local anesthetic action and provide postoperative analgesia[14,15]. However, clonidine does increase the likelihood of arterial hypotension, fainting, and bradycardia. Despite this, clonidine has analgesic, sedative-hypnotic, sympatholytic, and opioid-sparing properties that allow it to alleviate pain without impacting hemodynamic parameters[16]. Nowadays clonidine is being used invariably during hip replacement surgery. But still, in Bangladesh, there is a knowledge gap regarding the intra-operative and post-operative effects of clonidine. To fulfill the knowledge gap, this study was designed to determine the efficacy of Clonidine for sedation and analgesia in replacement surgery.

Methods

This open level, Randomized Control Trial (RCT) was done between October 2018 and April 2019 at the Department of Anesthesia, Analgesia, and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.

Selection of the participants and allocation of interventions Patients between the ages of 30 and 70 who were scheduled to undergo hip replacement surgery under epidural anesthesia, had ASA physical status I, II, III, did not have severe stenotic valvular heart disease or neurological disorder, did not take/receive sympatholytic drugs, and were willing to participate were included in the study. Patients who were unable to receive an epidural, who required conversion to general anesthesia, or who were allergic to clonidine were excluded from the study. Using a simple random sample procedure, 60 patients were involved in the trial; 30 were assigned to the Intervention (clonidine) group and got Tab. Clonidine (0.1 mg), whereas another 30 were assigned to the control group and were given Vitamin B complex injections as a placebo one hour before the neuraxial block. Each participant's written consent was obtained after informing him/her of the aims and objectives of the study.

As soon as the patients entered the operation room, their nil by mouth (NBM) status was confirmed and intravenous access was established. All patients were tracked using a pulse oximeter, electrocardiogram, noninvasive blood pressure measurement, and baseline parameters. Patients also received continuous nasal prong oxygen supplementation. After identifying the correct location of the patient's intervertebral space (L3 and L4). Painting draping and local infiltration were done. The epidural Tuohy needle was inserted, and the epidural space was identified using the loss of resistance technique. Then, a test dose of local anesthetic (2 ml of 2% lignocaine with adrenaline) was administered, followed by the insertion and fixation of an epidural

catheter. The initial bolus dose of local anesthetic was 15 ml of Bupivacaine 0.5%, followed as needed by a top-up dose of Bupivacaine 0.5% at a volume equal to one-third of the initial dose.

Outcome assessment

The sensory block (using alcohol-soaked cotton) and motor block (using the Bromage Scale 12) were evaluated 5 minutes after the deposition of local anesthetic into the epidural region and the time to onset of sensory and motor block was recorded. Up to 24 hours after surgery, the VAS was used in the post-anesthetic care unit (PACU) to assess the postoperative pain score. VAS pain scores ranged from 1 to 10, with 1 representing the least amount of pain and 10 indicating the greatest agony the individual has ever experienced. If the VAS is greater than four, the patient is given an analgesic dose of local anesthetic at a concentration of 0.125% and at a valium of 5 ml. The main outcome variables were documented. All vital indicators were observed (Spo2, pulse, blood pressure, respiration, and ECG). Bradycardia and hypotension were treated with atropine, ephedrine, and intravenous fluid administration. The first VAS in the PACU was done 2 hours after the previous intraoperative top-off dosage and continued at 5-minute intervals until a VAS score of 4 was achieved. From completed data sheets, data was extracted.

The VAS scores of the patients were then evaluated after they had been kept in recovery for one hour after the block had regressed to analyze the sensory block that had occurred in the PACU. All demographic data were retrieved from the patient profiles in their files, and all data obtained during the intraoperative and post-operative sessions were documented on patient-specific data sheets. Ethics permission was obtained from Bangabandhu Sheikh Mujib Medical University's institutional review board (Ref: No.BSMMU/2018/7047).

Data analysis

A questionnaire was used to obtain the data. To find data errors, every questionnaire that was collected underwent a thorough inspection. Data processing tasks include creating dummy tables, modifying computerized schedules, and analyzing, and matching data. Following the accumulation of all of this information, these data were examined, double-checked to ensure coherence, and revised to produce the final output. Data that had been edited and coded was then directly entered into the computer using SPSS. Version 22 of the SPSS (Statistical Package for Social Sciences) program was used to handle and analyze the data. The chi- square test and independent sample "t" test was used to get the p value. P value < 0.05 was fixed to determine the level of significance. Categorical data was displayed as a number percentage whereas data on continuous scales were presented as mean standard deviation. The summarized information was presented in the table as well as the graphic.

Results

Total 60 patients after fulfilling inclusion/exclusion criteria, were included in the study to determine the local anesthetic-sparing effect of oral clonidine on epidural anesthesia and analgesia in hip replacement surgery.

Table I: Distribution of the participant according to age and preoperative assessment of physical status

Baseline characteristics	Intervention group Frequency (%) (n=30)	Control group Frequency (%) (n=30	Total Frequency (%)	P value
Age (years)				
30-50	9 (30.0%)	8 (26.7%)	17 (28.3%)	0.78
51-70	21 (70.0%)	22(73.3%)	43 (71.7%)	
Physical status				
ASA II	23 (76.6%)	26 (86.6%)	49 (81.67)	0.32
ASA III	7(23.3%)	4 (13.3%)	11 (18.33)	

P value was obtained from Chi-square test

Distribution of the participant according to age and preoperative assessment of physical status is presented in **Table I**. Physical status was determined by American society of anesthesiologist (ASA). At baseline the patient of hip surgery in both groups were indifferent in respect of age (p value: 0.78) and physical status before surgery (p value: 0.32).

Table II: Assessment of anesthesia related variables

Sensory and motor blockage	Intervention group Frequency (%) (n=30)	Control group Frequency (%) (n=30)	P value
Onset of Sensory blockage			
5-10	0 (0.0)	0 (0.0)	
11-15	16 (53.3)	10 (33.3)	
16-20	12 (40.0)	14 (46.7)	0.019
>20	2 (6.7)	6 (20.0)	
Mean ± S.D.	15.8±1.3 min	19.4±2.0 min	a<0.001
Onset of motor blockage			
BS I	0	0	
BS II	0	0	
BS III	18	23	
BS IV	12	7	
Total duration of Sensory and motor blockage			
Mean ± S.D.	19.7 ± 2.1	20.1 ± 2.7	a0.524
Sensory block	256.1±18.7	192.9±16.1	a0.003
Motor block	209.4±15.4	185.3±15.6	a0.089

P value was obtained from Chi-square test and a independent sample t test

The mean ±SD time of onset of sensory blockage was significantly (p value: <0.001) lower in intervention group (15.8±1.3 min) than control group (19.4±2.0 min). And total duration of sensory block was also significantly (p value: 0.003) higher in intervention group (256.1±18.7 min) than control group (192.9±16.1 min). But the mean ±SD time of onset of motor blockage was similar (p value: 0.524) between intervention group (19.7 ± 2.1 min) and control group (20.1 ± 2.7 min) (**Table II**).

Table III: Trends of systolic blood pressure (SBP) between groups with respect to time

Blood pressure		Intervention group (n=30) Mean ± SD	Control group Frequency (%) (n=30)	P value
Systolic BP (mmHg)	Pre anesthesia	89.6±6.3	84.3±5.0	0.261
	5 min	86.5±6.8	84.4±9.2	0.098
	10 min	75.3±7.1	83.5±5.1	0.001
	15 min	75.6±11.2	82.3±4.8	0.001
	20 min	97.9±4.7	82.3±5.0	0.001
	30 min	94.6±15.6	84.8±5.0	0.002
	45 min	84.6±11.6	72.3±8.2	0.001
	60 min	59.6±6.0	61.2±9.4	0.467
Diastolic BP (mmHg)	Pre anesthesia	59.6±6.0	61.2±9.4	0.348
	5 min	63.9±5.2	61.2±9.6	0.213
	10 min	65.4±5.6	62.5±9.5	0.186
	15 min	67.6±7.4	61.5±9.7	0.013
	20 min	65.5±7.1	61.9±9.7	0.096
	30 min	66.0±6.8	61.2±9.4	0.039
	45 min	65.2±5.6	60.5±9.5	0.001
	60 min	59.5±5.0	60.2±7.4	0.432

P value was obtained from independent sample t test

At pre anesthesia stage, systolic and diastolic blood pressure was indifferent in between groups. But, after 5 and 10 minutes of intervention; significantly (p value: 0.001) lower systolic blood pressure was observed in intervention group. Whereas at 45-minute significant lower systolic blood pressure was observed in control group than intervention group. In 15 and 45-minutes, diastolic blood pressure was significantly (p value: 0.013, 0.001; respectively) higher in intervention group.

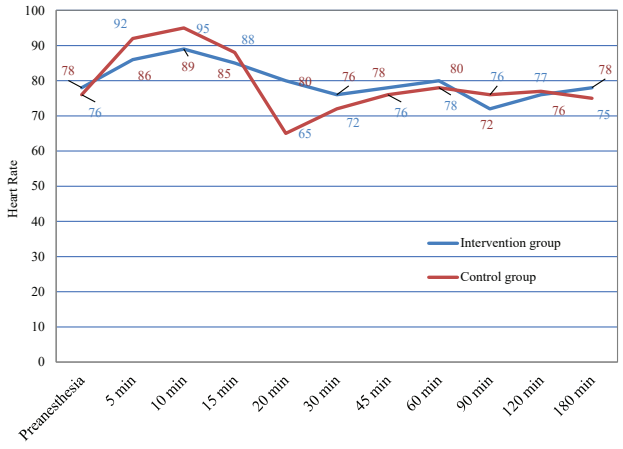

Fig- I: Trends of heart rate (HR) in the studied group

Fig. I shows the heart rate of the patients. No significant variation in the heart rate was observed between groups.

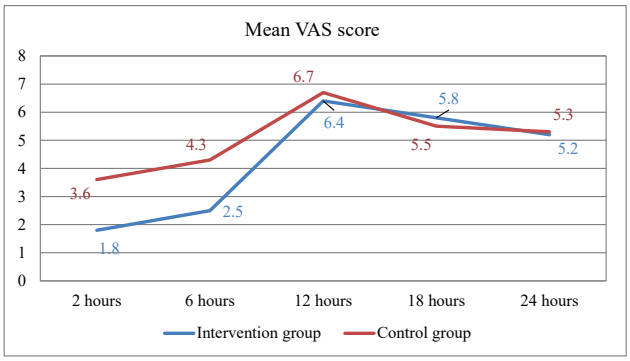

Figure II: Observation of intensity of pain by Visual Analogue Score after surgery (VAS)

The intensity of pain was assessed by Visual Analog Scale (VAS), where at 2 hours pain was significantly (p value: <0.001) less in intervention group (mean

VAS score:1.8) than control group (mean VAS score: 3.6) (Figure II). Similar significant less pain was reported at 6 hours in intervention group (mean VAS score:2.5) than control group (mean VAS score:4.3) (Figure II). Gradually as time passed, patients experiencing pain in each group was almost similar. Here Tab. Clonidine found to be significantly reduced the pain intensity up to 6 hours.

Table IV: Assessment of sedation according to Ramsay Sedation Scale (n=60)

Ramsay Sedation Scale	Intervention group (n=30) Mean ± SD	Control group Frequency (%) (n=30)	P value
After 45 minutes	4.38 ±0.57	3.52 ±0.27	0.001
After 90 minutes	4.13±0.32	3.89 ±0.51	0.001
After 180 minutes	1.39 ±0.47	1.46 ±0.51	0.131

P value was obtained from independent sample t test

After 45 and 90 minutes of epidural anesthesia, sedation was found significantly (p value :0.001) reduced by clonidine in comparison to placebo, where the mean Ramsay sedation scale was 4. 38 ±0.57 in intervention group and 3.52 ±0.27 in placebo group and 4.13±0.32 in intervention group and 3.89 ±0.51 in control group; respectively. But after 2hours of surgery sedation level gradually impaired in both groups and at 180 minutes it was found almost similar **(Table IV)**.

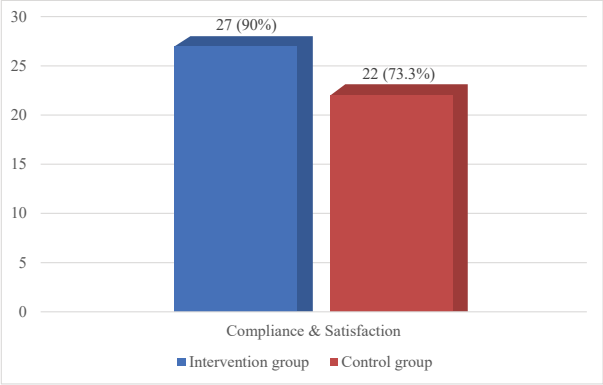

Figure III: Evaluation of Patients Compliance & Satisfaction

Subjective compliance & satisfaction revealed that total 27(90.0%) of patients in intervention group and 22 (73.3%) patients in control group were satisfied regarding remission of anxiety and agitation with maintenance of pleasant asleep (hypnosis) during operation (**Figure III**).

Discussion

Evidence has shown that the administration of clonidine during regional anesthesia accelerates the initiation of local anesthetic effects. This leads to a quick establishment of both sensory and motor blockade, prolongs pain relief after surgery, reduces the amount of local anesthetics needed, and maintains stable cardiovascular parameters [16]. However, in this study, the use of oral clonidine resulted in rapid and long-lasting sensory blocking, pain relief, and effective sedation management.

In this study, where the groups of patients were similar in terms of age and physical status, it was observed that the intervention group (clonidine) achieved near-maximum analgesia (sensory blockage) more quickly compared to the control group, with statistical significance. However, the time of onset of motor blockage was found to be similar between the intervention group (clonidine) and the control group. In the intervention group, the mean ±SD time of onset of motor blockade was 19.7 ± 2.1 minutes, while in the control group, it was 20.1 ± 2.7 minutes. The intervention group demonstrated a significantly higher total duration of analgesia compared to the control group. Based on the study conducted by Gupta et al (2010), it was observed that the group of patients who received clonidine epidurally experienced a significantly longer duration of postoperative analgesia (334.2 min) compared to the control group (161.4 min)[20]. In a recent study conducted by Arora et al., (2020), researchers examined the effects of clonidine on patients who had undergone lower abdominal and lower limb surgery. The results revealed a significant prolongation in the duration of analgesia in the clonidine group (380.84 ± 63.01) compared to the control group (136.06 ± 11.74)[21]. The variance in the average length of analgesia seen in the aforementioned trial was most likely caused by variations in the clonidine administration route.

After analyzing the results and making comparisons, it becomes clear that the group of patients who were administered clonidine reported lower levels of post-operative pain. The level of pain was measured using the Visual Analog Scale (VAS) at 2 hours and 6 hours. The results showed that the intervention group (clonidine group) experienced significantly less pain compared to the control group. Over time, the level of pain reported by patients in each group became nearly identical. A recent study has revealed that the use of clonidine has shown promising results in reducing pain intensity for up to 6 hours. Following epidural anesthesia, the intervention group (administered with clonidine) showed significantly improved sedation (motor blockage) compared to the control group. These results align with the findings of previous studies conducted by Arora et al. (2020) and Gupta et al. (2010)[20,21]. In a study conducted in 2003, Ikeda et al. found that the administration of clonidine through an epidural infusion can lead to a decrease in heart rate and blood pressure[22]. The most favorable approach is to find a balance between pain relief and potential side effects. It is important to note that side effects such as low blood pressure or slow heart rate may be linked to the absorption of medication into the body[23]. Research indicates that the use of epidural clonidine does not lead to any negative effects on hemodynamic stability. Administering 160 micrograms of clonidine can potentially result in a decrease in heart rate by 5% to 20% and arterial blood pressure by 18% to 20%[20].

The study conducted by Gupta et al. (2010) and Arora et al. (2020) found a substantial decrease in mean arterial pressure in the clonidine group at 30 minutes and 60 minutes, respectively[20,21]. In this study, during the pre-anesthesia stage, there were no significant differences in systolic and diastolic blood pressure between the groups. However, the intervention group experienced a significant decrease in systolic blood pressure after 5 and 10 minutes of receiving Clonidine. During the specified time intervals (15, 30,45 minutes), the diastolic blood pressure showed a significant increase in the intervention (clonidine) group compared to the control group. A study conducted by Arora et al., (2020) and Gupta et al., (2010) found that the intervention groups experienced fewer side effects such as nausea and vomiting [20,21]. In this study, the researchers found that patients in the intervention group reported higher levels of satisfaction and compliance with the treatment for anxiety and agitation during surgery. Specifically, the use of clonidine resulted in better maintenance of a pleasant asleep state, also known as hypnosis.

The study aimed for meticulousness, but encountered some limitations. The study conducted at a single institute with a small sample size may not provide a comprehensive representation of the entire country's situation.

Conclusion

Oral administration of clonidine led to prompt and enduring sensory blockade, alleviation of pain, and successful management of sedation, without significant post-operative complications. The patients had subtle, unnoticeable alterations in their hemodynamic status. Nevertheless, their hemodynamic status remained steady. Furthermore, Tab. Clonidine might be regularly prescribed for use in orthopedic interventions.

Declaration

Ethics approval

The study was approved by the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

Author Contributions

Conception and development of the idea *MN, DB, AKMA*
Writing *MN*
Data analysis *MN, ML*
Data collection *MN, ML*
Review and Editing *AKMA, DB*

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Conflict of interest None

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