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Original Research Article

Comparison of Two Different Doses of Clonidine Hydrochloride as An Adjuvant to Epidural Bupivacaine for Post-Operative Analgesia

Shatrughan Kumar[1], Shailesh Kumar[2]

[1]Junior Resident, Department of Anaesthesiology and Critical Care, Patna Medical College and Hospital, Patna, Bihar, India

[2]Associate Professor, Department of Anaesthesiology and Critical Care, Patna Medical College and Hospital, Patna, Bihar, India

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Corresponding author: Dr. Shatrughan Kumar

Conflict of interest: Nil

Abstract:

Objective: This study aimed to compare the block characteristics and hemodynamic or adverse effects of combining two distinct doses of clonidine with epidural Bupivacaine as an adjuvant for infraumbilical surgeries. This study sought to compare sensory and motor block onset factors between two groups.

Methods: This was an interventional, prospective, double-blind, parallel group, randomised clinical study involving patients undergoing elective lower abdominal and lower limb surgeries. During the 2015-2018 academic year, this investigation was conducted at the Patna Medical College and Hospital, Patna.

Results: In our study, the mean onset time for the sensory block was 8.17 ± 1.5 minutes in group A and 7.43 ± 1.01 minutes in group B. In group A, the mean time to onset of motor block was 19.55 ± 1.5 minutes, while in group B, it was 17.17 ± 1.37 minutes. In our study, the mean duration of sensory analgesia in group A was 351.10 ± 20.38 minutes, while in group B it was 372.32 ± 21.54 minutes, indicating a highly significant extension of analgesia duration in group B compared to group A.

Conclusion: During the intraoperative period, both concentrations of clonidine (60µg and 75µg) administered via the epidural route with 0.5% Bupivacaine provide effective analgesia. However, in the postoperative period, 75µg clonidine with 0.5% Bupivacaine provides longer-lasting analgesia than 60µg clonidine, without a significant increase in adverse effects or alteration of the hemodynamic profile.

Keywords: Clonidine, Epidural, Bupivacaine, Postoperative Analgesia, Haemodynamics.

Introduction

Recent advancements in the field of neurology have provided evidence indicating that peripheral tissue injury can result in persistent changes in central processing, leading to a decrease in pain threshold and an amplification of pain response. Postoperative pain may be intensified and prolonged as a result of surgical trauma, leading to similar modifications [1-3].

The inclusion of postoperative pain management in standard surgical and anaesthetic protocols is essential, not only from a humanitarian standpoint, but also due to its potential to mitigate morbidity, complications, and facilitate a faster recovery process. Despite significant advancements in the field of pain management, postoperative pain continues to be a significant contributor to patient distress [4]. The administration of drugs through neuraxial channels has been utilised for the purpose of postoperative analgesia for a considerable period of time [5]. Despite its efficacy in providing a reliable block, spinal anaesthesia is not without its drawbacks in the clinical setting. These limitations include the inability to alter the height of the block, the fixed duration of the block which cannot be extended, and the potential for consequences such as postdural puncture headache and neurological sequelae.

Bupivacaine (1-butyl-n-2,6-dimethylphenyl piperidine-2-carboxamide) is an injectable, long-acting local anaesthetic that was first synthesised by Ekenstam [6] in Sweden. It is one of the local anaesthetics with an extended duration of action that is widely used for intrathecal, extradural, and peripheral nerve blocks. It is a water-soluble white crystalline substance. Clonidine is a 2-adrenoreceptor and imidazoline receptor agonist with analgesic, sedative, minimal alveolar concentration- sparing, and no substantial respiratory depression effects. Clonidine has been utilised as an adjuvant in regional anaesthesia in a variety of contexts [7, 8], including postoperative epidural analgesia. Upon administration into the

subarachnoid or epidural space, clonidine exerts significant antinociceptive effects by acting on 2-receptors in the dorsal horn of the spinal cord and pain-related brain stem nuclei [9, 10]. As an adjunct to the local anaesthetic Bupivacaine, Clonidine prolongs the duration of analgesia. For infra-umbilical surgeries, we compared the block characteristics and hemodynamic or adverse effects of combining clonidine in two distinct doses with epidural Bupivacaine as an adjuvant. This study sought to compare sensory and motor block onset factors between two groups.

Methods

This was an interventional, prospective, double-blind, parallel-group, randomised clinical study involving patients undergoing elective lower abdominal and lower limb surgery. Institutional Ethical Committee approval and informed consent in writing were obtained. This research was conducted during the 2015-2018 academic year at the Patna Medical College and Hospital, Patna. The investigation included patients who reported to various outpatient departments of the centre.

Inclusion and Exclusion criteria

This study included patients between the ages of 18 and 59, of either gender, ASA grade I or II, and weighing between 45 and 65 kg who underwent elective surgery.

Patients who refused to give informed consent belonged to ASA grades III and IV, had an infection at the injection site, coagulopathy or were on anti-coagulation therapy, congenital abnormalities of lower spine and meninges, active disease of CNS, history of alcohol abuse, allergy to local anaesthetics, cardiopulmonary, renal, hepatic, neurological and psychiatric disorders, were taking any antihypertensive drugs, sedatives, anxiolytics,

Statistical Analysis

The predesigned patients record form (PRF), Case record form (CRF), and other required formats were utilised to collect and capture the data obtained at the time of the intervention within the operating room. The PRF will function as a source data verification document. The data was manually inspected for correction of trivial errors such as incorrect digits, incorrect units of measurement, improper data format, etc. The data were entered into a computer using the evaluation version of the statistical software graphpad instat 3.1, and the output was evaluated.

The demographic data was analysed using the two-tailed Student's t-test, assuming that both subject groups had the same variance. The maximum sensory level was analysed using the Chi-square test, the modified Bromage score, and the two-tailed Student's t-test to compare the onset and duration of sensory and motor blockade. We compared the incidence of adverse effects such as nausea, vomiting, hypotension, bradycardia, parched mouth, sedation, and urinary retention.

Results

The study cohort consisted of forty patients aged 18 to 59 with ASA grades I and II who were scheduled for lower abdominal and lower limb surgeries. For epidural anaesthesia and analgesia, Group A (n=20) received 15ml 0.5% Bupivacaine containing 60g clonidine while Group B (n=20) received 15ml 0.5% Bupivacaine containing 75g clonidine.

Table 1: Mean age and sex distribution

Age				
Age interval	**0.5%Bupivacaine + Clonidine 60µg (Group A)**		**0.5%Bupivacaine + Clonidine 75µg (Group B)**	
	No.	**%**	**No.**	**%**
18-29	4	20%	4	20%
30-39	5	25%	5	25%
40-49	5	25%	6	30%
50-59	6	30%	5	25%
Sex				
Male	12	60%	13	65%
Female	8	40%	7	35%

The minimum age of patients was 18 years old, while the maximum age was 59. In groups A and B, the average age was 39.3 ± 11.35 years and 40.2 ± 10.46 years, respectively. In this regard, there was no significant difference between the two groups (p = 0.74). There were 20 men (60%) and 8 women (40%) in group A. There were 13 males (65%) and 7 females (35%) in group B. The distribution of males and females in both categories was comparable (p = 0.80).

Table 2: Time of onset and duration

Parameter	0.5% Bupivacaine + Clonidine 60µg (Group A)		0.5% Bupivacaine + Clonidine 75µg (Group B)	
	Mean	SD	Mean	SD
Onset of sensory block (minutes)	8.16	1.16	7.40	1.00
Onset of motor block (minutes)	19.54	1.51	17.16	1.36
Duration of sensory analgesia	351.09	20.37	372.30	21.52

Group B experienced a quicker onset of anaesthesia compared to Group A. In group A, the onset of sensory block occurred 8.16 ± 1.16 minutes later than in group B (7.40 ± 1.00 minutes). Statistically, the difference was highly significant ($p < 0.001$). However, the sensory level was established at the T6-T7 level, there was no discernible difference in sensory anaesthesia throughout the surgical procedure between the two groups.

In group A, the average time to onset of motor block was 19.54 ± 1.51 minutes, while in group B it was 17.16 ± 1.41 minutes. Complete motor blockade was established earlier in group B, which was statistically significant. ($p < 0.001$). The duration of sensory analgesia was 351.09 ± 20.37 minutes in group A and 372.30 ± 21.52 minutes in group B. The duration of sensory analgesia was longer in Group B than in Group A, and the difference was statistically significant ($p < 0.001$).

Discussion

This study compared two distinct doses of clonidine with epidural bupivacaine for lower abdominal and lower limb surgery, focusing primarily on the onset, intensity, and duration of blocks, as well as cardiorespiratory parameters and postoperative analgesia. As previously stated, 80 patients between the ages of 18 and 59 with ASA physical status 1 and 2 and no significant illness were randomly divided into two equal groups: Group A (n=40) and Group B (n=40).

Epidural administration of 15 ml of 0.5% Bupivacaine and 60µg clonidine was administered to Group A patients. Patients who did not respond to the epidural technique and required conversion to general anaesthesia were excluded from the study and substituted with new patients who met the inclusion criteria. Group B patients received epidural administration of 15 ml of 0.5% Bupivacaine and 75µg clonidine. Also, in this case, non-compliant patients were substituted with patients who met the criteria.

Group A and Group B were made comparable by selecting surgeries with similar characteristics for both categories. In the present study, there were no significant differences in age, gender, or weight between the two categories of patients. The majority of patients were between the ages of 18 and 59, with a mean age of 39.3 ± 11.35 years in Group A and 40.2 ± 10.2 years in Group B. In both categories, the mean sex distribution and mean weight were also identical. These parameters were matched across both groups to prevent intraoperative and postoperative outcomes from changing.

Onset of sensory and motor blockade

In our study, the average duration for the onset of sensory block in group A was 8.17 ± 1.50 minutes and in group B it was 7.71 ± 1.01 minutes. The difference was extremely statistically significant. Therefore, it appears that the addition of 75µg of clonidine as an adjuvant delays the onset of sensory blockade in comparison to 60g ($p<0.001$). Similar to our study, Gupta S et al. [11] used 1mcg/kg of clonidine in conjunction with bupivacaine 1.5mg/kg in 30 adult patients (40-60 years) scheduled for postoperative pain relief in total knee replacement operations and compared this to bupivacaine 1.5mg/kg alone.

In the clonidine group, the time of sensory onset was 493.8 ± 31.66 seconds, which is significantly less than the control group, which was 686.4 ± 47.42 seconds with bupivacaine alone. Similar to our study, they conclude that the addition of clonidine as an adjuvant accelerates the onset of sensory blockade. In their study, Syal K et al [12] administered bupivacaine 0.125% with clonidine 60mcg to nulliparous healthy term parturients for epidural labour analgesia and compared it to bupivacaine 0.125% alone. In the combination group, the time of sensory onset was 8.04 1.77 minutes, compared to 8.64 ± 2.04 minutes in the bupivacaine group. Similar to our study, they found that the addition of clonidine shortens the sensory onset.

In group A, the mean time to onset of motor block was 19.55 ± 1.5 minutes, while in group B, it was 17.17 ± 1.37 minutes. Statistically, the difference between the two categories was significant. Therefore, it appears that 75µg of clonidine as an adjuvant reduces the onset of motor blockade compared to 60µg ($p<0.001$). In their study, Karki G et al. [13] compared 20ml 0.5% plain bupivacaine with 2µg/kg clonidine to 20ml 0.5% plain bupivacaine alone. A modified Bromage scale was used to determine the onset of Motor block.

The onset of grade 3 motor block was 17.80 ± 4.08 minutes earlier in the clonidine group than in the bupivacaine group (20.36 ± 3.4 minutes). Similar to our findings, they concluded that the addition of

clonidine delays the onset of sensory block. Gupta S. et al. [11] investigated the effect of clonidine 1mcg/kg as an adjuvant with bupivacaine 1.5mg/kg in epidural anaesthesia. In the clonidine group, the onset of motor function occurred 615.60 ± 31.99 seconds later than in the control group (808.00 ± 54.39 seconds). Similar to our study, they conclude that the addition of clonidine as an adjuvant accelerates the onset of motor blockade.

Duration of sensory analgesia

In our study, the mean duration of sensory analgesia in group A was 351.10 ± 20.38 minutes, while in group B it was 372.32 ± 21.54 minutes, indicating a highly significant extension of analgesia duration in group B compared to group A. S. Gupta et al. [11] In their study, they compared 1mcg/kg of clonidine with 1.5mg/kg of bupivacaine to 1.5mg/kg of bupivacaine alone. The duration of sensory analgesia in the clonidine group was 334.2 ± 38.61 minutes, which is significantly prolonged than in the control group (161.4 ± 26.98 minutes). Similar to our findings, they conclude that the addition of clonidine as an adjuvant lengthens the duration of analgesia. In their study, Krishnamoorthy K et al. [14] compared 50g of clonidine diluted to 1 ml with 14 ml Bupivacaine 0.5% to 14 ml Bupivacaine 0.5% and 1 ml saline. The clonidine group required first rescue analgesia 6.05 ± 0.65 hours later than the saline group (3.27 ± 0.53 hours). It indicates that the addition of clonidine lengthens the duration of analgesia, similar to our study.

Conclusion

On the basis of this comparative clinical investigation, it can be concluded that both doses of clonidine (60 µg and 75 µg) administered via the epidural route with 0.5% Bupivacaine provide effective intraoperative analgesia. However, in the postoperative period, 75µg clonidine with 0.5% Bupivacaine provides longer-lasting analgesia than 60µg clonidine, without a significant increase in adverse effects or alteration of the hemodynamic profile. Therefore, 75µg clonidine administered via the epidural route is more efficacious as an adjuvant to local anaesthetics for postoperative analgesia.

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