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Original Research Article

A Comparative Study of Two Doses of Clonidineas an Epidural Adjuvant in Combined Spinal Anaesthesia

Md. Imdad Ali[1], Dinbandhu Prasad[2], Prabhanjan Chaudhary[3]

[1]Senior Resident, Department of Anaesthesiology, NMCH Patna
[2]Senior Resident, Department of Anaesthesiology, NMCH Patna
[3]Assistant Prof. Department of Anaesthesiology, NMCH Patna

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Corresponding author: Dr. Prabhanjan Chaudhary
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Abstract

Background: This study was done to compare the effects of two different doses of Clonidine as a sole epidural adjuvant in CSE on SAB with 0.5% HyperbaricBupivacaine, on the onset and duration of sensory and motor blockade, duration of analgesia, level of sedation and hemodynamic changes.

Methods: A total number of 90 ASA I and II patients, between 18-60 years of height between 150-180 cm and of weight 40-80 kgs., undergoing infraumbilical surgeries, were randomized in three groups of 30 patients each; viz. Group G150, G300 and GNS. Group G150 received 150 µg Clonidine, G300 received 300 µg Clonidine and GNS received 0.9% Normal Saline (NS) through epidural route as a sole epidural adjuvant.

Conclusion: Our study showed that when Clonidine used as a sole epidural adjuvant in dose of 300 µg or 150 µg, for infraumbilical surgeries, has significantly faster onset of sensory and motor block with prolonged duration of analgesia and motor blockade and no significant side effects on a conventional SAB performed with 0.5% Hyperbaric Bupivacaine.

Keywords: Combined Spinal Epidural, Clonidine, Subarachnoid Block.

Introduction

Adjuvants are agents possessing little effect by themselves, but potentiate the actions of other drugs when given at the same time. Whether administered into the CSF in conjunction with a local anesthetic or alone, a variety of medications may exert a direct analgesic effect on the spinal cord and nerve roots, or prolong the duration of sensory and motor blockade. As such, the co-administration of these agents often allows for a reduction in the required dose of local anesthetic [1]. The α-2 adrenergic agonists are commonly used adjuvants. They have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia. Clonidine, the prototypical drug of this class, is a selective partial agonist for α2-adrenoreceptors with a ratio of approximately 200:1 (α2: α1) [2], and has long been used in variety of regional techniques. Clonidine, as an adjuvant with local anaesthetics, increases the duration of pain relief after intrathecal or epidural administration. In doses of

15 to 225 µg, Clonidine prolongs the duration of sensory and motor blockade by approximately 1 hour and improves analgesia, reducing morphine consumption by up to 40% [3]. Regional anaesthesia offers safe, effective, economical anaesthesia over general anaesthesia. Of the regional techniques described, Combined Spinal Anaesthesia (CSE) allows flexibility in a number of clinical settings because the more rapid onset of spinal block compared with epidural anesthesia allows the operative procedure to begin earlier, whereas the epidural catheter still provides both effective postoperative analgesia and allows anesthesia to be extended as the spinal resolves [4]. Although numerous studies have been made on Clonidine as an adjuvant in epidural or spinal anaesthesia, as a single or combined agent with local anaesthetic, the knowledge of its effect as an sole epidural adjuvant on a routine spinal block using 0.5 % Hyperbaric Bupivacaine is however limited.

Objectives

To study the onset and duration of sensory and motor block, haemodynamic variations and sedation following injection of the drugs.

Review of Literature

Leafing through the anaesthesia archives we learn that CSE anesthesia was first described in 1937 by Dr. A. Soresi, an Italian surgeon who injected medications in the subarachnoid and epidural space at the same time [5,6]. The procedure, as described by Soresi, was called "Episubdural Anesthesia" and involved use of the same fine needle for both the epidural and the subarachnoid injection. The needle was first advanced in the epidural space using the hanging drop technique, and 8 ml of Novocain solution were injected. Then, the needle was advanced further, until it perforated the dura, and Novocain 2 ml was injected in the subarachnoid space [7]. This CSE anesthesia study included over 200 patients and analgesia lasted for 24 to 48 [4]. "Episubdural anesthesia" did not involve placement of an epidural catheter, and Dr. Soresi concluded his paper stating that "the hanging drop method renders episubdural anesthesia the safest procedure giving perfect surgical anesthesia, ideal relaxation, and eliminating practically all postoperative pain and distress" [8]. prolonged postoperative analgesia, analgesia covering a satisfactory number of dermatomes, minimal local anesthetic toxicity and absence of pulmonary complications [9]. The same year, Brownridge proposed using CSE anesthesia for Cesarean section, and published his results, two years later in "Anaesthesia" [10]. Then, in 1982, Coates et al. and Mumtaz et al. described a technical innovation, introducing the "needle through needle" technique: local anesthetic was first injected in the subarachnoid space, and this injection was followed by placement of an epidural catheter [11,12] Collis et al. in 1995 made a randomized comparison of combined spinal epidural (CSE) and standard epidural in 197 labouring patients to assess maternal satisfaction. For CSE analgesia, Bupivacaine (2.5 mg) and fentanyl (25 µg) were initially injected into the subarachnoid space, followed by top-ups of 15 mL 0.1% bupivacaine with 2 µg/mL fentanyl into the epidural space, as required. For standard epidural analgesia, 25 mg (10 mL of 0.25%) Bupivacaine was injected into the epidural space, followed by top-ups of 6-10 mL 0.25% Bupivacaine, as required. Post-partum, each woman completed a questionnaire about her labour and scored various items on a visual analogue scale. Overall satisfaction was greater in the combined spinal-epidural group than in the standard epidural group (median [IQR] score 3 [2-10] vs. 9 [3-22]; p = 0.0002). Good

analgesia was achieved in both groups, but the CSE had faster onset of analgesia and more of this group were satisfied with analgesia at 20 min (92/98 vs 68/99, $p < 0.0001$). 12 women in the CSE group had leg weakness at 20 min., but this initial motor block had resolved in most of these mothers by 1 h. In the standard epidural group 32 had leg weakness at 20 min ($p = 0.001$), and the proportion of mothers with weakness increased in this group during labour. There were no differences in side-effects, except for mild pruritus, which was more common in the combined spinal-epidural group (42 vs. 1%; $p < 0.0001$). Overall, women seem to prefer the low-dose CSE to standard epidurals, perhaps because of the faster onset, less motor block, and feelings of greater self-control [13]. Froster et al. in 2004 conducted a study using Clonidine mixed with Ropivacaine and Fentanyl given epidurally for patients undergoing total knee arthoplasty. They randomized 72 patients into two groups which received 2 mg/mL Ropivacaine and Fentanyl 5 µg/mL either with or without Clonidine 2 µg/mL, after their total knee arthoplasty. Sethi et al. in 2007 conducted a study wherein they studied the analgesic effect of low dose Clonidine as an adjuvant to intrathecal Hyperbaric Bupivacaine. 60 patients were randomized into two groups of 30 each. Van de Velde et al. in 2009 took 70 labouring patients and studied the effects of epidural Clonidine and Neostigmine following intrathecal injection of Ropivacaine and Sufentanil. 15 minutes after the spinal drug administration, 10 mL of the study solution containing 500 µg Neostigmine with 75 µg Clonidine was given epidurally. After epidural injection, the peak arterial blood concentration is reached in 10 minutes and in venous blood it reaches by 30-45 min. Elimination from blood is very slow. Its maximally absorbed into the CSF compartment by 30-60 min. In contrast to blood levels, strong correlation exists between the level of analgesia and CSF concentration of drug of at least 130 ng/mL (EC) [14]. As with lipophilic opioids, Clonidine administration through various routes can cause analgesia. But the effect is twice as potent when given epidurally than IV [15]. In stress situation Clonidine can reduce but does not suppress the neurohormonal secretion (Nor Epinephrine, Epinephrine, Adrenocorticotrophic Hormone, cortisol) secondary to activation of sympathoadrenergic drive [16,17].

Material and methods

Prospective Randomized control study, Department of Anaesthesiology, NMCH, Patna, Bihar. Study duration of two years. A total number of 90 ASA I and II patients, between 18-60 years of height between 150-180 cm and of weight 40-80 kgs., undergoing infraumbilical surgeries, were randomized in three groups of 30 patients,

Group G150 received 150 µg Clonidine, G300 received 300 µg Clonidine and GNS received 0.9% Normal Saline (NS) through epidural route as a sole epidural adjuvant. Immediately followed by 3 mL of 0.5% Hyperbaric Bupivacaine intrathecally was then given to all the groups. Baseline hemodynamic parameters; onset of sensory block (time to T10) and motor block (time to Bromage 3), sedation level (Modified RSS Score) and hemodynamic changed were measured. Total duration of sensory block (time for 1st rescue analgesia) and motor block (time to Bromage 0) were recorded. Sample size for each group was calculated by keeping the confidence interval at 95% and power of the study at 80%. A total of 90 patients who were divided into 3 groups.

Group G150: received 150 µg of Clonidine epidurally, Group G300: received 300 µg of Clonidine epidurally. Group GNS: received 0.9% Normal Saline epidurally.

Inclusion Criteria

Patients aged between 18 to 60 years of either sex, Height 150-180 cm of either sex. ASA I or ASA II scheduled for elective infra-umbilical surgery.

Exclusion Criteria

ASA grade III and above. Patients weighing < 40kg and >80kg, Lack of patient consent or surgeon's consent. Contraindications of epidural anesthesia. mThey were randomly allocated to one of the following groups of 30 each: Group G150, Group G300 and Group GNS. History and general condition of the patient. Airway assessment by Mallampati grading. Nutritional status, height and weight of the patient.

The patient was then placed in a right or left lateral position. With strict aseptic precautions and after local anaesthetic infiltration with 2% Lignocaine at L_{1-2} interspace an 18G Touhy's needle was passed and epidural space was identified by the loss of resistance to air technique. An 18G epidural catheter was passed through epidural space in cephalad direction. Onset of sensory block was defined as time taken from SAB till the patient did not feel any sensation at T10 dermatome.m Onset of motor block**:** was defined as time taken from SAB till Bromage 3. **Total** analgesia duration: was defined as time taken from SAB till 1st rescue analgesia. Total duration of sensory block**:** was defined as time taken from SAB till two segment regression from the maximum block height. Descriptive and inferential statistical analysis has been carriedout in the present study.

Results

It was a clinical randomized double blind study with 90 patients randomly divided into three groups of 30 each, Group G150: received 150 µg of Clonidine, diluted to 5 cc, epidurally. Group G300: received 300 µg of Clonidine, diluted to 5 cc, epidurally. Group GNS: received 0.9% Normal Saline of 5 cc volume, epidurally. All groups then received 3 cc of 0.5 % Hyperbaric Bupivacaine intrathecally.

They were evaluated for onset and duration of sensory and motor blockade, haemodynamic variations, sedation scores and side effects if any.

Table 1: Weight and Height distribution of patients studied:

	Group G150	Group G300	Group GNS	P Value
Weight(Kg)	57.50±8.63	56.00±11.64	58.16±5.93	0.639
Height(cm)	156.27±5.76	156.67±6.69	157.73±3.45	0.567

Table 2: Comparison of side effects in the groups studied:

	Group G150 (n=30)	Group G300 (n=30)	Group GNS (n=30)	P value
Hypotension	2(6.6%)	3(10%)	1(3.3%)	0.692
Bradycardia	2(6.6%)	4(13.3%)	1(3.3%)	0.380

The side effect profile: Hypotension and Bradycardia was found to be clinically and statistically insignificant amongst the groups with p value 0.692and 0.380 respectively.

Table 3: Onset of sensory block at T10

Parameter	Group G150	Group G300	Group GNS	p Value
Onset of sensory Block at T10 (sec)	71.37±4.36	71.63±4.51	90.13±4.88	< 0.001

The onset of sensory block at T10 was faster in the Clonidine groups (71.37±4.36 and 71.63±4.51 sec. for G150 and G300 respectively) compared to the control group (90.13±4.88

sec) (p value <0.001). Amongst the Clonidine groups (G150 and G300) the onset was similar (p value 0.81).

Table 4: Total duration of Motor Block

Parameter	Group G150	Group G300	Group GNS	p Value
Total duration of Motor Block (min)	328.67±27.38	409.90±34.87	204.50±22.79	<0.001

The total duration of motor block (defined as time taken to return to Bromage score 0) was clinically and statistically prolonged for the Clonidine groups (328.67±27.38 and 409.90±34.87 min. for G150 and G300 respecively) with respect to control (204.50±22.79 min.) (p value <0.001). Amongst the Clonidine groups, G300 showed significantly prolonged duration. (p value<0.01).

Table 5: Total Analgesia duration (Time of request for first analgesicdose)

Parameter	Group G150	Group G300	Group GNS	p Value
Total Analgesia duration (min)	281.77±27.89	317.90±15.32	207.00±20.66	<0.001

The total analgesia duration (defined as time of request for first analgesia) was clinically and statistically prolonged for the Clonidine groups (281.77±27.89 and 317.90±15.32 min. for G150 and G300 respectively) with respect to control (207.00±20.66 min.) (p value <0.001). Amongst the Clonidine groups, G300 showed significantly prolonged duration. (p value <0.01).

Discussion

In this study, we have used 150 µg and 300 µg Clonidine alone via epidural route as adjuvant, to see its effect on SAB produced by 0.5% Hyperbaric Bupicavaine for infraumbilical surgeries. Some studies have shown that Clonidine can be used in 300-600 µg alone via epidural route [14]. Also, increased incidence of adverse effects such as bradycardia, hypotension and sedation with higher doses (>600 µg) of Clonidine have been reported [14]. In our study the onset of sensory block was taken as loss of cold sensation at T10 dermatome. The mean time for onset of sensory block was 71.37±4.36 sec. for Group G150, 71.63±4.51 sec. for Group G300 and 90.13±4.88 sec. forGroup GNS. This was found to be statistically significant (p value <0.01). Both the Groups G150 and G300 had much faster onset of sensory blockade when compared to Group GNS. Between Group G150 and G300, the onset was comparable with p value 0.81. Between G150 vs. GNS and G300 vs. GNS the onset was significantly faster in G150 and G300 respectively with p value <0.01.Saxena et al. [18] conducted a study wherein all the groups receiving Clonidine as an adjuvant intrathecally along with Hyperbaric Bupivacaine showed significantly (p value <0.01) faster onset at of sensory block and spread at T10. Bajwa et al. [19] study showed similarly, Clonidine as an adjuvant along with Ropivacaine vs. Ropivacaine alone given epidurally, showed a much faster onset at T10-11 level (8.64±2.56 min vs11.36±3.30 min.) and at T6-7 level (12.26±3.18 min. vs. 15.12±4.36) which was clinically and statistically significant with p value at <0.05. Gecaj-Gashi at al. [20] in their study showed similar fast onset at T10 level for patients group, which received Clonidine along with Bupivacaine intrathecally (11.39±2.15 min vs. 15.75±1.56 min) (p value <0.01). Thakur et al. [21] conducted a study, which showed that the groups receiving Clonidine as an intrathecal adjuvant had significantly prolonged 2 segment regression time (105.60±30.15, 110.60±26.22 min. vs. 72.60±15.42 min.;

pvalue <0.05). Sethi et al. [2**2]** evaluated the efficacy of low dose intrathecal Clonidine as an adjuvant to Bupivacaine and found similar prolongation of 2 segment regression time for the Clonidine group (218 min. vs. 136 min.; p value<0.001). Karki et al. [23] used epidural Clonidine as an adjuvant and found similar prolongation of the motor block for the Clonidine group (226.42±26.17 min. vs. 152±12.2 min.; p value <0.05). Sharma et al. [24] also found in their study, that the Clonidine group had longer mean duration of motor block when used as an epidural adjuvant. Prasad et al. [25] too had similar observations in their study with Clonidine adjuvant via epidural route with significantly prolonged duration of motor In our study, intraoperatively hypotension was observed in 2 patients (6.6%) in Group G150, 3 patients (10%) in Group G300 and in 1 patient (3.33%) in Group GNS, which was not statistically significant (p value 0.692). Incidence of bradycardia was 2 patients (6.6%) in Group G150, 4 patients (13.33%) in Group G300 and in 1 patient (3.33%) in Group GNS which again not significant (p value 0.380). Gautam et al. [26] in their study observed that the although SBP was lower in the Clonidine group, but it was statistically not significant. In our study plus other studies would infer that there were neither clinically nor statistically significant haemodynamic side effects when Clonidine was used as an adjuvant in a dose less than 300 µg. [27]

Conclusion

our study showed that when Clonidine used as a sole epidural adjuvant in dose of 300 µg or 150 µg, for infraumbilical surgeries, along with conventional SAB performed with 0.5 % Hyperbaric Bupivacaine has significantly faster onset of sensory and motor block with prolonged duration of analgesia and motor blockade and no significant side effects.

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