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Original Article

Anaesthesia Section

Comparison of Bupivacaine with Two Different Doses of Clonidine under Spinal Anaesthesia in Infraumbilical Surgeries- A Randomised Clinical Study

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ABSTRACT

Introduction: Spinal anaesthesia is known as a safe and effective way to give anaesthesia during infraumbilical and lower limb surgeries. Intrathecal clonidine is a safe non opioid adjuvant used with local anaesthetics to prolong sensory and motor block, promotes sedation and analgesia.

Aim: To compare the effects of bupivacaine with two different doses of clonidine under spinal anaesthesia in infraumbilical surgeries.

Materials and Methods: This randomised double-blinded study was conducted in the Department of Anaesthesiology at Hind Institute Of Medical Science, Sitapur, Uttar Pradesh, India. The duration of the study was 19 months, from January 2021 to August 2022. A total of 60 patients (36 males and 24 females) were enrolled in the study and were randomly assigned to one of two groups (group A and group B) of 30 patients each. Group A bupivacaine heavy 12.5 mg with 15 mcg of clonidine, total volume 3 mL and group B bupivacaine heavy 12.5 mg with 30 mcg of clonidine, total volume 3 mL. The study parameters were: onset of sensory and motor block, duration of postoperative analgesia and any side effects (hypotension, bradycardia, sedation or any other). The statistical analysis was done using Statistical Package for Social Sciences (SPSS) Version 21.0.

Results: The mean age of the study participants group A (44.51±12.84) years and group B (42.28±13.12) years. The demographical data showed comparable findings. The mean of onset of sensory (160.37±33.64) seconds and motor block (197.2±12.36) seconds in group B was statistically lower than group A. The mean duration of analgesia in group A (302.58±18.62) minutes was lower than group B (318.73±29.46) minutes. The mean Visual Analogue Scale (VAS) score was higher at every follow-up in group A as compared to in group B. The mean Ramsay sedation score was significantly higher in Group B at every follow-up than in group A.

Conclusion: Spinal anaesthesia performed with 0.5% bupivacaine heavy with 30 mcg clonidine was proven to be a more effective adjuvant in providing early onset of the sensory and motor blockade intraoperatively and prolongation of the duration of effective postoperative analgesia when compare to 15 mcg clonidine.

Keywords: Intrathecal, Non opioid, Postoperative analgesia, Sedation

INTRODUCTION

Spinal anaesthesia has established recognition for being a safe and effective technique for administering anaesthetic for infraumbilical and lower limb surgeries. It is a safe and efficient procedure to induce deep, reproducible sensory analgesia and motor blockade with a minimal volume of drug that is practically free of systemic pharmacologic effects. Even epidural anaesthesia requires the administration of a considerable amount of local anaesthetic medication, which results in pharmacologically active systemic blood levels, which may cause side effects and problems rarely seen with spinal anaesthesia [1,2]. Bupivacaine has a stabilising impact on all excitable membranes as a result of its pharmacological actions. It produces a different clinical profile of nerve blockage than lignocaine. It is four times more powerful than lignocaine and produces a more pronounced sensory block than lignocaine. However, its period of action is quite brief, ranging between 75 to 150 minutes [3,4].

Numerous adjuvants such as fentanyl, clonidine, ketamine, morphine, and buprenorphine have been used to prolong the effect of intrathecal bupivacaine and, therefore, extend analgesia's duration into the postoperative period as well. Alpha2 agonists are adjuvants used in anaesthesia and analgesia. They can be administered orally, transdermally, intravenously, perineurally, or neuraxial. Clonidine has been used as an anaesthetic adjuvant by anaesthesiologists to improve perioperative cardiovascular, sympathoadrenal stability, general and regional anaesthesia, sedation and analgesia [5]. Clonidine, prolongs sensory and motor block, promotes sedation, but may exacerbate hypotension and bradycardia when injected into spinal space [6-9]. Many studies already done in past using higher doses of clonidine (150 mcg) intrathecally were associated with haemodynamic instability, as well as, systemic side effects at cost of improved analgesia [10]. Hence, the aim of present study was to evaluate the two low doses (30 mcg vs 15 mcg) of clonidine as an adjuvant with bupivacaine for spinal anaesthesia during infraumbilical surgeries.

MATERIALS AND METHODS

This randomised double-blinded study was conducted in the Department of Anaesthesiology at Hind Institute Of Medical Science, Sitapur, Uttar Pradesh, India. The duration of the study was 19 months, from January 2021 to August 2022. The Institutional Ethics Committee approval was obtained {IHEC-HIMSA/MD/MS(20)/RD-11/01-21}

Inclusion criteria: A total of 60 patients between 20-50 years of age, American Society of Anesthesiologists (ASA) Physical Status (PS) I-II was planned for elective infraumblical surgeries.

Exclusion criteria: Patients with contraindication to subarachnoid block, having renal/haepatic dysfunction, haemodynamically unstable, allergic to study drugs and patients refusal to participate.

Sample size calculation: For sample size calculation, the study by Krishna K et al., was considered [11].

The sample size formulae:

$$n=\frac{(\sigma_1^2+\sigma_2^2/\kappa)\times(Z_{1-\alpha/2}+Z_{1-\beta})^2}{\Delta^2}$$

n=Sample size

σ=Standard Deviation

Δ=Difference of means

κ=Ratio

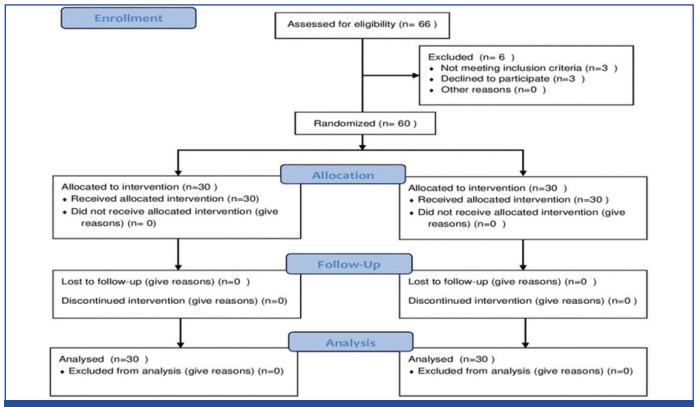
Z1-α/2=Two sided Z value

Z1-β=Power

Where, the confidence interval and power of study were 95% and 80%, respectively. Calculated sample size was 52 but considering drop out total sample size of 60 (30 in each group) was taken for study.

Study Procedure

After getting written and informed consent, patients were randomly divided into two groups, using computer-generated random number table, of 30 patients each. Group A-12.5 mg, 0.5% bupivacaine heavy (2.5 mL) +15 mcg clonidine (0.5 mL), group B-12.5 mg, 0.5% bupivacaine heavy (2.5 mL)+30 mcg clonidine (0.5 mL). Normal saline was used to make volume of clonidine upto 0.5 mL and total volume of drug kept 3.0 mL in both groups. For ensuring the double blinding drugs were prepared by anaesthesiologist, who did not perform subarachnoid block and not participating in data collection [Table/Fig-1]. A day before surgery preanaesthetic check-up with detailed physical and systemic examination was done. All relevant investigation was performed and reviewed. Patients were kept nil per oral for six hours before surgery. They were premedicated with tablet alprazolam 0.25 mg and capsule pantoprozol 40 mg orally on the night before surgery.



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

On the day of surgery, premedication was done with injection ondansetron 0.10 to 0.15 mg/kg Intravenous (i.v.), injection ranitidine 4-8 mg/kg i.v. and injection ceftriaxone 25-30 mg/kg i.v. after performing sensitivity test. In operation theater, monitors were attached to the patient and baseline parameters including Heart Rate (HR), systolic and diastolic Blood Pressure (BP), SpO_2 and respiratory rate were noted. All the patients were preloaded with 10 mL/kg of crystalloid solution after securing 18 G intravenous line over 10 minutes. After taking all aseptic precaution, spinal anaesthesia was given at level of L3-L4 or L2-L3 in seating position through a midline approach using 25 G quincke spinal needle. After confirmation of free flow of Cerebrospinal Fluid (CSF), a study drug was given which was prepared by another investigator to facilitate double blinding.

Sensory block and motor block were assessed by loss of sensation to a pin prick and by modified Bromage score, respectively. Sensory block onset time was defined as the time interval between the end of spinal anaesthesia administration and loss of pin prick sensation at T-10 level. While onset of complete motor block was defined as the time interval between completion of spinal anaesthesia and the absence of voluntary movement on feet, ankle, knee and hip (Bromage scale 3). These were assessed every one minute after performing spinal anaesthesia. Continuous monitoring of respiratory rate, HR, non invasive systolic and diastolic BP, SpO_2, and electrocardiogram was done for haemodynamic response. Events like hypotension, bradycardia sedation and any other were recorded. Bradycardia {defined as heart rate <50 Beats Per Minute (BPM)} was treated with injection atropine sulfate intravenously according to HR. Hypotension (defined as systolic blood pressure <20% less than base value) was treated with intravenous ephedrine intravenously, as per required and additional Ringer's lactate solution.

The operation was started when surgical anaesthesia (up to the T6 sensory dermatome) has developed. In case of failed or partial neuraxial block, the patient was given general anaesthesia and that patient was excluded from the study. The level of postoperative analgesia was assessed by using VAS with 0-10 cm line. The patients were made familiar to VAS scale a day before surgery during the preanaesthetic check-up. Rescue analgesia was given if (VAS>4). Time of administration of the study drug to time of administration rescue analgesic (VAS>4) was considered as the duration of analgesia of the study drug. Inj. diclofenac 75 mg was administered as a rescue analgesic. The changes in the cardiorespiratory parameters (HR, BP) were monitored, number of significant events (bradycardia, hypotenstion, sedation) were noted and data of these significant changes were compared between the two groups.

STATISTICAL ANALYSIS

The statistical analysis was done using SPSS version 21.0. The continuous data were summarised as Mean±SD while discrete (categorical) in percentage. To test the significance of two means the Student's t-test was used. The p-value <0.05 was considered statistically significant with 95% confidence interval.

RESULTS

A total of 60 individuals were included and randomly allocated into two study groups (group A and group B). Patients were comparable to each other in terms of demographic characteristics [Table/Fig-2]. There were 36 males and 24 females. There was no statistically significant difference in type of infraumbilical surgical procedures between the two groups [Table/Fig-3]. Fracture both bones, lower leg was the most common procedure in both groups followed by femur fracture, and vaginal hysterectomy [Table/Fig-3]. The mean time for the onset of sensory and motor block in group B was less than group A [Table/Fig-4]. The mean duration of analgesia of group A was significantly less than group B. The mean VAS score were higher at every follow-up in group A as compared to group B. The VAS score showed significant difference at every follow-up except at 15, 30 and 45 minutes of enrolled patients [Table/Fig-5]. Sedation was most common side effect in both groups followed by hypotension, bradycardia and dryness of mouth [Table/Fig-6]. The mean Ramsay sedation score was higher in group B at every follow-up than in group A. The mean sedation score showed a significant difference at every follow-up except at 12 hours [Table/Fig-7].

Variables	Group A (n =30)	Group B (n =30)	p-value
Age in years (Mean±SD)	44.51±12.84	42.28±13.12	0.5085
Weight in kilograms (Mean±SD)	69.94±7.86	70.04±10.16	0.9661
Height in centimeters (Mean±SD)	172.43±7.58	171.13±9.86	0.5692
Gender			
Male	17 (56.67%)	19 (63.33%)	0.5982
Female	13 (43.33%)	11 (36.67%)	
Mean duration of surgery in minutes	127.52± 46.71	115.62± 35.27	0.2700

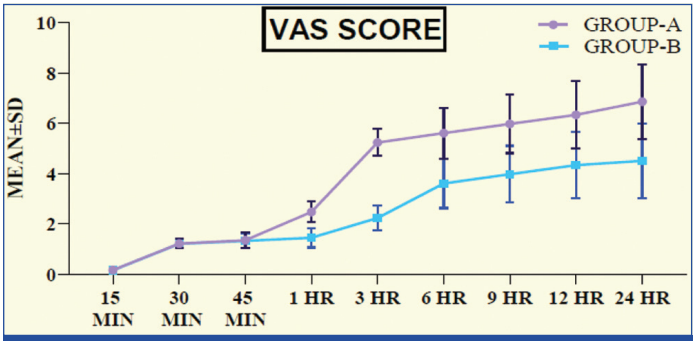
[Table/Fig-2]: Patients demography and duration of surgery (N=60).

Type of surgery	Group A (n=30) n (%)	Group B (n=30) n (%)	p-value
Total abdominal hysterectomy with bilateral salpingo oophorectomy	2 (6.67%)	3 (10.00%)	χ^2=2.133 p=0.9521
Vaginal hysterectomy	4 (13.33%)	2 (6.67%)	
Both bones lower limb	16 (53.33%)	13 (43.33%)	
Femur fracture	4 (13.33%)	6 (20.00%)	
Inguinal hernia	1 (3.33%)	1 (3.33%)	
Shaft of femur	1 (3.33%)	2 (6.67%)	
Implant exit	2 (6.67%)	3 (10.00%)	
Total	30 (100.00%)	30 (100.00%)	

[Table/Fig-3]: Tabular distribution of the type of surgery of the enrolled patients (N=60).

Parameters	Group A (n =30)	Group B (n=30)	p-value
Onset of sensory block in seconds (Mean±SD)	182.56±43.82	160.37±33.64	0.0318
Onset of motor block in seconds (Mean±SD)	205.61±16.82	197.24±12.36	0.0321
Duration of analgesia in minutes (Mean±SD)	302.58±18.62	318.73±29.46	0.0139

[Table/Fig-4]: Onset of sensory and motor block and duration of analgesia (N=60).



[Table/Fig-5]: Graphical representation of mean VAS score of the enrolled patients.

Parameters	Group A (n=30)	Group B (n=30)	p-value
Hypotension	2 (6.67%)	3 (10%)	0.6404
Bradycardia	2 (6.67%)	3 (10%)	0.6404
Sedation	15 (50%)	30 (100%)	<0.0001
Dryness of mouth	2 (6.67%)	3 (10%)	0.6404

[Table/Fig-6]: Tabular distribution of side effects of the enrolled patients (N=60).

Ramsay sedation score	Group A (n=30) (Mean±SD)	Group B (n=30) (Mean±SD)	t-value	p-value
30 minute	2.45±0.74	3.76±0.51	7.984	<0.0001*
1 hour	2.31±0.45	3.34±0.57	7.768	<0.0001*
3 hours	2.14±0.34	3.09±0.41	9.769	<0.0001*
6 hours	1.51±0.21	2.59±0.61	9.169	<0.0001*
9 hours	1.08±0.14	2.18±1.06	5.635	<0.0001*
12 hours	2.04±0.09	2.01±1.02	0.1244	0.9014

[Table/Fig-7]: Tabular distribution of mean Ramsay sedation score of the enrolled patients.
*: Highly significant; N=60

DISCUSSION

Clonidine used as an adjuvant with local anaesthetics produces analgesia of varying potency and duration and augments postoperative analgesia. There was no significant difference regarding the age, gender, body weight, height, type of surgeries and also mean duration of surgeries among the two groups. In present study, the mean time for the onset of sensory block of group B was significantly lower than group A. The present study is comparable to those reported by Menacherry VT et al., [9]. In the later study, it was found that, the mean time to onset of sensory block in the control group patient receiving 2.75 mL of 0.5% hyperbaric bupivacaine plus 0.4 mL saline was 103 seconds and in group C, one patient receiving 2.75 mL of 0.5% hyperbaric bupivacaine plus 45 mcg of clonidine, it was 77.25 seconds; in group C, two patients receiving 2.75 mL of 0.5% hyperbaric bupivacaine plus 60 mcg of clonidine, it was 156.25 seconds [9]. In group C, the onset time of sensory block was significantly prolonged. Klimscha W and Chiari A, investigated intrathecally administered 0.5% bupivacaine 5 mg and 150 g clonidine vs plain bupivacaine and found no statistically significant difference between the groups [10].

In the present study, the mean onset of the motor block of group B (bupivacaine heavy12.5 mg +30 mcg of clonidine) was significantly lower than group A (bupivacaine heavy12.5 mg +15 mcg of clonidine). The results obtained by Krishna K et al., and Saxena H et al., were comparable for motor block showing a significant difference in the beginning of motor block between the control group (hyperbaric bupivacaine 0.5%) and clonidine 30 mcg group [11,12]. In comparison to Krishna K et al., the duration of analgesia in the present study was shorter in both groups, owing to the use of a lower dose of bupivacaine (12.5 mg) in both groups in comparison to levobupivacaine 15 mg [11]. Similarly, the present study observed significantly longer duration of analgesia in group B (bupivacaine heavy12.5 mg +30 mcg of clonidine). In the present study, mean VAS score was higher at every follow-up in group A (bupivacaine heavy12.5 mg +15 mcg of clonidine) Dobrydnjov MD observed that, postoperative pain relief at rest was satisfactory in all patients (mean VAS approximately 2-3) irrespective of group. VAS at rest and on movement was significantly lower in group BC 15 (6 mg of bupivacaine +15 mcg of clonidine) and BC 30 (6 mg of bupivacaine +30 mcg of clonidine) compared with group B (6 mg of bupivacaine) during the first 210 minutes [13].

In the present study, mean Ramsay sedation score was higher in group B (bupivacaine heavy12.5 mg with+30 mcg of clonidine) at every follow-up. The mean sedation score showed a significant difference at every follow-up except at 12 hours. Gogoi S et al., found that, the mean Residual Sum of Squares (RSS) score was significantly lower in group BC (bupivacaine 0.25% +clonidine 1 mcg/kg) compared to group BD (bupivacaine 0.25% +dexmedetomidine 1 mcg/kg) at the end of two hours and three hours (p=0.0001) [14]. Menacherry VT et al., found that, the patients in both the clonidine groups (hyperbaric bupivacaine 2.75 mL+45 mcg vs hyperbaric bupivacaine 2.75 mL+ 60 mcg clonidine) had drowsiness with an RSS score of ≤3 that did not require active intervention [9]. Similarly, in the present study 100% patients of group B (bupivacaine heavy 12.5 mg +30 mcg of clonidine) were got sedation but did not required any active intervention. Other side effect was hypotension, bradycardia, and dryness of the mouth. However, statistically, a non significant difference was observed between both the groups.

Limitation(s)

New parameters like, motor coordination function test by Heel-Shin touch method, assessment of gait, the Analgesia Nociception Index (ANI) and Numeric Rating Scale (NRS) and controls are needed to account for confounding variables and boost study reliability.

CONCLUSION(S)

In conclusion, using clonidine as an adjuvant to bupivacaine in the treatment of subarachnoid blocks significantly increases the duration of both sensory and motor block. The authors conclude that, the clonidine hydrochloride (30 mcg) added to local anaesthetic in a subarachnoid block has proven to be a more effective adjuvant in prolonging the sensory and motor blockade intraoperatively and the duration of effective postoperative analgesia when compared to 15 mcg, with no significant adverse consequences.

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