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Intrathecal Bupivacaine with Different Doses of Clonidine in Elective Surgeries: A Comparative Study

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Abstract: Intrathecal clonidine is a very safe, nonopioid adjuvant to local anesthetics to prolong the duration of analgesia without any major side effects. The purpose of the present study was to evaluate the efficacy of clonidine in two different doses as an adjuvant to bupivacaine intrathecally in elective surgeries. This study include 80 patients aged between 20-60 years of both sexes divided in two two groups each consist of 40 patients. Group A received hyperbaric bupivacaine (2.5 ml) +50 µg clonidine (diluted to 0.5 ml) administered intrathecally and Group B– Received hyperbaric bupivacaine (2.5 ml) +75 µg clonidine (diluted to 0.5 ml) administered intrathecally. The mean time of onset of sensory block and motor block were comparable between two groups, but Duration of sensory block and motor block were significantly increased as the dose of clonidine increased and recue analgesia also decreased. Maximum fall in systolic blood pressure during first 15 min was noticed. There was no significant difference in the mean values of heart rate at different time intervals between the two groups. There was no significant difference in systolic blood pressure, diatolic blood pressure and mean arterial blood pressure in two groups. Sedation score were increased as the dose of clonidine is increased. Hence it is concluded that addition of intrathecal clonidine 50-75µg to small dose bupivacaine increased the spread, duration of analgesia, and produced effective spinal anesthesia with stable hemodynamics.
Keywords: clonidine, sensory blockade, motor blockade, side effects, sedation scores.

INTRODUCTION

Local anesthetic like bupivacaine is commonly used in spinal anesthesia, but the duration of spinal anesthesia may be short and limited, and higher doses of rescue analgesics may be required in the postoperative period. This can be avoided by using higher doses of bupivacaine which again can produce cardiac toxicity. Studies have shown that duration of analgesia due to bupivacaine in spinal anesthesia can be prolonged by using adjuvants such as midazolam, opioids, neostigmine, dexmedetomidine, and clonidine [1]. Almost all opioids have been used as adjuvants intrathecally.

Clinical studies have suggested that intrathecal clonidine, and α_2-receptor agonist, prolongs sensory and motor block in spinal anesthesia and provides prolonged postoperative analgesia. Clonidine has beneficial effects such as antiemesis, reduced postspinal shivering, anxiolysis, and sedation, thereby avoiding unwanted opioid-related side effects such as pruritus and respiratory depression [2, 3]. Many studies conducted in the past have used clonidine in doses of 15–150 µg intrathecally, but higher doses were associated with hemodynamic instability and systemic side effects at the cost of improved analgesia [4].

Hence, the present study is being undertaken to evaluate and compare the effects of different doses of clonidine a as intrathecal adjuvants to hyperbaric bupivacaine in patients undergoing lower limb orthopedic, general and gynecological surgeries and The primary objectives of this study were to evaluate and compare the effects of different doses of clonidine on time of request of first dose of rescue analgesic. Secondary objectives were to compare the effects different doses of clonidine on time of onset and duration of sensory and motor block, hemodynamic status, and side effects

MATERIALS & METHODS

This randomized controlled study was carried out from January 2016 to January 2017, after obtaining approval from the Hospital Ethics Committee and

written informed consent from the patients. Eighty patients of the American Society of Anesthesiologists Classes I or II of either sex and of age 20–60 years of age posted for elective surgery were randomly divided into two groups (n = 40) using computer-generated program. Assigned random group was enclosed in a sealed envelope to ensure concealment of allocation sequence. The anesthesiologist, who was not involved in the study, opened the envelope in Operation Theater and prepared the drug accordingly. The observation was done by the anesthesiologist who was blinded to the drug. Patients having severe systemic disorders such as diabetes mellitus, hypertension, heart disease, allergy to bupivacaine, spine deformity, increased intracranial pressure, neurological disorders, hemorrhagic diathesis, and infection at the puncture site were excluded from the study. Group A– Received hyperbaric bupivacaine (2.5 ml) +50 μg clonidine (diluted to 0.5 ml) administered intrathecally. Group B– Received hyperbaric bupivacaine (2.5 ml) +75 μg clonidine (diluted to 0.5 ml) administered intrathecally.

Total volume of study drug was 3 ml. Preanesthetic checkup was done, and visual analog scale (VAS) was explained to all patients. All the patients were kept nil orally for 6 h before surgery. After shifting the patients to Operation Theater, intravenous (IV) cannula was inserted, and preloading was done with Ringer solution (10 ml/kg). Preoperative parameters such as pulse rate, oxygen saturation, and blood pressure were recorded. Under all aseptic precaution, spinal anesthesia was administered at the level of L3–L4 intervertebral space in sitting position using midline approach by 25-gauge Quincke spinal needle. The anesthesiologist who administered anesthesia was blinded to the group allocation. Pulse rate, respiratory rate, electrocardiogram, SpO_2, and blood pressure were monitored. Pulse rate and blood pressure variations more than 20% of baseline were noted in both groups. Bradycardia and hypotension were treated with IV atropine and ephedrine, respectively. Sensory and motor block was monitored at 2, 4, 6, 8, 10, 15 min, and after that at 15 min interval. Sensory block was tested by pinprick method. The motor block was assessed according to the modified Bromage scale: Bromage 0: Patients able to move hip, knee, and ankle, Bromage 1: Patients unable to move hip but able to move the knee and ankle, Bromage 2: Patient unable to move hip and knee but able to move the ankle, Bromage 3: Patient unable to move hip, knee, and ankle[5]. The onset of sensory block was taken from the time of intrathecal injection till loss of pin prick sensation at T10. Duration of sensory block was taken as time from maximum height of block till regression to Level 1. The onset of motor block was defined as time from intrathecal injection to motor blockade Level 2 in Bromage scale. Duration of motor blockade was taken as time from intrathecal injection till no motor weakness (Bromage 0). Duration of analgesia was defined as time from intrathecal injection till administration of first rescue analgesic. Any side effects such as nausea, vomiting, pain, shivering, pruritus, sedation, hypotension, bradycardia, and respiratory discomfort were noted. Patients were assessed for degree of sedation, and scoring was done with Campbell sedation score as: 1: Wide awake, 2: Awake and comfortable, 3: Drowsy and difficult to arouse, and 4: Not arousable[5]. Postoperatively, the pain score was recorded by using VAS between 0 and 10 (0 = no pain, 10 = severe pain)[6]. Injection paracetamol (1 gm) was given intravenously as rescue analgesic when VAS was >5. Time of administering the first dose of rescue analgesia was noted

STATISTICAL METHODS

Power analysis suggested that a sample size of forty patients per group was required to achieve a power of 80% and a level significance of 0.05 to be able to detect a difference in the mean duration of analgesia by 60 min between the groups. Interpretation of the data was carried out and analyzed using statistical package for social sciences (SPSS version 19, IBM Corp, NY, USA). Data was represented as mean ± standard deviation for continuous data and frequency (percentage) or median (range) for nonparametric (categorical) data. The two groups were compared using analysis of variance. The proportion of adverse effects was compared using Chi-square test. $P < 0.05$ was considered statistically significant. $P < 0.001$ was considered highly statistically significant.

RESULTS

In our study, we observed that demographic data like age, height, weight, ASA grade, gender, and duration of surgery were comparable in two groups with $P > 0.05$(Table.1). Statistically these were not significant. Different types of surgeries conducted among the patients were shown in table 2.

Table-1: Demographic data

Character	A GROUP(50μg)	B GROUP((75μg)
Age in years	45.32±10.23	46.52±13.62
Height in cms	152.86±9.25	150.96±8.34
Weight in kgs	62.23±12.45	60.23±13.24
Sex male/female	18/22	21/19
ASA grade	1-2	1-2
Duration of surgery	174.32±50.12	172.52±48.23

Table-2: Showing Types of Surgery in Both Groups

Type of Surgery	A GROUP(50µg)	B GROUP((75µg)
Hernioplasty	10	12
Lower Limb	10	13
TAH	5	3
Ovariotomy	5	4
Appendicectomy	10	8
Total:	40	40

The mean time of onset of sensory block and motor block were comparable between two groups, but Duration of sensory block and motor block were significantly increased as the dose of clonidine increased and recue analgesia also decreased(table3).

Table-3: Comparision of different block characteristics

Time in min	A GROUP(50µg)	B GROUP((75µg)
On set of sensory block	6.52±1.45	5.23±1.22
On set of motor block	9.54±2.23	7.52±1.56
Duration of sensory block	204.54±13.20	242.36±20.28*
Duration of motor block	171.23±16.54	191.35±18.23*
Time for 1st dose of analgesic	420.56±30.45	480.35±24.10*

Maximum fall in systolic blood pressure during first 15 min was calculated and expressed as a percentage of baseline value in each patient in each group. The mean values were 24 ± 8.5% in Group A and 26.6 ± 9.2% in Group B, with no significant difference between the two groups. Injection mephentermine was used to treat hypotension in these patients. There was no significant difference in the mean values of heart rate at different time intervals between the two groups. There was no significant difference in systolic blood pressure; diatolic blood pressure and mean arterial blood pressure were shown in fig 1, 2&3 respectively.

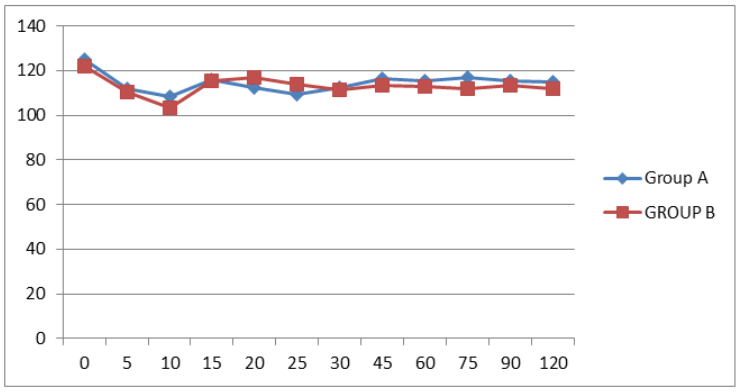

Fig-1: Systolic blood pressure

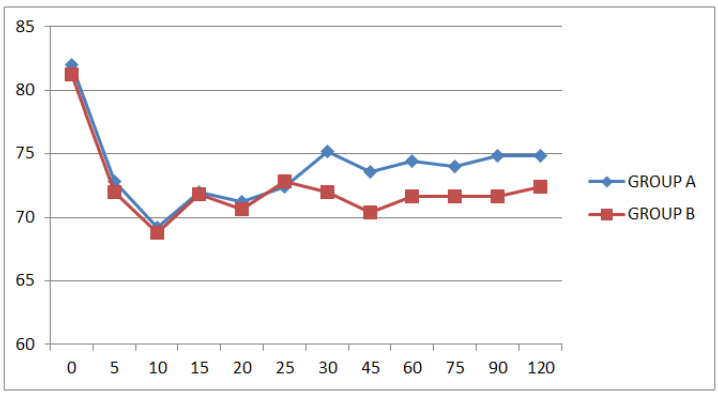

Fig-2: Diastolic blood pressure

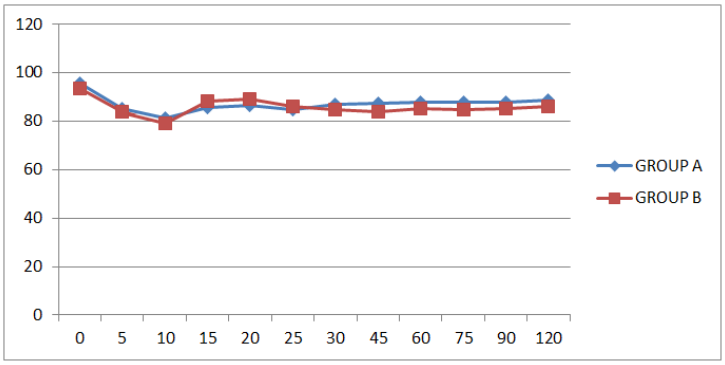

Fig-3: Mean arterial blood pressure

Among side effects, bradycardia occurred in 9 patients,hypotension occurred in 14 patients, Nausea occurred in 9 patients, dry mouth in occurred in 11 patients and vomition in one patient which was statistically not significant.. None of the patients in any group developed respiratory depression, pruritis and shivering.

Table-4: Side effects

Side effects	Group A No effected	Group B No effected
Bradycardia	5	4
Hypotension	6	8
Nausea	4	4
Vomiting	1	0
Shivering	0	0
Dry mouth	6	5
Respiratory Depression	0	0

Mean sedation scores were significantly higher in group B compared to group A as 64% patients in group B had a sedation score of 3 as compared to 32% in group A (P<0.0001). Only 16% of the patients in the B group had sedation scores of 1 compared to 52% wide and awake patients in A group, which was a highly significant statistical entity (p<0.0001)16% patients in group A, 20% patients in group B had score 2 which is statistically not significant.

DISCUSSION

Intrathecal clonidine is a α_2 adrenergic agonist having potent antinociceptive properties. It results in the prolongation of sensory and motor blockade and a reduction in the amount or concentration of local anesthetic required producing prolonged peri-operative analgesia, thereby reducing the incidence of side effects. The dosages used in our study are based on data from various studies, where hemodynamic stability and a significantly reduced incidence of side effects have been reported in dosages ranging between 15 and 150 µg of clonidine [7, 8].

Clonidine is commonly used because of its safety and various advantages over other adjuvants. The mechanism by which clonidine prolongs motor and sensory block is not well-known. It produces analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of postsynaptic dorsal horn neurons [9]. Binding of clonidine to motor neurons in the dorsal horn may prolong motor block [10]. Its effect in terms of potentiation of sensory and motor block of intrathecal bupivacaine has been studied with doses of 1-2 µg/kg[11,12]. Doses much less than 1 µg/kg have shown contradicting results in terms of augmenting the effects of local anesthetics, but with minimal side-effects in adult patients[13].

In present study the onset sensory block was 6.52±1.45 and 5.23±1.22 and on set of motor block 9.54±2.23 and 7.52±1.56 hence the dose of clonidine does not affect the onset of surgical anesthesia. In the present study, clonidine did not affect the onset of surgical anesthesia, similar results on the onset have been shown by other workers [14]. Clonidine in both doses increased the median highest sensory block level. In our study duration of sensory block and motor block were significantly increased as the dose of clonidine increased and recue analgesia also decreased. These results were in comparision with other studies [7, 8, 14].

Clonidine affects blood pressure in a complex fashion after neuraxial or systemic administration. It produces hypotension by activation of postsynaptic alpha 2 adrenoceptors in the brain stem and by directly inhibiting sympathetic presynaptic alpha 2 adrenoceptors neurons in the spinal cord [15]. In a

systemic review, the authors reported a 20% incidence of hypotension in controls and 31.3% incidence (relative risk, 1.81; 95% confidence intervals: 1.44-2.28) in patients receiving clonidine 15-150 μg without evidence of dose responsiveness [16].

Sedation score were increased as the dose of clonidine is increased. Markedly increased sedation scores were observed by with higher doses clonidine [17]. Kothari *et al*. also found 35%–45% patients drowsy by addition of 50 μg of clonidine to bupivacaine [18]. Clonidine is reported to cause a significant decrease in power of theta, α, and β bands of the electroencephalography. This hypnotic response may be mediated through locus coeruleus where α_2 adrenergic receptors are abundant.

CONCLUSION

The mean time of onset of sensory block and motor block were comparable between two groups, but Duration of sensory block and motor block were significantly increased as the dose of clonidine increased and recue analgesia also decreased. Hence addition of intrathecal clonidine 50-75μg to small dose bupivacaine increased the spread, duration of analgesia, and produced effective spinal anesthesia with stable hemodynamics.

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