A COMPARATIVE EVALUATION OF INTRAVENOUS DEXMEDETOMIDINE AND CLONIDINE AS PREMEDICATION FOR PROLONGATION OF BUPIVACAINE SUBARACHNOID BLOCK FOR LOWER LIMB ORTHOPAEDIC SURGERY

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ABSTRACT: BACKGROUND: Addition of α2 adrenergic agonists with local anaesthetics in bupivacaine spinal anaesthesia prolongs the duration of sensory and motor blockade and postoperative analgesia with minimal haemodynamic alterations.

AIM AND OBJECTIVES: To compare and evaluate the efficacy of intravenous dexmedetomidine and clonidine as premedication on subarachnoid blockade duration, postoperative analgesia, and sedation score in patients undergoing lower limb orthopaedic surgeries in bupivacaine (0.5%) heavy intrathecal block.

MATERIALS AND METHOD: S: We carried out a prospective, randomized, double blind study in which 60 patients of ASA status I or II, scheduled for orthopaedic lower limb surgery under spinal anaesthesia, were randomly allocated into two groups of 30 each group A and group B. Group A received dexmedetomidine 0.5µg/kg IV and group B received clonidine 1µg/kg in 10 ml of normal saline intravenously as premedication over 10 min., before subarachnoid blockade with 3.0 ml of 0.5% hyperbaric bupivacaine. Onset time and regression times of both sensory and motor blockade, haemodynamic parameters were recorded. Duration of postoperative analgesia and sedation score with adverse effects were also recorded.

RESULTS: The sensory block level was higher (T5-T7) and earlier in onset (1.81±1.75min.) in dexmedetomidine group than clonidine with level (T6-T8) and onset (2.56±1.62min.). Dexmedetomidine also increased the onset (3.54±3.07min.) and duration (265.45±41.50min.) of motor block achieved as compared to clonidine. The Ramsay sedation score was also greater in dexmedetomidine group than clonidine group (P<0.0001).

CONCLUSION: Single dose of premedication with intravenous dexmedetomidine is better than intravenous clonidine during bupivacaine spinal anaesthesia in orthopaedic lower limb surgeries for prolongation of sensory and motor blockade.

KEYWORDS: Dexmedetomidine, Clonidine, Intravenous, Premedication, Spinal anaesthesia.

INTRODUCTION: Spinal anaesthesia is the most commonly used anaesthetic technique for lower limb orthopaedic surgeries. It is considered a safer and more effective alternative to general anaesthesia.[1] Additional medications are frequently added to improve the quality and extend the duration of subarachnoid block.[2] Various previous studies suggest that clonidine and dexmedetomidine accelerate the onset, prolong the duration and improve the quality of neural blockade.

Clonidine, a selective partial α2 adrenergic agonist, is being extensively evaluated as an adjunct to intrathecal local anaesthetics and has proven to be a potent analgesic free of opioid related side effects.[3,4]
On the other hand dexmedetomidine\(^5\) is a highly selective \(\alpha_2\) adrenergic agonist which is gaining popularity nowadays. As compared to clonidine, it is 7-10 times more selective for \(\alpha_2\) receptors, has a shorter duration of action and is a better hypnotic, sedative and analgesic. It is used for general anaesthesia, post-operative analgesia and intrathecal spinal anaesthesia without any respiratory depression. It decreases sympathetic tone, attenuates the stress response to anaesthesia and surgery with mild cardio-vascular side effects.

The purpose of this study is to compare and observe prolongation of intrathecal spinal anaesthesia with intravenous dexmedetomidine and clonidine for assessment of cardio-vascular stability, level of sedation, postoperative analgesia using hyperbaric bupivacaine (0.5%) for intrathecal spinal anaesthesia.

**MATERIAL AND METHODS:** The study was undertaken in Department of Anaesthesia, MLB Medical College, Jhansi. After approval from ethical committee, written and informed consent was obtained from all patients. 60 patients belonging to ASA I & II, male & female adults between ages 20-50 years scheduled for various elective lower limb surgeries under subarachnoid block were included in study population.

**EXCLUSION CRITERIA:** Patients with contraindications to spinal anesthesia, eg., infection at surgical site, preexisting neurological deficit, coagulation defects, hypersensitivity to drug used, cardiorespiratory, neurological, hepatic and renal diseases, diabetes and patient refusal were excluded. The study was a prospective, randomized double blind clinical comparison study. 60 patients were randomly allocated into two groups by computerized generated table.

**Group A:** Patients received 0.5ug/kg dexmedetomidine diluted to 20 ml with normal saline over 10 min before ISA with (0.5%) heavy bupivacaine 3.0ml.

**Group B:** Patients received 1ug/kg clonidine diluted to 20 ml normal saline over 10 min before ISA with (0.5%) heavy bupivacaine 3.0ml.

**PROCEDURE:** After a thorough preanesthetic evaluation patients were advised to take 0.5mg alprazolam night before surgery and were kept nil per oral overnight.

On the day of surgery patients were shifted to OT after which routine noninvasive monitors were applied and basal parameters were recorded. An intravenous line was secured and preloading was done with 500 ml of Ringer lactate solution.

Premedication was done in group A patients by intravenous dexmedetomidine 0.5ug/kg diluted to 20ml over a period of 10min. while in group B intravenous clonidine 1ug/kg diluted to 20ml was given over a period of 10min.

Patients were kept in sitting position and lumbar puncture was performed at L3-L4 level by Quincke type point 25 gauge spinal needle. 15 mg (3.0 ml) hyperbaric bupivacaine was administered intrathecally and patient was turned supine. All patients received oxygen 4L/min via venti mask throughout the procedure.

Sensory blockade was assessed by pin prick method in midaxillary line, after which motor block was assessed using a modified Bromage scale.\(^6\) (Grade 0-No paralysis, 1- Unable to raise
extended leg, 2-Unable to flex knee, 3-Unable to flex ankle). Then the patients were put into the required surgical position.

Sensory and motor block was assessed every 2,5,10 min and thereafter 15 min during the surgery and postoperatively. Onset times of both sensory and motor blockade, highest dermatomal level of sensory blockade, recovery time for both were assessed and recorded. Recovery time for the sensory blockade was defined as two dermatomal regression of anesthesia from the maximal level while total duration of motor block was the time to return to grade 0 on the modified Bromage scale.

Post-operative pain was assessed by using VAS scale.\[7\] (VAS 0- No pain, 10 - worst possible pain), at 4, 6, 8, 10 and 12 hour. Patients with a VAS score of 3 or > received injection diclofenac intravenous 75mg. Ramsay sedation score (1. Anxious or agitated 2. Cooperative & tranquil 3. Drowsy but responsive to command. 4. Asleep and no response) was used to assess the sedation, it was re-evaluated every 10 min. after administration of block upto 4 hours and every 30 minutes thereafter.

Vital parameters e.g., Heart rate, Mean arterial pressure, Respiratory rate (RR) & Oxygen saturation (SP02) were recorded before premedication 10 min. before SAB, after SAB, and at 3, 10, 20, 30, 40, 50 min and thereafter hourly till 4 hours.

Hypotension (i.e., a decrease in MAP below 20% baseline or systolic blood pressure <90mmHg was treated with incremental doses of ephedrine 7.5mg IV, bradycardia (HR<50 beats/min) was treated with atropine 0.6 mg IV.

**STATISTICAL ANALYSIS:** All parametric data are presented as mean±SD and non-parametric data were tabulated. All parametric data were statistically analysed using student and non-parametric data analysed using chi-square and fisher test as appropriate. P value <0.05 was considered significant & <0.0001 was considered highly significant.

**RESULTS:** Spinal anaesthesia was successfully administered in 60 patients. The demographic data is presented in Table-1, age, sex, height and duration of surgery was comparable among the two groups.

Table-2 shows onset of sensory block was significantly earlier (P value <0.05) in group A (1.81±1.75min) than in group B (2.56±1.62min). The sensory level achieved is higher in group A (T5–T7) than in group B (T6–T8). The time required for two segment regression is significantly larger in group A (121.45±25.74 min) than in group B (87.38±15.94min). Total duration of sensory block was prolonged in group A (234.34±47.82min) than group B (141.66±30.20 min) which was highly significant (p<0.0001).

Table-3 shows mean time for onset of motor block in group A was 3.54±3.07 min and 4.64±2.91min. in group B i.e. it was faster in group A than group B. The duration of motor block was 265.45±41.50min in group A and in group B it was 223.12±26.43 min which was highly significant (p <0.0001).

In Table-4 there was a statistically significant (p<0.05) decrease in heart rate in group A 10 min. after premedication. Following SAB the trend continued for 60 min. This was not observed in group B. IV atropine 0.6mg was administered in 3 patients in group as compared to none in group B.

In Table-5 there was no significant difference in mean arterial pressure in 2 groups before premedication but in both groups there was a significantly lower MAP 10 min. after premedication. (P<0.05).

Preoperative MAP was above 80mmHg in both the groups indicating haemodynamic stability of two drugs in recommended doses.
In Table-6 mean sedation score was higher 16 in group A as compared to 3 is group B (P<0.0001).
Nausea/vomiting, bradycardia, hypotension were not significant among the groups.
Side effects e.g., nausea, vomiting, bradycardia, hypotension were not seen significantly among the two groups.
Mean sedation score was highly significantly (P<0.0001) in group A (16) than in group B (3).

**DISCUSSION:** Both of the adjuvant drugs dexmedetomidine and clonidine have been used by various routes with local anesthetics. Dexmedetomidine\(^8,^9\) acts on \(\alpha_2\) adrenergic receptors in a \(\alpha_2:\alpha_1\) binding ratio of 1620:1 of dexmedetomidine compared to 220: 1 for clonidine.

The analgesic effect of these drugs is at both spinal and supraspinal levels. The locus ceruleus and dorsal raphe nucleus are the important central neural areas where these drugs act to produce analgesia and sedation. Due to supraspinal action there is prolongation of subarachnoid blockade when these adjuvants are administered intravenously.

We selected a dose of 0.5 \(\mu\)g/kg of dexmedetomidine as premedication intravenously over a period of 10 min. in our study as higher doses upto 10\(\mu\)g/kg were associated with significant degree of haemodynamic derangements like bradycardia and hypotension.

Bajwa\(^{10}\) et al and Konacki\(^{11}\) et al elucidated that clonidine when used in doses of 0.1\(\mu\)g/kg produced minimal haemodynamic changes.

Onset time of sensory and motor block was prolonged by both the drugs and duration was prolonged as well. Similar results were observed by Kaya FN et al\(^{12}\) and Kabachi\(^{13}\) et al.

In our study two segment regression time was significantly longer in group A than in group B. This can be explained on the basis of mechanism of action of dexmedetomidine in being more selective (8-10 times) to \(\alpha_2\) adrenergic receptors.

However the duration of motor block was significantly higher in dexmedetomidine group than clonidine group.

Jaakola\(^{14}\) ML et al demonstrated the action of dexmedetomidine on \(\alpha_2\) receptors, the mechanism of motor block produced by \(\alpha_2\) against is unclear but there is evidence that clonidine inhibits impulse conduction in large myelinated A\(\alpha\) fibres directly. The 50% effective concentration (EC\(50\)) measured to produce block in motor fibres is 4 folds of block produced in small unmyelinated C fibres. Similar mechanism explains the prolongation of sensory & motor block in dexmedetomidine group.

The haemodynamic parameters both HR and MAP were stable throughout the perioperative period, and the fall in heart rate & MAP was less than 20% from the baseline among the group and the adverse effects like bradycardia and hypotension were more in dexmedetomidine group but not significant statistically. These side effects can be attributed to decrease in central sympathetic outflow. The sedation score was significantly higher in dexmedetomidine group and it differs from clonidine and other sedatives as the patient remains cooperative and arousable. Hall J.E et al\(^{15}\) reported that dexmedetomidine group produced minimal to none respiratory depression which has also been validated by results of our study.

**CONCLUSION:** Single dose of premedication with intravenous dexmedetomidine resulted in early onset of sensory & motor block in bupivacaine heavy (0.5%) spinal anaesthesia for lower limb orthopaedic surgeries with prolonged duration of analgesia post-operatively and stable...
haemodynamics variables. Thus establishing dexmedetomedine as an effective adjuvant than clonidine for bupivacaine subarachnoid blockade.

| Variables                      | Group A (n=30) | Group B (n=30) | P Value |
|--------------------------------|----------------|----------------|---------|
| Age (Years)                    | 39.34±7.92     | 40.56±10.8     |         |
| Sex (M:F)                      | 20:10          | 18:12          |         |
| Weight (kg)                    | 64.25±5.72     | 61.64±8.49     |         |
| Height (cm)                    | 165.81±11.2    | 161.84±6.40    |         |
| Duration of Surgery (min)      | 118.32±20.71   | 120.00±16.24   |         |

Table 1: Demographic Profile

| Variables                               | Group A (n=30) | Group B (n=30) | P Value |
|-----------------------------------------|----------------|----------------|---------|
| Onset of Sensory Block (min)            | 1.81±1.75      | 2.56±1.62      | <0.05   |
| Highest sensory level achieved (Segments)| T5-T7          | T6-T8          |         |
| Two segment regression of sensory block (min) | 121.45±5.74    | 87.38±15.94    | <0.05   |
| Total duration of block in (min)        | 234.34±47.82   | 141.66±30.20   | <0.0001 |

Table 2: Comparison of sensory & motor block

| Variables                               | Group A (n=30) | Group B (n=30) | P Value |
|-----------------------------------------|----------------|----------------|---------|
| Onset of Motor Block (min)              | 3.54±3.07      | 4.64±2.91      | >0.05   |
| Duration of motor block (min)           | 2.65±41.5      | 223.12±26.43   | <0.001  |

Table 3: Comparison of motor block

| Variables                               | Dexmedetonidine Group A (H. R./M) | Clonidine Group B (H. R./M) |
|-----------------------------------------|----------------------------------|-----------------------------|
| Before Premedication                    | 78                               | 88                          |
| After Premedication                     | 68                               | 90                          |
| Before Spinal                           | 66                               | 90                          |
| After Spinal                            | 70                               | 86                          |
| 3 Min                                   | 72                               | 84                          |
| 10 Min                                  | 68                               | 86                          |
| 20 Min                                  | 66                               | 85                          |
| 30 Min                                  | 64                               | 89                          |
| 40 Min                                  | 68                               | 80                          |
| 50Min                                   | 68                               | 78                          |
| 1 hr                                    | 70                               | 76                          |
| 1.5 hr                                  | 72                               | 75                          |
| 2 hr                                    | 76                               | 76                          |
| 3 hr                                    | 78                               | 78                          |
| 4 hr                                    | 82                               | 84                          |

Table 4: Heart rate (min.)
### Table 5: Mean Arterial Pressure (MAP) in mmHg

| Variables | Group A | Group B |
|-----------|---------|---------|
| Before Premedication | 100 | 102 |
| After Premedication | 84 | 89 |
| Before Spinal | 86 | 88 |
| After Spinal | 84 | 88 |
| 3 Min | 82 | 87 |
| 10 Min | 80 | 84 |
| 20 Min | 84 | 89 |
| 30 Min | 86 | 84 |
| 40 Min | 86 | 80 |
| 50 Min | 88 | 85 |
| 1 hr | 84 | 87 |
| 1.5 hr | 84 | 90 |
| 2 hr | 86 | 92 |
| 3 hr | 88 | 97 |
| 4 hr | 88 | 105 |

### Table 6: Adverse effects and sedation score

| Variables | Group A (n=30) | Group B (n=30) |
|-----------|----------------|----------------|
| Nausea/Vomiting | 1 | 1 |
| Bradycardia | 6 | 2 |
| Hypotension | 4 | 2 |
| Sedation Score (>3) | 16 | 5 |
Fig. 1: Comparison of heart rate (per minute) in Group A and Group B covering the pre, intra, and post-operative period

Fig. 2: Comparison of Mean Arterial Pressure (mm Hg) in Group A and Group B covering the pre, intra and post-operative period
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