

## Effect of intravenous dexmedetomidine on duration of spinal anaesthesia with hyperbaric bupivacaine - A comparative study

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### Abstract

**Introduction and Objectives:** Sub Arachnoid Block is one of the commonly used anaesthetic technique for lower limb surgeries, the duration and quality of block can be prolonged using several adjuvants. The objective of this study was to assess the quality, duration of block and time required for supplemental analgesia in patients undergoing lower limb surgeries.

**Materials and Methods:** Fifty ASA class I and II patients scheduled for lower limb surgeries, received Subarachnoid block with 15 mg hyperbaric bupivacaine or 15 mg hyperbaric bupivacaine plus intravenous dexmedetomidine 0.5microgm/kg body weight in 10ml saline as bolus dose prior to Sub Arachnoid Block. Outcome measures included onset and duration of sensory and motor block and duration of analgesia.

**Results:** Duration of sensory block ( $p=0.0001$ ), duration of motor block ( $p=0.0001$ ) and duration of analgesia ( $p=0.0001$ ) was significantly longer in dexmedetomidine group than the patients who received Subarachnoid block with 15 mg Bupivacaine alone. A significant decrease in heart rate, systolic blood pressure and mean arterial pressure was noted in dexmedetomidine group.

**Conclusion:** Intravenous dexmedetomidine in a single dose of 0.5µg/kg, administered over a period of 10 minutes prior to sub arachnoid block, prolongs the duration of sensory and motor blockade with arousable sedation, without any respiratory depression.

**Keywords:** Intravenous, Dexmedetomidine, Postoperative, Pain, Spinal anaesthesia, Analgesia, Sensory, Motor, Blockade.

### Introduction

Regional anaesthesia and analgesia has the potential to provide excellent operating conditions and prolonged postoperative pain relief. It is also known to reduce postoperative morbidity and mortality by its positive influence like improved blood flow and optimum tissue functionality and improved recovery, thereby leading to its widespread use. Among all the regional techniques, sub arachnoid block is the most commonly employed technique for lower abdominal and lower limb surgeries as it is very economical and easy to administer. Sub arachnoid block has many advantages such as easy to perform, rapid onset of action, less failure rate, cost-effectiveness, superior level of blockade and good muscle relaxation.<sup>1</sup> Hyperbaric bupivacaine is commonly used as local anaesthetic for administering sub arachnoid block. Subarachnoid block using local anaesthetic alone is associated with relatively short duration of action and hence early analgesic intervention is needed in the postoperative period. To improve the quality and duration of blockade, various adjuvants like opioids, ketamine, midazolam, clonidine, dexmedetomidine etc. have been used either intravenously and intrathecally.<sup>2</sup> But these adjuvants especially opioids are associated with side effects like pruritus, respiratory depression, urinary retention, postoperative nausea and vomiting. Hence alpha 2 agonists have recently been used as adjuvants to potentiate the effects of local anaesthesia without respiratory depression.

In our study, we have used Dexmedetomidine which is a selective  $\alpha_2$  adreno receptor agonist which has both analgesic and sedative properties when used as an adjuvant in regional

anaesthesia. In this study we have assessed the quality, duration of block and time required for supplemental analgesia with single dose of 0.5µg/kg of dexmedetomidine intravenously, as not many studies have been done using the same. Intravenous route is easy to administer and the single dose is associated with less side effects. The aim of this study was to evaluate the onset and duration of sensory and motor block, hemodynamic effect, postoperative analgesia, and adverse effects of dexmedetomidine given intravenously, with hyperbaric 0.5% bupivacaine given intrathecally.

### Materials and Methods

After the approval of the Hospital ethical Committee and written informed consent were obtained, the study was conducted on 60 patients with ASA physical status 1 and 2, of either sex, 18– 60 years of age, who were posted for elective lower limb surgeries under spinal anaesthesia. Patients having local infection at the site of block, severe hypovolemia, raised intracranial tension, deformities of the spine, bleeding and clotting disorders, allergy to local anaesthetics, patients on antiplatelet or anticoagulant drugs, patients with history of chronic headache, pregnant women, patients with pre-existing hepatic and renal diseases were excluded from the study.

Patients were randomly allocated into two groups by computer generated randomized tables. Group 1 received 15 mg of hyperbaric bupivacaine and group 2 received 15 mg hyperbaric bupivacaine plus intravenous dexmedetomidine 0.5 microgram/kg in 10ml normal saline as bolus dose, ten minutes prior to Sub Arachnoid block. After pre anaesthetic

evaluation, relevant investigations including haemoglobin estimation, total count, differential count, platelet count, liver function tests, renal function tests, serum electrolytes, coagulation profile, random blood sugar, electrocardiogram (ECG), chest x-ray, and urine routine and microscopy were done.

All patients were pre medicated with Tab. Alprazolam 0.25 mg and Tab. Pantoprazole 40 mg orally at 10 PM on the night before surgery. Patients, surgeons, anaesthesiologists, nurses and the investigator collecting the data were blinded as to which drug was being administered. Intraoperative monitoring included ECG, non-invasive blood pressure (NIBP) and pulse oximetry.

### Methodology

After obtaining Ethical committee approval subjects who were ASA I & 2 posted for lower limb surgeries were given sub arachnoid block by the qualified anaesthetist. He/she was also involved in giving Intra venous Dexmedetomidine 0.5 µg /kg body weight in 10 ml Normal saline as bolus injection over 10 minutes. This study was conducted on 50 adult patients aged between 18-50 years undergoing elective lower limb surgeries under spinal anaesthesia. Patients who were given sub arachnoid blockade alone or in combination with intravenous dexmedetomidine were studied till a total of 25 cases were obtained in each group. The patients were allocated randomly into two groups (control group and dexmed group) using a computer generated randomization table.

On admission a thorough pre-operative evaluation was done which included a detailed history, general physical examination, systemic examination and laboratory investigations. Then a written informed consent was taken after explaining the procedure, advantages and consequences to the patient in their own language.

### Procedure

Patient were premedicated with alprazolam 0.5 mg the day before and on the morning of surgery. Basal vital parameters like heart rate, blood pressure, SpO<sub>2</sub> were recorded. A bolus dose of 0.5 µg /kg body weight Dexmedetomidine in 10ml Normal Saline was given intravenously over 10 minutes before intrathecal deposition of bupivacaine in Group 2. Under aseptic conditions with patient in sitting position using a 25 gauge spinal needle at L3- L4 or L4-L5 interspace 3ml of 0.5% heavy bupivacaine (15mg) drug was deposited intrathecally after confirmation of free flow of CSF. Patients were positioned supine immediately after the administration of intrathecal agents.

Intra operatively, onset of sensory and motor blockade, maximum level of sensory blockade attained and the time for the same was recorded. Sedation using five point scale was noted. HR, NIBP, ECG and SpO<sub>2</sub> was recorded every 2 minutes for the first 20 minutes and every 5 minutes till the end of surgery and every 30 minutes thereafter. Also duration of analgesia, sensory and motor blockade and any adverse events like nausea, vomiting, shivering, postdural puncture headache, bradycardia, hypotension etc. was noted and

treated accordingly.

Duration of analgesia was recorded by using visual analogue pain score (VAS) between 0 and 10 (0 = no pain, 10 = most severe pain). Rescue analgesic (IM Tramadol 2mg/kg) was given when the patients began to experience uncomfortable pain (VAS ≥ 4).

Hemodynamic changes were also monitored at constant intervals. For the purpose of the study, heart rate less than 40 beats per min was considered as bradycardia and, if any, were treated with inj. atropine 0.6 mg IV. Systolic BP of less than 90 mmHg or fall in more than 30% of baseline value was considered as hypotension and was corrected with IV fluids and incremental IV doses of ephedrine 6 mg as required. Postoperatively sensory block, motor block and VAS scores were recorded in the post-anaesthetic care unit every 10 minutes until VAS 4 or more were attained.

### Statistical Analysis

All data was collected and coded, and entered in Microsoft Excel sheet and analysed using appropriate statistical software. The onset and duration of sensory and motor blockade was measured in terms of mean deviation +/- standard deviation. The groups were compared using independent t-test. A p value of ≤0.05 was considered significant. Analysis was done using SPSS 15.0 software.

### Results

Table 1, 2, 3 and 4 show the demographic data. Both groups were statistically comparable with respect to age, gender, ASA PS and body weight, height and BMI. The duration of surgery in control group was 104 minutes and in dexmed group was 106 mins. There was no significant difference in the duration of surgery between the groups (P = 0.640). There was significant decrease in heart rate in dexmed group compared to control group (with p value of 0.0001). There was also significant decrease in systolic (P = 0.0001) and mean arterial pressure (P = 0.0001), without a significant change in the diastolic blood pressure. (P = 0.06). The significant reduction in heart rate and blood pressure was evident after 15 minutes of completing the dexmedetomidine infusion. There was no significant difference in the onset of sensory (P = 0.128) and motor blockade (P = 1) in both groups. There was also no significant difference with the highest level of sensory block attained between the two groups (P = 1). However the mean duration of sensory block in control group was 167.08 +/- 7 minutes and that of the dexmed group was 185.4 +/- 7.1 minutes and the motor block in control group was 164.4 +/- 6 minutes and 192.00 +/- 7.9 minutes. The mean duration of analgesia (Table 5) in control group was 211.2 +/- 8.3 minutes and that of dexmed group was 239.560 +/- 5.9 minutes. There was significant prolongation of sensory and motor blockade and analgesia in dexmed group compared to control group with P value of 0.001.

**Table 1: Age distribution of patients in both groups**

Age in years	Group		Total
	Control	Dexmed	
≤20	2	1	3
21-30	8	6	14
31-40	3	7	10
41-50	6	5	11
51-60	6	6	12
Total	25	25	50
Mean ± SD	38.52±12.527	38.76±11.734	

**Table 2: Gender distribution of patients in both groups**

Sex	Group		Total
	Control	Dexmed	
Female	4	11	15
Male	21	14	35
Total	25	25	50

**Table 3: ASA physical status distribution in both groups**

ASA	Group		Total
	Control	Dexmed	
1	15	16	31
2	10	9	19
Total	25	25	50

**Table 4: Weight, Height and BMI distribution in both groups**

	Control (mean±SD)	Dexmed (mean±SD)	p value
Height (cm)	171.12±5.442	165.40±8.362	0.126
Weight (kg)	69.72±8.409	66.60±9.014	0.212
BMI (kg/m <sup>2</sup> )	23.77±2.41	24.31±2.61	0.198

**Table 5: Comparison of duration of sensory blockade, motor blockade and analgesia between two groups**

	Control (mean±SD)	Dexmed (mean±SD)	p value
Duration of sensory block	167.08±7.059	185.40±7.147	0.0001
Duration of motor block	164.400±6.0069	192.000±7.9057	0.0001
Duration of analgesia	211.200±8.3267	239.560±5.9166	0.0001

### Complications

Hypotension occurred in both groups but the difference was not significant. 5 patients in dexmed group developed hypotension compared to 4 patients in control group. 2 patients in dexmed group were given Atropine injection following bradycardia compared to 0 patients in control group. Three patients in both groups had nausea. There were no complications like vomiting, shivering, itching, pruritus and respiratory depression in patients of either group. Sedation among patients were more in dexmed group and was statistically significant ( $p=0.0001$ ). There was also statistically significant difference among both groups with respect to intra operative shivering which was more common in control group ( $p=0.0001$ ).

### Discussion

Different drugs have been used as adjuvants to local anesthetic drugs in order to prolong the duration of spinal anesthesia. Dexmedetomidine, an  $\alpha_2$  agonist produces sedation and anxiolysis by binding to  $\alpha_2$  receptors in the

Locus Ceruleus, which diminishes the release of norepinephrine and inhibits sympathetic activity, thus decreasing heart rate and blood pressure. It produces analgesia by binding to adrenoreceptors in the spinal cord. Dexmedetomidine, when used as an adjuvant either through intrathecal or intravenous route, has shown significant effect on onset and duration of spinal anesthesia. Side effects of dexmedetomidine, such as hypotension and bradycardia, are dose dependent. Loading dose given as an infusion over 10 minutes decreases the incidence of these side effects.

Our study compared the efficacy of intravenous dexmedetomidine as adjuvant with bupivacaine for spinal anesthesia against spinal anesthesia using bupivacaine alone. In the present study, we assessed 50 patients aged 18 to 50 years belonging to ASA class I and II posted for lower limb surgeries under spinal anesthesia. 25 patients fulfilling the inclusion criteria received dexmedetomidine bolus 0.5  $\mu\text{g}/\text{kg}/\text{hr}$  injected over 10 minutes intravenously prior to spinal anesthesia and remaining 25 patients did not receive dexmedetomidine bolus dose prior to spinal anesthesia. The

outcomes assessed were onset of motor and sensory blockade, highest level of block attained, duration of sensory and motor blockade, duration of analgesia, hemodynamic changes and complications. Both groups were comparable with respect to demographic data, duration of the surgery and ASA grading. The results of our study show that intravenous dexmedetomidine bolus injection of 0.5mcg/kg over 10 minutes followed by sub arachnoid block with hyperbaric bupivacaine 15mg significantly prolonged both sensory and motor block compared with spinal anaesthesia with bupivacaine alone.

Sule Akin et al<sup>3</sup> studied the effect of intra venous dexmedetomidine as adjuvant to epidural analgesia in elderly intensive care patients. Patients in the treatment group received 0.6 µg/kg loading dose over 30 minutes followed by continuous infusion at 0.2 µg/kg/hr. They observed that Visual analogue scale scores were significantly lower in dexmed group compared with control group with better hemodynamic stability. Mi Hyeon Lee et al<sup>4</sup> conducted a study comparing two bolus doses (0.5 µg/kg and 1 µg/kg) of intravenous dexmedetomidine as adjuvant to spinal anaesthesia against control group which receives only spinal anaesthesia. They found that both the bolus doses of intravenous dexmedetomidine prolonged the duration of spinal anaesthesia without any statistically significant differences in the duration of spinal anaesthesia between the two dexmedetomidine bolus groups. Chilkunda N et al<sup>5</sup> conducted a study on effects of intravenous dexmedetomidine on hyperbaric bupivacaine spinal anaesthesia using two groups with one group receiving dexmedetomidine infusion of 1 µg/kg bolus dose followed by 0.5 µg/kg/hr infusion and control group receiving normal saline infusion. They found that intra venous dexmedetomidine prolongs the duration of sensory and motor blockade of bupivacaine spinal anaesthesia with decrease in heart rate and mean/systolic/diastolic blood pressures with good sedation and less post-operative shivering. Hence, we have chosen to use lower dose of dexmedetomidine i.e., 0.5mcg/kg bolus dose as adjuvant to 0.5% hyperbaric Bupivacaine.

The mean age of patients in control group was 38.52±12.527 years and in dexmed group was 38.76±11.734 years. Maximum number of patients in either group belonged to the age group of 51- 60 years. The mean height of patients in our study was 171.12±5.442 cm and 165.40±8.362 cm in control group and dexmed group respectively. The mean weight of patients was 69.72±8.409 kg in control group and 66.60±9.014 kg in dexmed group. There was no statistically significant difference between the two groups with regard to their age, height and weight. Sule Akin et al<sup>3</sup> studied the effect of intra venous dexmedetomidine as adjuvant to epidural analgesia in elderly intensive care patients with mean age of 75.66±3.86years. Chilkunda N et al,<sup>5</sup> Deepika Shukla et al<sup>6</sup> and SS Harsoor et al<sup>7</sup> conducted study on the effects of intravenous dexmedetomidine on spinal block with bupivacaine on subjects with similar age distribution and anthropometric measurements comparable to our study.

Time of onset of sensory block and motor block was comparably similar in both the groups. These findings were in concordance with the results of Faraj W Abdullah et al<sup>8</sup> and Agarwal S et al<sup>9</sup> who observed no difference in the onset time in patients receiving dexmedetomidine infusion as adjuvant to spinal anaesthesia and spinal anaesthesia with only bupivacaine. Mi Hyeon Lee et al<sup>4</sup> also had observed that there was no significant difference in the onset of sensory and motor block between dexmedetomidine group and control group.

In the present study, majority of the patients in both the groups had T6 level of sensory block and there was no significant difference between the groups. This was similar to the findings made by Myoung Hun Kim et al<sup>10</sup> where they observed no significant difference in the level of block attained. But a similar study done by Mi Hyeon Lee et al<sup>4</sup> and SS Harsoor et al<sup>7</sup> showed that lower level of block was attained with dexmedetomidine possibly due to lesser dose of bupivacaine given intrathecally which was 12mg and 12.5mg of 0.5% hyperbaric bupivacaine respectively. Dose of bupivacaine which we used for the present study was 15mg of 0.5% hyperbaric bupivacaine.

Mi Hyeon Lee et al<sup>4</sup> compared the doses of dexmedetomidine 0.5µg/kg, 1µg/kg with bupivacaine and found the effect to be dose dependent on the onset and regression of sensory and motor block. The intravenous 0.5µg/kg bolus dose of dexmedetomidine used in our study has shown prolonged duration of sensory block, which is in concordance with the results observed by Faraj W Abdullah et al<sup>8</sup> while comparing dexmedetomidine group and control group. Similar study done by Murat Tetkin et al<sup>11</sup> and Velayudha Sidda et al<sup>12</sup> showed prolongation of sensory block with dexmedetomidine infusion intravenously. Intra venous dexmedetomidine when combined with spinal bupivacaine prolongs the sensory block. The mechanism of intravenous dexmedetomidine on prolonging sensory blockade of spinal anaesthesia remains unclear; however, at supra spinal level α<sub>2</sub> receptors are present in high concentration at the locus ceruleus in the brain stem. Medullo-spinal nor-adrenergic pathway originates from this region and it is an important modulator of nociceptive neurotransmission. Dexmedetomidine acting on these receptors at locus ceruleus results in prolongation of sensory blockade.<sup>13</sup>

Our present study also showed that there was significant prolongation of motor block with dexmedetomidine infusion group compared to only spinal anaesthesia group. This was comparable with the results obtained by Faraj W Abdullah et al<sup>8</sup> and Murat Tekin et al.<sup>11</sup> In a similar study conducted by Velayudha Sidda et al,<sup>12</sup> dexmedetomidine was found to have a significantly prolonged duration of motor block compared to control group. Dexmedetomidine produces a greater degree of differential blockade by preferentially blocking the myelinated Aα fibers involved in sensory conduction over the unmyelinated C fibers involved in motor conduction.<sup>13</sup>

Mi Hyeon Lee et al<sup>4</sup> and Faraj W Abdullah et al<sup>8</sup> had showed that dexmedetomidine infusion significantly prolonged the duration of analgesia. The results of the present

study concurs with the findings of the above authors as we had a statistically significant prolonged duration of analgesia. SS Harsoor et al,<sup>7</sup> Velayudha Sidda et al<sup>12</sup> also demonstrated that dexmedetomidine infusion as adjuvant to spinal anesthesia prolonged the duration of analgesia compared to sole spinal anesthesia. Stimulation of the  $\alpha_{2C}$  and  $\alpha_{2A}$  receptors in the dorsal horn, reduces the release of nociceptive transmitters, substance P and glutamate, the analgesic effect is prolonged also due to hyperpolarization of the unmyelinated C fibres (sensory).<sup>13</sup>

In our study we found that intra operative systolic blood pressure and mean arterial pressure were lower in the dexmedetomidine group than in the control group which were statistically significant. This finding was in concordance with the results obtained by Mi Hyeon Lee et al<sup>4</sup> and Chilkunda et al<sup>5</sup> where they demonstrated significant difference in blood pressure variation between the two groups. But this finding was contradictory to studies done by Harsoor et al<sup>7</sup> and Murat Tekin et al<sup>11</sup> where the difference in blood pressure were not statistically significant. This present study showed that there was a significant decrease in the heart rate in dexmed group when compared to control group. Most of the studies have noted bradycardia as a prominent side effect with incidence varying from 30% to 40%, sometimes requiring treatment with atropine. But in our study, the incidence of bradycardia was low owing to a lower bolus dose used and augers well with observations of Harsoor et al<sup>7</sup> and Faraj W Abdullah et al.<sup>8</sup>

Our present study showed that dexmedetomidine group has less intra operative shivering and more sedation compared to control group. These findings were in concordance with the results of Murat Tekin et al.<sup>11</sup> Studies by Chilkunda et al<sup>5</sup> and Myoung et al<sup>10</sup> showed no significant difference in intra operative shivering between dexmed and control group. IV dexmedetomidine not only increases the duration of local anaesthetic, but also provides sedation.

## Conclusion

Intravenous dexmedetomidine as a bolus dose of 0.5microgram/kg when used as an adjuvant to spinal anaesthesia prolongs sensory and motor blockade. It provides excellent postoperative pain relief. It causes significant decrease in heart rate and blood pressure. The frequency of complications like bradycardia, respiratory depression and hypotension are less when intravenous dexmedetomidine is given as bolus dose of 0.5 microgram/kg over a period of 10 minutes.

**Conflict of Interest:** None.

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