

## Intravenous Versus Epidural Dexmedetomidine: Comparison of Effect on Prolongation of Analgesia after Subarachnoid Block with Bupivacaine in lower limb Surgery

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### How to cite this article:

Nirmala Kumari, Jyoti V Kulkarni, Nidhi Chitravanshi. Intravenous Versus Epidural Dexmedetomidine: Comparison of Effect on Prolongation of Analgesia after Subarachnoid Block with Bupivacaine in lower limb Surgery. Indian J Anesth Analg. 2020;7(4):957-962.

### Abstract

**Introduction:** Subarachnoid block is the most common technique amongst regional anesthesia for lower abdomen and lower limb surgeries. Dexmedetomidine, a new highly selective  $\alpha_2$ -agonist, is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects. In this study we want to compare efficacy of Epidural Dexmedetomidine with Intravenous Dexmedetomidine in subarachnoid block with Inj. Bupivacaine.

**Aims and objectives:** Primary objective of this study is to compare the duration of post-operative analgesia of IV Dexmedetomidine with epidural Dexmedetomidine in subarachnoid block given for lower limb surgeries. Our secondary objective is to compare the onset of sensory blockade, onset of motor blockade, sedation Score and any complications like bradycardia, hypotension in both groups.

**Methodology:** Sixty patients posted for lower limb surgeries were included in this study. In Group I Inj Dexmedetomidine 0.5 ug/kg diluted in 100 ml NS was given as infusion over 15 minutes and Group E received, 100 ml NS as infusion over 15 minutes. Epidural space was identified with Tuohy needle by LOR resistance and 10 ml NS was given epidurally in Group I and 0.5 ug/kg of Inj dexmedetomidine in 9.5 ml of NS was given epidurally in Group E. Subarachnoid block was given by 25G spinal needle in L3-L4 space in sitting position using all aseptic precautions in both the groups with 3.5 ml 0.5% hyperbaric Bupivacaine. Onset of sensory and motor blockade, pulse rate, MAP, sedation score, time for two segment regression and the time when patients request first analgesic were noted and analysed.

**Result:** The mean time of onset of sensory blockade and mean time of onset of motor blockade were comparable between the groups, in Group I onset of sensory blockade was 7.27±2.75 min while in Group E 8.17±2.03 min with P >0.05 while onset of motor blockade was 11.33±3.45 min in Group I and 12.03±2.07 min in Group E with p >0.05. The time taken for two-segment regression was significantly earlier in Group I 157.5 ±22.35 min than in Group E 171.03±13.01 min. with P <0.006. The mean duration of post-operative analgesia was significantly longer in Group E 447.33±41.78 while in Group I 425.5±27.16 min with P <0.02. The mean of RSS (Ramsay sedation score) in Group I was 3±0.12 and in Group E was 2±0.24, the difference was clinically significant with P = 0.036.

**Conclusion:** Administration of Epidural Dexmedetomidine 0.5 ug/kg leads to prolongation of sensory blockade after intrathecal Bupivacaine and prolongs postoperative analgesia than Intravenous Dexmedetomidine.

**Keywords:** Dexmedetomidine; Intravenous; Epidural; Subarachnoid.

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## Introduction

Subarachnoid block is the most common technique amongst regional anesthesia for lower abdomen and lower limb surgeries. Intense anesthesia, good muscle relaxation, less bleeding, good cardiovascular stability, early ambulation, less chances of post-operative respiratory infection and embolization and postoperative analgesia are the advantages of Subarachnoid block. With use of only LA, there is limited post-operative analgesia, so different additives are used along with LA. Dexmedetomidine, a new highly selective  $\alpha_2$ -agonist, is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.<sup>1</sup> The unique analgesic properties have encouraged anesthesiologists to use it perineurally. Previous studies have declared that dexmedetomidine potentiates local anesthetic effect when administered by neuraxial route. We carried out a study with an aim to compare the duration of post-operative analgesia in patients receiving intravenous dexmedetomidine with epidural dexmedetomidine in patients operated under subarachnoid block for lower limb surgery.

## Objectives

Primary objective of this study is to compare the duration of postoperative analgesia of IV Dexmedetomidine with epidural Dexmedetomidine in subarachnoid block given for lower limb surgeries. Our secondary objective is to compare the onset of sensory blockade, onset of motor blockade, sedation Score and any complications like bradycardia, hypotension in both groups.

## Methodology

It is a prospective, randomized, double blind, comparative study conducted in Government Medical College, Aurangabad. The study was carried out in 60 ASA Gr I and II patients posted for elective lower limb surgeries. Patients were randomly allocated into 2 groups. After detail preoperative evaluation, consent and confirming the NBM status, patients were posted for the surgery. All patients were monitored with continuous ECG, Pulse oximetry, Non-invasive blood pressure. IV line was secured with angiocath no 18G and 0.9% NS 500 ml infusion was given. In Group I Inj Dexmedetomidine 0.5 ug/kg diluted in 100 ml NS was given as infusion over 15 minutes and Group E received, 100 ml NS as infusion over 15 minutes. Epidural space was identified with

Tuohy needle by LOR resistance and 10 ml NS was given epidurally in Group I and 0.5 ug/kg of inj dexmedetomidine in 9.5ml of NS was given epidurally in Group E. Subarachnoid block was given by 25G spinal needle in L3-L4 space in sitting position using all aseptic precautions in both the groups with 3.5 ml 0.5% hyperbaric Bupivacaine.

Immediately after completion of the injection patients were made to lie supine hemodynamic monitoring was done at 5 min interval. Oxygen was administered via face mask (at 4l/min). The onset time of sensory blockade at T10 dermatome was considered as the time of onset of analgesia. Sensory testing was assessed by loss of pinprick sensation to 23G hypodermic needle. Onset of motor blockade was noted and assessed by Modified Bromage criteria. Sedation was assessed by Modified Ramsay Score. NIBP, PR, SpO<sub>2</sub> and continuous ECG were monitored till the end of surgery and thereafter at every 15 min in the 1st post-operative hour followed by every half hourly for next 3 hours. The time when patient requests first analgesic dose was noted and it was considered as duration of postoperative analgesia.

Sedation was assessed by Modified Ramsay Score.

- 1-anxious and agitated
- 2-alert and wide awake
- 3-arousable to verbal command
- 4-arousable to gentle tactile stimulation
- 5-arousable to vigorous shaking 6-unarousable.

## Observations and Results

In our study, the demographic profile of the patients of both the groups are comparable with no significant difference. The age distribution of patients between both the groups are comparable with Mean age in group I was 41.37 years and in group E was 42 years with  $P = 0.741$ . The groups are comparable as per height with mean height of the patients in Group I was 165.87 cms and in Group E 166.33 cms with  $P = 0.298$ , the difference is insignificant. The mean weight of the patients in Group I was  $61.86 \pm 19.19$  kg and  $59.79 \pm 18.38$  kg in Group E, ( $P = 0.0744$ ), the difference is insignificant.

The mean time of onset of sensory blockade and mean time of onset of motor blockade were comparable between the groups, in Group I onset of sensory blockade was  $7.27 \pm 2.75$  min while in Group E  $8.17 \pm 2.03$  min with  $P > 0.05$  while onset of motor blockade was  $11.33 \pm 3.45$  min in Group I and  $12.03 \pm 2.07$  min in Group E with  $p > 0.05$ .

The mean time of onset of sensory blockade were comparable between the groups,  $P > 0.05$  Fig. 1.

The mean time of onset of motor blockade were comparable between the groups,  $P > 0.05$  Fig. 2.

The time taken for two-segment regression was significantly earlier in Group I  $157.5 \pm 22.35$  min than in Group E  $171.03 \pm 13.01$  min. with  $P < 0.006$ . The mean duration of post-operative analgesia was significantly longer in Group E  $447.33 \pm 41.78$  while in Group I  $425.5 \pm 27.16$  min with  $P < 0.02$ .

The time taken for two-segment regression was earlier in Grp I,  $P < 0.006$  Fig. 3.

The mean duration of post-operative analgesia was significantly longer in Grp E,  $P < 0.02$  Fig. 4.

The mean of RSS (Ramsay sedation score) in Group I was  $3 \pm 0.12$  and in Group E was  $2 \pm 0.24$ , the difference was clinically significant with  $P = 0.036$ . Thus, suggesting the sedation due to dexmedetomidine was more than in the intravenous group than in the epidural group.

Repeated measures ANOVA (Green house-Geisser) was used to compare pulse rate (PR) at 17 time points for two different routes namely Intravenous and Epidural. The pulse rate between these two groups was not found to be statistically significant ( $F=0.705$ ,  $df = 4.8$ ,  $p=0.6153$ ). Similarly the same test was applied to compare the mean arterial pressure (MAP) at same 17 different time points. This too was not found to be statistically significant. ( $F=2.247$ ,  $df=4.8$ ,  $p=0.52$ .)

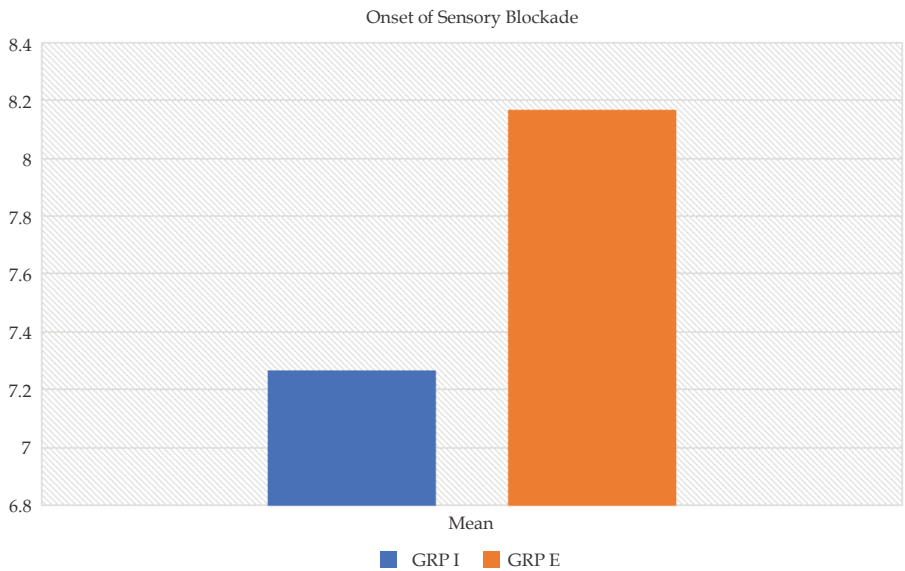


Fig. 1:

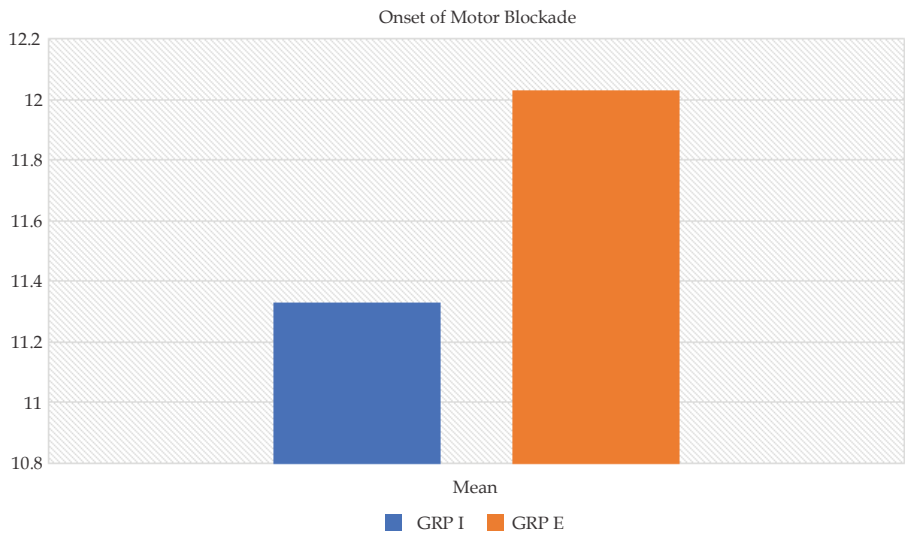


Fig. 2:



Fig. 3:

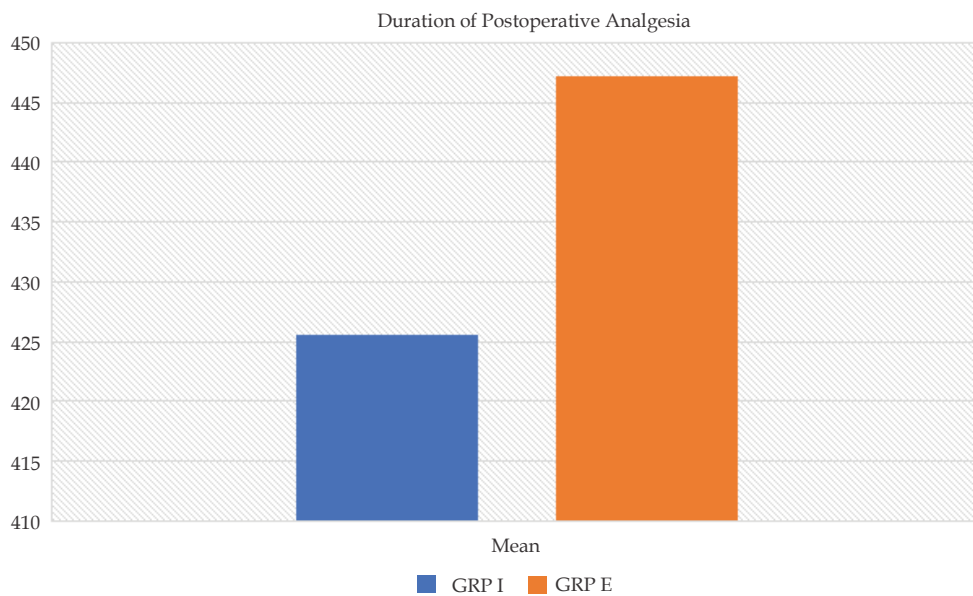


Fig. 4:

### Discussion

This study was conducted to evaluate and compare the effect of epidural Dexmedetomidine with Intravenous Dexmedetomidine for potentiating perioperative analgesia in spinal anesthesia with Bupivacaine in patients undergoing elective lower-limb surgery. The mean time of onset of sensory and motor blockade was comparable in both groups while we found that two segment regression and time of first request of analgesic in group E was significantly prolonged than in group I which indicates epidural Dexmedetomidine prolongs duration of sensory blockade more than

Intravenous Dexmedetomidine. Similar findings were noted in the study conducted by SI Shaikh and et al.,<sup>4</sup> who compared epidural dexmedetomidine (1.5 µg/kg) or clonidine (2 µg/kg) in 10 ml normal saline along with 0.5% isobaric levobupivacaine 15 mg (3 ml) and found that mean time taken for rescue analgesia in Group A (Clonidine) was 363.73 min and that of Group B (Dexmedetomidine) was 456.87 min.

In literature we found comparative study of IV versus Intrathecal Dexmedetomidine but we didn't find any study comparing Intravenous versus Epidural Dexmedetomidine. Ahmed

M.S. Hamed, Sahar M. Talaat<sup>2</sup> reported that durations of sensory and motor blockade and postoperative analgesia were significantly longer in the IT group. Annamalai A, Singh S, Singh A, Mahrous DE<sup>3</sup> compared effect of IV saline with IV Dexmedetomidine 10 minutes prior to spinal anesthesia and IV Dexmedetomidine 10 minutes after spinal anesthesia and concluded that Intravenous dexmedetomidine prolonged spinal bupivacaine sensory blockade in both the groups. Our findings were comparable with these studies which indicates that intravenous or Epidural administration of Dexmedetomidine prolongs postoperative analgesia but it is more with Epidural administration.

Epidural administrations of  $\alpha_2$  agonists lead to anxiolysis, sedation, analgesia, and hypnosis.<sup>4,5</sup> The anesthetic and the analgesic requirement get reduced because of their analgesic properties and augmentation of local anesthetic effects as they cause hyperpolarization of nerve tissues by altering transmembrane potential and ion conductance at locus coeruleus in the brainstem.<sup>4</sup> Dexmedetomidine may exert its effect on sensory and motor block through the supraspinal, spinal, and peripheral action.<sup>6</sup> It acts on both presynaptic and postsynaptic sympathetic nerve terminal and central nervous system, thereby decreasing the sympathetic outflow and norepinephrine release causing sedative, antianxiety, analgesic, sympatholytic, and hemodynamic effects.<sup>7</sup> Even with the evidence of both the supraspinal and peripheral sites of action of dexmedetomidine, the spinal mechanism may be mainly responsible for the analgesic effects.<sup>4,8,9</sup> Epidural dexmedetomidine has greater selectivity for  $\alpha_2$  receptors with greater lipid solubility which might be the reason for early onset of sensory and motor blockade. Reduction of the systemic absorption of the local anesthetic caused by local vasoconstrictor subtypes mediated by the C2 in smooth muscle and venous epidural plexus might be responsible for prolongation of analgesia. All these factors might be responsible for prolonged analgesia we found in epidural Dexmedetomidine group than in Intravenous group.

Intravenous dexmedetomidine may also augment the effect of the intrathecal block. Although the mechanism remains unclear, the supraspinal direct analgesic and the vasoconstrictive effect of dexmedetomidine are likely to be involved. Neurons in the locus coeruleus are connected to the noradrenergic nuclei in the brain stem. The activity of noradrenergic neurons is decreased by agonists acting at  $\alpha_2$ -adrenergic receptors in the

locus coeruleus cell bodies, and therefore exerts a descending inhibitory effect on nociception in the spinal cord.<sup>6,10</sup>

Administration of dexmedetomidine intravenously reduces the release of norepinephrine and inhibits sympathetic activity, thus resulting in decreasing heart rate and blood pressure.<sup>10</sup> As we infuse Dexmedetomidine over a period of 15 min and 500 ml of Normal Saline before administration of spinal anesthesia we didn't observe significant bradycardia or hypotension in both groups.<sup>6</sup> Bradycardia during spinal anesthesia is believed to be secondary to decreased venous return and from the blockade of sympathetic stimulation to the heart that arise from the first four thoracic spinal segments.<sup>11</sup> The hypnotic and supraspinal analgesic effects of dexmedetomidine are mediated by the hyperpolarization of noradrenergic neurons, which suppresses neuronal firing in the locus coeruleus along with inhibition of norepinephrine release and activity in the descending medullospinal noradrenergic pathway. We didn't observed sedation or respiratory depression in both groups.

So we could say that epidural Dexmedetomidine is a better option for providing prolonged analgesia than Intravenous Dexmedetomidine.

## Conclusion

Epidural Dexmedetomidine 0.5 microgram/kg leads to prolongation of sensory blockade after intrathecal Bupivacaine and also prolongs postoperative analgesia than Intravenous Dexmedetomidine. Also it provides good cardiovascular stability without sedation and respiratory depression. We can conclude that Epidural Dexmedetomidine prolongs sensory blockade significantly than Intravenous Dexmedetomidine.

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