

# Effect of supplementation of low dose intravenous dexmedetomidine on characteristics of spinal anaesthesia with hyperbaric bupivacaine

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## ABSTRACT

**Aims:** Intravenous (IV) dexmedetomidine with excellent sedative properties has been shown to reduce analgesic requirements during general anaesthesia. A study was conducted to assess the effects of IV dexmedetomidine on sensory, motor, haemodynamic parameters and sedation during subarachnoid block (SAB). **Methods:** A total of 50 patients undergoing infraumbilical and lower limb surgeries under SAB were selected. Group D received IV dexmedetomidine 0.5 mcg/kg bolus over 10 min prior to SAB, followed by an infusion of 0.5 mcg/kg/h for the duration of the surgery. Group C received similar volume of normal saline infusion. Time for the onset of sensory and motor blockade, cephalad level of analgesia and duration of analgesia were noted. Sedation scores using Ramsay Sedation Score (RSS) and haemodynamic parameters were assessed. **Results:** Demographic parameters, duration and type of surgery were comparable. Onset of sensory block was  $66 \pm 44.14$  s in Group D compared with  $129.6 \pm 102.4$  s in Group C. The time for two segment regression was  $111.52 \pm 30.9$  min in Group D and  $53.6 \pm 18.22$  min in Group C and duration of analgesia was  $222.8 \pm 123.4$  min in Group D and  $138.36 \pm 21.62$  min in Group C. The duration of motor blockade was prolonged in Group D compared with Group C. There was clinically and statistically significant decrease in heart rate and blood pressures in Group D. The mean intraoperative RSS was higher in Group D. **Conclusion:** Administration of IV dexmedetomidine during SAB hastens the onset of sensory block and prolongs the duration of sensory and motor block with satisfactory arousable sedation.

**Key words:** Dexmedetomidine, intravenous, subarachnoid block, supplementation

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## INTRODUCTION

Subarachnoid block (SAB) is a widely used regional anaesthetic technique, particularly advantageous for lower abdominal and lower limb surgeries.<sup>[1]</sup> The intrathecal local anaesthetic 0.5% bupivacaine with dextrose, is appropriate for surgeries lasting for 2-2.5 h.<sup>[2]</sup> Several additives such as opioids, alpha agonists among others have been used with local anaesthetics to prolong the duration of SAB.<sup>[3]</sup> Alpha 2 adrenoceptor agonists have been studied as adjuvants to spinal anaesthesia with promising results. Clonidine, an alpha 2 adrenoceptor agonist was found to prolong the duration of sensory and motor block

when administered intrathecally.<sup>[2]</sup> It was also found to prolong spinal anaesthesia when administered as an oral premedication and when administered by the intravenous (IV) route.<sup>[4,5]</sup>

Dexmedetomidine is a more selective alpha 2 adrenoceptor agonist with sedative and analgesic properties. Though approved for intensive care unit sedation, studies are being conducted on its off-label uses. IV dexmedetomidine has been found to reduce the anaesthetic requirements during the general anaesthesia.<sup>[6]</sup> Dexmedetomidine has been found to exert its analgesic actions both at the spinal and supraspinal levels.<sup>[7]</sup> Kanazi *et al.* demonstrated a significant

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prolongation in the duration of sensory and motor block with dexmedetomidine used as intrathecal additive for 0.5% heavy bupivacaine.<sup>[8]</sup> However, literature pertaining to effect of IV administered dexmedetomidine on spinal anaesthesia are sparse and all published studies have used 1 mcg/kg bolus followed by infusion.<sup>[9,10]</sup>

We hypothesised that IV dexmedetomidine at a lower loading dose followed by infusion might prolong the duration of SAB with 0.5% heavy bupivacaine. The primary aim of this study was to assess the onset and duration of sensory and motor blockade following IV dexmedetomidine supplementation during SAB. We also evaluated the effect of IV dexmedetomidine supplementation on haemodynamic parameters, sedation and adverse effects if any.

## METHODS

A randomised, double-blind, prospective study was conducted on 50 patients of American Society of Anaesthesiologists Grades I and II, aged between 18 and 55 years undergoing lower abdominal and lower limb surgeries under SAB.

After obtaining institutional ethical approval and informed consent, patients were randomly allocated into 2 groups, Group D (dexmedetomidine) and Group C (control) using computer generated random numbers. Patients with infection at the puncture site, coagulopathy, having true hypersensitivity to drugs used, diabetes and hypertension, psychiatric and neurological diseases were excluded from the study. All patients were kept nil per oral overnight and pre-medicated on the previous night of surgery with oral tablet alprazolam 0.5 mg. In the operation theatre, all patients were connected to electrocardiography, peripheral oxygen saturation (SpO<sub>2</sub>) and non-invasive blood pressure monitor and all the basal parameters were recorded. An IV line was obtained with 18 gauge cannula and all patients were preloaded with Ringer lactate solution 10 ml/kg body weight.

Group D patients received IV dexmedetomidine 0.5 mcg/kg diluted to 20 ml with normal saline and infused over 10 min as a loading dose, prior to SAB. Group C received similar volume of normal saline. Immediately following the initial loading dose, patients were put in lateral position and operating table was kept flat. SAB was administered at L3-L4 or L4-L5 level using standard technique with 12.5 mg of hyperbaric bupivacaine. After SAB, patients in Group D received

maintenance infusion of dexmedetomidine at the rate of 0.5 mcg/kg/h and the same rate of infusion of normal saline was administered in Group C, throughout the duration of surgery. Sensory block was assessed by loss of temperature sensation and motor blockade was determined using Bromage Scale<sup>[11]</sup> (0 = no paralysis; 1 = unable to raise extended leg; 2 = unable to flex knee; 3 = unable to flex ankle).

The level of sensory and motor blockade was checked every 2 min until the maximum level of the block was achieved and at 5 min interval subsequently. The level of sedation was evaluated throughout the study period using Ramsay Sedation Score (RSS).<sup>[12]</sup> Intraoperatively, heart rate, blood pressures and SpO<sub>2</sub> were recorded every 5 min until the end of surgery and every 15 min in the first post-operative hour followed by every half hourly for next 3 h. Hypotension was defined as more than 25% decrease in mean arterial pressure and was treated with fluid boluses and injection ephedrine 6 mg IV. Bradycardia was defined as heart rate less than 50 beats/min and treated with injection atropine 0.6 mg IV.

Parameters observed were time for the onset of sensory and motor blockade, maximum cephalad level of sensory block achieved, time for two segment regression, total duration of analgesia and motor blockade.

Onset of sensory block was considered when the loss of temperature sensation to cold was noted at T10 and onset of motor block when complete loss of motor power was achieved (Bromage Scale 3). Post-operatively, pain was assessed using visual analogue scale (VAS). Total duration of analgesia was defined as time from administration of SAB until the first complaint of pain (VAS  $\geq$  3). Injection diclofenac 75 mg intramuscular was used as rescue analgesic. Complications such as hypotension, bradycardia, nausea, vomiting, shivering, urinary retention and headache were noted and treated accordingly. An Anaesthesiologist, who was blinded to the study drug used, documented all the parameters.

Keeping the power at 80% and confidence interval at 95%, to detect at least 15% difference in duration of analgesia, the minimum sample size required was 16 patients in each group. However, we included 25 patients in each group for better validation of results.

All parametric data are presented as mean  $\pm$  SD and non-parametric data tabulated. All parametric data

were statistically analysed using Student's *t*-test and non-parametric data analysed using Chi-square test and Fischer exact test as appropriate.  $P < 0.05$  was considered as statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences version 16.0 (IL, Chicago) software.

## RESULTS

The demographic data are presented in Table 1. Age, gender, height, weight and duration of surgery were comparable. Type of surgeries was uniformly distributed between the groups.

Onset of sensory block was significantly faster in Group D ( $66 \pm 44.14$  s) compared to Group C ( $129.6 \pm 102.4$  s) with  $P < 0.001$ . The time required for two segment regression was also significantly prolonged in Group D ( $111.52 \pm 30.9$  min) compared with Group C ( $53.6 \pm 18.22$  min),  $P < 0.001$ . The duration of analgesia was significantly prolonged in Group D ( $222.8 \pm 123.4$  min in Group D,  $138.36 \pm 21.62$  min in Group C,  $P < 0.001$ ). The median level of cephalad spread of sensory blockade in Group D was T10 (T8-T12) compared with T8 (T6-10) in Group C. Mean time for the onset of motor blockade in Group D was  $3.76 \pm 2.02$  min whereas in Group C, it was  $4.2 \pm 2.08$  min,  $P = 0.136$ . Complete regression of motor blockade took longer time in Group D ( $256.44 \pm 53.10$  min) compared with Group C ( $231.16 \pm 32.2$  min),  $P < 0.001$  [Table 2].

Basal haemodynamic variables were comparable between the groups. Intra-operatively, there was a clinically and statistically significant decrease in heart rate in Group D from 15 min following SAB and persisted to be lower for 90 min. Bradycardia requiring atropine administration was noted in four patients in Group D compared with none in Group C ( $P = 0.055$ ). Similar trend was observed in systolic, diastolic and mean arterial pressures 60 min following SAB in Group D [Figure 1]. Hypotension was observed in two patients in Group D and in one patient belonging to Group C ( $P = 0.5$ ).

Post-operatively, heart rate was comparable between the groups, but the systolic, diastolic and mean arterial pressures continued to be significantly lower in Group D for the initial 2 h [Figure 2].

The mean intra-operative RSS in Group D was  $2.34 \pm 1.1$  whereas in Group C, it was  $2.0 \pm 0.0$  ( $P = 0.034$ ). However, RSS was comparable in both groups in the post-operative period. Respiratory rate

was lower in Group D (Group D -  $14.81 \pm 0.96$  vs. Group C -  $16.64 \pm 1.26$ /min,  $P < 0.001$ ), but oxygen saturation was comparable between both groups (Group D 98% vs. Group C 97.85%,  $P = 0.153$ ). Respiratory rate and oxygen saturation were comparable between both groups in the post-operative period.

The incidences of side effects were comparable between the two groups [Table 3].

## DISCUSSION

IV administered dexmedetomidine has been shown to produce analgesic effects by acting at both spinal and supraspinal levels. The analgesic effect primarily results from the inhibition of locus ceruleus at the brain stem. In addition, dexmedetomidine infusion may result in increased activation of alpha-2 receptors at the spinal cord resulting in inhibition of nociceptive impulse transmission. The effect seems to be mediated through both presynaptic and the post-synaptic

Table 1: Demographic data

Parameters	Group D	Group C	P value
Age (in years)	40.72±8.92	39.8±11.51	0.753
Gender (M: F)	15:10	18:7	0.557
Height (in m)	1.68±0.14	1.7±0.14	0.489
Weight (in kg)	61.52±22	63.08±18.52	0.590
Duration of surgery (in min)	63.84±30.5	69.4±40.34	0.277
Type of surgeries			
Lower abdominal	12	9	0.560
Lower limb	13	16	

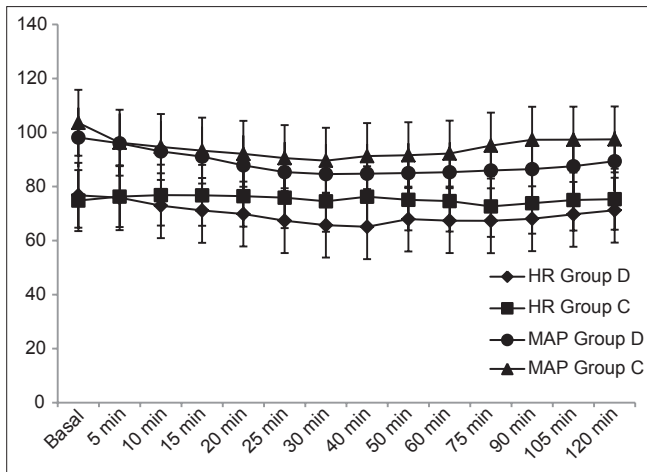
Table 2: Comparison sensory and motor parameters

Parameters	Group D	Group C	P value
Onset of sensory block (to T10) in s	66±44.14	129.6±102.4	<0.001*
Median maximum level of sensory blockade	T10 (T8-T12)	T8 (T6-T10)	0.362
Two segment regression (in min)	111.52±30.9	53.6±18.22	<0.001**
Duration of analgesia (in min)	222.8±123.4	138.36±21.62	<0.001**
Onset of motor blockade (in min)	3.76±2.02	4.2±2.08	0.136
Duration of motor blockade (in min)	256.44±53.10	231.16±32.2	<0.001**

\*Statistically significant, \*\*Statistically highly significant

Table 3: Comparison of incidence of side effects

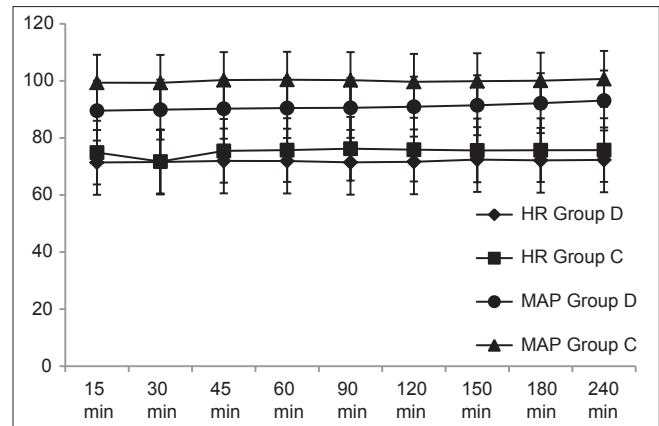
Side effects	Group D (n=25)	Group C (n=25)	P value
Hypotension	2	1	0.500
Bradycardia	4	0	0.055
Shivering	1	5	0.095
Nausea	0	0	-
Vomiting	0	0	-



**Figure 1:** Comparison of intra-operative haemodynamic parameters. Heart rate significantly low ( $P<0.05$ ) in Group D from 30<sup>th</sup> min to 60<sup>th</sup> min. MAP significantly low ( $P<0.05$ ) from 60<sup>th</sup> min until the end of surgery

alpha-2 receptors.<sup>[7,13]</sup> The results of this study indicate that infusion of dexmedetomidine hastens the onset of sensory block, though the onset of motor blockade was not affected. Faster onset of the sensory block may be due to alpha-2 receptor activation induced inhibition of nociceptive impulse transmission.

Dexmedetomidine infusion used as a loading dose followed by an infusion has been found to prolong the duration of analgesia and motor blockade in the present study. Lugo *et al.*<sup>[9]</sup> in their study noted prolongation of sensory block and duration of analgesia without significant effect on motor block while using 1 mcg/kg bolus followed by 0.5 mcg/kg/h infusion of dexmedetomidine. Al-Mustafa *et al.*<sup>[10]</sup> also observed similar findings in their study and in addition, there was prolongation of motor blockade with a similar dose of dexmedetomidine. In another study observing the effect of dexmedetomidine infusion on spinal anaesthesia with ropivacaine, it was observed that dexmedetomidine bolus of 1 mcg/kg followed by infusion at 0.4 mcg/kg/h prolonged the duration of sensory and motor regression.<sup>[14]</sup> Recently, administration of a single bolus of 1 mcg/kg,<sup>[15]</sup> and 0.5 mcg/kg,<sup>[16]</sup> also were reported to prolong the duration of analgesia and sensory blockade. The duration of sensory block and analgesia in our study were comparable with above studies despite using a lower initial loading dose of 0.5 mcg/kg, compared with 1 mcg/kg. Furthermore, an evaluation of the analgesic effect of different doses of IV dexmedetomidine (0.25, 0.5 and 1 mcg/kg) on ischemic pain in healthy volunteers demonstrated moderate analgesia with a ceiling effect at 0.5 mcg/kg.<sup>[17]</sup>



**Figure 2:** Post-operative haemodynamic parameters. MAP significantly low ( $P<0.05$ ) in Group D for initial 2 h

Several studies reported prolonged duration of motor block following use of 1 mcg/kg initial bolus dose followed by infusion. However, in a study by Kaya *et al.*<sup>[16]</sup> use of a single dose of 0.5 mcg/kg of dexmedetomidine did not affect the duration of motor block. It was observed that effect of clonidine on motor blockade was concentration dependant<sup>[4]</sup> and the same theory might explain this phenomenon with dexmedetomidine as well. The prolongation of motor block in spite of use of 0.5 mcg/kg initial loading dose, observed by us may be attributed to continuous infusion following loading dose.

Haemodynamic response following dexmedetomidine infusion depends upon the dose and speed of infusion. A sequence of transient hypertension with reflex bradycardia, followed by hypotension is seen with higher dose and rapid infusion.<sup>[18,19]</sup> The subsequent decrease in heart rate and blood pressure may be due to decrease in central sympathetic outflow.<sup>[19]</sup> There was a minimal decrease in heart rate and blood pressure in patients receiving dexmedetomidine in our study, similar to observations of other authors.<sup>[10]</sup> Most of studies have noted bradycardia as a prominent side effect, with incidence varying from 30% to 40% sometimes requiring treatment with atropine, following use of a bolus dose of 1 mcg/kg and infusion greater than 0.4 mcg/kg/h.<sup>[9,14,15,19]</sup> However, the incidence of bradycardia in our study was low and also transient, probably owing to a lower bolus dose used and augers well with observations of Kaya *et al.*<sup>[16]</sup> Incidence of hypotension in our study was comparable with other studies.<sup>[10,15]</sup> The infusions were continued during episodes of hypotension and/or bradycardia and the severity of these effects did not warrant stoppage of infusions at any point of time.



Intra-operative sedation provided by dexmedetomidine eliminates the need for additional sedatives. Dexmedetomidine produces sedation by its central effect and seems to be dose dependant.<sup>[20,21]</sup> Most of patients receiving dexmedetomidine were sedated, but easily arousable in the present study. Contrary to observations of Al-Mustafa *et al.*<sup>[10]</sup> and Hong *et al.*<sup>[15]</sup> who used higher doses of dexmedetomidine and noted excessive sedation in 3 out of 25 and 2 out of 26 patients respectively in their study, none of our patients had RSS greater than 3 at any point of observation highlighting the advantage of lower dose. Kaya *et al.*<sup>[16]</sup> also had similar observations regarding sedation in their study.

Respiratory rate was lower in patients receiving dexmedetomidine, but clinically not significant enough to be considered as respiratory depression and oxygen saturation was maintained equally well in both groups. However, Hong *et al.* noted desaturation in two patients, which was attributed to the advanced age of the patients in their study, though Jaakola<sup>[22]</sup> did not observe similar incidence of desaturation.

## CONCLUSION

IV supplementation of loading dose of dexmedetomidine 0.5 mcg/kg followed by infusion at 0.5 mcg/kg/h hastens the onset of sensory block and prolongs the duration of sensory block, analgesia and motor block with lesser incidence of bradycardia. Further, IV dexmedetomidine supplementation during SAB produces satisfactory arousable sedation without causing respiratory depression.

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