

## Assessment of the three Different Dexmedetomidine Doses and their Effects on the Duration of Spinal Anaesthesia: A Comparative Research

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### Abstract

**Aim:** The aim of the present study to comparison of 3 Different Dexmedetomidine Doses and Their Effect on the Duration of Spinal Anesthesia. **Methods:** Any gender between 18 and 65 years with American Society of Anesthesia physical state I or II (ASA I or II) with body mass index (BMI) 40 kg/m<sup>2</sup> or below were included in this study. All patients that were included were randomized, using computer generated random number table, to four groups: control group (group C) and three experimental groups (groups D1.5, D3 and D5). At the site of local anesthesia, a spinal needle 25G was advanced till reaching the intrathecal space and cerebrospinal fluid (CSF) flows through the needle, and then the following were injected according to the groups: Total 100 Patients were included in this study 25 in each group. **Results:** Regarding the onset of the sensory block, there were statistical differences among groups as group C showed onset after  $1.7 \pm 1.7$  min while group D1.5 showed onset of sensory block after  $2.5 \pm 1.88$  min while in group D3 it was  $3.12 \pm 2.54$  min and in group D5 it was  $2.63 \pm 3.34$  min. The previous results showed a dose-response prolongation to the Dexmedetomidine; this prolongation shows a statistically significant between the control group C and the other three groups (p-value 0.001). On the other hand, there were no statistical differences among the study groups (p-value 0.57). Moreover, this prolongation has no clinical significance. Regarding the duration of the sensory block there is, again, a dose-related prolongation with a crescendo pattern (group C  $217.21 \pm 81.69$  min), group D1.5 ( $221.22 \pm 50$  min), group D3 ( $303.56 \pm 43.01$  min), group D5 ( $367.75 \pm 97.68$  min)). However, there was no statistical significance between the control group and group D1.5 (p-value was 0.24). On the contrary, there was a prolongation in both groups D3 and D5 which have achieved a statistical significance (p value was <0.001) in comparison with the control group. The same pattern was achieved in the duration of the motor block as it was ( $207.25 \pm 45.26$  min) in group C, ( $250.27 \pm 82.69$  min) in group D1.5, ( $269.67 \pm 33.61$  min) in group D3 and ( $320.64 \pm 93.12$  min) in group D5. **Conclusion:** The Dexmedetomidine can prolong the duration of the spinal anesthesia with a high safety profile and no complications in both doses 3 and 5  $\mu$ g but not with a dose of 1.5  $\mu$ g.

**Keywords:** Dexmedetomidine, spinal, anesthesia

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## Introduction

Spinal anesthesia is the most commonly used technique for lower abdominal surgeries as it is very economical and easy to administer[1]. Postoperative pain is a major problem in infraumbilical surgeries because shorter duration of spinal anesthesia using only local anesthetics, and thus, early analgesic intervention is needed in postoperative period. Various adjuvants such as fentanyl, midazolam, and clonidine have been tried along with local anesthetics, to prolong the intraoperative block and postoperative analgesia.

A most common problem during infraumbilical surgeries under subarachnoid block is visceral pain, nausea, and vomiting[2]. Addition of an adjuvant to the intrathecal local anesthetics will improve the quality of the intraoperative block and early postoperative analgesia. The addition of opioids to local anesthetics has disadvantages, such as pruritus and respiratory depression, nausea, vomiting.

In recent years,  $\alpha_2$  adrenoreceptor gains wide popularity as an anesthetic adjuvants and also as analgesics. Their primary effect is sympatholytic. They reduce peripheral norepinephrine release by the stimulation of prejunctional inhibitory  $\alpha_2$  adrenoceptors. They also inhibit the central neural transmission in dorsal horn by presynaptic and postsynaptic mechanism. They also have direct sympatholytic effect on spinal preganglionic sympathetic neurons. Sedative, anxiolytic, and analgesic properties of alpha agonists favour the wide clinical use. The addition of dexmedetomidine to the local anesthetics provides effective analgesia for acute and chronic pain[3].

Dexmedetomidine is a selective alpha 2 agonist when compared to clonidine (affinity for alpha 2 receptor is 1600:1, clonidine 200:1). Hence, it is used in clinical practice as an adjuvant to regional,

local, and general anesthesia. Dexmedetomidine is approved by the Food and Drug Administration as an intravenous (IV) additive for Intensive Care Unit (ICU) sedation, but recently, it is widely used an adjuvant to the local anesthetics. The addition of dexmedetomidine for intrathecal local anesthetics prolongs the duration of both sensory block, motor block, and postoperative analgesia without severe sedation. This effect is due to the sparing of supraspinal central nervous system so that it reduces the requirement of immediate postoperative analgesics[3,4].

It produces dose-dependent sedation, anxiolysis, and analgesia without respiratory depression. Activation of the receptors in the brain and spinal cord inhibits neuronal firing causing hypotension, bradycardia, sedation, and analgesia[4].

The previous studies revealed prolongation of spinal block by intrathecal 5 and 10  $\mu\text{g}$  dexmedetomidine as an adjuvant with no significant effect on blood pressure or heart rate (HR)[5].

Not many studies have been done to compare the effect of different doses of dexmedetomidine as an adjuvant with intrathecal bupivacaine in infraumbilical surgeries, and hence, we designed this study to evaluate the effects of different doses of dexmedetomidine as an adjuvant to hyperbaric bupivacaine.

## Materials and methods

A prospective double blind randomized controlled study was conducted in the Department of Anaesthesiology and Critical Care, Patna Medical College and Hospital, Patna, Bihar, India for 12 months, after taking the approval of the protocol review committee and institutional ethics committee.

## Inclusion criteria

Any gender between 18 and 65 years with American Society of Anaesthesiologist physical state I or II (ASA I or II) with body mass index (BMI) 40 kg/m<sup>2</sup> or below (considered obesity with potential difficulty and complications).

### Exclusion criteria

Any gender with age below 18 or above 65 and or BMI more than 40 kg/m<sup>2</sup>, patient refusal, coagulopathy, allergy to the used drugs ASA more than II, obstacles in communications such as mental retardation, dementia, deaf, mute etc. Also, patients that were under treatment with  $\alpha$ 2-adrenergic agonist or transformed to general anaesthesia were excluded.

All patients that were included were randomized, using computer generated random number table, to four groups: control group (group C) and three experimental groups (groups D1.5, D3 and D5). All patients were subjected to detailed history, thorough examinations, and full laboratories before the procedure, consent was signed after detailed explanation and finally; patients were included randomly in one of the four groups.

An intravenous (IV) line was inserted and crystalloid solution 15 ml/kg was given to each patient, full monitoring was connected (blood pressure, heart rate (HR), peripheral oxygen saturation (SpO<sub>2</sub>) and electrocardiography), baseline data were recorded. The patient was in the sitting position; the back was sterilized by Povidone iodine. The L<sub>3</sub>/L<sub>4</sub> or L<sub>4</sub>/L<sub>5</sub> intervertebral space was located. 3 mL of 2% lidocaine was infiltrated subcutaneously and into a deeper ligament.

At the site of local anesthesia, a spinal needle 25G was advanced till reaching the intrathecal space and cerebrospinal fluid (CSF) flows through the needle, and then the following were injected according to the groups: Total 100 Patients were included in this study 25 in each group.

- Group C: 3 mL (15 mg) of 0.5% levobupivacaine+0.5 mL normal saline.

- Group D1.5: 3 mL (15mg) of 0.5% levobupivacaine+0.5 mL (1.5 $\mu$ g) Dexmedetomidine.
- Group D3: 3 mL (15 mg) of 0.5% levobupivacaine+0.5 mL (3 $\mu$ g) Dexmedetomidine.
- Group D5: 3 mL (15mg) of 0.5% levobupivacaine+0.5 mL (5 $\mu$ g) Dexmedetomidine.

Dexmedetomidine was prepared by dilution on saline to reach the needed dose under complete sterile precautions. For instance; 0.3ml of Dexmedetomidine with 30 $\mu$ g was diluted on 100 ml saline to become 3 $\mu$ g/ml to achieve 1.5 $\mu$ g per 0.5 ml.

The spinal needle was then withdrawn and a dressing was placed over the puncture site and rapidly the patient was set in the supine position with continuous recording of the vitals every 5 min.

The patients in all the four groups were looked for the following outcomes:

Duration of the spinal sensory blockade (primary outcome), the onset of the blockade, the level of sedation, duration of motor blockade, hemodynamics, complications (hypotension, nausea, vomiting, allergy, any adverse effect specified by the patients). Also, patient's demographic data were collected (age, sex, BMI and duration of surgery).

Duration of the block was considered as the time from solid and stable sensory block to the time of two segment regression using the skin pricks every 5 min, while the onset of the block was considered as the time elapsed from the needle withdrawal to the time with a full sensory block with stationary sensor level.

Sensory block was assessed using a loss of cold sensation every 2 min till having a stable sensory level for the next 20 min.

Motor block was assessed by modified Bromage scale[6] (0=free movement of legs and feet, 1=just able to flex knees with free movement of feet, 2=unable to flex

knees, but with free movement of feet, 3=unable to move legs or feet.

Sedation was assessed using Ramsay scale[7] 1-patient anxious, agitated or restless scale 2-patient cooperative, oriented and tranquil alert scale 3-patient responds to commands scale 4-asleep but with brisk response to light glabellar tap or loud auditory. Scale 5-asleep, sluggish response to glabellar tap or loud auditory stimulus scale 6- asleep no response.

Hypotension was considered as 20% reduction of the mean arterial pressure from the baseline and was treated by ephedrine increments 9 mg each.

### Statistical analysis

Data were recorded and entered using the statistical package SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 25. Data were summarized using mean and standard deviation in quantitative data and using

frequency (count) and relative frequency (percentage) for categorical data. Comparisons between groups were done using ANOVA with post hoc test in normally distributed quantitative variables while non-parametric Kruskal-Wallis test and Mann-Whitney test were used for non-normally distributed quantitative variables. For comparison of serial measurements within each group repeated measures ANOVA was used in normally distributed quantitative variables while non-parametric Friedman test was used for non-normally distributed quantitative variables. For comparing categorical data, Chi-square test was performed. The exact test was used instead when the expected frequency is less than 5. P- values less than 0.05 were considered as statistically significant

### Results

Regarding the demographic data and their durations, there were no statistical differences between the groups (Table 1).

**Table 1: Demographic and clinical characteristics. Numerical data were presented as Mean  $\pm$  Standard deviation (SD), P\* value<0.05 was considered statistically significant.**

	Group C (n=25)	Group D1.5 (n=25)	Group D3 (n=25)	Group D5 (n=25)	P value
Age	41.5 $\pm$ 12.4	39.2 $\pm$ 10.7	42.6 $\pm$ 10.5	42.77 $\pm$ 9.36	0.57
Gender (m/F)	17/8	16/9	19/6	16/9	0.27
BMI (Kg/m <sup>2</sup> )	27.77 $\pm$ 3.57	29.55 $\pm$ 3.16	31.03 $\pm$ 1.87	28.88 $\pm$ 3.01	0.25
Duration of surgeries (min)	78.98 $\pm$ 19.68	83.55 $\pm$ 20.36	81.66 $\pm$ 22.39	83.99 $\pm$ 20.98	0.77
ASA (I/II)	22/3	23/2	20/5	19/6	0.79

Regarding the onset of the sensory block, there were statistical differences among groups as group C showed onset after 1.7  $\pm$  1.7 min while group D1.5 showed onset of sensory block after 2.5  $\pm$  1.88 min while in group D3 it was 3.12  $\pm$  2.54 min and in group D5 it was 2.63  $\pm$  3.34 min.

The previous results showed a dose-response prolongation to the Dexmedetomidine; this prolongation shows a statistically significant between the control group C and the other three groups (p-value 0.001). On the other hand, there

were no statistical differences among the study groups (p-value 0.57). Moreover, this prolongation has no clinical significance.

Regarding the duration of the sensory block there is, again, a dose-related prolongation with a crescendo pattern (group C 217.21  $\pm$  81.69 min), group D1.5 (221.22  $\pm$  50 min), group D3 (303.56 $\pm$  43.01 min), group D5 (367.75  $\pm$  97.68 min)). However, there was no statistical significance between the control group and group D1.5 (p-value was 0.24). On the contrary, there was a prolongation in both groups D3 and D5

which have achieved a statistical significance (p value was <0.001) in comparison with the control group (Table 2).

The same pattern was achieved in the duration of the motor block as it was (207.25 ± 45.26min) in group C, (250.27 ± 82.69 min) in group D1.5, (269.67 ± 33.61 min) in group D3 and (320.64 ± 93.12 min) in

group D5. The above results showed a statistical difference with significance between groups D5 and D3 on one hand and control group C on the other hand with p-value 0.004. Likewise, there was no statistical significance between both groups C and D1.5 with p-value 0.57 and even more among any experimental groups (D1.5, D3 and D5 vs. each other) (Table 2).

**Table 2: Sensory and motor block pattern. Numerical data were presented as Mean ± Slandered deviation (SD), P\* value<0.05 was considered statistically significant**

	Group C (n=25)	Group D1.5 (n=25)	Group D3 (n=25)	Group D5 (n=25)	P value
Onset of the sensory block (min)	1.7±1.7	2.5±1.88	3.12 ± 2.54	2.63 ± 3.34	0.001
Duration of the sensory block (min)	217.21±81.69	221.22±50 min p value 0.24 vs. C	303.56±43.01 min	367.75±97.68	<0.001
Duration of the motor block (min)	207.25±45.26	250.27±82.69 p value 0.57 vs. C	269.67±33.61	320.64±93.12	0.004

Regarding the heart rate and mean blood pressure there were neither clinical nor statistical differences among the four groups while the patients were under anesthesia and till the first-hour intra-operatively (Figures 2 and 3).

Sedation score showed a statistical significance between the control group C on one hand and the other three groups

D1.5, D3 and D5 on the other hand as Ramsay score was reached 2.5 Dier 30 min and kept on the same level for the next 180 min in all the study groups but maintained at 1 in the control group C (Table 3). Here were no complications recorded in all groups apart from few cases of nausea and vomiting with neither statistical nor clinical relevance (Table 4)

**Table 3: Ramsay sedation score values in different groups Values are presented as median (inter-quartile range).**

	Group C (n=25)	Group D1.5 (n=25)	Group D3 (n=25)	Group D5 (n=25)	P value
T0	1 (1-1.5)	1 (1-1.5)	1 (1-1.5)	1 (1-1.5)	1
T30 min	1 (1-1.5)	2 (1-2.5) *	2 (1-2.5)	2 (1-2.5)	0.001
T60 min	1 (1-1.5)	2 (2-2.5) *	2 (2-2.5)	2 (2-2.5)	<0.001
T120 min	1 (1-1.5)	2 (2-2.5) *	2 (2-2.5)	2 (2-2.5)	<0.001
T180 min	1 (1-1.5)	2 (2-2.5) *	2 (2-2.5)	2 (2-2.5)	<0.001

\*Denotes statistical significance compared to control group

**Table 4: cases with complications (number of cases and percentage)**

	Group C	Group D1.5	Group D3	Group D5	P value
Nausea	2(8%)	2 (8%)	3 (12%)	2 (8%)	1

<b>Vomiting</b>	<b>0 (%)</b>	<b>2(8%)</b>	<b>2 (8%)</b>	<b>0 (%)</b>	<b>1</b>
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## Discussion

This study is answering the question of; what is the least dose of Dexmedetomidine that will cause a clinical effect when injected intrathecally? It showed that there is an effect on the duration of the spinal anesthesia when Dexmedetomidine was added. There is a prolonged duration regarding both sensory and motor block. Moreover, there is a sedative effect which is favored in the spinal anesthesia. This sedative effect is safe and accepted and will encourage the usage of Dexmedetomidine in combination with levobupivacaine in spinal anesthesia. Likewise, there were a few adverse effects in the form of nausea and vomiting with neither statistical nor clinical relevance.

Also, this study showed that there is a relation between the dose of Dexmedetomidine and its effect. However, this relation has no statistical significance in small doses (1.5 $\mu$ g) but has both clinical and statistical significance when increased to 3 $\mu$ g and 5 $\mu$ g respectively.

Although there was a sedative effect, this effect was very mild as it was scored as 2 in Ramsay score. These results conclude that there is a weak relation between Dexmedetomidine and the level of sedation if it was injected intrathecally.

We have chosen these doses under the theory that 1/10 dose of the drug will be effective when injected into the intrathecal space. This was tested before by Kanzani[8] in the humans but in a dose of 3 $\mu$ g, he found that this dose is equivalent to 30 $\mu$ g intravenously.

There were many studies that have tested the effect of Dexmedetomidine when injected into the cerebrospinal fluid either in animals or humans or with different doses in comparison with saline or Clonidine[9-19] however, this is the first study to test the same drug with different doses, especially with the very small dose 1.5 $\mu$ g.

In this study, no cases were reported with hypotension or bradycardia to the limit of intervention. However, there is a study[20] reported more hypotension and sedation with the 5mcg dose. The explanation of this difference may be because of the type of surgery (hysterectomy) mandated a higher level of block and consequently hypotension was reported.

This study has limitations in the form of the type of surgery as we did not restrict to a single type of surgery which may have an influence on the results. Moreover, adding Dexmedetomidine will not increase the sensory block duration alone, but also, will increase the duration of the motor block duration which considered as a limitation to the drug itself (not to the study) and may lead to prolonged recovery or hospital stay. Moreover, there is still a question regarding a dose of 2 $\mu$ g which was not tested in this study and needs further research. In this study, the protocol was to start with 1.5 $\mu$ g and increase in a manner of duplication and subsequently dose of 2 $\mu$ g was not tested.

## Conclusion

The present study concluded that Dexmedetomidine can prolong the duration of the spinal anesthesia with a high safety profile and no complications in both doses 3 and 5 $\mu$ g but not with a dose of 1.5 $\mu$ g.

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