



## Anaesthesiology

## COMPARISON OF EFFECTIVENESS BETWEEN TWO DIFFERENT DOSES OF INTRAVENOUS DEXMEDETOMIDINE AS ADJUVANT TO SUBARACHNOID BLOCK FOR SUB UMBILICAL SURGERIES - A RANDOMISED TRIAL.

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### KEYWORDS :

#### Introduction

Spinal anesthesia, commonly used technique in anesthetic practice for infraumbilical surgeries. Subarachnoid block is preferred to epidural anesthesia for its faster onset and denser block<sup>1</sup>. Bupivacaine is used for surgeries lasting for 2 to 2.5 hours<sup>2</sup>. To prolong the duration of spinal anesthesia adjuvants like epinephrine, opioids, magnesium sulphate and  $\alpha 2$  agonists like clonidine, dexmedetomidine have been used intrathecally<sup>3</sup>.  $\alpha 2$  agonists have also been found to extend the duration of spinal anesthesia when given intravenously<sup>4,5,6,7,8</sup>.

In addition to sedation and analgesia they also reduce sympathetic tone and attenuate the stress response to surgery. Sedation and anxiolysis are by activation of presynaptic  $\alpha 2$  receptors in locus coeruleus. Inhibition of sympathetic activity is by post synaptic activation which reduces heart rate and blood pressure. Activation of and  $\alpha 2A$  and  $\alpha 2B$  adrenergic receptors situated in the neurons of the superficial dorsal horn (especially lamina II) of spinal cord, reduces pain transmission directly by reducing the discharge of pro-nociceptive transmitter, glutamate and substance P from primary afferent terminals and also by hyperpolarization of spinal interneurons through G protein mediated potassium channel activation<sup>9,10,11</sup>.

The principal for the analgesic effects of dexmedetomidine is by spinal mechanism even though there is evidence for both supraspinal and peripheral sites of action<sup>12</sup>.

Dexmedetomidine is preferred over clonidine as adjuvant to spinal anesthesia due to its more selective  $\alpha 2A$  receptor agonist activity which produces more sedative and analgesic effect<sup>13</sup>. Present study is designed to compare the effect of two different loading doses of intravenous dexmedetomidine on subarachnoid block with hyperbaric bupivacaine.

#### Structures pierced during subarachnoid block

Following structures are traversed when needle is passed into subarachnoid space Skin → Subcutaneous tissue → Supraspinatus ligament → Interspinous ligament → Ligamentum flavum → Areolar tissue or epidural space → Dura matter

#### Pharmacology

Bupivacaine inhibits nerve impulse generation and transmission, likely via raising the threshold for electrical excitation in the neuron, slowing nerve impulse propagation, and lowering the rate of rise of the action potential.

Excessive plasma levels, which can be caused by overdosing, inadvertent intravascular injection, or poor metabolic degradation, are a major cause of adverse reactions to this drug.

Clonidine, the first and most well-known  $\alpha 2$  agonist, is classified as a partial  $\alpha 2$  agonist since its  $\alpha 2/\alpha 1$  selectivity is 200, whereas dexmedetomidine's is 1620. As a result, dexmedetomidine is 8 times more selective for the  $\alpha 2$  adrenoceptor than clonidine and is termed a complete agonist of the  $\alpha 2$  adrenoceptor. Dexmedetomidine's  $\alpha 2$  adrenoceptor selectivity is dosage dependent. High selectivity of the  $\alpha 2$  adrenoceptor are reported at low to medium doses or at slow rates of

infusion, whereas high doses or rapid infusions of low doses are associated with both  $\alpha 1$  and  $\alpha 2$  activity. Dexmedetomidine's high  $\alpha 1$  adrenoceptor selectivity allows it to be used in reasonably large dosages for sedation and analgesia without causing undesirable vascular effects from activation of  $\alpha 1$  receptors.

#### MATERIALS AND METHODS

Sixty patients scheduled for surgeries under Subarachnoid block in NRI INSTITUTE OF MEDICAL SCIENCES, Sangivalasa, Visakhapatnam, meeting the following criteria were included in the study. Sixty patients were divided by computer generated random number An informed and written consent was taken from patients who were included in the study. All patients in study groups were kept nil Before commencement of anesthesia, patient was instructed on the methods of sensory and motor assessments.

#### Inclusion criteria Age: 18 – 60 years

ASA grade: I – II

Patients undergoing infra umbilical surgeries

#### Exclusion criteria

Contraindication for spinal anesthesia

ASA grade III – V

Systolic blood pressure <90mm Hg, heart rate less than 50/min Patients on Calcium channel blockers, ACE inhibitors, clonidine Patients on opioid, antidepressants a week prior to surgery Cesarean section surgery.

Intravenous line was secured with 18-gauge cannula. Preloading was done with 15ml/kg Ringer Lactate 30 min prior to procedure. Pulse oximeter, noninvasive blood pressure (NIBP), and electrocardiography monitors were connected to all patients on arrival to operating room and baseline parameters were noted. The patient and anesthesiologist were blinded to the study groups, and all the recordings were noted by an anesthesiologist, who was blinded to randomization schedule.

Under strict aseptic precautions, lumbar puncture was done at the level of L3–L4 intervertebral space through midline approach by using a 25-gauge Quincke spinal needle. After confirmation of free flow of cerebrospinal fluid 0.5% hyperbaric bupivacaine, 17.5mg was given intrathecally.

Group A: Intravenous dexmedetomidine 0.5 $\mu$ g/kg in 100ml NS loading dose was administered in the first 10min immediately after spinal anesthesia.

Group B: Intravenous dexmedetomidine 1 $\mu$ g/kg in 100ml NS loading dose was administered in the first 10min immediately after spinal anesthesia.

#### DATA ANALYSIS

Descriptive statistical analysis was done in present study. Results of continuous measurements are represented as Mean  $\pm$  SD and results of categorical measurements are represented in Number (%). Chi-square

test was used for calculation of significance of study parameters on categorical scale between two or more groups. Fishers exact test was used for calculation of significance of the study parameters on categorical scale (frequency tables). Paired t test was used for calculation of significance of the study parameters on continuous scale within group. Student independent t test was used for calculation of significance of the study parameters on continuous scale between groups. P value <0.05 was considered as statistically significant.

Statistical software: SPSS 22 was used for analysis of the data and Microsoft word and excel were used to generate graphs, tables.

All the patients participated throughout the study. There was no significant difference in the demographic characteristics between two groups. Table 1 illustrates the distribution, percentage mean age ,BMI,ASA and sex distribution in the two groups, which was found to be comparable.

The mean heart rate(HR), systolic blood pressure (SBP),diastolic blood pressure(DBP), mean arterial blood pressure(MAP), Ramsay sedation score (RSS ),Oxygen saturation SPO2 duration of surgery Atropin usage ,there was no significant difference in above mentioned parametresas shown in table 2,3 and 4.

		Group A Frequency	Group B Frequency	Group A	Group B	PVAL UE
BMI		30	30	24.91±4.94	23.23±3.02	0.118
ASA	GRADE 1	18	21			0.4170
	GRADE 2	12	9			
GEN DER	Male	18	20			0.592
	Female	12	10			
AGE	20-30	6	6	42.03±10.85	41.27±8.20	0.759
	31-40	9	9			
	41-50	8	8			
	51-60	7	7			

**Table 1 Demographic data of two groups**

	Heart rate (beats/min)			Diastolic blood pressure (mmHg)		
	Group A	Group B	p-value	Group A	Group B	p-value
PRE-OP	81.60±9.87	78.90±8.87	0.2700	79.87±8.24	78.9±12.1	0.7190
0 min	82.60±9.69	79.03±8.74	0.1400	80.3±8.04	79.1±9.76	0.6050
5 min	75.30±10.59	74.67±8.69	0.8010	78.63±7.88	76.63±11.03	0.4220
10 min	71.83±10.80	70.27±8.91	0.5430	75.77±9.45	70.6±11.05	0.0560
15 min	70.00±10.88	68.00±9.26	0.4467	74.6±9.23	66.1±11.17	0.0020*
20 min	70.63±9.32	66.67±9.88	0.1150	72.37±8.65	65.2±8.61	0.0020*
25 min	69.80±9.09	66.27±10.50	0.1690	70.37±8.47	64.4±7.85	0.0060*
30 min	70.67±9.40	66.30±11.22	0.1080	69.53±9.98	63.5±8.14	0.0130*
45 min	72.93±8.65	69.10±9.69	0.1180	68.67±9.72	62.17±8.61	0.0080*
60 min	75.30±8.46	69.13±9.12	0.0070	70.67±10.21	64.13±8.65	0.0100*
75 min	76.30±7.36	64.47±7.60	0.0010	69.4±9.23	64.8±8.79	0.0530
90 min	76.33±7.61	67.50±8.13	0.0001	67.27±9.65	67.21±9.37	0.9810
120 min	76.56±7.70	76.56±7.7	0.0020	69.67±9.24	74.14±9.09	0.2000
150 min	82.67±12.01	71.00±1.41	0.2850	62±7.07	74.67±3.21	0.0650
POST OP	74.87±7.33	67.37±7.30	0.0010	70.37±8.47	65.4±9.64	0.0380*

**Table 2**

	Systolic Blood Pressure (mmHg)			Mean arterial Pressure (mmHg)		
	Group A	Group B	p-value	Group A	Group B	p-value
PRE-OP	133.63±14.22	133.5±13.95	0.9710			
0 min	134.57±14.21	134.17±15.45	0.9170	96.63±7.96	97.67±9.5	0.6500
5 min	133.47±13.06	130.83±13.09	0.4390	95.1±7.72	95.17±10.12	0.9770
10 min	129.07±17.64	119.67±12.89	0.0220	91.73±11.29	86.9±11	0.0730
15 min	124.5±19.23	115.6±14.5	0.0480	89.67±11.25	82.93±10.5	0.0200*
20 min	121.73±16.92	114.67±14.67	0.0890	87.3±10.56	81.9±8.84	0.0360*
25 min	117.27±17.02	110.5±10.7	0.0700	84.57±9.95	79.6±7.8	0.0360*
30 min	115.97±16.52	109.83±13.35	0.1190	83.5±11.38	78.63±9.3	0.0750
45 min	113.77±16.61	109.5±12.92	0.2710	82.23±11.23	77.23±8.39	0.0560
60 min	112.97±15.36	109.7±13.52	0.3860	83.37±11.19	78.87±8.67	0.0870
75 min	112.63±14.31	110.83±12.55	0.6060	82.33±9.99	80.07±9.66	0.3750
90 min	112.07±15.36	112.64±13.16	0.8790	80.73±10.19	81.38±9.61	0.8030
120 min	115.06±15.45	119.47±15.96	0.4340	83.27±10.62	88.13±10.84	0.2240
150 min	106±4.24	122±11.79	0.1760	75.5±6.36	92.33±4.73	0.0410*
POST OP	117.27±17.021	112±12.964	0.1830			

**Table 3**

	Ramsay Sedation Score		
	Group A	Group B	p-value
RSS 0 min	1.37±0.49	1.87±0.35	<0.05*
RSS 5 min	2.47±0.57	2.97±0.18	<0.05*
RSS 10 min	3.10±0.40	3.1±0.30	0.9999
RSS 15 min	3.20±0.41	3.13±0.35	0.4950
RSS 20 min	3.13±0.57	3.73±0.45	<0.05*
RSS 25 min	3.20±0.66	3.93±0.25	<0.05*
RSS 30 min	3.10±0.61	3.27±0.45	0.2320
RSS 45 min	2.87±0.57	3.37±0.49	0.0010*
RSS 60 min	2.73±0.52	2.93±0.36	0.0900
RSS 75 min	2.63±0.49	2.63±0.49	0.9999
RSS 90 min	1.97±0.49	2.13±0.35	0.1330
RSS 120 min	1.64±0.49	2.13±0.35	0.0020*
POST OP RSS 0 min	1.70±0.47	2.10±0.61	0.0060*
POST OP RSS 30 min	1.63±0.49	1.93±0.45	0.0160*
POST OP RSS 1h	1.63±0.49	1.67±0.48	0.7910

**Table 4**

In our study Intraoperative Ramsay Sedation Scores in series were slightly high in Group B compared to Group A. Maximum mean score in Group B was 3.93±0.25, whereas it was 3.20±0.66, P value < 0.05 by using Student unpaired T test. There was no excessive sedation (RSS>4) was observed in both the groups. Postoperative period the maximum mean score of sedation in Group B was 2.10±0.61, whereas it was 1.70±0.61 in Group A, P value is 0.006, which is statistically significant. Though it is statistically significant, it is clinically insignificant In our study the time for first request of analgesic in Group A was 265.5±15.11 minutes, where as it was 276±13.8 minutes in Group B. student unpaired T test is used to compare the above data and calculated P value is 0.007. The mean time for rescue analgesic was slightly higher in Group B compared to Group A, which is

statistically significant. we observed that duration of motor block (regression to Bromage 0) is  $265 \pm 19.61$  minutes in Group A compared to  $276.83 \pm 20.53$  minutes in Group B. Student unpaired T test is used to compare the above data and calculated P value is 0.026, which is statistically significant. Mean duration of motor block was slightly higher in Group B compared to Group A, which is statistically significant. we observed that onset of motor and sensory blockade there is no difference in mean duration of onset of motor blockade and sensory blockade between both the groups, which is statistically not significant.

we observed that two segment regression had mean duration of  $116.83 \pm 11.33$  minutes in Group A (Dexmedetomidine  $0.5 \mu\text{g}/\text{kg}$ ) where as it was  $123 \pm 9.34$  minutes in Group B (Dexmedetomidine  $1 \mu\text{g}/\text{kg}$ ). Student unpaired T test is used to compare the above data and the resultant P value is 0.025. Mean duration of two segment regression is slightly higher in Group B compared to Group A, which is statistically significant. The highest level of sensory block is comparable in both groups, there is no difference in highest level of sensory block achieved in both the groups, which is not statistically significant

Variable	Study groups	Mean $\pm$ SD	p-value
TIME TO TWO SEGMENT REGRESSION (min)	Group A	$116.83 \pm 11.33$	0.02 50*
	Group B	$123 \pm 9.34$	
SENSORY ONSET (min)	Group A	$2.96 \pm 0.52$	0.18 4
	Group B	$2.78 \pm 0.54$	
MOTOR BLOCK ONSET (min)	Group A	$5.19 \pm 1.01$	0.44 8
	Group B	$4.99 \pm 0.99$	
DURATION OF MOTOR BLOCK (min)	Group A	$265.00 \pm 19.6111$	0.0260*
	Group B	$276.83 \pm 20.53$	

## Discussion

60 patients between the age 18 – 60 years, came for elective lower abdominal and lower limb surgeries under subarachnoid block were selected 30 patients were randomly allocated either to Group A (Dexmedetomidine  $0.5 \mu\text{g}/\text{kg}$ ) or Group B (Dexmedetomidine  $1.0 \mu\text{g}/\text{kg}$ ). The study drugs were infused as loading dose over 10 minutes immediately after subarachnoid block. The objective of the study was to compare onset and duration of sensory and motor blockade, time for rescue analgesic, intraoperative and postoperative sedation scores, intraoperative hemodynamics parameters.

Sensory blockade was checked with pin prick in mid axillary line from caudal to cephalad direction and time taken for onset of sensory blockade at T10 dermatome, highest level of sensory blockade and time taken for two segment regression from highest level were noted. Motor blockade was assessed by Modified Bromage Scale. Time taken for motor blockade to reach Modified Bromage Scale 3 and regression of motor blockade to Modified Bromage Scale 0 was noted. Hemodynamic parameters heart rate, systolic, diastolic, mean arterial blood pressures were monitored intraoperatively and in immediate postoperative period. The level of sedation was assessed using Ramsay Level of Sedation Scale. Time for rescue analgesic in postoperative period was noted.

We noted slight prolongation of time for two segment regression of sensory blockade, time taken for regression of motor blockade to Modified Bromage Scale 0 and time for rescue analgesic. There was no excessive sedation ( $>4$ ) intraoperatively in both the groups. The incidence of bradycardia requiring atropine was high in Group B (Dexmedetomidine  $1.0 \mu\text{g}/\text{kg}$ ). However bradycardia was brief and responded well to atropine. The difference is statistically not significant for hypotension requiring mephenteramine between the groups.

We conclude that Dexmedetomidine administered as isolated loading dose of  $1.0 \mu\text{g}/\text{kg}$  over 10 minutes immediately after spinal anesthesia slightly increased the duration of sensory blockade, motor blockade and time for rescue analgesia than loading dose of  $0.5 \mu\text{g}/\text{kg}$  in patients undergoing lower abdominal and lower limb surgeries.

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