



### Clinical Investigation

## Haemodynamic changes with lower dose of Hyperbaric Bupivacaine with Dexmedetomidine and Conventional dose of Hyperbaric Bupivacaine for Subarachnoid Block in Lower Limb Surgeries (Orthopaedic Cases)

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### **Abstract**

**Background and Aims:** *It is universally agreed that the anaesthesia of choice for lower limb surgeries is a subarachnoid block and a sensory level of T – 10 is recommended to provide excellent anaesthesia for the patient. It is well established that opioids has got a prominent analgesic action at the spinal cord level and it can be used safely for subarachnoid block. If you can add a  $\alpha$ -2 adrenoreceptor agonist like Dexmedetomidine to hyperbaric bupivacaine (the standard drug used for sub arachnoid block) and thus reduce the dose of bupivacaine used, without compromising on the analgesic effect and haemodynamic changes.*

**Aim of the study:** *Primary aim: To measure the Haemodynamic changes like Blood Pressure and Pulse rate by adding dexmedetomidine to lower dose Hyperbaric bupivacaine and Hyperbaric bupivacaine alone. Secondary aim: Compare the side effects like nausea, vomiting, sedation, shivering and pruritis.*

**Methods:** *This study was prospective, randomized, comparative study double blind in nature and conducted after obtaining institutional Ethics Committee approval and written informed consent. The person giving the drug and the monitoring personnel were blinded 60 adult patients of ASA grade I and II aged between 20 – 50 year. Undergoing various elective lower limb (Orthopaedics) surgeries.*

**Results:** *Dexmedetomidine in a dose of 5 $\mu$ g was used for supplementation spinal Bupivacaine, showed that Haemodynamic changes like blood pressure and pulse rate is more on the bupivacaine group than dexmedetomidine group.*

**Conclusion:** *5  $\mu$ g Dexmedetomidine to 2cc of hyperbaric Bupivacaine 0.5% is associated with lessor incidence of Hypotension and less Bradycardia compare to bupivacaine group had more incidence of hypotension and bradycardia.*

**Keywords:** *Dexmedetomidine, Hyperbaric Bupivacaine, Spinal anaesthesia.*

### **Introduction**

Dexmedetomidine is an  $\alpha$ -2 adreno receptor agonist, which is approved as an intravenous sedative and analgesic drug. It is useful adjuvant

in regional anesthesia. Kanazi et al, found that 5 $\mu$ g clonidine are equipotent intrathecally when added to Bupivacaine in patients undergoing major surgeries in the abdomen and lower

extremities. Dexmedetomidine given intrathecally along with Bupivacaine produce significantly longer duration of sensory and motor block than Bupivacaine alone without serious side effects less Hypotension and Bradycardia compare to Bupivacaine. It maintains patient arousability and respiratory function. Bupivacaine: is a synthetic local anesthetic drug and it belongs to Amide group, Pka = 8.1 ph 0.5% bupivacaine is 5.5 specific gravity of 1.0227 – 1.0278. protein binding 95% its volume of distribution is 73L and clearance is 0.47lt/min. Elimination half-life is 210 minutes. Bupivacaine act as a conduction blocker of nerve impulses by sodium pump inhibition. More specifically bupivacaine is classified as pipercoloxylides.

### Materials and Methods

This prospective comparative study was conducted after obtaining institutional Ethics Committee approval and written informed consent. The person giving the drug and the monitoring personnel were blinded 60 adult patients of ASA grade I and II aged between 20 – 50 year. Undergoing various elective lower limb (Orthopaedics) surgeries. Patient were randomly allocated to one of the two group of 30 each according to computer generated randomized table satisfying inclusion and exclusion criteria's.

### Inclusion Criteria

- ASA-I/II
- Age group between 20 - 50
- Height- 155-175 cm

### Exclusion Criteria

- History of allergy to local anaesthetics.
- Patients with spinal deformities, peripheral neuropathy, bleeding disorders or anticoagulation therapy.
- Patients with serious systemic illness, psychiatric illness, mental retardation. Patients with Diabetes mellitus ,systemic Hypertension and Ischaemic heart disease, Patients satisfying the selection criteria were randomly divided into two groups of 30 each as per the random number chart. Both the patient and

the principal investigator were blinded for the drug, which was being administered during the period of observation and the drug being prepared by a qualified assistant.

### Monitors

- Non-invasive Blood pressure monitoring
- Pulse oximeter
- ECG
- Visual assessment of respiration

### Interventions

**Preparation:** All the patients were selected after pre-op evaluation and written informed consent from all the patients. Psychological preparation was done and the procedure explained to all the patients in advance.

**On the table:** An IV access was secured using an 18G cannula under local anesthesia in the left forearm vein and an isotonic saline drip was started at a rate of 8ml/kg/hr. Monitors including a pulse oxymeter, B.P apparatus & an ECG monitor were routinely used. Midazolam was titrated with increments of 0.25 mg each and used up to a maximum dose of 0.025mg/kg to have sufficient anxiolysis without producing too much sedation. The patient was kept left lateral and positioned for a subarachnoid block. Under strict aseptic precautions after giving local anaesthesia with a 26 G needle, lumbar puncture was done with a Quinke needle of 23 G size using either the midline or paramedian approach in the L 3/4 or L 2/3 space. After clear CSF was flowing freely, (the Dexmedetomidine group received 5µg (0.5) cc of Dexmedetomidine with 0.5% 2 cc (10 mg) hyperbaric bupivacaine and the Bupivacaine group who received of 0.5% 2.5cc of hyperbaric bupivacaine) was injected into the subarachnoid space. The table was kept horizontal throughout. The patient was turned supine immediately. Throughout the procedure patient received an oxygen supplementation of 4L/minute via a simple oxygen mask.

### Main outcome and measurements

To measure the haemodynamic changes like

changes in pulse rate and blood pressure and other side effects like nausea, vomiting, sedation, shivering and pruritis in the group with Dexmedetomidine-Bupivacaine group and Bupivacaine group alone.

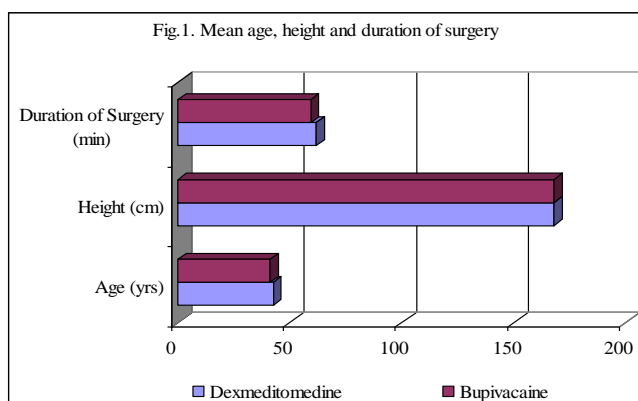
**Data Collection:** The principal investigator himself collected the data. Pulse rate and blood pressure were checked every minute for the first 20 minutes and every two-minute for the next 20 minutes and every five minutes till the end of surgery and then every 10-15 minutes for three hours post operatively. They were followed up for 24 hours thereafter with routine post-op care in the post-surgical wards.

Complications during surgery were treated as follows: Hypotension (defined as a systolic blood pressure of < 100 mm Hg or fall of 30% or more of initial reading, whichever was higher) was treated with 6mg increments of iv ephedrine and 200 ml normal saline. Bradycardia (defined as a heart rate < 50bpm) was treated with iv atropine 0.3-0.5 mg, if it was associated with hypotension.

**Observations and Results**

The observations made were tabulated and analysed using appropriate statistical tools. The patients in both Dexmedetomidine group & the Bupivacaine group were comparable with respect to their age, height and duration of surgery (unpaired t test)

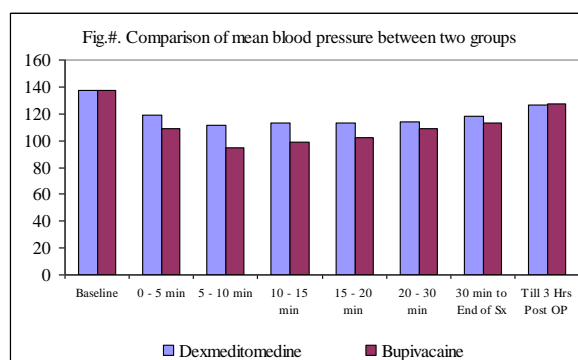
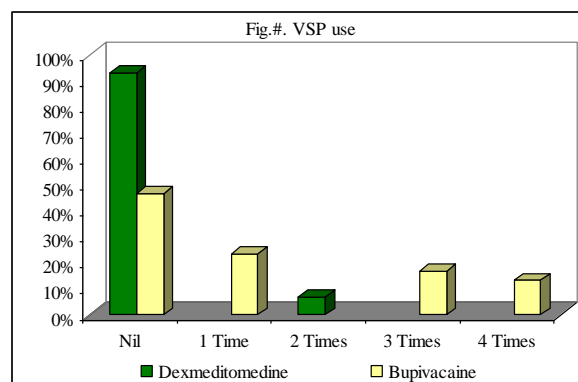
Parameter	Group	Mean	± SD	t value	P value	Comments
Age (yrs)	Dex	42.53	5.64	0.959	> 0.05	Not significant
	bupivacaine	41.17	5.40			
Height (cm)	Dexmed	168.07	4.21	- 0.059	> 0.05	Not significant
	bupivacaine	168.13	4.49			
Duration of Surgery (min)	Dexmed	61.73	10.88	0.835	> 0.05	Not significant
	bupivacaine	59.37	11.08			



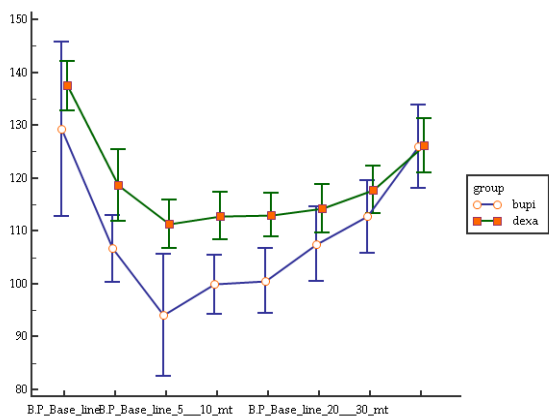
**Haemodynamic Changes**

Pulse rate & blood pressure were checked every minute for the first 20 minutes and every two - minute for the next 10 minute for the next 10 minutes and every five minutes till the end of surgery and then every 10-15 minutes for three hours post operatively. They were followed up to 24 hours thereafter with routine post-op care in the post-surgical wards.

**Hypotension and Bradycardia:** While analyzing the two parameters - pulse rate & blood pressure, we included the data of only the first 30 minutes of these variables for our statistical analysis because it is the period during which the intrathecal drug usually gets fixed and exerts its significant sympatholytic effect. Only two subjects among the Dexmedetomidine group had episodes of hypotension that required vasopressors, whereas 16 among the Bupivacaine group had incidence of hypotension in the first 30 minutes after administering the subarachnoid block. Moreover 9 among these 16 subjects, among Bupivacaine group, had persistence of hypotension that required more than two boluses of the vasopressor (VSP), while none among the Dexmedetomidine group required that.



	N	Minimum	Maximum	Mean	95% CI	Median	95% CI	SD	Normal Distr.
B.P_Base_line	60	1.220	164.000	135.520	130.121 to 140.919	140.000	135.878 to 144.000	20.9000	<0.0001
B.P_Base_line_0_5_mt	60	86.000	180.000	113.667	109.596 to 117.737	110.000	108.000 to 120.000	15.7573	0.0005
B.P_Base_line_5_10_mt	59	18.000	136.000	102.746	98.059 to 107.432	106.000	96.000 to 110.000	17.9843	<0.0001
B.P_Base_line_10_15_mt	57	70.000	146.000	105.579	101.790 to 109.368	106.000	100.000 to 110.736	14.2815	0.6428
B.P_Base_line_15_20_mt	57	76.000	160.000	107.684	103.699 to 111.669	110.000	105.264 to 110.736	15.0180	0.0021
B.P_Base_line_20_30_mt	59	84.000	152.000	111.576	108.341 to 114.811	110.000	107.006 to 114.000	12.4141	0.0006
B.P_Base_line_30_end_of_surgery	53	94.000	160.000	116.528	112.907 to 120.150	114.000	110.000 to 118.000	13.1392	0.0002
B.P_Base_line_Till_3_h_post_op	59	100.000	170.000	127.085	123.332 to 130.837	128.000	120.000 to 130.000	14.3998	0.0543

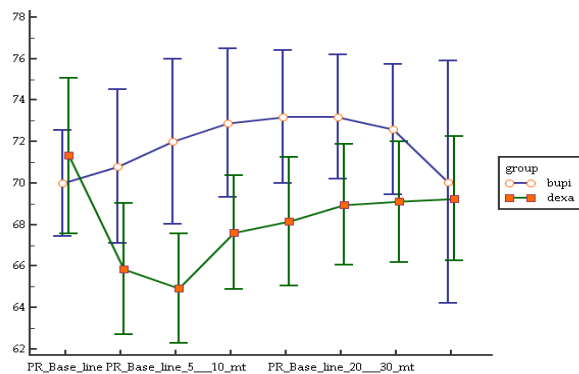
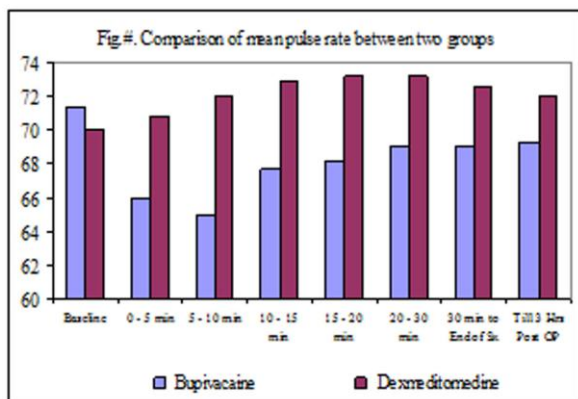


Parameter	Group	Mean	± SD	t value	P value	Comments
Vasopressor use	exmeditomedine	0.13	0.51	-3.851	< 0.001	Clinically Significant
	Bupavacaine	1.27	1.53			

The most significant side effects reported about the use of intrathecal  $\alpha_2$  - adrenoreceptor agonists are bradycardia and Hypotension. In present study hypotension Bradycardia was more in the Bupivacane group than in the Dexmeditomedine group.

**Comparison of Pulse Rate between two groups**

	PR_Base_line	PR_Base_line_0_5_mt	PR_Base_line_5_10_mt	PR_Base_line_10_15_mt	PR_Base_line_15_20_mt	PR_Base_line_20_30_mt	PR_Base_line_30_end_of_surgery	PR_Base_line_Till_3_h_post_op
N	60	60	60	60	60	60	60	60
Minimum	56.000	49.000	56.000	54.000	56.000	56.000	56.000	0.600
Maximum	94.000	90.000	96.000	88.000	88.000	88.000	92.000	88.000
Mean	70.667	68.333	68.467	70.267	70.683	71.083	70.850	69.660
95% CI	68.457 to 72.876	65.883 to 70.784	65.971 to 70.962	67.965 to 72.569	68.421 to 72.946	68.990 to 73.176	68.726 to 72.974	66.475 to 72.845
Median	70.000	68.000	68.000	69.000	69.000	70.500	70.000	69.000
95% CI	68.000 to 74.000	64.000 to 70.000	62.000 to 70.000	66.000 to 76.000	66.000 to 72.000	67.878 to 72.000	66.000 to 74.000	66.939 to 74.000
SD	8.5542	9.4862	9.6612	8.9117	8.7575	8.1017	8.2211	12.3291
Normal Distr.	0.1415	0.2557	0.0008	0.0164	0.0035	0.0362	0.0437	<0.0001



**Summary statistics table**

	N	Minimum	Maximum	Mean	95% CI	Median	95% CI	SD	Normal Distr.
PR_Base_line	60	56.000	94.000	70.667	68.457 to 72.876	70.000	68.000 to 74.000	8.5542	0.1415
PR_Base_line_0_5_mt	60	49.000	90.000	68.333	65.883 to 70.784	68.000	64.000 to 70.000	9.4862	0.2557
PR_Base_line_5_10_mt	60	56.000	96.000	68.467	65.971 to 70.962	68.000	62.000 to 70.000	9.6612	0.0008
PR_Base_line_10_15_mt	60	54.000	88.000	70.267	67.965 to 72.569	69.000	66.000 to 76.000	8.9117	0.0164
PR_Base_line_15_20_mt	60	56.000	88.000	70.683	68.421 to 72.946	69.000	66.000 to 72.000	8.7575	0.0035
PR_Base_line_20_30_mt	60	56.000	88.000	71.083	68.990 to 73.176	70.500	67.878 to 72.000	8.1017	0.0362
PR_Base_line_30_end_of_surgery	60	58.000	92.000	70.850	68.726 to 72.974	70.000	66.000 to 74.000	8.2211	0.0437
PR_Base_line_Till_3_h_post_op	60	0.600	88.000	69.660	66.475 to 72.845	69.000	66.939 to 74.000	12.3291	<0.0001

**Other Side Effects**

No subjects among either group had any incidence of sedation or respiratory depression or pruritis. 2 subjects from Bupivacaine group had intra operative nausea and vomiting, while only one subject among the Dexmedetomidine group had it. The incidence of shivering was higher among the Bupivacaine group with 9 subjects experienced shivering, while none had in Dexmedetomidine group.

**Discussion**

Here we discuss the Haemodynamic changes like blood pressure and pulse rate these parameters checked the every 5 minutes till the end of surgery and every 10 – 15 minutes for three hours post operatively. The result of the study shows that the supplementation of lower dose of Bupivacaine with 5 µg Dexmedetomidine significantly<sup>1-5</sup> prolonged sensory block and less hypotension and bradycardia compared with intrathecal Bupivacaine alone. Intrathecal bupivacaine group alone significantly reduces blood pressure and heart rate from this study.

The American Journal of applied sciences, Publication effect of adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on spinal block in Gynaecological procedures, the purpose of this study was evaluated the onset and duration of sensory and block as well as operative analgesia and Haemodynamic changes of Dexmedetomidine or fentanyl given intrathecally with plain 0.5% Bupivacaine for spinal anaesthesia. Patient were randomly allocated to receive either 10 mg isobasic bupivacaine plus 5 µg dexmedetomidine (group D n=38) or 10 mg isobaric bupivacaine plus 25 mg fentanyl (group Fn = 38), results patients in group D had significant

longer sensory and motor block and less hypotension and bradycardia than patients in group F. The bupivacaine group had more hypotension and bradycardia than Dexmedetomidine group.

In the present study and based on the above study's findings Dexmedetomidine in a dose of 5µg was used for supplementation spinal Bupivacaine, showed the duration of sensory block in (Dexmedetomidine) group is 295±40 min and bupivacaine group 219±15 (P< 0.001) and it is highly significant. Dexmedetomidine is a highly selective α<sub>2</sub> adrenoreceptor agonist approved as intravenous sedative and adjuvant to anesthesia. Dexmedetomidine when used intravenously during anesthesia reduces opioid and Inhalational anesthetics requirements. Compared with clonidine a α<sub>2</sub> adrenoreceptor agonist, the affinity of Dexmedetomidine to α<sub>2</sub> receptors has been reported to be 10 times more than clonidine. Moreover, Kalso et al. and post et al. reported a 1:10 dose ratio between intrathecal Dexmedetomidine and clonidine in animals. Clinical studies in surgical patients showed that intrathecal clonidine increases the duration of sensory block when added to spinal local anesthetics and this effect of clonidine in dose dependent. From Kanazi study and animal studies, we assumed that 3 - 5 µg Dexmedetomidine would be equipotent to 30 - 45 µg clonidine when used for supplementation of spinal Bupivacaine.

In this study intrathecal Dexmedetomidine and Bupivacaine block has resulted in significantly less side effects like hypotension and bradycardia than intrathecal Bupivacaine alone. The most significant side effects reported about the use of intrathecal α<sub>2</sub> adrenoreceptor agonist are bradycardia and hypotension, in present study

these side effects were not significant probably because we used small dose of intrathecal Dexmedetomidine, which was confirmed by the findings of Kanazi report. In present study hypotension and bradycardia was more in the Bupivacaine group than in the Dexmedetomidine group.

### Conclusion

After analyzing the results our study, Dexmedetomidine group is associated lesser incidence of Hypotension and bradycardia, lesser degree of motor blockade and improved analgesic efficacy. Intrathecal Dexmedetomidine supplementation of spinal block seems to be less haemodynamic changes and a good alternative to intrathecal fentanyl. However, Intrathecal dose of Dexmedetomidine to hyperbaric bupivacaine, use in present study needs further clinical studies to prove its efficacy and safety and sample size is adequate randomization not done and recommends further clinical evaluation.

In conclusion, 5 µg Dexmedetomidine seems to be an attractive alternative as adjuvant to spinal bupivacaine in surgical procedures especially in those that need quite long time with minimal side effects like less hypotension bradycardia and excellent quality of spinal analgesia compared to hyperbaric Bupivacaine alone. In this study we concluded that Hyperbaric Bupivacaine group had more incidence of hypotension and bradycardia compared to Dexmedetomidine group.

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**Conflicts of Interest:** There are no conflicts of Interest

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