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## A study on hemodynamic changes and adverse reactions between isobaric levobupivacaine 0.5% versus isobaric levobupivacaine 0.5% with 3mcg dexmedetomidine

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### Abstract

Hypotension during spinal anaesthesia is because of the physiologic effects of central Neuraxial blockade, which is due to two major alterations in cardiovascular systems. First is blockade of sympathetic vasoconstrictor Fibers of the arterioles. Arteriolar dilatation results in a decrease in peripheral vascular resistance. The second is actual dilatation of peripheral veins and Venules with pooling of blood. This combined with paralysis of skeletal muscle and the loss of muscular milking action plus the interference with the thoracic respiratory pump decreases venous return. Sixty patients in the age group between 20 and 60 years belonging to ASA Grade-I and Grade-II posted for elective lower limb surgeries were grouped randomly into two groups(n=30). Randomization was done using simple sealed envelope technique. Based on outcome variables namely mean sensory and motor block time, significance detection of mean difference of 20 minutes, with 90% statistical power and 5% level of significance, the sample of 60 was adequate.

There was a statistically significant changes in the pulse rate between two groups during first 60 minutes. Two patients in Group LD had bradycardia and no patients in Group LF. There is no statistically significant difference in systolic blood pressure between the groups. Two patients in Group L and Two patients in Group LD had hypotension. Two patients in Group L developed adverse effects (Bradycardia-2), and Four patients in Group LD (Hypotension -2, Bradycardia - 2). There was no statistically significant difference between the groups regarding adverse effects ( $p=0.671$ ).

**Keywords:** Hemodynamic changes, adverse reactions, isobaric levobupivacaine

### Introduction

The cardiovascular effects of spinal anaesthesia are similar in some ways to the combined use of intravenous  $\alpha_1$  and  $\beta$ - adrenergic blockers. It decreases heart rate and arterial blood pressure. The sympathectomy that accompanies the technique depends on the height of the block, with the sympathectomy extending for two to six dermatomes above the sensory level. This results in venous and arterial vasodilatation, but because of the large amount of blood in the venous system (approximately 75% of total blood volume), the venodilation effect predominates because of the limited amount of smooth muscle in arteries. If normal cardiac output is maintained, total peripheral resistance should decrease only 15% to 18% in normovolemic healthy patients, even with near total sympathectomy. Heart rate during high spinal anaesthesia typically decreases as a result of blockade of the Cardioaccelerator Fibers arising from T1 to T4. The heart rate may decrease as a result of a fall in right atrial filling, which decreases outflow from intrinsic chronotropic stretch receptors located in the right atrium and great veins <sup>[1, 2]</sup>.

Tidal volume remains unchanged during high spinal anaesthesia. Vital capacity decreases from 4.05 to 3.73 litres and is due to decrease in expiratory reserve volume related to paralysis of abdominal muscles necessary for forced exhalation.

The rare respiratory arrest associated with spinal anaesthesia is unrelated to phrenic or inspiratory dysfunction, but rather to Hypoperfusion of the respiratory centres in the brainstem. This rare respiratory arrest almost always disappears as soon as pharmacologic and fluid therapies have restored cardiac output and blood pressure. This would not be the case if phrenic paralysis due to high levels of local anaesthetic was the cause of apnoea. The physiological consideration related to muscle paralysis with spinal anaesthesia should focus on the expiratory muscles which are important for effective coughing and clearing of intrapulmonary secretions <sup>[3]</sup>.

Loss of the Mandibulo-Temporal-Joint [MTJ] sense or position sense in the thoracic cage structures may provoke a sensation of not breathing and has been termed affective dyspnoea. It can be combated simply by having the patient voluntarily take deep breaths or by having the patient smell aromatic spirit <sup>[4]</sup>.

Nausea and vomiting may be associated with spinal anaesthesia and are primarily related to gastrointestinal hyperperistalsis due to unopposed parasympathetic activity. This gastrointestinal hyperperistalsis has the advantage of providing excellent surgical condition because of contracted gut. Blockade of the thoracolumbar sympathetic outflow at levels up to T5 will promote gastric emptying. Motor activity of the gut is enhanced with an increase in peristaltic and segmental motility, with sphincter relaxation <sup>[5]</sup>.

Symptoms are related to the tissue hypoxia that results from diminished blood pressure. Hypotension during spinal anaesthesia is because of the physiologic effects of central Neuraxial blockade, which is due to two major alterations in cardiovascular systems. First is blockade of sympathetic vasoconstrictor Fibers of the arterioles. Arteriolar dilatation results in a decrease in peripheral vascular resistance. The second is actual dilatation of peripheral veins and Venules with pooling of blood. This combined with paralysis of skeletal muscle and the loss of muscular milking action plus the interference with the thoracic respiratory pump decreases venous return.

Adequate hydration that is replacement of fluid deficit prior to induction of spinal anaesthesia and proper positioning of the patient after spinal anaesthesia will improve venous return, cardiac output and blood pressure. Once the diagnosis of hypotension is established four procedures are of practical importance <sup>[6]</sup>.

The quest for newer and safer anaesthetic agents has always been one of the primary needs in anaesthesiology practice. Regional anaesthesia techniques have seen numerous modifications over the last two decades with the advent of many new and safer local anaesthetics. Bupivacaine, the widely used local anaesthetic in regional anaesthesia is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers Levobupivacaine S (–) isomer and Dextrobupivacaine R (+) isomer. Severe central nervous system (CNS) and cardiovascular adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anaesthesia have been linked to the R (+) isomer of Bupivacaine <sup>[7]</sup>.

Levorotatory isomers were shown to have a safer pharmacological profile with less cardiac and neurotoxic

adverse effects. The pure S (–) enantiomers of Bupivacaine i.e., Levobupivacaine was thus introduced into clinical anaesthesia practice. Levobupivacaine has been recently introduced into the Indian market (2012) and is being widely used in various health set-ups. The decreased toxicity of Levobupivacaine is attributed to its faster protein binding rate <sup>[8]</sup>.

### Methodology

Sixty patients in the age group between 20 and 60 years belonging to ASA Grade-I and Grade-II posted for elective lower limb surgeries were grouped randomly into two groups (n=30). Randomization was done using simple sealed envelope technique. Based on outcome variables namely mean sensory and motor block time, significance detection of mean difference of 20 minutes, with 90% statistical power and 5% level of significance, the sample of 60 was adequate.

**Group LF (n=30):** Levobupivacaine 0.5% isobaric (3ml) with normal saline (0.3ml) (Total 3.3 ml).

**Group LD (n=35):** Levobupivacaine 0.5% isobaric (3ml) with Dexmedetomidine 3µg (0.3ml) (Total 3.3 ml).

### Inclusion criteria

Adult patients aged between 20-60 years, belonging to ASA grade I and II posted for elective Lower limb surgeries were included in the study with.

1. Weight >50kgs
2. Height >150cm.

### Exclusion criteria

Patients belonging to the following classes:

- Age group less than 20 years and more than 60 years,
- Patients with ASA Grade > II,
- Patients with spinal deformities or injection site infection,
- Patients posted for emergency surgeries,
- Patients with morbid obesity,
- Patients shorter than 150 cm,
- Patients having any absolute contraindications for spinal anaesthesia like raised intracranial pressure, severe hypovolemia, bleeding diathesis,

### Results

**Table 1:** Age distribution of patients studied

Age in years	Levobupivacaine		Levobupivacaine + dexmedetomidine	
	No	%	No	%
21-30	4	13.3	7	23.3
31-40	6	20.0	7	23.3
41-50	15	50.0	10	33.3
51-60	5	16.7	6	20.0
Total	30	100.0	30	100.0
Mean ± SD	43.57±8.94		42.00±9.38	

Table 1 shows age distribution of the patients in two groups. There is no statistically significant difference in the age wise

distribution of patients between the groups (p=0.510)

**Table 2:** ASA Grade distribution of patients studied

ASA Grade	Levobupivacaine		Levobupivacaine + dexmedetomidine	
	No	%	No	%
Grade 1	15	50.0	15	50.0
Grade 2	15	50.0	15	50.0
Total	30	100.0	30	100.0

Samples are ASA matched with P=1.000

Table 2 shows the ASA Grade distribution in both the groups. There is no statistically significant difference between the groups (p=1.000).

**Table 3:** Comparison of Pulse Rate in two groups of patients studied

Heart rate (bpm)	Levobupivacaine	Levobupivacaine + dexmedetomidine	P value
Basal	72.80±11.95	69.10±11.86	0.233
2min	77.40±11.66	71.10±12.15	0.045*
5min	77.60±10.48	71.10±10.51	0.020*
10min	79.90±7.62	72.30±10.19	0.002**
20min	81.00±6.45	71.20±9.20	<0.001**
30min	83.40±7.05	73.70±9.26	<0.001**
40min	83.40±6.56	74.20±8.60	<0.001**
60min	82.70±6.65	76.60±8.39	0.003**
90min	73.75±9.11	63.43±6.13	0.050+
120min	74.00±8.49	74.00±0.00	1.000
At the end of surgery	72.67±4.21	74.40±10.11	0.639

Table 3 shows the comparison of Pulse Rate in two groups of patients studied. There was a statistically significant changes in the pulse rate between two groups during first 60

minutes. Two patients in Group LD had bradycardia and no patients in Group LF.

**Table 4:** Comparison of SBP (mm Hg) in two groups of patients studied

SBP (mm Hg)	Levobupivacaine	Levobupivacaine + dexmedetomidine	P value
Basal	130.16±10.27	128.17±9.72	0.442
2min	122.03±13.88	120.70±13.42	0.707
5min	118.00±13.42	113.60±6.22	0.109
10min	107.30±17.68	113.00±12.89	0.159
20min	115.00±9.63	115.60±11.13	0.824
30min	112.60±15.14	110.80±12.90	0.622
40min	107.30±15.06	99.20±31.42	0.208
60min	109.40±8.49	112.20±13.25	0.334
90min	111.75±7.37	120.43±13.20	0.263
120min	113.50±4.95	107.50±4.95	0.349
At the end of surgery	113.22±8.15	113.60±14.32	0.945

Table 4 shows the mean SBP (mm Hg) in two groups of patients studied. There is no statistically significant difference in systolic blood pressure between the groups.

Two patients in Group L and Two patients in Group LD had hypotension.

**Table 5:** Comparison of DBP (mm Hg) in two groups of patients studied

DBP (mm Hg)	Levobupivacaine	Levobupivacaine + dexmedetomidine	P value
Basal	79.70±10.83	80.90±17.86	0.754
2min	72.40±8.00	68.70±11.09	0.144
5min	68.60±9.40	70.10±11.03	0.573
10min	61.80±12.66	73.10±15.67	0.003**
20min	63.80±9.99	69.30±12.08	0.060+
30min	67.20±13.62	68.00±12.48	0.813
40min	63.40±10.37	66.00±10.46	0.338
60min	64.70±9.49	67.90±11.39	0.242
90min	59.75±14.73	72.00±8.60	0.110
120min	69.00±5.66	60.50±12.02	0.461
At the end of surgery	67.67±9.97	70.30±14.02	0.647

Table 5 shows Mean DBP (mm Hg) in two groups of patients studied. There was statistically significant

difference in diastolic blood pressure at 10 mins between the groups.

**Table 6:** Comparison of MAP (mm Hg) in two groups of patients studied

MAP (mm Hg)	Levobupivacaine	Levobupivacaine + dexmedetomidine	P value
Basal	96.00±9.14	95.10±13.90	0.768
2min	86.17±9.38	86.71±8.92	0.823
5min	83.60±10.35	84.20±8.29	0.805
10min	75.33±13.53	73.27±14.29	0.567
20min	77.90±10.07	80.50±10.74	0.337
30min	80.80±16.13	79.20±11.30	0.658
40min	76.40±12.38	79.30±10.80	0.338
60min	76.70±8.62	80.20±12.00	0.200
90min	77.60±8.99	84.88±7.36	0.138
120min	79.50±12.02	78.00±8.49	0.899
At the end of surgery	80.78±9.38	79.2.00±11.84	0.753

Table 6 shows the mean MAP (mm Hg) in two groups of patients studied. There is no statistically significant difference in Mean arterial pressure between the groups

**Table 7:** Comparison of SpO<sub>2</sub> % in two groups of patients studied

SpO <sub>2</sub> %	Group L	Group LD	P value
Basal	100.00±0.00	100.00±0.00	-
2 min	100.00±0.00	100.00±0.00	-
5 min	100.00±0.00	100.00±0.00	-
10 min	100.00±0.00	100.00±0.00	-
20 min	100.00±0.00	100.00±0.00	-
30 min	100.00±0.00	100.00±0.00	-
40 min	100.00±0.00	100.00±0.00	-
60 min	100.00±0.00	100.00±0.00	-
90 min	100.00±0.00	100.00±0.00	-
120 min	100.00±0.00	100.00±0.00	-
At end of surgery	100.00±0.00	100.00±0.00	-

Table 7 shows the mean SpO<sub>2</sub> % in two groups of patients studied. All the patients in both the groups maintained 100% saturation.

**Table 8:** Adverse Effects

ADR	Levobupivacaine (n=30)		Levobupivacaine + dexmedetomidine (n=30)	
	No	%	No	%
No	28	93.3	26	86.7
Yes	2	6.7	4	13.3
• Bradycardia	2	6.7	2	6.7
• Hypotension	0	0.0	2	6.7

P=0.671, not significant, Fisher Exact test

Table 8 shows the adverse effects in both the groups. Two patients in Group L developed adverse effects (Bradycardia-2), and Four patients in Group LD (Hypotension -2,

Bradycardia - 2). There was no statistically significant difference between the groups regarding adverse effects (p=0.671).

**Table 9:** Dose of Atropine

Atropine Dose Used	Levobupivacaine (n=30)		Levobupivacaine + dexmedetomidine (n=30)	
	No	%	No	%
No	28	93.3	28	93.3
Yes	2	6.7	2	6.7
0.6 mg	2	6.7	2	6.7

p=1.000, Not significant, Fisher Exact test

Table 9 shows the dose of atropine required to treat hypotension. There was no statistically significant difference between the dose of ephedrine required in two groups (p=1.000).

## Discussion

The aim of good post-operative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. Spinal anaesthesia is a commonly used

technique for lower limb surgeries, as it provides faster and effective onset of sensory and motor block and also extended postoperative analgesia. Levobupivacaine is a preferred local anaesthetic due to its longer sensory block, lower cardiac and central nervous system toxicity. Opioids and  $\alpha_2$ -agonists are commonly used Neuraxial adjuvants to improve the quality of perioperative analgesia.

In current study 60 patients undergoing elective lower limb surgeries were included. The demographic data in terms of

age, height, weight showed no statistical difference. The drug selected for subarachnoid block was 15mg of 0.5% isobaric levobupivacaine. Similarly Sathitkarnmanee T *et al.* <sup>[9]</sup> and Mantouvalou M *et al.* <sup>[10]</sup> used 15mg of levobupivacaine which provided adequate sensory and motor block for abdominal surgeries. Lee YY *et al.* <sup>[11]</sup> concluded that 2.6ml of 0.5% levobupivacaine can be used as an alternative to 0.5% racemic bupivacaine in spinal anaesthesia.

In our study we added dexmedetomidine 3µg in group LD to levobupivacaine. Similarly Esmoğlu *et al.* <sup>[12]</sup> hypothesised that Intrathecal 3µg dexmedetomidine shortens sensory and motor block onset time and prolongs block duration without any significant adverse effects.

So we have chosen 3µgdexmedetomidine as adjuvant with levobupivacaine to avoid undue length of motor block and also to minimise the cardiovascular side effects like bradycardia.

There is a statistically significant changes in pulse rate between two groups in first 60min. 2 Patients in group L and group LD developed Bradycardia similarly in the study conducted by Esmoğlu *et al.* <sup>[12]</sup> reported 3 patients in group L and 2 patients in group LD developed bradycardia.

In present study two patients in Group LD had hypotension of more than 20% fall in basal blood pressure similar to a study conducted by Esmoğlu *et al.* <sup>[12]</sup> wherein 2 patients in group LD developed hypotension of more than 20% fall in basal value.

In the current study none of our patients had any evidence of respiratory depression, sedation, episodes of nausea, vomiting, shivering, hypersensitivity reactions to any of the study drug whereas Esmoğlu *et al.* <sup>[12]</sup> reported 1 patient with nausea and 1 patient with vomiting in Levobupivacaine group and one patient with nausea and 2 patient with nausea and 1 patient with vomiting in dexmedetomidine group.

## Conclusion

To conclude patients who received dexmedetomidine 3µg along with levobupivacaine showed a better quality and prolonged duration of sensory and motor block with better hemodynamic stability.

The bradycardia response was more pronounced in dexmedetomidine group which requires constant vigilant monitoring. Finally we conclude that dexmedetomidine is an important agent in the armamentarium of various adjuvants to local anaesthetic being used for lower limb surgeries.

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