ORIGINAL RESEARCH

Intrathecal levobupivacaine and bupivacaine with buprenorphine in elective lower abdominal surgeries and lower limb surgeries: Hemodynamic changes

[1]Dr. Mohammed Naveed Nadaf, [2]Dr. Rahul Bankapur, [3]Dr. Ajay BC, [4]Dr. Srinivas Kurahatti

[1]Senior Resident, Department of Anesthesiology, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India

[2, 4]Assistant Professor, Department of Anesthesiology, KAHER's Jagadguru Gangadhar Mahaswamigalu Moorsavirmath Medical College and Hospital, Hubli, Karnataka, India

[3]Assistant Professor, Department of Anesthesiology, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India

Corresponding Author
Dr. Srinivas Kurahatti
Assistant Professor, Department of Anesthesiology, KAHER's Jagadguru Gangadhar Mahaswamigalu Moorsavirmath Medical College and Hospital, Hubli, Karnataka, India

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ABSTRACT
In the last two decades, regional anesthesia has emerged as an important and safer alternative to general anesthesia as it offers good muscle relaxation with rapid onset of action and fewer adverse effects. A prospective randomized controlled study was conducted on 60 patients of physical status ASA I & II, aged 20-60 years of either sex posted for lower abdominal and lower limb surgeries at Hospital. There was no statistically significant difference in the mean heart rate between the 2 groups at various time intervals. None of the patients required atropine for bradycardia. Overall, the intraoperative mean systolic blood pressure decreased in both the groups after anesthesia. However, there is no statistically significant difference in Intraoperative mean systolic blood pressure between groups at various time intervals.

Key words: Intrathecal levobupivacaine, buprenorphine, hemodynamic changes

INTRODUCTION

Spinal anaesthesia is the most suitable modality of anaesthesia for lower abdominal and lower limb surgeries. As compared to other techniques, it is cost effective, has rapid onset of action and achieves sensory, motor and autonomic blockade depending on the level administered. However it is limited by side effects such as hypotension, bradycardia and short duration of action. In most cases, the drug administered is hyperbaric bupivacaine (0.5%), a local anaesthetic. For years, the practice was to administer only a local anaesthetic and it was effective in almost every way in terms of motor, sensory and autonomic blockade [1, 2].

In the last two decades, regional anaesthesia has emerged as an important and safer alternative to general anaesthesia as it offers good muscle relaxation with rapid onset of action and fewer adverse effects.

Hyperbaric tracemict bupivacaine is one of the most frequently used long acting agents for intrathecal anaesthesia. But adverse effects such as prolonged motor blockade postoperatively, cardiotoxicity and CNS toxicity have been documented which can be attributed to the R (+) isomer of bupivacaine [3].

Withtthet advent toftlevobupivacaine, the pure tStenantiomert of tbupivacaine, titt has been found tha tit has at safer pharmacological profile than its trace mic sibling due to low cardio oxicity as well as adverse neurological effects [4].

Both levobupuvacaine and racemic bupivacaine have been used effective elytast long acting local anaes he icstintrathec ally with good sensory as well as mot or blockade [5].

Because of its significantly lower side effects, levobupivacaine appears to be a safer alternative to bupivacaine especially in elderly patients and in those with cardiovascular risk factors [6].

METHODOLOGY

A prospective randomized controlled study was conducted on 60 patients of physical status ASA I & II, aged 20-60 years of either sex posted for lower abdominal and lower limb surgeries at Hospital.

Ethical committee clearance and written informed consent of the patients were obtained before proceeding with the study.

INCLUSION CRITERIA

1. Between the ages of 20-60 years.
2. Patients posted for elective lower limb surgeries.
3. ASA class I or II.

EXCLUSION CRITERIA

1. Contraindications to intrathecal anaesthesia.
2. Patients with disorders of spine, alcoholic patients, cardiopulmonary diseases, BP >140/90mmhg.
3. BMI >35kg/m^2
4. Height <150 cm or >180 cm
5. History of drug abuse, collagen vascular diseases, bleeding disorders, space occupying lesions of brain.
6. Known hypersensitivity of local anaesthesia.

- Preoperative assessment was done for each patient and written informed consent was taken.
- Basic lab investigations like haemoglobin (Hb) %, fasting blood sugar (FBS) or random blood sugar (RBS), blood urea, serum creatinine and electrocardiogram (ECG) was done routinely in all patients.
- Chest X-ray was done when indicated.
- Written and informed consent was taken prior to scheduled operation. Patients were explained about the procedure of spinal anaesthesia.
- All patients were premedicated with a tablet premedication with tablet Ranitidine 150mg and tablet Diazepam 5mg orally the night before surgery.
- Anaesthesia machine, circuits, emergency drugs and equipments and monitors were checked before starting the case. The monitors used were-electrocardiogram (ECG), pulse oximetry, non-invasive blood pressure (NIBP). Invasive vascular access was secured depending on the need.
- IV line secured using 18 gauge cannula.
- Base line blood pressure, heart rate, respiratory rate and SPO2 noted.
- On arrival in the operating room, patients were preloaded with lactated ringer's solution at 15 ml/ kg.

The study population was divided into two groups of 30 patients in each group.

Patients were randomized into two groups on the basis of a sealed envelope technique to receive one of the following into the subarachnoid block:

GROUP X: received 2.7ml of 0.5% hyperbaric levobupivacaine plus 0.3 ml buprenorphine (90 mcg)

GROUP Y: received 2.7ml of 0.5% hyperbaric bupivacaine plus 0.3 ml buprenorphine (90 mcg).

- The patient placed in lateral position. With all aseptic precautions a skin wheal raised in L3-L4 interspace with 2ml of 2% lignocaine
- Under asepsis, 25G Quincke Babcock spinal needle was used to enter L3-4 interspace.
- The needle was slowly advanced until it enters the subarachnoid space, which was identified by the loss of resistance.
- Once free flow of CSF was confirmed, pre-loaded drug injections were given over approximately 10 to 15 seconds to each group as specified
- After completion of the block, patients were turned back to supine position.
- Oxygen was administrated through a mask.
- The surgeon and the observing anaesthetist were blinded to the patient groups.

RESULTS

Table 1: Intraoperative mean heart rate at different time intervals between the two groups

Time (min)	Group X (n=30)	Group Y (n=30)	p value
Baseline	73.93±11.197	73.17±10.069	0.781
2	72.57±11.863	70.77±10.348	0.534
4	70.63±10.953	69.63±11.251	0.728
6	68.87±10.477	67.17±10.515	0.533
8	68.03±10.759	65.53±11.491	0.388
10	67.27±10.602	67.3±10.895	0.529
15	68.86±10.313	67.33±10.373	0.543
20	67.23±10.625	64.77±10.439	0.25
25	67.43±10.585	65.73±10.794	0.534
30	67.4±8.764	67.67±7.126	0.575
50	68.03±8.269	68.9±7.136	0.543
70	67.97±8.442	67.97±8.785	0.548
90	68.53±9.359	68.17±6.756	0.568
110	67±7.793	65.83±6.52	0.639

130	67±9.899	67.91±8.905	0.898

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

There was no statistically significant difference in the mean heart rate between the 2 groups at various time intervals. None of the patients required atropine for bradycardia.

Table 2: Postoperative mean heart rate at different time intervals between the two groups

Time (min x 10)	Group X (n=30)	Group Y (n=30)	p value
9	68.55±6.639	54	0.062
11	69.94±8.707	59.75±4.2	0.001#
13	68.43±8.526	62.9±5.674	0.009*
15	68.83±8.107	64.6±7.059	0.046*
17	69.43±7.829	65.78±8.243	0.092
19	69.7±7.91	65.43±7.753	0.039*
21	69.83±8.082	66±7.865	0.068
24	69.97±8.211	66.13±7.001	0.057
27	70.07±8.051	65.7±7.042	0.029*
30	70.07±7.79	65.67±6.9	0.024*
42	70.17±8.205	66.43±7.195	0.066
66	71.07±7.956	66.9±6.272	0.028*
90	70.43±8.541	66.8±6.408	0.068
114	70.7±8.583	67.5±6.323	0.106
138	71.37±8.101	67.8±6.738	0.069
144	71.83±8.146	67.87±6.678	0.044*

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

The postoperative mean heart rate values were significantly ($p< 0.05$) lower in Group Y than in Group X at 110 min, 130 min, 150 min, 190 min, 270 min, 300 min, 660 min and 1440 min (Table 7). The maximum difference was noted at 110 min wherein the values were (69.94±8.707 bpm) and (59.75±4.2 bpm) in Group X and Group Y respectively which was highly significant ($p< 0.001$).

Heart rate intraoperative and postoperative were stable in both drug groups and didn't cause significant bradycardia.

Table 3: Intraoperative mean systolic blood pressure at different time intervals between the two groups

Time (min)	Group X (n=30)	Group Y (n=30)	p value
Baseline	135.13±14.822	136.33±15.897	0.763
2	128.7±13.792	126.63±17.433	0.613
4	121.5±10.712	120.9±14.358	0.855
6	120.8±10.111	117.7±14.589	0.343
8	117.07±10.184	115.97±15.032	0.741
10	114.17±10.684	114.17±14.847	1
15	113.83±11.579	114.73±15.008	0.796
20	116.43±9.518	114.9±13.842	0.619
25	116.9±6.925	115.8±14.968	0.717
30	118.6±7.356	118.43±13.343	0.952
50	118.93±8.403	117.93±11.353	0.7
70	117.83±9.976	117.53±11.808	0.916
90	121.37±9.719	117.66±7.729	0.149
110	120.67±8.595	117.83±8.063	0.338
130	114.5±7.778	120±7.483	0.356

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

Apart from baseline values, maximum systolic blood pressure was noted at 4 min (121.5±10.712 mm Hg) in Group X and at 2 min (126.63±17.433 mm Hg) in Group Y.

Minimum systolic blood pressure was noted at 15 min (113.83±11.579 mm Hg) in Group X and at 20 min (114.9±13.842 mm Hg) in Group Y.

Overall, the intraoperative mean systolic blood pressure decreased in both the groups after anesthesia. However, there is no statistically significant difference in Intraoperative mean systolic blood pressure between groups at various time intervals.

Table 4: Postoperative mean systolic blood pressure at different time intervals between the two groups

Time (min x 10)	Group X (n=30)	Group Y (n=30)	p value
9	120.36±6.667	130	0.197
11	125.68±9.673	128±21.175	0.709
13	124.07±9.475	117.47±8.434	0.023*
15	121.3±8.991	122.33±7.493	0.654
17	123.4±9.968	123.44±8.126	0.985
19	124.23±8.435	124.27±6.802	0.987
21	124.47±9.047	124.3±6.732	0.936
24	124.63±8.311	125.9±6.989	0.525
27	125.03±7.337	125.5±6.73	0.798
30	125.23±7.319	126.27±6.186	0.557
42	123.87±9.016	126.6±8.885	0.242
66	127.63±9.665	127.87±8.131	0.92
90	129.17±10.079	128.63±7.563	0.817
114	129.7±8.359	128.8±7.867	0.669
138	130.73±9.044	130.27±7.803	0.831
144	131.13±8.862	127.2±19.852	0.326

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

There is no statistically significant difference in mean postoperative systolic blood pressure between groups at various time intervals except at 130 min which was (124.07±9.475 mmHg) in Group X and (117.47± 8.434 mm Hg) in Group Y. Both groups maintained a haemodynamically stable systolic blood pressure.

Table 5: Intraoperative mean diastolic blood pressure at different time intervals between the two groups

Time (min)	Group X (n=30)	Group Y (n=30)	p value
Baseline	81.5±8.08	82.17±8.263	0.753
2	79.2±7.73	79.77±9.354	0.799
4	74.9±7.954	75.67±10.548	0.752
6	73.43±8.951	73.53±7.366	0.962
8	73.37±9.182	73.33±8.644	0.988
10	71.4±8.85	72.97±8.915	0.497
15	70.67±9.415	73.3±10.35	0.307
20	71.1±9.011	71.3±9.997	0.935
25	72.77±10.078	72.73±10.305	0.99
30	72.93±9.505	74.17±9.229	0.612
50	73.1±8.88	74.5±9.306	0.553
70	73.87±7.505	74.5±9.001	0.768
90	72.58±8.099	74.14±6.76	0.474
110	71.92±6.999	74.17±7.088	0.376
130	68±5.657	74.67±7.843	0.278

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

The Intraoperative mean diastolic blood pressure values did not differ significantly between the two groups. The fall in DBP was noted in both the groups following subarachnoid block.

Apart from baseline values, maximum diastolic blood pressure was noted on 4 min (74.9±7.954 mmHg) in Group X and on 2 min (79.77±9.354 mmHg) in Group Y. Minimum diastolic blood pressure was noted at 15 min (70.67±9.011 mm Hg) in Group X and at 20 min (71.3±9.97 mmHg) in Group Y.

Table 6: Postoperative mean diastolic blood pressure at different time intervals between the two groups

Time (min x 10)	Group X (n=30)	Group Y (n=30)	p value
9	78.45±7.005	94	0.06
11	78.28±5.312	77.43±11.872	0.861
13	77.32±5.498	75.39±7.563	0.321
15	78.87±6.917	75.88±8.558	0.161
17	78.17±5.471	77.85±8.934	0.875
19	77.87±5.374	77.67±8.053	0.91
21	78.23±5.029	77.77±7.802	0.784

24	78.8±4.852	78.83±7.657	0.984
27	78.87±4.988	79.57±7.65	0.676
30	78.9±5.287	79.43±6.981	0.74
42	80.87±5.782	78.77±8.148	0.254
66	80.5±7.07	79.9±6.738	0.738
900	80.9±5.294	80.47±5.776	0.763
114	80.53±4.833	80.73±6.633	0.894
138	81.17±4.829	81±6.4	0.91
144	81.33±4.105	81.07±6.297	0.847

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

There is no statistically significant difference in postoperative mean diastolic blood pressure between groups at various time intervals. The maximum difference was noted at 90 min with the value of (78.45±7.005 mmHg) in Group X and (94mmHg) in Group Y with *p=0.06* which was not statistically significant.

Table 7: Intraoperative mean arterial pressure at different time intervals between the two groups

Time(min)	Group X(n=30)	Group Y(n=30)	p value
Baseline	95±11.893	97.83±12.072	0.364
2	90.13±10.657	93.73±11.662	0.217
4	87.37±12.333	87.6±12.555	0.942
6	85.57±12.364	83.5±12.241	0.518
8	82.5±12.207	81.8±12.274	0.825
10	79.4±10.711	82.43±11.886	0.303
15	80.87±12.525	81.03±10.918	0.956
20	80.27±12.063	79.53±12.202	0.816
25	79.6±10.634	80.23±13.008	0.837
30	79.17±10.92	81.8±10.473	0.344
50	78.6±10.842	82.2±8.688	0.161
70	80.97±10.186	82.67±11.442	0.546
90	81.42±9.53	77.52±16.556	0.357
110	80.92±8.826	79.83±7.142	0.694
130	78±5.657	81.92±9.01	0.57

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

After subarachnoid block, fall in MAP was noted in both the groups. There is no statistically significant difference in intraoperative mean arterial pressure between groups at various time intervals. It ranged from 79 mmHg to 95 mmHg in Group X and 77 mmHg to 93 mmHg in Group Y.

Table 8: Postoperative mean arterial pressure at different time intervals between the two groups

Time (min x 10)	Group X (n=30)	Group Y (n=30)	p value
9	85.92±8.785	110	0.023*
11	84.17±7.823	87.17±12.465	0.491
13	84.21±7.104	84.65±7.945	0.851
15	83.87±8.114	85.24±6.48	0.523
17	84.63±8.282	84.62±6.204	0.993
19	85.07±8.283	83.77±6.725	0.507
21	85.67±7.703	84.27±7.329	0.474
24	85.83±7.349	83.97±6.896	0.315
27	85.8±7.346	84.37±6.473	0.426
30	85.7±7.283	84.37±6.239	0.449
42	86.63±8.122	84.6±7.618	0.321
66	87.1±8.277	85.57±8.577	0.484
90	86.17±7.154	85.9±8.743	0.898
114	87.53±7.267	85.83±7.479	0.376
138	87.6±7.113	85.17±7.135	0.191
144	87.53±7.272	85.33±7.303	0.247

Values are in mean ± SD, *p value < 0.05 is significant, #p value < 0.001 is highly significant

There is no statistically significant difference in postoperative mean arterial pressure between groups at various time intervals except at 90 min which shows higher MAP in Group Y when compared to Group X (85.92±8.785 mmHg) and is statistically significant.

DISCUSSION

Currently-it-has become more popular because of addition-] of opioids-tonlocal anesthetics in central neuraxial blockade which-provides-better intra-operative-analgesia-and-early-postoperative-nalgesia.

Levobupivacine is the pure S (-) enantiomer of racemic bupivacaine and is less cardiotoxic. Because of it's significantly fewer adverse effects, levobupivacaine seems to be a better alternative to bupivacaine especially in elderly patients and those with cardiovascular risk factors.

In the intrathecal space, opioids activate the opioid receptors present in the gray matter of the spinal cord and thereby exerts their actions. There are several studies that support the combination of local anesthetics with opioids in providing safe anaesthesia with good analgesia while reducing the dose requirements and adverse effects of each agent.

In the recent times, highly lipid soluble opioids such as fentanyl and buprenorphine are being used as adjuvants to low concentrations of local anesthetics as these agents produces a synergistic effect without causing prolonged sympathetic blockade.

In a study by K.R. Milligan [7] levobupivacaine, produced a less intense motor block of shorter duration. In our study also, levobupivacaine with buprenorphine group demonstrated dense motor blockade with prolonged sensory analgesia in comparison to bupivacaine with buprenorphine group.

There was no significant difference between the two groups in terms of hemodyanamic parameters like systolic blood pressure, diastolic blood pressure and heart rate with a p value >0.05 stating indirectly that the pharmacological profile of both the drugs was almost the same. This is comparable with studies by Lacassie*et al.* [8], Camorcia*et al.* [9], Glasser*et al.* [10] Lee *et al.* [11] and Karaca*et al.* [12].

In our study we found the analgesia was good in both the groups in the post-operative period with the addition of buprenorphine. However the sensory analgesia was prolonged in the group that received levobupivacine with buprenorphine.

Krishnan S H *et al.*[13] showed that 200 µg buprenorphine when added to local anesthetic for adductor canal block in patients undergoing unilateral total knee arthroplasty,reduced the postoperative opioid consumption significantly. Similarly in our study the addition of buprenorphine had good outcomes in both the groups, more so in the levobupivacaine with buprenorphine group.

Thus in our pilot study it was shown that levobupivacaine produced more prolonged sensory levels when combined with buprenorphine. This is comparable to the study by Lipp M *et al.* [14].

Hypotension is a frequent side effect after spinal anaesthesia. However, five to seven patients in either of our study groups demonstrated significant hypotension. This is probably due to the low volume (2.7 ml) of local anesthetic that was used for the study and also because all the patients were adequately preloaded prior to the procedure. The most common side effect observed with intrathecal opioids is pruritis. However in our study none of patient in the levobupivacaine with buprenorphine group or bupivacaine with buprenorphine group complained of pruritis. In contrast, a study conducted by Erdil*et al.*[15]demonstrated pruritis in 75% of patients. This may be due to the higher dose of opioid used in the study [16].

Another frequently seen side effect following spinal anaesthesia is shivering. Six patients in both the study groups demonstrated shivering. However it was not found to be statistically significant. Regarding shivering our results doesn't match with that of the study conducted by Erdil*et al.* [15]. This is probably because of the study being conducted on elderly patients.

CONCLUSION

- Based on the study, we conclude that both levobupivacaine with buprenorphine and bupivacaine with buprenorphine regimes were effective in providing hemodynamic stability.
- Two episode of bradycardia was observed in both group, that was not deleterious to the patient and there were no other significant side effects.

REFERENCES

1. Gautam B, Niroula S, Sharma M, Lama SM. Effects of Intrathecal Dexmedetomidine as an Adjuvant to Hyperbaric Bupivacaine for Spinal Anaesthesia in Adults Undergoing Elective Infra-umbilical Surgery. J Nepal Med Assoc. 2017;56:379-87.
2. Ravindran R, Sajid B, Ramadas KT, Susheela I. Intrathecal Hyperbaric Bupivacaine with Varying Doses of Buprenorphine for Postoperative Analgesia after Cesarean Section: A Comparative Study. Anesth Essays Res. 2017;11:952-7.
3. Ture P, Ramaswamy AH, Shaikh SI, Alur JB, Ture AV. Comparative evaluation of anaesthetic efficacy and haemodynamic effects of a combination of isobaric bupivacaine with buprenorphine vs. isobaric levobupivacaine with buprenorphine for spinal anaesthesia – A double blinded randomised clinical trial. Indian J Anaesth. 2019;63:49-54.
4. El-Rakhawy M, Labib I, El-Shahat. Lumbar vertebral canal stenosis: Concept of morphometric and radiometric study of the human lumbar vertebral canal. AAMJ; c2010.
5. Crafts RC. A textbook of human anatomy. 3rd ed. Canada: John Wiley and Sons Canada, Limited; c1985. p. 99-107.
6. Clarke E, Charles DO. The human brain and spinal cord: a historical study illustrated by writings from

antiquity to the twentieth century. 2nd ed. San Francisco: Norman Publishing; c1996. p. 260-90.
7. Milligan KR. Recent advances in local anaesthetics for spinal anaesthesia. European journal of anaesthesiology. 2004 Nov;21(11):837-47.
8. Lacassie HJ, Columb MO. The relative motor blocking potencies of bupivacaine and levobupivacaine in labor Anesthesia Analgoue. 2003;97:1509-1513.
9. Camorcia M, Capogna G, Berritta C, Columb MO. The relative potencies for motor block after intrathecal ropivacaine, levobupivacaine, and bupivacaine Anesthesia Analgoue. 2007;104:904-907.
10. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. AnesthAnalg, table of contents. 2002;94:194-198.
11. Lee YY, Muchhal K, Chan CK. Levobupivacaine versus racemic bupivacaine in spinal anaesthesia for urological surgery. Anaesthesia Intensive Care. 2003;31:637-641.
12. Karaca F, Erkılıç E, Akdıkan A, Gümüş T, Kanbak O. Assessment of the Effect of Intrathecal Low Dose Levobupivacaine or Bupivacaine Combined with Fentanyl in Patients Undergoing Cesarean Section. J AnesthClin Res. 2014;5:465.
13. Krishnan SH, Gilbert LA, Ghoddoussi F, Applefield DJ, Kassab SS, Ellis TA, *et al*. Addition of buprenorphine to local anesthetic in adductor canal blocks after total knee arthroplasty improves postoperative pain relief: a randomized controlled trial. Journal of clinical anesthesia. 2016 Sep 30;33:432-7.
14. Lipp M, Daubländer M, Lanz EO. 15 mg Intrathecal buprenorphine applied for postoperative analgesia. A clinical double-blind study. Der Anaesthesist. 1987 May;36(5):233-8.
15. Erdil F, Bulut S, Demirbilek S, Gedik E, Gulhas N, Ersoy MO, *et al*. The effects of intrathecal levobupivacaine and bupivacaine in the elderly. Anaesthesia. 2009 Sep 1;64(9):942-6.
16. Goerig M, Agarwal K, am Esch JS. The versatile August Bier (1861-1949), father of spinal anesthesia. Journal of clinical anesthesia. 2000;12(7):561-569.