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Corresponding Author
Sanhita Kulkarni,
Department of Anaesthesia, MGM Medical College and Hospital, Aurangabad, India
drsanhitakulkarni@gmail.com

Author Designation
[1]Senior Resident
[2,4,5]Professor
[3]Associate Professor
[6]Professor and Head

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A Comparative Study of Two Doses of Buprenorphine as an Adjuvant to 0.5% Hyperbaric Bupivacaine for Spinal Anesthesia in Lower Limb Surgeries

[1]Ashik Sreekumar, [2]Sanhita Kulkarni, [3]Anuradha Mohite, [4]Pradnya Joshi, [5]Vasanti Sasturkar and [6]Pramod Bhale
[1-6]Department of Anaesthesia, MGM Medical College and Hospital, Aurangabad, India

ABSTRACT
Buprenorphine is an agonist-antagonist opioid. Intrathecal buprenorphine in different doses along with local anaesthetics is safe and known to increase the postoperative analgesia without affecting sensory or motor blockade. Aim of the study is to compare the efficacy and safety of two doses of buprenorphine (45 mcg and 60 mcg) as an adjuvant to 0.5% hyperbaric bupivacaine for spinal anesthesia in lower limb surgeries. Prospective randomized double blind study in sixty patients posted for lower limb orthopaedic surgeries under spinal anaesthesia. Group B1 (n=30) received 3 ml of 0.5% hyperbaric bupivacaine with 45 mcg buprenorphine, Group B2 (n=30) received 3 ml 0.5% hyperbaric bupivacaine with 60 mcg buprenorphine, respectively. Following parameters were observed: onset and duration of sensory block and motor block, maximum height of sensory block and duration of postoperative analgesia and side effects if any. Group B2 (3.92±1.47 min) had a faster onset of sensory block when compared to group B1 (4.88± 1.17 min) which was statistically significant (p=0.014). T6 was the maximum height of sensory block attained in both the groups. The mean duration of sensory block was prolonged in Group B2 (182.0±31.1 min) than Group B1 (152.8±16.7 min). This difference was highly significant statistically. (P=0.0000). Group B2 (5.76±1.45 min) had a faster onset of motor block when compared to group B1 (6.88±1.17 min) the results being statistically significant (P=0.004). The mean duration of motor block was prolonged in group B2 (213.6±32.5 min) when compared to group B1 (185.2±21.4 min), the results were statistically highly significant (p=0.001). The duration of analgesia was prolonged in group B2 (306.0±34.4 min) when compared to group B1 (277.2±31.4 min). The results were statistically significant (p=0.003). No major side effects observed in both the groups. Addition of buprenorphine as an adjuvant to hyperbaric bupivacaine in doses of 60 mcg as compared to 45 mcg provides faster onset of sensory and motor block along with prolonged duration of sensory, motor block and post operative analgesia without significant increase in adverse effects.

INTRODUCTION

Spinal anaesthesia is routinely employed in lower limb surgeries. Bupivacaine, a racaemic mixture of dextrobupivacaine and levobupivacaine had been the gold standard for intrathecal use in spinal anaesthesia for many years[1]. Bupivacaine alone in spinal anesthesia may not be sufficient for prolonged surgeries. To overcome this problem various adjuvants like opioids, α2agonists are used in combination with local anaesthetic agents. Opioids such as fentanyl and buprenorphine are commonly used intrathecal adjuvants.

Buprenorphine an agonist and antagonist at mu and kappa receptor respectively is about 30 times more potent than morphine[2]. It was studied by various authors in different doses ranging from 15 mcg to 150 mcg in intrathecal use. There is paucity in literature comparing buprenorphine in doses of 45 mcg and 60 mcg along with hyperbaric bupivacaine in lower limb surgeries.

Our aim of this study was to compare the sensory and motor block characteristics, duration of postoperative analgesia along with haemodynamic stability of two different doses of buprenorphine (45 mcg and 60 mcg) as an adjuvant to hyperbaric bupivacaine in patients undergoing lower limb surgeries.

MATERIALS AND METHODS

The study was conducted at a tertiary care center after obtaining approval from the Institution Ethics Committee and written informed consent from all patients who participated in the study. This was a prospective, randomized, double-blind controlled study.

Fifty ASA physical status Class I to III posted for elective lower limb between the age of 18 and 65 years were selected for this Study. The sealed envelope random sampling procedure was used to allocate the subjects into two groups B1 and B2 of 25 each. Exclusion criteria were coexisting systemic illness, emergency surgery, history of allergy to local anaesthetics or opioids, patient refusal, or any contraindication to SAB. Those with failed or partial block were excluded from the study.

The Study will Include 2 Groups:

- **Group B1:** 3 ml 0.5% hyperbaric bupivacaine with 45 mcg Inj. buprenorphine
- **Group B2:** 3ml 0.5%hyperbaric bupivacaine with 60 mcg Inj. buprenorphine.

The procedure was explained to the patient and informed written consent was taken for participation in the study. Prior to enrolment of the first patient the study was registered with the Clinical Trials Registry-India (CTRI) with the registration number CTRI/2022/01/039545. One anaesthesiologist administered the drug intrathecal while another anaesthesiologist (observer) who was blind to the drug administered, recorded the findings.

For calculating sample size, we conducted pilot study with10 patients in each group. On the basis of the results of this pilot study and setting the error at 0.05 and βerror at 0.9, A power analysis indicated that 25 patients per group were required to detect a 10% difference in duration of analgesia. Considering the dropouts, we recruited 31 patients in each group.

On the day of surgery in the operation theatre, monitors were attached and baseline parameters like heart rate (HR), Non invasive mean blood pressure (MAP), Oxygen Saturation (SPO2) and ECG were recorded. Intravenous access was established using 20 G angiocath. Co-loading was done by infusion of 500ml ringer lactate. As per the allocated groups subarachnoid block was administered in sitting position in L3-L4 interspace with 23G quincke needle. After clear CSF tap, the drug was injected into the subarachnoid space. Group A received 3ml (15 mg) of 0.5% hyperbaric bupivacaine with 45 mcg buprenorphine Group B received 3 ml (15 mg) of 0.5% hyperbaric bupivacaine with 60 mcg buprenorphine Buprenorphine was taken in tuberculin syringe so as to add it precisely.

The patient was made supine and sensory block was tested by pin prick method in the midaxillary line every 2 min till maximum height of sensory level which is two consecutive reading at the same dermatome level was achieved. Thereafter sensory block was tested every 20 min till the block regressed to L1 level. The time from spinal injection (T-0) to time taken to achieve T10 level was considered as onset of sensory blockade. The time from T-0 toL1 regression was taken as total duration of sensory block. Motor block was tested every 2 min using Bromage scale till the start of surgery. Thereafter motor block was tested in post operative period every 20min for the first 2 hours and thereafter every 2 hours till complete recovery (grade 0) and duration of motor block were noted. Surgery was allowed after achieving sensory block uptoT10 and grade2 motor block. Failure to achieve the required block in 20 min was considered as failure of block and general anaesthesia was given. After spinal anaesthesia was administered, heart rate and mean blood pressure was recorded every 2 min for the first 20 min. Thereafter it was taken every 10 min till regression of block toL1. Fall of mean arterial pressure by more than 20% of baseline was considered as hypotension and was treated with inj. mephenteramine 3 mg intravenously. Fall in heart rate to less than 50 beats per minute was taken as bradycardia and treated with injection atropine 0.6mg. Inj. Ondansetron 4 mg IV was given to

treat intra operative nausea and vomiting. The patients were also observed for pruritis and urinary retention.

Post operatively, pain was assessed using visual analog scale (VAS) every 30 minutes for the first 2 hours and then every 2 hourly till the VAS score reached >4 and rescue analgesia given with Inj. Diclofenac75mg diluted in 100 ml of water.

Statistical Analysis: All data was systematically compiled and statistically analyzed after the completion of the study. Quantitative data was expressed as mean±standard deviation. Qualitative data was expressed as frequency and percentages. Student's paired "t"test was applied when comparing two means. Chi square test was used to compare qualitative parameters. P<0.05 was considered as statistically significant and <0.001 as statistically highly significant

RESULTS AND DISCUSSIONS

All the patients in both the groups were comparable in terms of age, sex, ASA grading and duration of surgery. The onset of sensory and motor block was faster in group B2 3.92±1.47 min as compared to group B1 4.88±1.17 min which was statistically significant (p value 0.014). T6 was the maximum level of sensory block attained in both the groups with statistically insignificant value (p value 0.223). The duration of sensory block was prolonged in group B2 182.0±31.1 min as compared to group B1 152.8±16.7 min which was statistically highly significant (p value0.0000).

Group B2 had a faster onset of motor block of 5.76±1.45 min when compared to group B1 of 6.88±1.17 min which was statistically significant (p value 0.004). Group B2 also showed a prolonged duration of motor block of 213.6±32.5min as compared to the 185.2±21.4 min of group B1which was statistically highly significant (p value 0.001).

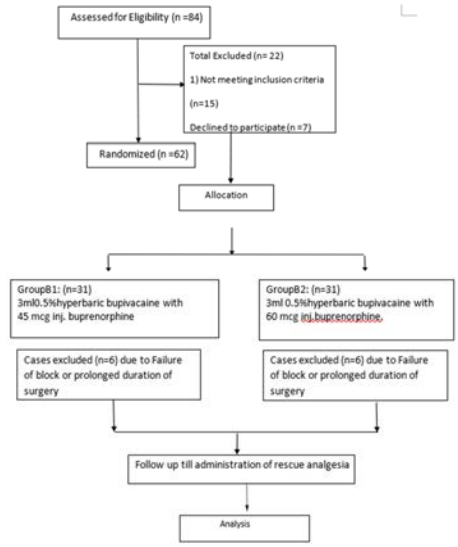

Fig. 1: Consort Flow Diagram of Study Methodology

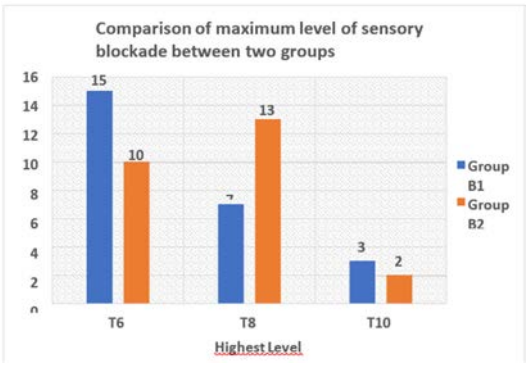

Fig. 2: Comparison of maximum level of sensory blockade between two groups

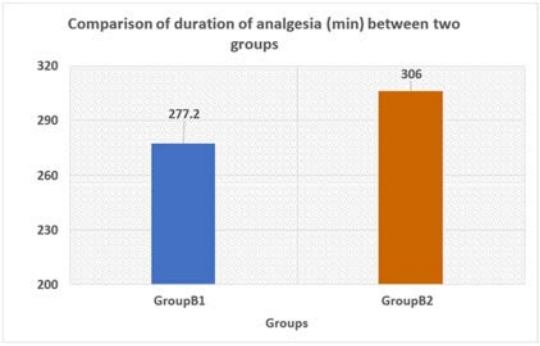

Fig. 3: Comparison of duration of analgesia between two groups

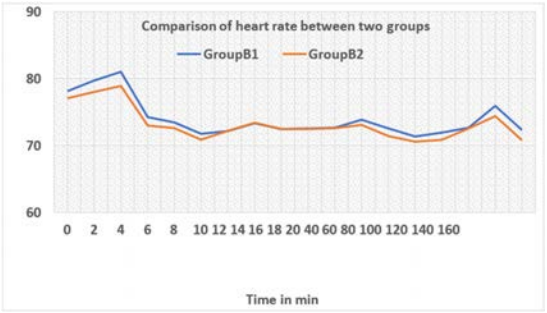

Fig. 4: Comparison of heart rate between the two groups

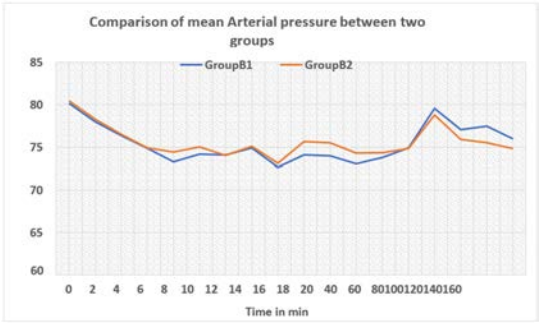

Fig. 5: Comparison of Mean arterial pressure between the two groups

Table 1: Demographic data

Parameters	Group B1	Group B2	P-Value
Duration of surgery in hrs	118.7±28.6	120.7±39.8	P=0.824 NS
Age	40.7±14.0	45.0±15.0	
Sex			
Male	80%	64%	P=0.765 NS
Female	20%	36%	
ASA Grade			
I	4%	12%	P=0.571 NS
II	72%	68%	
III	24%	20%	

Table 2: Comparison of sensory and motor block characteristics

Parameters	Group B 1 (n = 30)	Group B2 (n = 30)	p-value
Onset of sensory block (min)	4.88± 1.17	3.92±1.47	0.014
Onset of sensory block (min)	T6	T6	0.223
Duration of Sensory Blockade (min)	152.8±16.7	182.0±31.	0.000 HS
Onset of motor block (min)	6.88±1.17	5.76±1.45	0.004 S
Duration of motor block (min)	185.2±21.4	213.6±32.5	0.001HS
Duration of analgesia (min)	277.2±31.4	306.0±34.4	0.003 S

S = significant, HS = highly significant Mean ± standard deviation (S

Table 3: Distribution of patients according to adverse effects

Adverse effects	Group B1n =25		Group B2n =25		Z-value	P-value
	No	Percentage	No	Percentage		
Nausea	00	0	00	0	0	0
Vomiting	00	0	00	0	0	0
Respiratory depression	00	0	00	0	0	0
Hypotension	5	20	6	24	0.3414	0.7278NS
Bradycardia	1	4	1	4	0	1NS

The duration of analgesia was significantly prolonged in group B2 (306.0±34.4min) as compared to groupB1 (277.2±31.4min) which was statistically significant (p value 0.003).Though we observed hypotension and bradycardia during our study in both the groups they were statistically insignificant. There were no any adverse effects like nausea, vomiting, or pruritis in both the groups.

Spinal anaesthesia has been routinely used in lower limb surgeries and bupivacaine being the gold standard for intrathecal use. The duration of action attained with bupivacaine alone may be inadequate for prolonged surgeries, however this can be circumvented with the use of adjuvants which when used in combination with local anaesthetic agents not only prolong the duration but also the quality of analgesia while maintaining hemodynamic stability. These adjuvants help in reducing the dose of local anesthetics thereby helping in early mobilization of patients[3] Buprenorphine,a highly potent and lipophilic agonist-antagonist opioid with long duration of action which makes it an excellent choice for postoperative analgesia[4,5].

It is highly lipid soluble and diffuses quickly into neural tissue, decreasing the chances of rostral spread leading to lesser side effects in the post-operative period[6]. Buprenorphine as an intrathecal adjuvant was studied by various authors in different dosages ranging from 15-150 mcg. There was lacunae in the literature comparing buprenorphine in doses of 45 and 60 mcg along with hyperbaric bupivacaine in lower limb surgeries hence we have undertaken this study of comparing two doses of buprenorphine.

The onset of sensory and motor block in our study was comparable with the studies done by Ravindra[6] and Bhukya[3] T6 was the maximum height of sensory block achieved in both the groups in our study which was statistically insignificant. Ture[7] had similar findings with our study but Reddy[8] observed sensory level at T4 which may be due to the higher dose of bupivacaine and buprenorphine used.

In our study, duration of sensory block was statistically highly significant in group B1 which was152.8±16.7 min while in group B2 was 182.0±31.1min, with highly statistically significant difference. From the studies done by Palet[2], Bhukya[3] and Dhawale[9], it was concluded that increase in dose of buprenorphine increases duration of sensory block. The onset of motor block in group B1 and B2 was 6.88±1.17 min and 5.76±1.45 min respectively in our study which was statistically significant.

Alugolu[10] had similar observations in onset of motor block which are there in our study. The duration of motor block was found to be longer in group B2 than group B1 in our study and their difference was statistically highly significant. Pal[2] also found that addition of buprenorphine 75mcg to bupivacaine prolonged the duration of motor to 222.66±24.34min Gupta[11] had similar observation with our studies that addition of 60 mcg of buprenorphine resulted in

duration of motor block of 205.17±63.0 min.

The total duration of analgesia in group B1 was 277.2±31.4 min while in group B2 was 306.0±34 min which was statistically significant. A study done by Pal[3] found that the duration of analgesia in buprenorphine group was 294.00±17.93 min which was comparable to our study. It was observed in the study conducted by Bhukya[3] that the duration of analgesia in buprenorphine group was 292 min which was comparable to our study

Reddy[8] concluded that the duration of analgesia was 378±63.81min when buprenorphine was used in the dose of 150 mcg. This duration of analgesia was more than our study may be because of more buprenorphine used by them. Dhawale[9] observed 412.17 min of duration of analgesia in their study which was more than our study, which could be attributed to the use of larger dose of buprenorphine. here was no statistically significant difference in heart rate in both the groups with the p>0.05. There was incidence of bradycardia in one patient in each group which required inj atropine. This was similar to the observed by Mishra[12], Layek[13] and Ture[7]

Although we had observed hypotension in both the groups it was not statistically significant (p>0.05). These observations were comparable to the studies done by Ravindran *et al.* Ture[7] and Bhukya[3].

There was no significant difference in the incidence of side effects when comparing 45 mcg and 60 mcg buprenorphine groups like respiratory depression, pruritis or nausea. Rudra[14] and Alugolu[10] also noted no adverse events in their study

Limitations of the Study: In this study, we chose a maximum dose of 60 mcg of buprenorphine though higher doses might have resulted in further prolongation of analgesia. However, higher doses have been reported to cause more adverse effects. To observe significant changes in haemodynamic responses more sample size would have been included in the study.

CONCLUSION

Our study demonstrated that buprenorphine when added as an adjuvant to hyperbaric bupivacaine in the doses of 60 mcg causes a faster onset of sensory and motor block along with prolonged duration of sensory, motor block and post operative analgesia without significant adverse effects.

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