Original Research Article

Indian Journal of Anesthesia and Analgesia
2018; 5(7): 1159-1169
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.5718.12

A Comparative Evaluation of Efficacy of Intrathecal Nalbuphine and Butorphanol as Adjuvant to Hyperbaric Bupivacaine 0.5% for Lower Limb Surgery

Mohit Gupta[1], Neeharika Arora[2]

[1]3rd year Resident [2]Associate Professor, Department of Anaesthesiology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh 243001, India.

Abstract

Background: Subarachnoid block is the most preferred technique for anaesthetic management for lower limb surgeries. Various adjuvants have been used to improve the efficacy local anaesthetics by hastening the onset and prolonging the duration of sensory and motor block. The present study aims to compare the efficacy of intrathecal nalbuphine with butorphanol as adjuvant to 0.5% hyperbaric bupivacaine for lower limb surgery. *Methods:* 90 patients belonging to ASA status I and II of either sex were randomly divided into three groups of 30 each to receive either butorphanol 25 µg (Group A) or nalbuphine 400 mcg (Group B) or normal saline 0.5 ml (Group C) with 2.5 mL 0.5% hyperbaric bupivacaine, making intrathecal drug volume to 3mL in each group. Sensory and motor block characteristics in terms of time to onset and duration were recorded as the primary end points. Drug related side effects of pruritus, nausea/vomiting, and respiratory depression were recorded as the secondary outcomes. *Results:* The three groups were comparable regarding the demographic profile. The time to onset of sensory block was shortened in patients of group A and B as compared to group C, more so in group A. The mean time of 2 dermatomal regression was significantly more in Group B as compared to Group A and Group C ($p=0.003$, $p<0.001$) and significantly more in Group A as compared to Group C ($p<0.001$). Onset of motor block and time required to attain complete motor block (motor bromage 2 and 3 respectively) were comparable between the three groups and statistically not significant Duration of motor block was significantly more in group B as compared to Group A and Group C ($p<0.001$, $p<0.001$) and comparable between Group A and Group C .Furthermore, duration of motor block was maximum in Group B as compared to Group A (<0.001). No drug related side effects were observed in either group. *Conclusions:* Intrathecal Butorphanol 25 mcg showed faster onset of sensory block whereas nalbuphine 400 mcg showed prolonged duration of sensory and motor block as adjuvant to hyperbaric bupivacaine 0.5%.

Keywords: Intrathecal; Nalbuphine; Butorphanol.

How to cite this article:

Mohit Gupta & Neeharika Arora. A Comparative Evaluation of Efficacy of Intrathecal Nalbuphine and Butorphanol as Adjuvant to Hyperbaric Bupivacaine 0.5% for Lower Limb Surgery. Indian J Anesth Analg. 2018;5(7):1159-69.

Introduction

Spinal anesthesia is the most preferred technique for conduct of anaesthesia management for lower limb surgeries.it provides benifits of lesser blood loss, lower incidence of deep vein thrombosis and postoperative analgesia. A limited duration of action is a major drawback of this technique. Even though major advances have been made in local anesthetic chemistry, synthesis of an ideal agent remains elusive. An agent with a longer duration of action, shorter onset time, and a more selective sight of action is sought. Adjuvants are those drugs which, when co-administered with local anesthetic agents, may improve the speed of onset and

Corresponding Author: Neeharika Arora, Associate Professor, Department of Anaesthesiology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh 243001, India.
E-mail: acadneeharika@rediffmail.com

Received on 16.05.2018, **Accepted on** 31.05.2018

duration of analgesia and counteract disadvantageous effects of local anesthetics. By adding these adjuvants, the dose of local anesthetics like bupivacaine can be reduced, thereby reducing its side effects. Combination allows for a reduction in doses of both classes of drugs, thus lessening the likelihood of side effects attributable to each.

The mechanism by which opioids affect LA action is through a G-protein-coupled-receptor system. Opioids competitively bind to specific receptors to induce pain relief by hyperpolarizing the afferent sensory neurons in which the receptors are imbedded. Hyperpolarization of the cell membrane by an opiate decreases the propagation of neuronal action potentials thereby inhibiting afferent pain signals. Eventually this produces a decrease in the perception of pain [1]. Factors such as dose, lipophilicity, site of injection and condition of the milieu into which the injection is made, play an important role on the eventual effect produced [2,3].

Nalbuphine and Butorphanol belong to phenanthrene group of agonist antagonists, having agonist action on kappa receptor and antagonistic or partial agonist property at mu receptor. They are synthetically prepared, having similar pharmacological properties [5,6].

Therefore, in this study, an attempt was made to compare the efficacy of intrathecal Butorphanol and Nalbuphine as an adjuvant to Bupivacaine 0.5% heavy for lower limb surgeries.

Methods

After obtaining institutional ethical committee approval and informed written consent from the patients this randomised controlled study was carried out in the department of anaesthesiology, SRMSIMS, Bareilly, on 90 patients between 18-60 years of age and ASA grade I and II physical status scheduled to undergo lower limb sungeries under SAB.

Patient denying consent, allergy to any anesthetic drug, infection at the site of injection,patient on anticoagulants or bleeding disorder, ASA III and IVand patients on tranquilizers, hypnotics, sedatives, and other psychotropicdrugs were excluded from the study.

Pre anesthetic checkup was done on the previous day and on morning of surgery. Routine and specific investigations were noted.

Patients were randomly allocated into 3 groups each having 30 patients.

Group A - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + butorphanol 25μg (0.5 ml)

Group B - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + nalbuphine 400ug (0.5 ml)

Group C - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + normal saline (0.5 ml)

All the patients were kept fasting overnight prior to the scheduled day of operation.

Patients received Inj. Ranitidine 50mg IV as premedication after entering the operation theatre. All standard monitors (ECG, NIBP, SpO2) were applied. Baseline BP, PR, RR were recorded. All patients were preloaded through 18 G cannula with 10 ml/kg of RL solution. Under all aseptic precautions, lumbar puncture was performed in the L3-4. Intervertebral space using 25 G Quincke's spinal needle in sitting position. The patient received either one of the drug solution. Patients were turned supine and position of table was kept horizontal. Recording of HR, SBP, DBP, MAP, SpO2 and RR was done every 3 min. for 15 min., every 5 min. for 30 min., every 15 min. till 3 hours. In the intra operative period, crystalloid solutions (Ringer Lactate) 4ml/kg/hr was infused. The onset of sensory block was tested by pin-prick method using a 24G hypodermic needle every 2 minutes until the level had stabilized for 4 consecutive tests. Motor block was assessed by modified Bromage scale.

The following parameters were noted:

1. Time to onset of sensory block (i.e. time from intrathecal injection of drug to complete loss of sensation to pin prick at T10).
2. Time taken to achieve the highest level of sensory block (time from intrathecal injection to highest level of sensory block).
3. The time for two dermatomal segments regression of sensory level.
4. Time to onset of motor block by Modified Bromage Score (time from intrathecal injection to achievement of Bromage 2).
5. Time taken to achieve complete motor block by Modified Bromage Score (time from intrathecal injection to achievement of Bromage 3).
6. Duration of motor block will be noted (time from Bromage 3 to Bromage 2).

Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables are presented as mean±SD, and categorical variables are presented as absolute numbers and

percentage. Data were checked for normality before statistical analysis using Shaipro Wilk test. Normally distributed continuous variables were compared using ANOVA. If the F value was significant and variance was homogeneous, Tukey multiplecomparison test was used to assess the differences between the individual groups; otherwise, Tamhane's T2 test was used. Categorical variables were analyzed using the chi square test. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

Results

The present study compared effect of nalbuphine (400 mcg in 0.5 ml), butorphanol (25 mcg in 0.5 ml) and normal saline (0.5 ml) with bupivacaine on the onset and duration of sensory and motor block when administered by intrathecal route as an adjuvant to bupivacaine 0.5% heavy (2.5 ml)

There was no significant difference in age, sex, ASA physical status, preoperative vitals among the three groups. Thus, we conclude that age, sex and ASA physical status and preoperative vitals in three groups were comparable.

The Mean±SD onset of sensory block in Group A, Group B and Group C respectively. It was found that there was significant difference among three groups ($p<0.001$). Post hoc analysis showed that mean onset of sensory block was significantly early in Group A and Group B as compared to Group C ($p<0.001$, $p<0.001$). Furthermore, mean onset of sensory block was faster in Group A as compared to Group B (<0.001).

The Mean±SD time of 2 dermatomal regression was121.33±3.51,125.07±4.74 and 148.7±5.38 in Group

Demographic Profile

Table 1: Comparison of age in study groups

	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	P Value
Age	34.10 ± 12.17	31.53 ± 11.39	36.07 ± 12.91	0.05

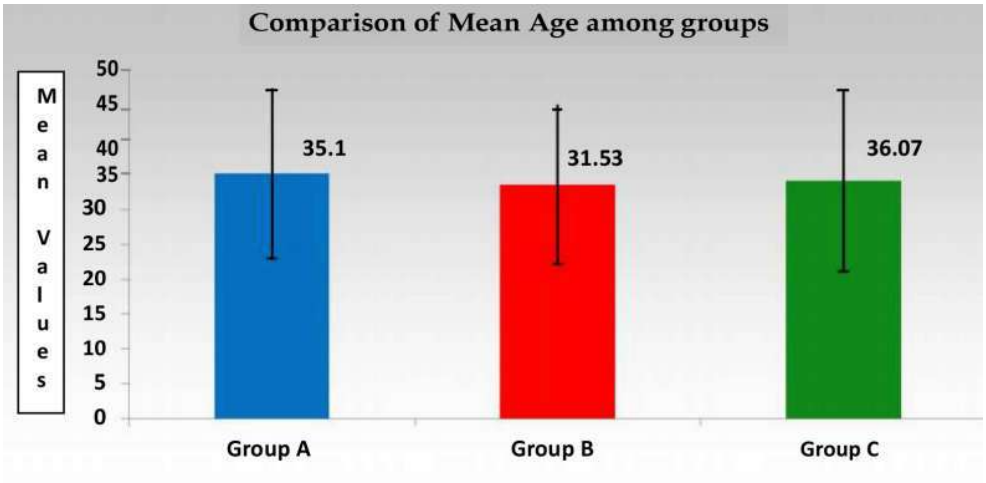

Fig. 1: Comparison of age in study groups

Table 2: Comparison of height and weight in study groups

	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	P Value
Height (cm)	162 ± 4.63	163.23 ± 4.23	161.67 ± 4.41	0.057
Weight (KG)	65.93 ± 4.97	64.43 ± 6.66	63.50 ± 4.91	0.639

A, Group B and Group C respectively. It was found that there was significant difference among three groups (p<0.001). Post hoc analysis showed that mean time of 2 dermatomal regression was significantly more in Group B as compared to Group A and Group C (p=0.003, p<0.001) and significantly more in Group A as compared to Group C (p<0.001).

The Mean ± SD for the time to onset of motor block was 2.53±0.86, 2.87±0.97 and 2.87±1.07 in Group A, Group B and Group C respectively. It was found that there was no significant difference among three groups (p = 0.314) .

The Mean±SD for the time to motor bromage 3 was 5.17±0.98, 5.50±1.07 and 5.63±0.85 in Group A, Group B and Group C respectively. It was found that there was no significant difference among three groups (p = 0.167) .

The Mean±SD duration of motor block in Group A, Group B and Group C was 120.37±2.31, 127.9±6.82, 120.63±4.37 respectively. It was found that there was significant difference among three groups (p<0.001). Post hoc analysis showed that duration of motor block was significantly more in Group B as compared to Group A and Group C (p<0.001, p<0.001) and comparable between Group A and Group C (p = 0.988). Furthermore, duration of motor block was maximum in Group B as compared to Group A (<0.001).

Table 3: Comparison of gender distribution among groups

Sex	Group A Frequency (%)	Group B Frequency (%)	Group C Frequency (%)	P Value
F	8 (26.7%)	4 (13.3%)	3 (10.0%)	
M	22(73.3%)	26(86.7%)	27(90.0%)	
Total	30(100%)	30(100%)	30(100%)	

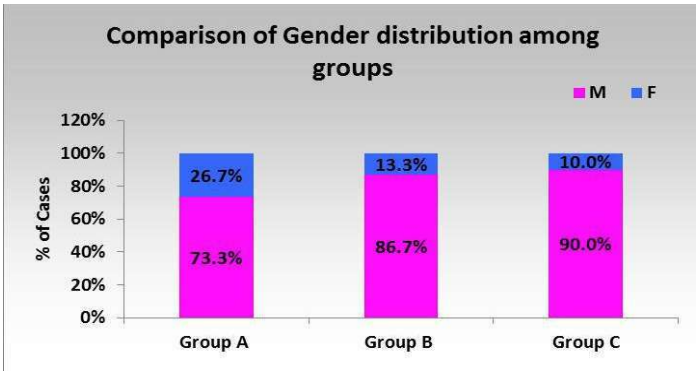

Fig. 2: Comparison of gender distribution among groups

Table 4: Comparison of ASA grade between groups

ASA	Group A (n=30) Frequency (%)	Group B (n=30) Frequency (%)	Group C (n=30) Frequency (%)	P Value
I	19 (63.3%)	17 (63.3%)	16 (53.3%)	0.049
II	11 (36.7%)	13 (36.7%)	14 (46.7%)	
Total	30 (100%)	30 (100%)	30 (100%)	

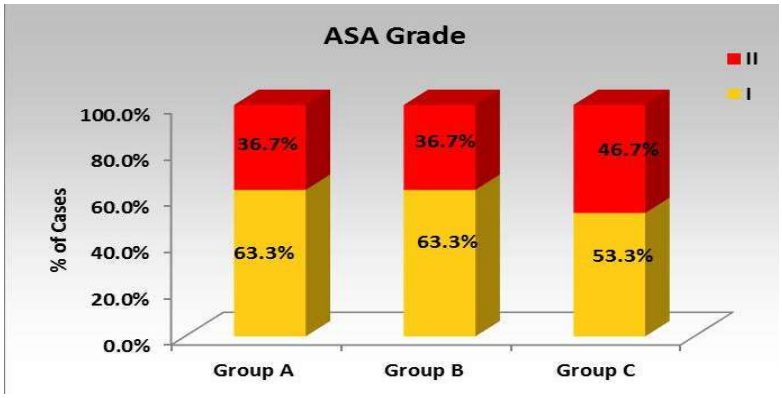

Fig. 3: Comparison of ASA grade between groups

Hemodynamics Changes

Table 5: Comparison of Heart Rate (HR) changes among groups

HR (per min)	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	P Value Group A V/S Group B	P Value Group A V/S Group C	P Value Group B V/S Group C
00 min	80.83±10.76	79.43±9.9	81.2±12.67	0.879	0.991	
03 min	72.67±11.57	72.13±8.2	74.67±11.9	0.98	0.751	0.632
06 min	72.53±12.78	70.2±7.53	73.37±12.7	0.703	0.956	0.525
09 min	72.40±11.29	69.67±8.4	72.67± 1.86	0.581	0.995	0.521
12 min	69.97± 12.27	69.43±9.3	71.77±13.1	0.698	0.823	0.721
15 min	73.30 ± 11.59	70.93±8.3	73.63±12.7	0.685	0.992	0.612
20 min	70.77 ± 12.56	70.33±8.7	71.83±12.4	0.988	0.930	0.867
25 min	70.87 ± 11.51	70.87±9.1	71.60±11.6	1.000	0.963	0.963
30 min	71.03 ± 10.74	70.00±7.8	71.07±10.8	0.914	1.000	0.909
45min	69.89 ± 11.08	69.37±9.2	69.05±11.3	0.980	0.950	0.993
60min	71.15 ± 9.81	71.20±8.8	70.88 ± 9.79	1.000	0.994	0.991
75min	70.77 ± 9.19	70.80±7.3	70.23 ± 8.76	1.000	0.968	0.964
90min	72.20 ± 9.06	72.17±7.1	71.90 ± 8.58	1.000	0.989	0.992
105min	71.13 ± 8.06	uu.53±7.2	70.73 ± 7.33	0.754	0.977	0.628
120min	70.10 ± 8.27	72.53±8.0	69.90 ± 7.85	0.476	0.995	0.419
135min	70.30 ± 8.4	73.306	71.17 ± 7.63	0.282	0.898	0.524
150min	72.73 ± 12.49	73.63±7.0	73.47±12.3	0.945	0.963	0.988
165 min	72.33 ± 12.54	73.03±6.4	72.53±12.1	0.965	0.997	0.982
180min	70.67±16.77	73.83±5.8	71.03±16.3	0.654	0.994	0.717

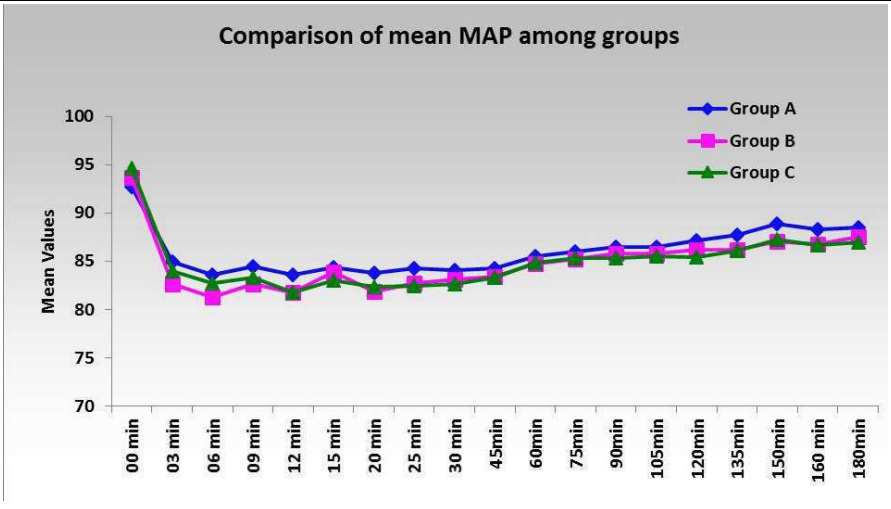

Fig. 4: Comparison of Heart Rate (HR) changes among groups

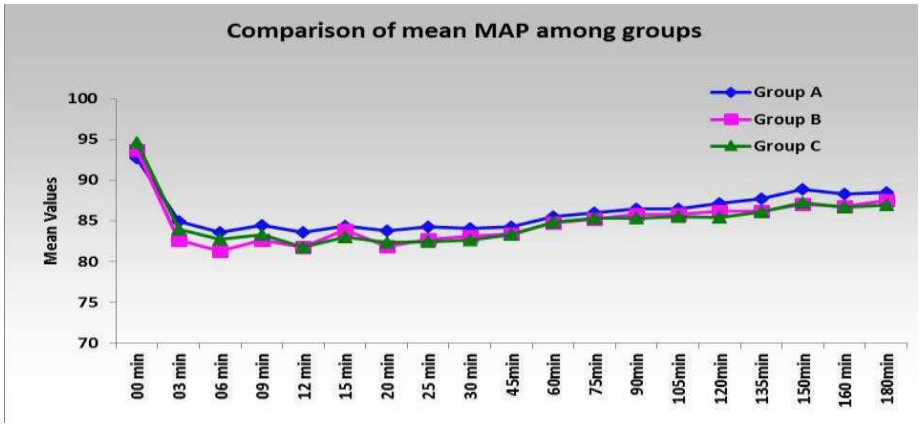

Fig. 5: Comparison of Mean Arterial Pressure (MAP) among groups

Table 6: Comparison of Mean Arterial Pressure (MAP) among groups

MAP (mm of Hg)	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	P Value Group A V/S Group B	Group A V/S Group C	Group B V/S Group C
00 min	92.69±6.4	93.64 ± 8.79	94.64 ± 8.49	0.888	0.610	0.878
03 min	84.89±5.5	82.59 ± 7.15	83.98 ± 10.82	0.521	0.902	0.787
06 min	83.54±5.7	81.31 ± 7.01	82.71 ± 10.78	0.539	0.917	0.783
09 min	84.48±7.1	82.59 ± 7.32	83.31 ± 11.43	0.687	0.866	0.946
12 min	83.59±7.0	81.74 ± 7.74	81.72 ± 11.33	0.702	0.696	1.000
15 min	84.38±6.1	83.83 ± 7.26	83.00 ± 10.97	0.966	0.800	0.922
20 min	83.74±7.2	81.87 ± 8.83	82.36 ± 12.01	0.728	0.840	0.979
25 min	84.21±7.1	82.74 ± 9.12	82.46 ± 12.12	0.827	0.762	0.993
30 min	84.06±6.6	83.09 ± 8.42	82.63 ± 11.88	0.913	0.822	0.980
45min	84.27±7.9	83.37 ± 9.82	83.29 ± 12.88	0.940	0.930	1.000
60min	85.54±7.3	84.72 ± 9.35	84.81 ± 12.32	0.944	0.956	0.999
75min	86.00±6.8	85.24 ± 9.19	85.36 ±11.46	0.948	0.962	0.999
90min	86.49±6.8	85.79 ±9.15	85.33 ± 11.95	0.957	0.886	0.981
105min	86.51±6.8	85.77 ± 8.79	85.53 ± 12.11	0.951	0.916	0.995
120min	87.13±7.0	86.14 ± 7.97	85.44 ± 11.74	0.908	0.756	0.953
135min	87.71±7.2	86.19 ± 8.55	86.09 ± 12.2	0.811	0.789	0.999
150min	88.87±6.5	87.07 ± 7.88	87.2 ± 11.64	0.716	0.751	0.998
165 min	88.33±6.3	86.73 ± 8.46	86.64 ±11.53	0.773	0.750	0.999
180min	88.52±6.1	87.49 ± 8.30	86.97 ± 11.49	0.895	0.779	0.972

Table 7: Comparison of changes in Respiratory Rate (RR) between groups

RR (cpm)	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	Group A V/S Group B	P Value Group A V/S Group C	Group B V/S Group C
00 min	13.97 ± 1.69	14.23 ± 1.72	13.63 ± 1.65	0.814	0.725	0.357
03 min	12.83 ± 1.12	12.73 ± 1.05	12.73 ± 1.05	0.931	0.931	1.000
06 min	13.13 ± 1.48	13.03 ± 1.38	13.03 ± 1.38	0.959	0.959	1.000
09 min	13.50 ± 1.17	13.37 ± 1.19	13.37 ± 1.19	0.900	0.900	1.000
12 min	13.37 ± 0.96	13.30 ± 0.84	13.30 ± 0.84	0.954	0.954	1.000
15 min	13.80 ± 1.06	13.77 ± 0.94	13.77 ± 0.94	0.990	0.990	1.000
20 min	13.60 ± 1.22	13.47 ± 1.17	13.47 ± 1.17	0.901	0.901	1.000
25 min	13.80 ± 1.10	13.73 ± 1.08	13.73 ± 1.08	0.969	0.969	1.000
30 min	13.23 ± 1.22	13.13 ± 1.22	13.13 ± 1.22	0.946	0.946	1.000
45min	13.50 ± 1.23	13.37 ± 1.27	13.37 ± 1.27	0.911	0.911	1.000
60min	12.97 ± 1.54	12.83 ± 1.44	12.83 ± 1.44	9.350	0.935	1.000
75min	13.20 ± 1.03	13.10 ± 1.00	13.10 ± 1.00	0.922	0.922	1.000
90min	12.80 ± 1.24	12.7 ± 1.21	12.77 ± 1.19	0.946	0.994	0.975
105min	12.97 ± 1.27	12.9 ± 1.30	13.00 ± 1.26	0.978	0.994	0.951
120min	13.13 ± 0.94	13.03 ± 0.89	13.00 ± 0.91	0.906	0.839	0.989
135min	13.17 ± 1.02	13.03 ± 1.03	13.07 ± 0.98	0.866	0.922	0.991
150min	12.87 ± 0.90	12.90 ± 0.96	12.93 ± 0.98	0.990	0.960	0.990
165min	12.97 ± 1.00	12.93 ± 1.02	12.97 ± 0.96	0.991	1.000	0.991
180min	12.97 ± 0.96	13.00 ± 0.95	13.03 ± 0.96	0.990	0.961	0.990

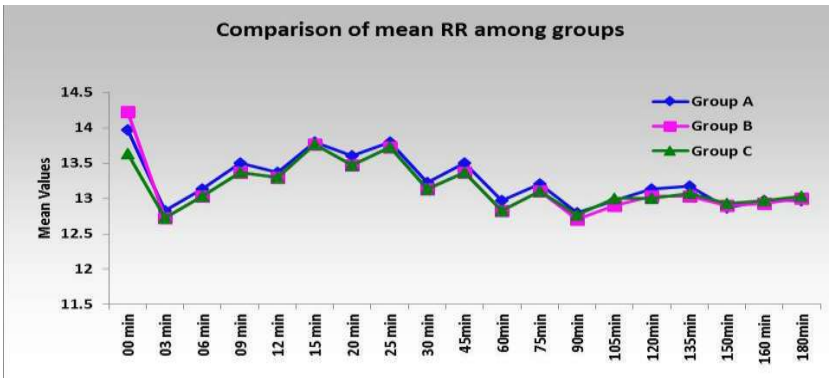

Fig. 6: Comparison of changes in Respiratory Rate (RR) between groups

Onset of Sensory Block

Table 8: Comparison of time to Sensory Onset

	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	Group A V/S Group B	P Value Group A V/S Group C	Group B V/S Group C
Time of onset of sensory block (T10) (sec)	108.63 ± 2.54	162.9 ± 2.4	65.67 ± 6.32	<0.001	<0.001	<0.001

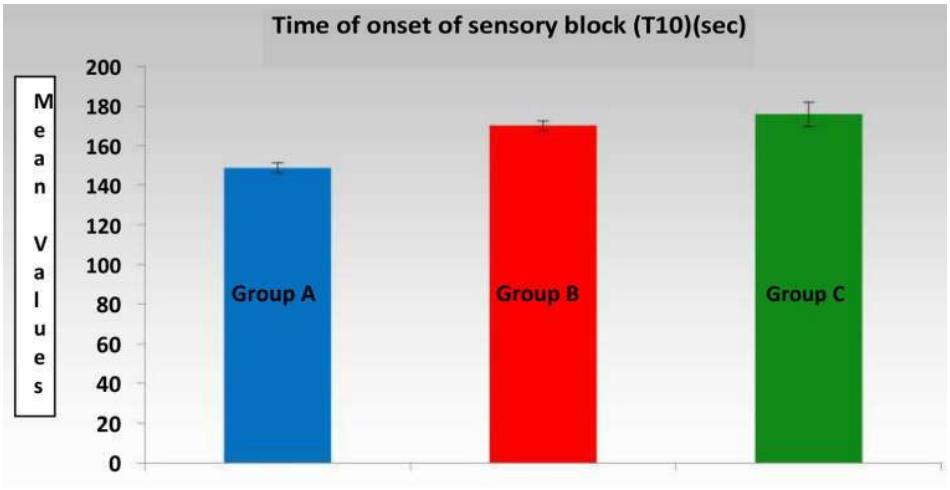

Fig. 7: Comparison of time to Sensory Onset

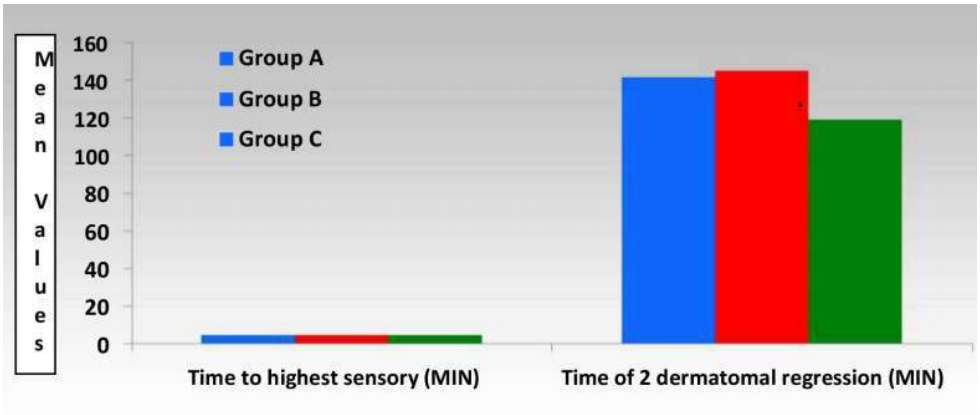

Fig. 8: Comparison of Time to achieve Highest Sensory Level and Duration of Sensory Block

Table 9: Comparison of Time to achieve Highest Sensory Level and Duration of Sensory Block

	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	Group A V/S Group B	P Value Group A V/S Group C	Group B V/S Group C
Time to highest Sensory (MIN)	2.3 ± 0.92	2.63 ± 1.16	42.70 ± 1.12	0.228	0.253	0.294
Time of 2 dermatomal regression (MIN)	121.33 ± 3.51	125.07 ± 4.74	148.70 ± 5.38	0.003	<0.001	<0.001

Table 10: Comparison of Onset and Duration of Motor Block

	Group A (n=30) Mean ± SD	Group B (n=30) Mean ± SD	Group C (n=30) Mean ± SD	Group A V/S Group B	P Value Group A V/S Group C	Group B V/S Group C
onset of motor block (Time to motor bromage 2 MIN)	3.53 ± 0.86	3.87 ± 0.97	3.87 ± 1.07	0.418	0.469	1
time to complete motor block (motor bromage 3 min)	4.17 ± 0.98	4.50 ± 1.07	4.63 ± 0.85	0.218	0.057	0.604
Duration of motor block (MIN)	120.37 ± 2.31	127.90 ± 6.82	120.63 ± 4.37	<0.001	0.988	<0.001

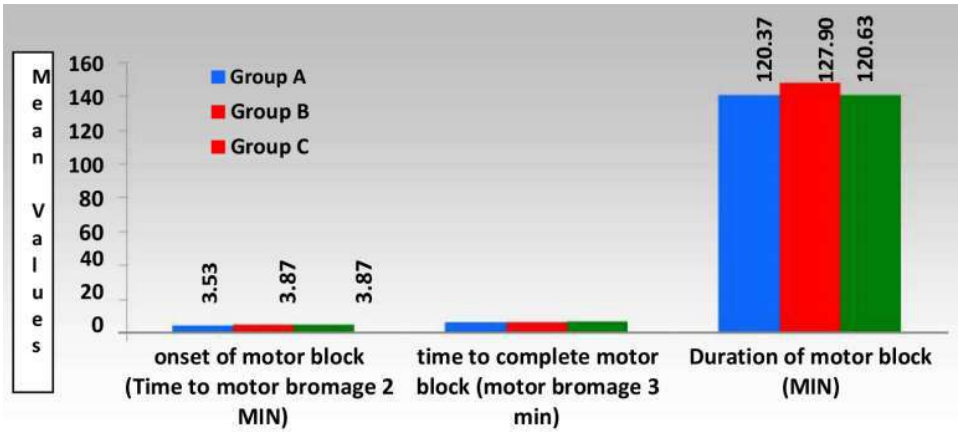

Fig. 9: Comparison of Onset and Duration of Motor Block

Adverse Effects

Table 11: Comparison of adverse effects among groups

Adverse effects	Group A Frequency (%)	Group B Frequency (%)	Group C Frequency (%)	P Value
Pruritus	0	0	0	
Nausea/vomiting	0	0	0	
Respiratory depression	0	0	0	

Discussion

In the present study we have compared the efficacy of nalbuphine (400 mcg in 0.5 ml), butorphanol (25 mcg in 0.5 ml) and normal saline (0.5 ml) with bupivacaine when administered by intrathecal route as an adjuvant to bupivacaine 0.5 % heavy (2.5 ml).

We have conducted this study on patients undergoing elective lower limb surgeries under spinal anesthesia.

90 patients of ASA grade I and II were divided into 3 equal groups of 30 patients each i.e. Group A (butorphanol), Group B (nalbuphine) and Group C (normal saline).

Group A - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + Butorphanol 25µg (0.5 ml)

Group B - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + nalbuphine 400ug (0.5 ml)

Group C - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + normal saline (0.5 ml)

Patient characteristics across the groups

There were no significant differences in patient's age, sex distribution, weight, height and ASA status. Thus all 3 groups were comparable with respect to their demographic profile.

Onset of Sensory Blockade

Onset of sensory block was considered as the time

from intrathecal injection of drug to complete loss of sensation to pin prick at T10 level.

The onset of sensory block during present study was found to be earliest with Butorphanol (148.63± 2.54 sec) followed by Nalbuphine (169.90±2.40 sec) and Control (175.67±6.32 seconds) respectively and difference among them was found to be significant, ($p<0.001$). The onset was significantly faster with butorphanol and nalbuphine as compared to control group ($p<0.001$) ($p<0.001$). Also butorphanol group showed significantly earlier onset as compared to nalbuphine group ($p<0.001$).

Shaheda P et al, in their study to evaluate of the effect of intrathecal Nalbuphine as an adjuvant to spinal Bupivacaine for postoperative analgesia in patients undergoing abdominal hysterectomy found that the onset of sensory block was faster with Nalbuphine 1mg Group (1.63±0.57) as compared to control group (3.23±1.03) which was both statistically and clinically significant. Also similar results were observed by Ahluwalia P and Shakooh S in their respective studies that the onset of sensory block was faster with Nalbuphine (0.8 mg) Group as compared to control group which was both statistically and clinically significant [10,20]. Mukherjee et al in their study on intrathecal Nalbuphine as an adjuvant to subarachnoid block at doses of 0.2mg, 0.4mg and 0.8mg observed earlier sensory onset with nalbuphine groups without significant difference between different doses of nalbuphine [14].

Meitei AJ et al recorded delayed sensory onset with butorphanol group 25mcg (31.68+5.436) compared to control group (29.87+5.673) which was statistically and clinically insignificant whereas we found that butorphanol group shows significantly early onset of sensory block as compared to control group [21].

Also study done by Chari VR et al. on addition of intrathecal Butorphanol 25µg to bupivacaine 0.5% heavy to patients undergoing lower segment caesarean section, showed that onset of sensory block was comparable between both the butorphanol and control groups [15]. Also study conducted by Jyothi B. et al. on comparison of analgesic effect of different doses of intrathecal nalbuphine – 0.8, 1.6 and 2.5 mg with Bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries, they found that onset was comparable among the groups with no difference on addition of increased doses of nalbuphine [18].

Similarly Tiwari A.K. et al. in their study compared intrathecal bupivacaine with a combination of nalbuphine and bupivacaine for subarachnoid block at doses of 0.2mg and 0.4 mg observed that onset of sensory block was comparable in all the groups [16].

Time Taken to Achieve the Highest level of Sensory Block

In our study, the time to attain highest level of sensory block was 4.3±0.92, 4.63±1.16 and 4.70±1.12 in Butorphanol, Nalbuphine and control group respectively. It was found that there was no significant difference among three groups ($p= 0.305$) and the groups were comparable.

In the study conducted by Meitei A.J. et al. on evaluation of intrathecal Bupivacaine alone and bupivacaine with butorphanol for lower segment caesarean section, they found that time taken to attain highest level of sensory blockade was similar and clinically and statistically insignificant ($p= 0.196$) between Butorphanol (297.50±115.1) and control group (242.80±89.7) [21] .

Similar results were observed by Chari VR et al. in their study of addition of intrathecal Butorphanol 25µg to bupivacaine 0.5% heavy to patients undergoing lower segment caesarean section, where they found that highest level of sensory block was attained by butorphanol group in 5.53±1.5 min and by control in 4.77±1.46 min which was statistically insignificant.($p>0.05$) [15].

This finding does not correlate with the values observed by Kaur M. et al. who in their study on comparison of intrathecal bupivacaine alone, sufentanil or butorphanol in combination with bupivacaine for endoscopic urological surgery, recorded delay in time required to attain highest sensory with butorphanol group (10.43±1.63) compared to control group (9.17±1.64) which was statistically and clinically significant [12].

The time for Two Dermatomal Segments Regression of sensory level

Duration of sensory block i.e. time to 2 dermatomal segment regression was longest with Nalbuphine group (145.07±4.74 min) followed by Butorphanol group (141.33±3.51 min) and Control group (118.70±5.38 min) in that order with significant difference ($p<0.001$). Duration of sensory block was significantly more with nalbuphine as compared to butorphanol ($p= 0.003$) and control group ($p<0.001$). Moreover, duration of sensory block was more with butorphanol as compared to control ($p<0.001$). Similarly, in study by Kaur M, Chari VR and Meitei AJ the duration of sensory block was found to be

prolonged with butorphanol as compared to control group [12,15,20]. Also Ahluwalia P, Shahedha P and Shakooh S, in their respective studies observed that addition of nalbuphine prolongs the duration of sensory block which was in agreement with the present study [10,20]. Similarly Jyothi B. et al in their study on comparison of analgesic effect of different doses of intrathecal nalbuphine – 0.8, 1.6 and 2.5 mg with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries observed significantly prolonged duration of sensory block in groups containing nalbuphine but was comparable among the different doses [18]. Whereas Mukherjee A and Tiwari AK observed that sensory block duration was significantly prolonged with higher doses of nalbuphine [14,16].

Onset of motor block and time to complete motor block

The time to onset of motor block (i.e. time from intrathecal injection to achievement of bromage 2) was 4.53±0.86, 4.87±0.97 and 4.87±1.07 minutes in Butorphanol, Nalbuphine and control group respectively. Also, the time taken to attain complete motor block (i.e. time from intrathecal injection to achievement of motor bromage 3) was 6.17±0.98, 6.50±1.07 and 6.63±0.85 minutes in Butorphanol, Nalbuphine and control group respectively. It was found that there was no significant difference among three groups regarding onset time and time to complete motor block ($p=0.314$), ($p=0.167$) respectively and the groups were comparable. Similarly Chari VR observed that time to onset ofmotor block and time to complete motor block were comparable in both butorphanol and control group [15]. Similar results were seen in studies done by Mukherjee A, Tiwari AK and Ahluwalia P were they observed that onset of motor block was comparable between nalbuphine and control group [14,16,20]. Also Meitei AJ observed that onset of motor block was comparable but control group reached complete motor block earlier as compared to butorphanol [21].

Whereas Shahedha P and Shakooh S in their respective studies observed faster onset of motor block with nalbuphine which was not in concordance to our study [21].

Duration of Motor Block

In our study, the duration of motor block was significantly prolonged in nalbuphine group (147.90±6.82 min) as compared to butorphanol and control ($p<0.001$). Whereas, the duration was comparable with butorphanol and control ($p = 0.988$).

Similar results were seen in studies conducted by Kaur M and Meitei AJ who observed comparable duration of motor block in butorphanol and control groups [12,20]. Also Ahluwalia P and Shakooh S in their respective studies observed that nalbuphine significantly prolongs the duration of motor block which were in agreement to our study [20,21]. Whereas Mukherjee A and Tiwari AK observed comparable duration of motor block between nalbuphine and control group despite increasing the dose of nalbuphine [14,16].

Conclusion

The addition of Nalbuphine in strength of 400 mcg and Butorphanol in strength of 25 mcg to 0.5% hyperbaric Bupivacaine intrathecally provide rapid onset and longer duration of sensory block. Though butorphanol showed rapid onset of sensory block as compared to Nalbuphine, the sensory block was longer lasting with Nalbuphine. Nalbuphine also increases the duration of motor block whereas Butorphanol does not.

Thus from our study, we conclude that both Butorphanol and Nalbuphine can be used as a safe adjuvant to local anesthetic for spinal anesthesia. Butorphanol showed faster onset of action and more prolonged duration of analgesia whereas Nalbuphine showed prolonged duration of sensor and motor block. This could be of value in geriatric patients undergoing lower limb surgeries as the quality and duration of block may be improved with a lower dose of local anaesthetic. Also the side effects like pruritus and the risk of respiratory depression may be obviated with the use of opioid agonist antagonist.

Since these two adjuvants have not been compared prior to the present study further studies are required in different centers with larger sample size.

Declarations

Funding: none

Conflict of interest: none

Ethical approval

Institutional ethical committee

References

1. Busch-Dienstfertig, M. & Stein, C. Opioid receptors and opioid peptide-producing leukocytes in inflammatory pain—basic and therapeutic aspects. Brain Behav. Immun. 2010;24:683–694.
2. Stein, C., Millan, M. J., Shippenberg, T.S., Peter, K. & Herz, A. Peripheral opioid receptors mediating antinociception in inflammation. Evidence for involvement of mu, delta and kappa receptors. J Pharmacol Exp Ther 1989;248:1269–1275.
3. Tegeder, I., Meier, S., Burian, M., Schmidt, H., Geisslinger, G. & Lötsch, J. Peripheral opioid analgesia in experimental human pain models. Brain 2003;126, 1092–1102.
4. Saxena AK, Arava AK. Current concepts in neuraxial administration of opioids and non opioids: an overview and future perspectives. Indian J. Anaesth. 2004;48(1):13-24.
5. Hindle A.Intrathecal opioids in the management of acute postoperative pain.Continuing Education in Anaesthesia. Critical Care & Pain J; 2008:8(3):81-85
6. Pallasch TJ, Gill CJ. Butorphanol and Nalbuphine: a pharmacological comparison. Oral Surgery & Oral Pathology. 1985;59(1):15–20.
7. Fournier R, Van GE, Macksay M, Gamulin Z. Onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. ActaAnaesthesiol Scand. 2000;44:940-5.
8. Culebras X, Giovanni G, Jiri Z, Christian K, and Rene AM. Advantages of Intrathecal Nalbuphine Compared with Intrathecal Morphine, After Cesarean Delivery: An Evaluation of Postoperative Analgesia and Adverse Effects. AnesthAnalg. 2000;91:601–5.
9. Yoon HJ, Jee YS, Hong JY. A Comparison of Analgesic Effects and Side Effects of Intrathecal Morphine, Nalbuphine and a Morphine-Nalbuphine Mixture for PainRelief during a Cesarean Section. Korean J Anesthesiol; 2002 May:42(5):627-63.
10. Shakooh S, Bhosle P. Intrathecal nalbuphine: An effective adjuvant for post-operative analgesia. Innovative J Med Health Sci 2004;4:79-82.
11. Singh V, Gupta LK, Singh GP. Comparison among intrathecal fentanyl and butorphanol in combination with bupivacaine for lower limb surgeries. J AnesthClinPharmacol. 2006;22:371–5.
12. Kaur M, Katyal S, Kathuria S, Singh P. A comparative evaluation of intrathecal bupivacaine alone, sufentanil or butorphanol in combination with bupivacaine for endoscopic urological surgery. Saudi Journal of Anaesthesia. 2011;5(2):202-207.
13. Kumar B, Williams A, Lidddle D, Verghese M. Comparison of intrathecal bupivacaine–fentanyl and bupivacaine - butorphanol mixtures for lower limb orthopedic procedures Anesthesia: Essay and Researches. 2011;5(2)190-95.
14. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N. Intrathecal nalbuphine as an adjuvant to subarachnoid block: what is the most effective dose? Anesth Essays Research. 2011;5:171-5.
15. Chari VR, Goyal AA, Singh V. A study of addition of injection butorphanol to hyperbaric injection bupivacaine given intrathecally to patients undergoing lower segment caesarean section: a randomized controlled trial. Med J of Dr. DY Patil Univ. 2013;6(2):156-60.
16. Tiwari AK, Tomar GS, Agrawal J. Intrathecal bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid blockA randomized prospective double-blind clinical study. Am J Ther 2013;20:592-5.
17. Nag S, Kumar R, Naifi S, Lakhanpal M. A comparative study of Butorphanol as an adjuvant to bupivacaine in comparison to bupivacaine alone. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2014 Feb;13(1, Ver X):32-36.
18. Jyothi B, Gowda S, Shaikh SI. A comparison of analgesic effect of different doses of intrathecal Nalbuphine hydrochloride with bupivacaine and bupivacaine alone lower abdominal and orthopedic surgeries. Indian J Pain. 2014;28:18-23.
19. Gomaa HM, Mohamed NN, Zoheir HA, Ali MS. A comparison between postoperative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section. Egypt J Anaesth. 2014;03:8-14.
20. Ahluwalia P, Ahluwalia A, Varshney R, Thakur S, Bhandari S. A prospective randomized double blind study to evaluate the effects of intrathecal nalbuphine in patients of lower abdominal surgeries under spinal anesthesia. Int J Sci Study. 2015;3(3):19-23.
21. Meitei AJ, Rubina O, Laithangbam PK, Singh JI, Ingudum D, Mithun Raj R. Evaluation of intrathecal bupivacaine alone, bupivacaine with butorphanol and bupivacaine with dexmedetomidine for lower segment caesarean section: a randomized control trial. Int J Basic ClinPharmacol 2016;5:2675-82.