Original Research Article

Comparative study of bupivacaine with nalbuphine and buprenorphine intrathecally for postoperative analgesia in lower limb surgeries

Manjula R[1], Karthik Kumar[2], Damodar Reddy Y[3*], Ranjitha C[2]

[1]Professor, [2]Post Graduates, Department of Anesthesiology, Adichunchanagiri Institute of Medical Sciences, Adichunchanagiri University, BG Nagara, Mandya, Karnataka, INDIA.
[3]Consultant, Department of Anesthesiology, KIMS-SAVEERA Hospital, Andhra Pradesh, INDIA.
Email: statisticsclinic2018@gmail.com

Abstract

Background: Spinal anaesthesia is the commonly used technique for lower limb surgeries as it is very economical and easy to administer. Its main disadvantage remains the short duration of action. Hence different additives have been used. Since there are no studies comparing Buprenorphine and Nalbuphine we have selected this study to evaluate the potentiating effect of intrathecal Bupivacaine with Buprenorphine compared with Nalbuphine for postoperative analgesia. **Materials and Methods:** In this prospective randomised controlled study, 60 patients of ASA physical status I and II belonging to age group of 18-60years undergoing elective lower limb surgery under sub-arachnoid block were randomly allocated into 2 groups of 30patients each, group BN and group BB. Group BN received 3ml of 0.5%(H)Bupivacaine(15mg)+1mg(0.1ml) of Nalbuphine+normalsaline(0.4ml) and group BB received 3ml of 0.5%(H)Bupivacaine(15 mg)+0.5ml(150µg) of buprenorphine for spinal anaesthesia. The onset and duration of sensory and motor blockade, 2 segment regression, duration of postoperative analgesia, side-effects and haemodynamic parameters were compared between the groups. **Results:** The mean time of onset of sensory and motor block, 2 segment regression and duration of motor block was comparable and statistically not significant between the two groups. The duration of postoperative analgesia was significantly prolonged with Buprenorphine compared to Nalbuphine with Bupivacaine($p<0.05$). **Conclusion:** Intrathecal Bupivacaine with Buprenorphine 150µg caused prolonged duration of postoperative analgesia when compared to intrathecal Bupivacaine with Nalbuphine 1mg..

Key Word: Intrathecal; Bupivacaine; Buprenorphine; Nalbuphine; Postoperative analgesia

[*]**Address for Correspondence:**
Dr. Damodar Reddy Y, Department of Anesthesiology, KIMS-SAVEERA Hospital, Andhra Pradesh, INDIA.
Email: statisticsclinic2018@gmail.com
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INTRODUCTION

Opioids have been used along with Bupivacaine in subarachnoid block to prolong its effect, to improve the quality of analgesia and minimize the requirement of postoperative analgesics. The reason for mixing of opioids and local anaesthetics is that this combination will terminate the pain by acting at two different sites, local anaesthetics acting at the nerve axon and the opioids at the receptor site in the spinal cord. Nalbuphine is a semisynthetic opioid, which is structurally related to oxymorphone, highly lipid soluble with an agonist activity at kappa and an antagonist activity at µ opioid receptor[1,2]. When Nalbuphine is added as an adjuvant to intrathecal Bupivacaine, it has potential to provide good intraoperative and postoperative analgesia with decreased incidence of µ receptor side effects like respiratory depression. Nalbuphine has short duration of action due to its lipid solubility and rapid clearance when compared to Morphine. The side effects of Nalbuphine are dizziness, bradycardia, nausea, vomiting, pruritis, urinary

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retention and sedation. Buprenorphine is also a highly lipid soluble The baine derivative with a partial agonist activity at the μ-opioid receptor and antagonist at kappa receptor. 33 times more potent than morphine. It has higher affinity than the full agonist at μ-receptor [3]. Partial agonist has a dose-effect ceiling that is lower than that of a full agonist.[4] Here we compared the effect of Nalbuphine and Buprenorphine as an adjuvant to hyperbaric Bupivacaine intrathecallyin terms of duration of action, quality of postoperative analgesia and any side effects.

AIMS AND OBJECTIVES

To compare the

- Onset of sensory and motor blockade.
- Duration of sensory and motor blockade.
- 2 segment regression.
- Duration of postoperative analgesia achieved
- To study any side-effects withaddition of Nalbuphine and Buprenorphine
- Haemodynamic parameters

MATERIALS AND METHODS

This prospective randomised controlled study was done at department of anaesthesiology, Adichunchanagiri Institute of Medical Sciences, BG Nagara, Mandya. After approval from the ethical committee of the institution, informed written consent was taken from all 60 patients of ASA physical status I and II belonging to age group of 18- 60 years undergoing elective lowerlimb surgery. Exclusion criteria were Infection at the site of sub arachnoid block, bleeding disorders, patient receiving anticoagulants, cardiac diseases, renal diseases, Allergic reaction to any anaesthetic drug, patients on tranquilizers, hypnotics, sedatives and other psychotropic drugs. Patients were randomly allocated into 2 groups of 30 patients each, group BN and group BB by computerized randomization method. Group BN received 3ml of 0.5% (H) Bupivacaine (15mg) + 1mg(0.1ml) of Nalbuphine + normal saline(0.4ml) and group BB received 3ml of 0.5% (H) Bupivacaine (15 mg)+0.5ml(150μg) of Buprenorphine for spinal anaesthesia. A thorough pre-anaesthetic evaluation was done for the study population a day prior to the surgery. Detailed history, airway examination and cardiorespiratory examination with emphasis on the Mallampatti grading and rule of 1-2-3 was performed. Relevant clinical investigations which were done on the study population - Blood investigations: Hb,TC, DC, Platelet count, BT, CT, Blood grouping and Rh typing, Blood sugar, Urine analysis, RFT, HIV, HBsAg, ECG, Chest x-ray (if necessary). Preoperative orders advised for the patients include written informed consent, Nil per oral status for a minimum of 8 hours. Pre-medications – Tablet Ranitidine 150mg and Tablet *al*prazolam 0.5mg were prescribed. The entire procedure of spinal anaesthesia was explained to the patient in the regional language that they could understand. Patients were explained about visual analogue scale (VAS) and were taught how to express the degree of pain on the scale. Patients (was) were shifted to OT, intra operatively an IV line was secured with IV cannula, standard monitors(NIBP, SpO2, ECG) connected and baseline vitals recorded, patients were preloaded with 10-15 ml/kg ringer lactate solution. Sub arachnoid block was (given) performed under strict aseptic precautions in sitting position preferably in L3-L4 interspinous space using 25G spinal needle after free flow of CSF.The study medication was prepared by the person who was not involved in the study to ensure blinding of anaesthesiologist. Group BN received 3ml of 0.5% (H) Bupivacaine (15mg) + 1mg(0.1ml) of Nalbuphine + Normal Saline(0.4ml) and group BB received 3ml of 0.5% (H) Bupivacaine (15 mg)+0.5ml(150μg) of Buprenorphine for spinal anaesthesia. Then patients were shifted to supine position, intraoperatively haemodynamic parameters and the following parameters were noted and used for comparison between the groups.

- Time of drug administration.
- Time of onset and complete sensory and motor block
- 2 segment regression of sensory block.
- Duration of sensory block (sensory level was assessed by pin prick method)
- Duration of post-operative analgesia (Effective analgesia-time of onset of sensory block to the first request of rescue analgesics by using VAS score).
- Duration of motor block (which was assessed by Modified Bromage scale)

Score	Score Criteria
1	Complete block (unable to move feet and knee)
2	Almost complete block (unable to move feet and knee)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

This was performed every 2 minutes until complete motor block and every 30minutes until return of normal motor function. Post operatively pain, sensory level, motor level were evaluated every 30mins for first 2 hours, every 60mins for next 6 hours and at 12 hours and 24 hours in recovery room. Pain was assessed by VAS(visual analogue scale), patient was given a scale marked from 0-10 and was asked to mark on the scale the degree of pain

he /she experiencing from 0-no pain to 10 maximum pain , when VAS>4, rescue analgesia given with inj. Diclofenac sodium 1.5mg/kg IM.

Side effects like pruritis, urinary retention, respiratory depression, postoperative nausea and vomiting etc were recorded for 24 hours.

Statistical Analysis: The sample size was decided in consultation with the statistician and was based on initial pilot study observations, indicating that approximately 23 patients should be included in each group in order to ensure a power of 0.80. Assuming a 5% drop out rate, the final sample size was set at 30 patients in each group, which would permit a type 1 alpha error =0.05, with a type 2 error of beta=0.2. Data analysis was done with the help of computer using SPSS statistical package- Version 17**.** A 'p' value less than 0.05 (will denote significant relationship)was considered statistically significant. Demographic characteristics of cases studied, outcome variables and the significance of the relationship between the outcomes variables of the two groups were analysed using the appropriate tests.

RESULTS

60 patients of ASA physical status 1 and 2 posted for lower limb surgeries under Subarachnoid block, were randomly selected and divided into 2 groups of 30 patients each. Group BN- received 3ml of 0.5% (H)Bupivacaine(15mg) + 1mg(0.1ml) of Nalbuphine+normalsaline(0.4ml) Group BB- received 3ml of 0.5%(H)Bupivacaine(15 mg)+0.5ml(150µg) of buprenorphine

Table 1: Social Profile of the study participants

		Group BN	Group BB	Total	P-Value
Age Group	21-30	7 (23.3%)	8 (26.7%)	15	0.402
	31-40	10 (33.3%)	6 (20%)	16	
	41-50	13 (43.5%)	16 (53.3%)	29	
Gender	Male	10 (33%)	19 (63%)	29	0.020
	Female	20 (67%)	11 (37%)	31	
ASA	I	27 (90%)	20 (67%)	47	0.028
	II	3 (10%)	10 (33%)	13	

In BN group, 7 patients (23.3%) were in 21-30 yrs age group, 10 patients (33.3%) were in 31-40 yrs age group and 13 patients (43.5%) were in 41-50 yrs age group. In BB group, 8 patients (26.7%) were in 21-30 yrs, 6 patients (20%) were in 31-40 yrs and 16 patients (53.3%) were in 41-50 yrs age group. The average age of patients in BN group was 38.23±8.28, whereas it was 38.90±9.63 in BB group. The sample with a P-value 0.775 There were 10 (33%) male patients and 20 (67%) female patients in BN group and 19 male patients (63%) and 11 (37%) in BB group with the P-value 0.071. All the patients enrolled in the study in two groups were comparable according to body weight, height and body mass index. In present study it was observed that group BN had 27 (90%) patients with ASA Grade 1, and 3 (10%) with ASA Grade 2, while Group BB had 20 (67%) and 10 (33%) patients of ASA Grade 1 and 2 respectively.

Table 2: Comparison of sensory and motor blockade between two groups

	Group BN	Group BB	P p value
Onset of sensory	1.68±0.21	1.72±0.24	0.4948
Onset of motor	5.76±0.60	6.00±0.57	0.1176
Two Segment regression	132.9±5.23	135.4±6.11	0.094
Duration of Motor block	141.2±5.93	144.4±7.03	0.0616
Duration of effective analgesia	261±25.34	392±32.4	<0.001

The mean onset of loss of sensory sensation in group BN was 1.68 where as in Group BB was 1.72 minutes. The loss of motor sensation was seen in 5.76 minutes in Group BN and 6 Minutes in Group BB. The two segment regression was seen more in Group BB (135 minutes) than Group BN (132.9 minutes). The total duration of Motor Blockade was also more in Group BB with 144.4 minutes and 141.2 minutes in Group BN. The total duration of effective analgesia was seen more in group BB where it lasted for 392 minutes where as in Group BN it was 261 minutes. All the parameters were found to be not significant statistically when compared between both the groups. The mean time of onset of sensory and motor block,2 segment regression and duration of motor block (is)was comparable (between two groups but) and statistically not significant between the two groups. The duration of postoperative analgesia (is)was significantly prolonged with addition of Buprenorphine compared to Nalbuphine with Bupivacaine **(p<0.05)**.There were no statistically significant differences in the demographic

profile of patients in either group in terms of age, body weights, or male/female (M/F) ratio ($p > 0.05$). There was no significant difference found in various haemodynamic vital parameters intra operatively between the two groups.

DISCUSSION

Subarachnoid block is a common regional technique for lower limb surgeries, which is simpler and cost-effective. The combination of local anaesthetics with adjuvant enables us for the use of lesser dose of local anaesthetics and increases the success of anaesthesia. Intrathecal opioidsused as an adjunct to local anaesthetic Bupivacaine vary widely thereby decreasing the adverse effects associated with the use of higher dose of Local anaesthetics like hypotension, bradycardia, high level of motor blockade. Spinal opioids have been proven to provide profound postoperative analgesia with fewer central and systemic adverse effects as compared to opioids administered systemically. Nalbuphine is an opioid structurally related to oxymorphone. It is a highly lipid soluble opioid with an agonist action at the k opioid receptor and an antagonist activity at the mu opioid receptor. There are few studies done previously on intrathecal Nalbuphine as an adjuvant. Various studies on usage of intrathecal Nalbuphine (compared) by Arghya Mukherjee *et al*[5], Manisha Sapate *et al*, compared the effect of adding 0.5 mg of Nalbuphine to spinal bupivacaine[6], Lin *et al*, found that the addition of intrathecal Nalbuphine 0.4 mg to hyperbaric Tetracaine, compared with intrathecal Morphine 0.4 mg for SAB, improved the quality of intraoperative and postoperative analgesia with fewer side effects[7]. These studies found that postoperative analgesia prolong around 200-600 minute by adding various dose of intrathecal Nalbuphine. SapkalPravin S. *et al*,[8] in their study concluded that intrathecal Clonidine 60mcg significantly prolongs the duration of spinal anaesthesia and quality of spinal analgesia was acceptable to patients in both groups though VAS assessment was better in Buprenorphine group. SoumyaSamal *et al*[9] administered intrathecal Buprenorphine and intrathecal Dexmedetomidine for postoperative analgesia and found that intrathecal Buprenorphine provides longer duration of postoperative analgesia than intrathecal Dexmedetomidine without significant hemodynamic changes. P HarshaVardhan *et al*,[10] in their study to compare the efficacy of hyperbaric Bupivacaine with Buprenorphine combination in lower abdominal and lower limb surgeries for prolonging the duration of postoperative analgesia, concluded that low dose buprenorphine potentiates the action of bupivacaine in spinal anaesthesia thereby decreasing the time taken for onset of analgesia, prolonging the duration of analgesia, delays postoperative pain and thus reduces the analgesic requirement in the early postoperative period. S Kumaresan *et al*,[11] in their study of intrathecal Nalbuphine as an adjuvant to spinal anaesthesia showed that in a dose of 0.6mg to prolong the duration of anaesthesia without increased adverse effects. Fournier *et al*[12] compared between intrathecal Nalbuphine 0.4mg and Morphine 160µg in patients undergoing TKR. They concluded that Nalbuphine produces faster onset of pain relieving but duration of analgesia shorter than Morphine. Tiwari *et al*[13] had compared intrathecal Nalbuphine 0.2 and 0.4mg added to hyperbaric Bupivacaine alone. They concluded that prolonged duration of analgesia was seen in Nalbuphine 0.4mg without adverse effects. Since there are no proper study comparing intrathecal Buprenorphine with Nalbuphine as adjuvant in potentiating postoperative analgesia we have selected these two drugs for comparison in our study. Our study shows effective analgesia in BB group is 392±32.4 min and in BN group 261±25.34 minutes,this prolongation of postoperative analgesia is supported by previous studies mention above. Our study shows no statistically significant difference between onset of sensory and motor block, duration of motor block and two-segment regression time among both groups. Intrathecal Buprenorphine 150 µg as an adjuvant provide significantly longer duration of postoperative analgesia when compared to 1 mg Nalbuphine. Adverse effects like nausea,vomiting, urinary retention and shivering were statistically insignificant in our study.

CONCLUSION

Present study shows effective analgesia in BB group is 392±32.4min while compared to BN group effective analgesia is 261±25.34min.**(P<0.001)**. Hence we concluded that intrathecal Buprenorphine 150µg when compared to intrathecal Nalbuphine 1mg causes prolonged duration of postoperative analgesia.

REFERENCES

1 Zarr GD, Werling LL, Brown SR, Cox BM. Opioid ligand binding sites in the spinalcord of the guinea-pig. Neuropharmacology 1986; 25: 471-80.

2 De Souza EB, Schmidt WK, Kuhar MJ. Nalbuphine : An autoradiographic opioid receptor binding profile in the central nervous system of an agonist/antagonist analgesic. J PharmacolExpTher1988; 244: 391-402.

3 Huang, A., Katznelson, R., Perrot, M., and Clark, H. (2014). Perioperative management of a patient undergoing Clagett window closer stabilized on Suboxone for chronic pain: a case report. Canadian Journal of Anesthesia, 61. P826-831. Retrieved on: 1/3/2015. DOI: 10. 1007/s12630-014-0193-y.

4 Barash, P., Cullen, B., Stoelting, R., Cahalan, M., and Stock, M. (2009). Clinical anaesthesia (6thed). Philadelphia, PA: Lippincott, Williams, and Wilkins

5 Mukherjee, *et al*.: Optimal dose of intrathecal nalbuphine. Anesthesia: Essays and Researches; 5(2); Jul-Dec 2011.
6 Manisha Sapate, MD, DA*, PreetySahu**, W. S. Thatte, A randomized, double blind, control study of the effect of adding nalbuphine to spinal bupivacaine for lower abdominal surgeries in elderly patients. Apicare ISSN 1607-8322, ISSN (Online) 22205799.
7 Lin ML *et al*, The analgesic effect of subarachnoid administration of tetracaine combined with low dose of morphine or nalbuphine for spinal anaesthesia. Ma ZuiXueZaZhi. 1992 Jun;30(2):101-5
8 SapkalPravin S., *et al*, Comparative study of intrathecal clonidine and intrathecal buprenorphine for postoperative analgesia after lower limb orthopaedic surgery. IJCRR. 2013;5(6): 87-91
9 SoumyaSamal *et al*, Intrathecal Buprenoephine or intrathecal Dexmedetomidine for postoperative analgesia: A comparative study. The Health Agenda, Online ISSN No: 2320-3749
10 P HarshaVardhan *et al*, Combination of hyperbaric bupivacaine with buprenorphine in lower abdominal surgery- A comparative study. Journal of science, vol 5 / Issue 7 / 2015/484-488
11 S Kumaresan *et al*, Intrathecal Nalbuphine as an adjuvant to spinal anaesthesia: What is most optimum dose? International Journal of Scientific Study / April 2017 / vol 5 / Issue 1
12 Fournier R, Van Gessel E, Macksay M, Gamulin Z. Onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. Anaesthesiology. 1998; 89: 867.
13 Tiwari *et al*, Intrathecal Bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block: A randomised prospective double-blind clinical study. American Journal of Therapeutics: November/December 2013 – volume 20 – Issue 6 – p 592-595.

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