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Comparative Study of Bupivacaine with Nalbuphine and Buprenorphine Intrathecally for Postoperative Analgesia in Lower Limb Surgeries

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ABSTRACT: Background*: Analgesia, one of the components of triad of anaesthesia, has now extended to relief of postoperative pain, chronic pain and cancer pain. The spinal cord has taken the center stage in analgesia practice and Spinal anaesthesia is the commonly used technique for lower limb surgeries as it is easy to administer, economical and causes less hemodynamic variation than general anaesthesia. Hence different additives can be used to increase the duration of postoperative analgesia. Since there are no studies comparing Buprenorphine and Nalbuphine, we have selected this study to evaluate the 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 A (Bupivacaine and Nalbuphine) and Group B (Bupivacaine and Buprenorphine). Group A received 2.8ml of 0.5%(H)Bupivacaine+[0.2 ml (2mg) of Nalbuphine (undiluted) taken in 1ml tuberculin syringe 1mg/0.1ml] and group B received 2.8ml of 0.5%(H)Bupivacaine+0.2ml(60µg) 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 60µg caused prolonged duration of postoperative analgesia when compared to intrathecal Bupivacaine with Nalbuphine 2mg.*

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

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I. Introduction

Analgesia, one of the components of triad of anaesthesia, has now extended to relief of postoperative pain, chronic pain and cancer pain. The spinal cord has taken the center stage in analgesia practice following the demonstration of analgesia with intrathecal morphine by Yaksh and Rudy (1977)[1]. Deposition of drugs in the epidural and subarachnoid space paved a new era for pain relief. Spinal anesthesia is the best anesthetic technique for lower limb surgeries as it is simple to perform, with fast onset of anaesthesia and complete muscle relaxation. Intrathecal opioids are synergistic with local anesthetics and intensify the sensory blockade. The first report on the use of intrathecal opioids (ITO) for acute pain treatment was in 1979 by Wang and colleagues.[2]Use of ITO as an adjuncts has a definite place in the present regional anesthesia practice. Various opioids have been used along with bupivacaine to prolong its effect, to improve the quality of analgesia and minimize the requirement of postoperative analgesics. Nalbuphine is a semisynthetic opioid with mixed mu antagonist and k agonist properties.[3,4]Previous studies have shown that epidural or intrathecal administration of nalbuphine produces a significant analgesia accompanied by minimal pruritus and respiratory depression.

The knowledge of specific opiate receptors in the substantia gelatinosa of the posterior horn of spinal cord resulted in wide spread use of intathecal opiates in the treatment of acute and chronic pain (Pert and Snyder, 1973)[5]. A local anaesthetic – opioid combination provides superior analgesia during perioperative and postoperative period.

Intrathecal opioids have unique advantages over conventional, intermittent IV/ IM administration, in that patients given opioids have fewer respiratory complications and can be mobilized sooner in the postoperative period. Though pure opioid agonists like morphine and fentanyl has already established its role in epidural administration for pain relief, its side effects like respiratory depression, nausea, vomiting, urinary retention etc., has made physician to search for a better drug for epidural employment. The agonist/antagonist opioid agent Nalbuphine can be expected to offer some scope in this respect, since the respiratory depression reaches ceiling level at higher dose of this drug. 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[6,7] Buprenorphine is also a highly lipid soluble Thebaine derivative with a partial agonist activity at the μ-opioid receptor and antagonist at kappa receptor. It is 33 times more potent than morphine. It has higher affinity than the full agonist at μ-receptor.[8] Here we compared the effect of Nalbuphine and Buprenorphine as an adjuvant to hyperbaric Bupivacaine intrathecally in terms of duration of action, quality of postoperative analgesia and any side effects.

II. 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.
- Any side-effects with addition of Nalbuphine and Buprenorphine.
- Haemodynamic parameters.

III. Materials And Methods

This prospective randomised controlled study was done 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 A and group B by computerized randomization method. Group A received 2.8ml of 0.5% (H) Bupivacaine (14mg) + 2mg(0.2ml) of Nalbuphine and group B received 2.8 ml of 0.5% (H) Bupivacaine (14 mg)+0.2ml(60μg) 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 was performed. Relevant clinical investigations which were done on the study population - Blood investigations: Hb,TLC, DLC, Platelet count, BT, CT, Blood grouping and Rh typing, Blood sugar, Urine analysis, LFT, RFT, HIV, HBsAg, HCV, ECG, Chest x-ray (if necessary). Preoperative orders advised for the patients included written informed consent, Nil per oral status for a minimum of 8 hours. Pre-medications – Tablet Ranitidine 150mg and Tablet alprazolam 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 which when shifted to OT, an IV line was secured with 18G IV cannula, standard monitors (NIBP, SpO2, ECG) were connected and baseline vitals were recorded, patients were preloaded with 10-15 ml/kg Ringer Lactate Solution. Sub arachnoid block was performed under strict aseptic precautions in sitting position preferably in L3-L4 space using 25G spinal needle after assuring clear and free flow of CSF. The study medication was prepared by the person who was not involved in the study to ensure

blinding of the anaesthesiologist. Group A received 2.8 ml of 0.5% (H) Bupivacaine (14mg) + 2mg(0.2ml) of Nalbuphine and Group B received 2.8 ml of 0.5% (H) Bupivacaine (14 mg) + 0.2ml(60µg) of Buprenorphine for spinal anaesthesia. After this the patients were shifted to supine position where intraoperative haemodynamic parameters along with other 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)

Grades	Description
1	Complete block (unable to move feet or knees)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion (between scores 3 and 5)
5	No detectable weakness of hip flexion while supine (full flexion of knees)
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 levelwereevaluated every 30mins for first 2 hours, every 60mins for next 6 hours and at 12 hours and 24 hours in the 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 is experiencing from 0-no pain to 10 maximum pain , when VAS>4, rescue analgesia was 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.

IV. 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 beta error =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)and 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.

V. 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 A- received 2.8 ml of 0.5% (H)Bupivacaine(14mg) + 2mg(0.2ml) of Nalbuphine + Group B- received 3ml of 0.5%(H)Bupivacaine(14 mg) + 0.2ml(60µg) of buprenorphine.

In A group, 7 patients (23.3%) were in 21-30 years age group, 10 patients (33.3%) were in 31-40 years age group and 13 patients (43.5%) were in 41-50 years age group.

TABLE:1 *SOCIAL PROFILE OF THE STUDY POPULATION*

		GROUP A	GROUP B	TOTAL	P VALUE
	21-30	7(23.3%)	8(26.7%)	15	
AGE GROUP	31-40	10(33.3%)	6(20%)	16	0.402
	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	
	II	3(10%)	10(33%)	13	0.028

In B group, 8 patients (26.7%) were in 21-30 years, 6 patients (20%) were in 31-40 years and 16 patients (53.3%) were in 41-50 years age group. The average age of patients in A group was 38.23±8.28, whereas it was 38.90±9.63 in B group. The sample with a P-value 0.775 .There were 10 (33%) male patients and 20 (67%) female patients in A group and 19 male patients (63%) and 11 (37%) in B 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 A had 27 (90%) patients with ASA Grade 1, and 3 (10%) with ASA Grade 2, while Group B 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 A	GROUP B	p VALUE
ONSET OF SENSORY BLOCK	1.68±0.21	1.72±0.24	0.4948
ONSET OF MOTOR BLOCK	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 A was 1.68 where as in Group B was 1.72 minutes. The loss of motor sensation was seen in 5.76 minutes in Group A and 6 Minutes in Group B. The two segment regression was seen more in Group B(135 minutes) than Group A (132.9 minutes). The total duration of Motor Blockade was also more in Group B with 144.4 minutes and 141.2 minutes in Group A. The total duration of effective analgesia was seen more in group B where it lasted for 392 minutes where as in Group B 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.

VI. 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 opioidscan be used as an adjunct to local anaesthetics. 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[9] , Manisha Sapate et al, compared the effect of adding 0.5 mg of Nalbuphine to spinal bupivacaine[10] , 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[11] . These studies found that postoperative analgesia prolong around 200-600 minute by adding various dose of intrathecal Nalbuphine. SapkalPravin S. et al, [12] 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[13] 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,[14]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 theanalgesic requirement in the early postoperative period. S Kumaresan et al,[15] 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[16] 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[17] 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 60µg as an adjuvant provide significantly longer duration of postoperative analgesia when compared to 2mg Nalbuphine. Adverse effects like nausea,vomiting, urinary retention and shivering were statistically insignificant in our study.

VII. Conclusion

Present study shows effective analgesia in B group is 392±32.4min while the effective analgesia in A group is 261±25.34min.($P<0.001$). Hence we concluded that intrathecal Buprenorphine 60µg when compared to intrathecal Nalbuphine 2mg causes prolonged duration of postoperative analgesia.

References

[1]. Yaksh T. L. Rudy T. A. Studies on the direct spinal action of narcotics in the production of analgesia in the rat. Joumal of Pharmacology & Experimental Therapeutics, 1977; 202: 411-428.
[2]. Wang JK, Nauss LA, Thomas JE-pain relief by intrathecally applied in man-Anaesthesiology 1979; 50: 149-51.
[3]. Culebras X, Gaggero G, Zatloukal J, Kern C, Marti RA. Advantages of Intrathecal nalbuphine, compared with intrathecal morphine, after Cesarean delivery: An evaluation of postoperative analgesia and adverse effects. Anesth Analg 2000; 91(3): 601-5.
[4]. Mikuni I, Hirai H, Toyama Y, Takahata O, Iwasaki H. Efficacy of intrathecal morphine with epidural ropivacaine infusion for postcesarean analgesia. J Clin Anesth. 2010 Jun; 22(4): 268-73. doi: 10.1016/j.jclinane.2009.09.003.
[5]. Pert CB, Snyder SH. Opiate receptor: demonstration in nervous tissue. Science, 1973 Mar 9; 179(4077): 1011–1014.
[6]. Zarr GD, Werling LL, Brown SR, Cox BM. Opioid ligand binding sites in the spinalcord of the guinea-pig. Neuropharmacology 1986; 25: 471-80.
[7]. 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.
[8]. 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.
[9]. Mukherjee, et al.: Optimal dose of intrathecal nalbuphine. Anesthesia: Essays and Researches; 5(2); Jul-Dec 2011.
[10]. 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.

[11]. 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
[12]. 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
[13]. SoumyaSamal et al, Intrathecal Buprenoephine or intrathecal Dexmedetomidine for postoperative analgesia: A comparative study. The Health Agenda, Online ISSN No: 2320-3749
[14]. 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
[15]. 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
[16]. 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.
[17]. Tiwari et al, Intrathecal Bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block: A randomised prospective doubleblind clinical study. American Journal of Therapeutics: November/December 2013 – volume 20 – Issue 6 – p 592-595.

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