

# Comparitive Study of Bupivacaine with Nalbuphine and Bupivacaine alone for Post-Operative Analgesia in SubArachniod Block for Lower Limb Surgeries- Prospective Randomised Study

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Submission: March 06, 2017; Published: April 05, 2017

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## Abstract

**Background:** Nalbuphine is a synthetic opioid, with kappa agonist or partial  $\mu$  antagonist action. When added as an adjuvant to intrathecal bupivacaine, it acts on dorsal horn of spinal cord producing analgesia with decreased incidence of  $\mu$  receptor side effects.

**Aims and Objectives:** To compare the onset, duration of sensory blockade, duration of motor blockade, 2 segment regression and duration of post operative analgesia achieved, by comparing hyperbaric bupivacaine alone with hyperbaric bupivacaine and nalbuphine after intrathecal administration.

**Material and Methods:** Randomised double blind study done on 60 patients, who were undergoing lower limb surgeries under sub-arachnoid block. Patients were divided into two groups, group B receiving 15mg of 0.5% hyperbaric bupivacaine+0.1ml of normal saline and group N receiving 15mg of hyperbaric bupivacaine+0.1ml of nalbuphine (1mg). Assessment of duration of motor and sensory blockade was done by modified bromage scale and pin prick method respectively.

**Results:** There was no significant variation in onset of motor and sensory blockade in two groups, but mean time of post-operative analgesia in group N was highly significant than group B ( $P < 0.001$ ).

**Conclusion:** Thus we conclude that intrathecal nalbuphine at dosage of 1mg can be used as effective adjuvant along with 0.5% of hyperbaric bupivacaine intrathecally to have good post-operative analgesia.

**Keywords:** Nalbuphine; Modified bromage scale; Sub-arachnoid block; hyperbaric bupivacaine

## Introduction

Analgesia during post operative period is of main demand these days. A pain free and stress free postoperative definitely helps in early mobilization and recovery. Intrathecal administration of opioids in conjunction with local anaesthetics improves the quality of intraoperative analgesia and provides superior quality and duration of analgesia post-operatively [1,2].

Nalbuphine is an opioid, which is structurally related to oxymorphone, highly lipid soluble with an agonist activity at kappa and an antagonist activity at  $\mu$  opioid receptor [3].

When nalbuphine is added as an adjuvant to intrathecal bupivacaine, it has potential to provide good intraoperative and post operative analgesia with decreased incidence of  $\mu$  receptor

side effects like respiratory depression [4]. The side effects of nalbuphine are like dizziness, bradycardia, nausea, vomiting, pruritis, urinary retention and sedation. Nalbuphine has short duration of action due to its lipid solubility and rapid clearance when compared to morphine [5].

Here we compared the effect of nalbuphine addition to hyperbaric bupivacaine intrathecally with hyperbaric bupivacaine alone for duration, quality of post operative analgesia and any side effects.

## Aims and Objectives

To compare the

- Onset of sensory and motor blockade.

- b. Duration of sensory and motor blockade.
- c. 2 segment regression.
- d. Duration of post operative analgesia achieved
- e. To study any side-effects with addition of nalbuphine.
- f. Haemodynamic parameters.

### Materials and Methods

This double blind prospective randomized study was done from may 2016 to august 2016, on patients who were admitted at Adichunchanagiri institute of medical sciences, posted for lower limb surgery under sub arachnoid block.

The study was undertaken after obtaining ethical committee clearance as well as informed consent from all patients. 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.

Study consists of 60 patients of both genders belonging to ASA I and II aged between 18-65 years, who were undergoing lower limb surgeries under sub arachnoid block. Patients were randomly allocated into 2 groups of 30 patients each, group N and group B by computerized randomization method. Group N received 3ml of 0.5% Bupivacaine(15mg)+1mg of Nalbuphine, group B received 3ml of 0.5% of Bupivacaine (15 mg)+0.1ml of normal saline for spinal anaesthesia. Pre anaesthetic check up was done and patients were kept nil per oral for about 6-8 hours. Patient was pre medicated with Tb- Alprazolam 0.5mg and Tb-rantidine 150 mg night before surgery.

### Inclusion criteria

- a. American Society of Anaesthesiologists (ASA) I and II patients.
- b. Age group of 18-65 years.
- c. Patient with written valid consent.
- d. Patient undergoing elective lower limb surgery.

### Exclusion criteria

- a. Infection at the site.
- b. Bleeding disorder.
- c. Allergic reaction to any anaesthetic drug.
- d. Patients on tranquilizers, hypnotics, sedatives and other psychotropic drugs.

Patient was shifted to OT, intra operatively an IV line was secured with 18 G iv cannula, standard monitors(NIBP, SpO<sub>2</sub>, ECG) connected and vitals recorded, patients were preloaded

with 10ml/kg ringer lactate solution. Sub arachnoid block was given under strict aseptic precautions in sitting position preferably in L3-L4 interspinous space with 25G quinkies spinal needle. The study medication was prepared by the person who was not involved in the study to ensure blinding of anaesthetist. Respective agents were injected according to the group, intra operatively haemodynamic parameters and the following parameters were noted and used for comparison between the groups.

### Time of spinal anaesthesia (drug administration time)

- a. Time of onset and complete sensory and motor block
- b. 2 segment regression of the block.
- c. Duration of sensory block (sensory level was assessed by pin prick method)
- d. Duration of post-operative analgesia(effective analgesia-time of onset of sensory block to the first request of analgesia by using VAS score).
- e. Duration of motor block (which was assessed by modified bromage scale)

### Modified bromage scale

0-no motor block with full flexion of knees and feet

1-just able to flex knees, full flexion of feet

2- unable to flex knees, but some flexion of feet possible.

3-unable to move legs/feet

Post operatively pain, sensory level, motor level was 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). Here 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>3, rescue analgesia given with injdiclofenac sodium.

Side effects like (pruritis, urinary retention, respiratory depression, post operative nausea and vomiting etc) were recorded for 24 hours.

### Statistical analysis

Data analysis was done with the help of computer using SPSS statistical package- Version 17. Using this software, measures of central tendency, measures of dispersion, 't' value, chi square and 'p' values was calculated. 't' test was used to test the significance of difference between quantitative variables and Yate's and Fisher's chi square tests for qualitative variables. A 'p' value less than 0.05 will denote significant relationship. Demographic characteristics of cases studied, outcome variables and the significance of the relationship between the outcomes variables of the two groups was analyzed using the above tests.

**Results**

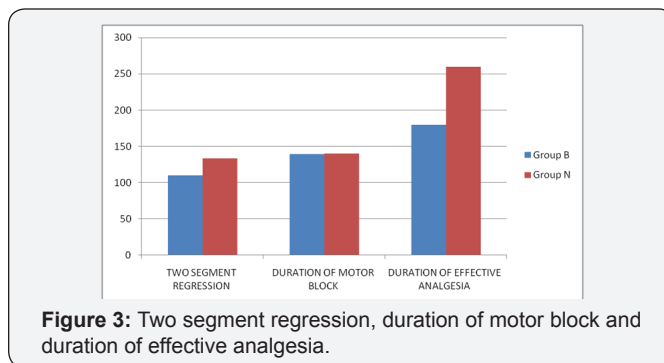
Both groups were compared on various variables like age, weight, sex ratio and duration of surgery. There was no significant difference found in various haemodynamic vital parameters intra operatively between the two groups (Table 1,2) (Figure 1-3).

**Table 1:** Demographic Data and Duration of Surgery.

Variable	Group B	Group N	
Age(yrs)	40.8±11.2	41.2±11.0	P=0.8891(NS)
Weight(kg)	65.2±5.41	63.0±10.38	P=0.3075(NS)
Sex(M:F)	15:11	14:12	P=0.7377(NS)
Duration of surgery(minutes)	119.3±17.14	121.4±25.16	P=0.7069(NS)

**Table 2:** Sensory and motor block compared between two groups.

	Group B	Group N	P Value
Onset of Sensory(minutes)	1.74±0.24	1.69±0.20	P=0.3843(NS)
Onset of Motor(minutes)	6.0±0.59	5.8±0.64	P=0.2133(NS)
Two Segment Regression	110.2±6.80	133.5±5.83	P<0.0001(S)
Duration of Motor Block	139.1±5.86	140.7±6.01	P=0.3008(NS)
Duration of Effective Analgesia	180±5.85	260±5.64	P<0.0001(S)



**Figure 3:** Two segment regression, duration of motor block and duration of effective analgesia.

**Summary of Results**

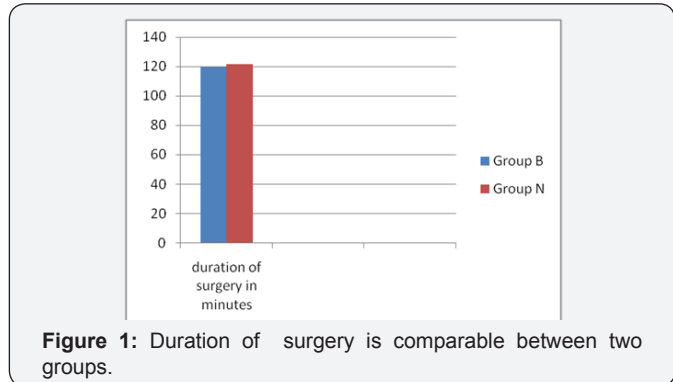
The mean time of onset of sensory blockade and motor blockade between the two groups is comparable with p value of (0.3843) and (p=0.2133) which is not statistically significant. Two segment regression of sensory blockade is significantly prolonged by addition of intrathecalnalbuphine as seen in group N. The duration of analgesia is significantly prolonged with addition of nalbuphine compared with bupivacaine alone.

**Discussion**

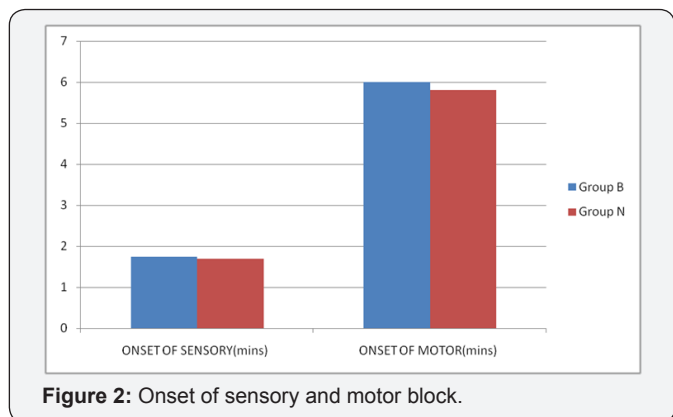
Subarachnoid block is the first choice for lower abdominal and lower extremity surgeries. Sub arachnoid block with bupivacaine alone has short period of post operative analgesia. Many adjuvants like fentanyl,morphine,clonidine has been used to prolong post operative analgesia. Spinal opioids can provide profound post operative analgesia with fewer central and systemic adverse effects than with opioids administered systematically [6]. Most commonly used opioids are usually  $\mu$  agonist drugs, which has excellent analgesic effect with various  $\mu$  related side effects. Eventually it was found that significant analgesia can be obtained by action on kappa binding sites also by bypassing  $\mu$  related side effects [7,8]. As there was less studies on opioids like Nalbuphine as an adjuvant in spinal anaesthesia. We have conducted this study.

Nalbuphine hydrochloride is a kappa agonist/partial  $\mu$  antagonist analgesic [8,9]. Whennalbuphine binds to  $\mu$  receptor,it serves only to competitively displace other  $\mu$  agonists from the receptor without itself displacing any agonist activity similar to those of nalaxone. It binds to kappa receptor; it has agonist effect, so nalbuphine has mixed agonist-antagonistic effect. These affects inhibit release of neurotransmitter that mediates pain such as substance p and in addition to this it also inhibits post synaptic interneuron and outer neuron of spinothalamic tract which transports nociceptive information.

Local anesthetic bupivacaine acts mainly by blockade of voltage gated sodium channels in the axonal membranes, and also by further effect on presynaptic inhibition of calcium channels [10]. A combination of these affects may explain the observed synergism between bupivacaine and nalbuphine in our study.



**Figure 1:** Duration of surgery is comparable between two groups.



**Figure 2:** Onset of sensory and motor block.

The principle finding of this study is that addition of 1mg of intrathecal nalbuphine to spinal anaesthesia in patients undergoing lower limb surgery with hyperbaric 0.5% bupivacaine intensifies the sensory blockade and increases the duration of sensory blockade without  $\mu$  related side effects. Two segment regression, time of sensory blockade and duration of analgesia were maximally prolonged with nalbuphine 1mg with minimum effects over haemodynamic and respiratory parameters [11].

Previous studies have demonstrated that visceral analgesia is mediated by both  $\mu$  and kappa receptors and that intrathecal nalbuphine suppresses response to visceral pain [12]. In our study 2 segment regression of sensory block was prolonged with addition of nalbuphine to bupivacaine which correlated with that of tiwari et al who also found that with addition of 0.8mg of nalbuphine to 0.5% bupivacaine for subarachnoid block provides excellent analgesia with longer duration of action compared with 1.6 and 2.4mg of nalbuphine [13].

Large number of animal studies has been undertaken to prove that intrathecal nalbuphine was not neurotoxic. Rawal et al showed in sheep model using histopathological methods that, intrathecal nalbuphine even at large doses 15-24mg were not associated with histopathological changes of the spinal cord [9].

From our study we can also conclude that use of nalbuphine in dosage of 1mg along with bupivacaine 0.5% H<sub>2</sub>O does not cause any gross haemodynamic disturbances. Similar findings are seen in study conducted by culebras et al, tiwari et al [13], mortafa et al [14].

In our study none of the patients had respiratory depression since nalbuphine is  $\mu$  antagonist, respiratory depression is predominantly  $\mu$  mediated. Respiratory depression effect is expected to be attenuated by nalbuphine, so nalbuphine exhibits ceiling effect for respiratory depression [RR < 30cpm, spo<sub>2</sub> > 90%] this is proved in studies done by romagnoli and keats [15].

Our study also concludes that addition of nalbuphine had significantly longer duration of first request of analgesia, compared to patients who received bupivacaine alone and it also prolongs duration of analgesia which correlates to result of studies done by lin [16] found that intrathecal nalbuphine at dosage of 0.8-1.6mg improved quality of intraoperative analgesia during cesarean section with good visceral analgesia, our study showed excellent analgesia at dosage of 1mg as an adjuvant to intrathecal bupivacaine [5]. Adverse effects like nausea, vomiting, urinary retention and shivering were statistically insignificant.

## Conclusion

On the basis of this study, in conclusion, addition of nalbuphine hydrochloride in dosage of 1mg to intrathecal bupivacaine 0.5% H<sub>2</sub>O prolongs the duration of sensory block provides excellent and longer duration of post operative analgesia, prolongs the 2 segment regression with maintaining stable haemodynamics

without any significant side effects in patients undergoing lower limb orthopaedic surgeries.

Thus we conclude that intrathecal nalbuphine at dosage of 1mg can be used as an effective adjuvant along with intrathecal hyperbaric bupivacaine 0.5% to have a good post operative analgesia.

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DOI: [10.19080/JAICM.2017.02.555581](https://doi.org/10.19080/JAICM.2017.02.555581)

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