*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*
*e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 8 Ver. VIII (Aug. 2015), PP 122-127*
*www.iosrjournals.org*

# A Comparative Study of Intra Muscular Nalbuphine with Intra Muscular Butorphanol for the Relief of Postoperative Pain

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***Abstract:***
***Aims And Objectives:*** *This study compared the analgesic efficacy of intramuscularly administered Nalbuphine with respect to onset, quality and duration of pain relief and side effect profile with to those of Butorphanol IM in the immediate postoperative period.*
***Materials And Methods:*** *60 adult patients of ASA Class 1 and 2 of either sex, belonging to age 21-60 years, posted for lower abdominal and lower limb surgeries done under spinal anaesthesia were randomly divided into 2 groups-Group A-Nalbuphine group and Group B-Butorphanol group. In the postoperative period patients were asked to express the intensity of pain on the VAS scale. When it reached >5 mark on the scale, patients in Group A received Nalbuphine 10mg and patients in Group B received Butorphanol 2mg intramuscularly. Thereafter, onsets, duration, quality of analgesia were recorded at regular intervals for 24hours postoperatively.*
***Results:*** *The mean time of onset of analgesia in Group A was 14.66±4.34 minutes and in Group B was 34.76±5.73. Duration of analgesia in Group A ranged from 4-12 hours with a mean 6.05 ± 3.14 hours. In Group B, it ranged from 4-8 hours with a mean 5.20 ± 0.71 hours. Regarding quality of analgesia, in Group A, 43.3% of patients had pain score of 3 with 36.7% of patients had pain score of 3 in Group B.*
***Conclusion:*** *Intra muscular Nalbuphine, when compared to Butorphanol, provides an effective analgesia with rapid onset, prolonged duration and stable hemodynamic parameters for postoperative pain relief. This drug is suitable for providing postoperative analgesia following moderate duration of surgical procedures.*
***Keywords:*** *Postoperative pain relief, intramuscular, Nalbuphine, Butorphanol.*

## I. Introduction

Perception of pain is a major concern for most of the surgical patients. Postoperative pain[1] is an acute pain which initiate a systemic stress response[2] that encompasses a wide range of neuroendocrine, immunological, and haematological responses. The overall metabolic effect is one of catabolism of stored body fuels .

Despite the efforts and innovations in pain management, many patients continue to experience intense pain after surgery[3]. Modern day anaesthesia is not just concerned with relieving pain but also to improve quality of life of the patient and fast recovery and thus to reduce medical cost.

Opioids have long been the mainstay of therapy for the treatment of acute postoperative pain, especially for moderate to severe pain. However, the use of mu agonists like morphine may result in serious side effects e.g. pruritus, urinary retention, nausea and vomiting and delayed respiratory depression. These side effects may lead to patient discomfort and prolonged hospital stay thus limiting their usefulness for postoperative pain.

Nalbuphine and Butorphanol are partial agonist–antagonists, having agonist action on kappa receptor and antagonistic or partial agonist property at mu receptor. Benefits of a partial agonist include analgesia with a decrease in unwanted side effects, such as respiratory depression. They can be given through intramuscular, intravenous, epidural, and transnasal routes. They are widely available without restriction as compared to some of the potent opioids like morphine or fentanyl. Various modalities have been tried for the management of postoperative pain out of which intramuscularly injectable opioids is an established and accepted technique.

**Aims and Objectives**: To compare the analgesic efficacy and other effects of Nalbuphine and Butorphanol, administered intramuscularly, in postoperative patients who have undergone lower abdominal and lower limb surgeries under spinal anaethesia.

## II. Material And Methods

After obtaining institutional ethical committee approval and written informed consent, sixty adult patients of ASA class 1 and 2, weighing 45 to 60 kgs of either sex, belonging to 21-60 years of age, posted for elective lower abdominal and lower limb surgeries in orthopaedics, gynaecological, urological and plastic surgeries were selected for the study. Patients with ventricular dysfunction, coronary insufficiency, valvular heart diseases, hypertension, physical dependency on opioids, and history of drug allergy, bronchial asthma, COPD, renal and hepatic diseases were excluded from study.

Patients were premedicated with 0.25 mg of oral alprazolam given on the night before and on the morning of surgery. Patients, after being shifted to the operation theatre, were subjected to monitoring of ECG, pulse oximetry, and noninvasive blood pressure and continued into postoperative period. All patients were operated under spinal blockade using 0.5% bupivacaine heavy.

Visual Analogue Scale (VAS) was used to assess the intensity of pain and pain relief. Before the surgery patients were shown a VAS scale consisting of a 10cms`line with 0 being no pain and 10 being worst pain ever felt and they were asked to express the intensity of pain on the scale.

The patients, when they first complained of pain, were asked to express the intensity on the pain scale. When it reached 5 mark on the scale, patients in Group A received IM Nalbuphine 10mg and patients in Group B received IM Butorphanol 2mg. Intensity of pain was assessed at every 5 minutes for the first hour and thereafter at 1 hour interval for 8 hours and then at 4 hours interval for 24 hours post operative period.

Onset of analgesia is time interval from drug administration till VAS score came down to 5. Readings of >5 was considered as unsatisfactory analgesia and rescue analgesia was given. Duration of analgesia is time interval between the start of analgesia (i.e when the VAS score is at 5), till the patient complaints of pain (i.e when VAS score is >5) when rescue analgesia was given.

The following parameters were recorded
1. Onset of analgesia
2. Duration of analgesia
3. Quality of analgesia: assessed by pain score
4. Cardiorespiratory effects: pulse rate, blood pressure, and respiratory rate
5. Side effects: drowsiness pruritis, nausea, vomiting, urinary retention, respiratory depression and hypotension.

**Statistical analysis**

Continuous data was analysed by student t-test and categorical data by Chi-square test. Any possible significance has been determined considering it statistically significant if the p<5% level of significance**.**

**Observations and Results**

Demographic data: minimum age of the patients in this study was 21 and maximum being 60 years. The mean age of the patients in group A was 40.66± 8.90 and in Group B was 40.70 ±10.69. In both groups both male and female patients were equally distributed. Both groups were comparable with regard to age, sex, weight and height distribution.

**Table 1: Demographic Data**

| Parameter | Group A (n=30) | Group B (n=30) |
|---|---|---|
| Age(Mean± SD) | 40.66± 8.90 | 40.70 ±10.69 |
| Sex(M/F) | 15/15 | 17/13 |
| Weight(Mean± SD) | 63.8 ±8.2 | 65.3 ±7.6 |
| Height(m)(Mean±SD | 1.56± 0.07 | 1.57± 0.57 |

**Onset of Analgesia**

The mean time of onset of analgesia in group A was 14.66±4.34 (SD) minutes and in group B was 34.76±5.73 (SD) minutes. In group A, 43.3% of patients had onset of analgesia between 11-15 minutes and about 40% of patients in group B had onset of analgesia between 36-40 minutes. The statistical analysis by Student's unpaired t-test showed that time of onset of analgesia in group A was significantly less when compared to group B (t-15.29 with df-54. p<0.0001.

**Table 2: Onset Of Analgesia**

| Onset of analgesia(min) | Group a Nalbuphine No.of cases (%) | Group b Butorphanol No of cases (%) |
|---|---|---|
| 6-10 | 0 | 0 |
| 11-15 | 5(16.7%) | 0 |
| 16-20 | 13(43.3%) | 0 |
| 21-25 | 10(33.3%) | 0 |
| 26-30 | 2(6.7%) | 2(6.6%) |
| 31-35 | 0 | 3(9.9%) |
| 36-40 | 0 | 11(36.7%) |
| 41-45 | 0 | 12(40%) |
| 46-50 | 0 | 2(6.7%) |

**Duration of analgesia**

Duration of analgesia was observed in both groups for a period of twenty four hours at regular intervals during postoperative period. In group A, 53% of patients had duration of analgesia ranging 4-12hours, mean duration of analgesia being 6.05± 3.14hours with minimum of 4 hours duration was observed in 9.9% patients and a maximum duration of 12 hours was observed in 3.3% patients.

In group B, 50% of patients had duration of analgesia ranging from 4-8 hours with mean duration being 5.20± 0.71 hours with minimum duration of 4 hours was observed in 50% cases and a maximum of 8hours was observed in 2% patients.Statistical analysis by student unpaired t-test showed that increase in duration of analgesia in group A was statistically significant when compared to group B ($t=18.41$ with df-31, $p<0.0001$).

**Table 3: Duration Of Analgesia**

| Duration of Analgesia (Hours) | Group A No of cases (%) | Group B No of cases (%) |
|---|---|---|
| 4-5 | 3(9.9%) | 15(50%) |
| 5-6 | 8(26.7%) | 13(43.3%) |
| 6-8 | 8(26.7%) | 2(6.7%) |
| 8-10 | 2(6.7%) | 0 |
| 10-12 | 2(6.7%) | 0 |
| 12-14 | 1(3.3%) | 0 |
| 14-24 | 0 | 0 |

**Quality of analgesia**

Quality of analgesia was assessed at the time at which rescue analgesia was given to the patient. This was assessed by pain score system. Patient was asked to give a global assessment of the overall effectiveness of the analgesic treatment.

**Table 4: Quality of analgesia**

| Pain score | Quality of analgesia | Group A (Nalbuphine) No of cases (%) | Group B (Butorphanol) No of cases (%) |
|---|---|---|---|
| 0 | No pain relief | 0 | 0 |
| 1 | Poor pain relief | 0 | 0 |
| 2 | Fair pain relief | 1(3.3%) | 2(3.7%) |
| 3 | Good pain relief | 11(36.7%) | 13(43.3%) |
| 4 | Excellent pain relief | 18(60%) | 15(50%) |

A pain score of 3(good pain relief) was observed in 36.7% of group A patients compared to 43.3% of patients in group B. A pain score of 4(excellent pain relief) was observed in 60% of group A patients compared to 50% in group B patients. This difference was statistically insignificant by chi-square test($X^2=0.60$, $p>0.05$).

**Cardiovascular and respiratory effects**

**Table 5: Changes In Cardiorespiratory Parameters**

| VITALS | GROUP A | | | | GROUP B | | | |
|---|---|---|---|---|---|---|---|---|
| | BEFORE | | AFTER | | BEFORE | | AFTER | |
| | Range | Mean±S.D | Range | Mean±S.D | Range | Mean±S.D | Range | Mean±S.D |
| Pulse rate(bpm) | 64-90 | 75.70± 7.83 | 65-88 | 74.20 ±6.61 | 64-94 | 78.30 ±8.58 | 60-90 | 74.20± 8.05 |
| Systolic blood pressure (mmHg) | 110-130 | 121.33±5.99 | 100-130 | 118.40 ±6.50 | 110-130 | 121.20 ±6.33 | 86-128 | 115.00 ±9.60 |
| Diastolic blood pressure (mmHg) | 70-90 | 79.86 ±5.91 | 66-88 | 76.80 ±5.90 | 68-90 | 81.00 ±6.78 | 54-88 | 76.60± 8.77 |
| Respiratory rate(cpm) | 12-18 | 14.63 ±2.07 | 12-17 | 13.53 ±1.56 | 12-18 | 14.56± 2.22 | 11-17 | 13.10± 1.64 |

In group A, before giving Nalbuphine, pulse rate ranged between 64-90(75.70±7.83) bpm, systolic blood pressure between 110-130(121.33±5.99)mmHg, diastolic blood pressure 70-90(79.86 ±5.91)mmHg and respiratory rate ranged between 12-18(14.63 ±2.07)breaths/min. But after giving Nalbuphine (which marks onset of analgesia) pulse rate ranged between 65-88(74.20 ±6.61) bpm, systolic blood pressure between 100-130 (118.40 ±6.50) mmHg, diastolic blood pressure ranged 66-88(76.80 ±5.90) mmHg and respiratory rate ranged between12-17(13.53 ±1.56) breaths/min.

In group B before giving Butorphanol, pulse rate ranged between 64-99(78.30 ±8.58)bpm, systolic blood pressure between 110-130(121.20±6.33)mmHg, diastolic blood pressure 68-90(81.00 ±6.78)mmHg and respiratory rate ranged between 12-18(14.56 ±2.22)breaths/min But after giving Butorphanol (which marks onset of analgesia) pulse rate ranged between 60-90(74.20 ±8.015)bpm, systolic blood pressure between 86-128(115.0 ±9.60)mmHg, diastolic blood pressure ranged 54-88(76.60 ±8.77)mmHg and respiratory rate ranged between 11-17(13.10 ±1.64) breaths/min. We did not observe respiratory depression (defined as respiratory rate less than 10 breaths/min or SpO2<90%) in any of the patients in both groups in postoperative period.

**Side Effects**

In group A side effects like nausea(9.9%), vomiting(6.7%) and pruritis(0%) were less when compared to group B nausea(33.3%), vomiting(33,3%), vomiting(26.7%), pruritis(0%). These differences were statistically significant by chi-square test ($p<0.05$).none of our patients reported pruritis during study duration. Pruritis is a common side effect of use of opioids and occurs via agonism at mu receptors. Nalbuphine, on the other hand, is an antagonist at mu receptors and thus does not cause any pruritis. Absence of pruritus with Nalbuphine has also been reported by other authors.[3,7]

Incidence of sedation was less in group A (26.7%) when compared to group B (66.7%) which is statistically significant by chi-square test ($p<0.05$). Incidence of hypotension was more in group B (6.7%) when compared to group A (0%). This difference was statistically significant by chi-square test ($p>0.05$). Urinary retention could not be assessed because indwelling urinary catheter was left in place for 24 hours in most of the patients. Overall frequency of side effects were more in group B when compared to group A.

**Table 6: Incidence of side effects**

| SIDE EFFECTS | GROUP A | GROUP B | $X^2$ VALUE | P VALUE |
|---|---|---|---|---|
| Nausea | 3(9.9%) | 10(33.3%) | 4.31 | p<0.05 |
| Vomiting | 2(6.7%) | 8(26.7%) | 4.32 | p<0.05 |
| Pruritis | 0 | O | 0 | 0 |
| Sedation | 8(26.7%) | 20(66.7%) | 9.64 | p<0.05 |
| Hypotension | 0 | 2(6.7%) | 2.06 | p>0.05 |
| Respiratoty depression | 0 | 0 | 0 | 0 |

## III. Discussion

Management of postoperative pain still remains an enigma.Uncontrolled pain in the post operative period has detrimental effects. In recent times, the role of intramuscularly injectable opioids for the relief of postoperative pain promises a good platform in this field.

In an attempt to find out a good analgesic to alleviate postoperative pain, this clinical study was conducted to assess the efficacy and safety of equianalgesic doses of IM Nalbuphine (10mg) and compared with IM Butorphanol(2mg) in the management of postoperative field. There was no significant difference in the demographic profile of the patients in the study.

**Onset of analgesia**: in our study the mean time of onset of analgesia in group A (Nalbuphine) and group B(Butorphanol) was 14.66±4.34 min and 34.76±5.73 min respectively. Time of onset of analgesia in group A was statistically significantly less when compared to group B ($t=15.29$ with df-54,$p<0.0001$). Onset of pain relief with intramuscular Nalbuphine appeared at 15min, peaked at 30min where as for Butorphanol onset of analgesia appeared at 25 min with peak action at 1hour.

**Duration of analgesia**: in our study the duration of analgesia in group A Nalbuphine ranged between 4-12h with mean of 6.05±3.14 hours and in group B Butorphanol it ranged between 4-8h with mean of 5.20±0.71 hours which was statistically significantly more in group A when compared to group B ($t-18.41$ with df-31, $p<0.0001$). a study, in patients undergoing craniotomy, reported duration of analgesia in Butorphanol Group and Nalbuphine Group was 253.33±34.97 and 327.33±42.99 min. respectively which is statistically significant ($p<0.05$)[4.] Del Pizzo found the duration of analgesia provided by intravenous Butorphanol to be about 2 hour (0.5 mg dose) or 2-4 hours (1-2 mg dose)[5]. Our results are comparable to those of above studies.

**Quality of analgesia** : Quality of analgesia was assessed at the time at which rescue analgesia(diclofenac sodium) was given to the patient. In Nalbuphine group, 60% of patients graded their pain relief as excellent, but in Butorphanol group 50% patients graded as excellent. This difference was statistically insignificant by chi-square test.($X^2$=0.6,df-1,p>0.05). However in both groups majority of patients expressed their analgesia as good to excellent.

In a comparative study by Hanumantharao et al, fentanyl group required rescue analgesia in 30 min in comparison to Butorphanol group who reported pain after 3 hours of post-operative period (P<0.001)[6]. F. N. Minai and F. A. Khan, comparing with morphine, concluded that Nalbuphine in a dose of 0.2 mg/kg provided better quality of analgesia with greater hemodynamic stability, significantly longer duration of analgesia for about 5.8hr, reducing the need for supplements in the immediate postoperative period.[7]

Beaver,Feise, and Robbe concluded that intramuscular and oral Nalbuphine is more potent and well tolerated analgesic than Butorphanol for moderate to severe postoperative pain.[8] Intramuscular Nalbuphine found it to be 0.7-0.8 times as potent as morphine for peak analgesia and 0.8-0.9 times as potent for total analgesia while possessing slightly greater duration of action than morphine.[9] Intramuscular Butorphanol to be 7 times more potent than morphine for postoperative analgesia.[10]

**Cardiorespiratory Effects**

The cardiovascular parameters monitored were heart rate, systolic blood pressure and diastolic blood pressure. Mean changes in these parameters showed no statistically significant changes in both groups. Nalbuphine reported to decrease in heart rate and myocardial contractility while maintaining aortic perfusion thereby maintaining balance between myocardial oxygen supply and demand[12]. Nalbuphine did not produce any significant changes in systemic, pulmonary arterial, and pulmonary capillary wedge pressure in patients experiencing myocardial infarction[11].

However, Butorphanol causes significant increases in cardiac index, left ventricular end-diastolic pressure, and pulmonary artery pressure[13]. Therefore use of Butorphanol should be restricted in patients with acute myocardial infarction, coronary insufficiency and ventricular dysfunction.

It is fortuitous that we did not encounter any serious or clinically significant fluctuations in haemodynamic parameters within each group nor did we observe a difference in values between the two groups.

In this study the respiratory parameters monitored were respiratory rate and Spo2. Mean changes in these parameters showed no significant changes in both groups. All patients received supplemental oxygen by face mask for first four hours postoperatively. Comparing morphine, Nalbuphine, being mu antagonist and kappa agonist, has a ceiling effect in its respiratory depression hence it is considered to be safer than morphine[14,15]. This is a significant advantage in recovery room areas.

**Side effects:** In our study group A(Nalbuphine) patients had less incidence of side effects like nausea(9.9%) and vomiting(6.7%) when compared to group B(Butorphanol), nausea(33.3%),vomiting(26.7%) and this was statistically significant(p<0.05). We consider this lower incidence of nausea and vomiting in the Nalbuphine group, which is consistent with lesser inhibition of gastrointestinal motility by partial agonists[16].

Nalbuphine, an antagonist at mu receptors, unlike pure mu receptor agonists does not cause any pruritis. Absence of pruritus with Nalbuphine has also been reported by other authors[17]. None of our patients reported pruritis in this study.

In our study sedation was more in Butorphanol group (66.7%) when compared to Nalbuphine group (26.7%) and this was statistically significant. At no occasion did the severity of sedation evoke concern on the possibility of the patient going into respiratory depression. Sedation is unavoidable side effect of both Butorphanol and Nalbuphine when given in adequate doses with possible peak plasma concentrations of the drug at 60 to 180 minutes. Such sedation relieves surgery related anxiety, provides the much needed comfort for a post-operative patient and should therefore be considered a beneficial effect of the study drug.

Safety of Nalbuphine was been widely accecpted in many studies, producing beneficial sedation which was maximum at 60 min after injection. Increasing the dose of Nalbuphine from 10 mg to 20 mg produced no significant additional sedation or intraoperative benefit.[18,19]

## IV. Conclusion

It was concluded that Nalbuphine provides a rapid, excellent but with equal and slightly longer duration of analgesia and minimal side effects when compared to Butorphanol.Nalbuphine is also superior to Butorphanol as it does not increase cardiac oxygen requirements and cardiac work in compromised patients nor does it prolong the duration of respiratory depression with higher doses.

In view of safety and superiority of Nalbuphine when compared to Butorphanol, Nalbuphine can be routinely employed in the treatment of postoperative pain with a continuous vigilant monitoring for complications of injectible opoids.

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