Intrathecal Nalbuphine an Effective Adjuvant for Post Operative Analgesia (A Comparitive Study with Fentanil)

Jaideep Singh[1], Aditya Agarwal[2], Ajay Vatal[3]

ABSTRACT

Introduction: Various adjuvants have been used along with local anaesthetics for prolongation of analgesia post operatively in neuraxial blockade. The frequently used adjuvants are opioids, midazolam, neostigmine, ketamine etc. Neuraxial opioids bind to intrathecal opioid receptors and produce effective pain relief post operatively with minimal untoward effects. Nalbuphine is an opioid drug with mixed μ antagonist and κ agonist properties. Thus we conducted a prospective, randomized, comparative study to observe the effect of 0.5% hyperbaric Bupivacaine 3 ml on pain relief after lower limb and lower abdominal surgeries and compare it with effect of intrathecal Nalbuphine + 0.5% hyperbaric Bupivacaine 3 ml.

Material and methods: 60 patients of ASA grades I and II of either sex in the age group of 20-60 years will be randomly allocated to one of the two groups. Group B (n = 30) received 3 ml of 0.5% hyperbaric bupivacaine intrathecally; group N (n = 30) received 3 ml of 0.5% hyperbaric bupivacaine + 1 mg nalbuphine intrathecally. The onset of sensory and motor blockade, duration of motor blockade and analgesia, VAS score, haemodynamic and side effects will be recorded, tabulated, and analysed.

Result: The onset of complete motor block was more rapid with fentanyl than nalbuphine and this was statistically significant ($p<0.05$). The duration of post-operative analgesia and the effective analgesic time were more prolonged in nalbuphine group than in fentanyl group with no statistically significant difference. As regards the side effects, they were less in nalbuphine group than the fentanyl group

Conclusion: In our study we conclude that both Nalbuphine or Fentanyl in combination with low dose hyperbaric bupivacaine (15mg) are equally efficacious and haemodynamically stable in patients undergoing lower limb surgeries. However, Nalbuphine with comparatively prolonged post operative analgesia and effective analgesia time and lesser side effects is a better adjuvant than Fentanyl for intrathecal injections of Bupivacaine 0.5%(H) in surgeries undergoing spinal anaesthesia. with no statistically significant difference.

Keywords: Intrathecal Nalbuphine, Adjuvant, Analgesia

INTRODUCTION

Various adjuvants have been used along with local anaesthetics for prolongation of postoperative analgesia in neuraxial blockade. The frequently used adjuvants are opioids,midazolam,ketamine,neostigmine etc. Neuraxial opioids bind to intrathecal opioid receptors and produce effective pain relief postoperatively with minimal side effects.

Analgesia is one of the main demands of all patients postoperatively. There has been a radical improvement in the quality of pain relief ever since W.T.G. Morton demonstrated anaesthesia. There is still scope to make analgesia not only more effective but also less hazardous.

Various types of medications can be used to overcome pain but opioids provide the most effective pain relief and are a standard of care. 1 The major problems encountered with opioids are their side effects which includes pruritus, nausea, constipation, respiratory depression, undesirable sedation and urinary retention. In this scenario, the use of Nalbuphine, a mixed opioid kappa agonist –mu antagonist can prove to be a boon because when used singly or in combination with other agents it has the potential to maintain or even enhance opioid based analgesia while simultaneously mitigating the common mu-opioid side effects. The binding of nalbuphine to mu receptors will only competitively displace other mu agonists without itself displaying any agonist properties. However, when it binds with Kappa receptors it displays agonist properties. Kappa opioid receptors are distributed throughout brain and spinal cord involved in nociception. Nalbuphine avidly binds to Kappa opioid receptors in these areas to produce analgesia. This pattern of binding and effects defines Nalbuphine as a mixed agonist-antagonist.1

There are a very few studies of Intrathecal Nalbuphine for postoperative analgesia. Hence we have tried to study and compare the intra-operative and postoperative analgesic effect of more commonly used intrathecal Fentanyl and intrathecal nalbuphine as an adjuvant to Bupivacaine.In this study we also assess and compare the haemodynamic conditions and side effects between Intrathecal Fentanyl and Intrathecal Nalbuphine as an adjuvant to Bupivacaine.

MATERIAL AND METHODS

After approval by institutional ethical committee, a bilingual written informed consent was obtained from all patients. It was a Randomised, prospective, comparative and double blinded study. Sixty patients, ASA physical status i and ii, aged 18-60 years scheduled for elective lowerlimb surgeries of duration less than 3 hours were selected. 30 patients each were randomly divided into two groups using sequentially numbered, sealed opaque envelope technique:

Group A- Received 25 mcg of Fentanyl as an adjuvant with Bupivacaine 0.5% (H) 3ml intrathecally

Group B- Received 0.8 mg of Nalbuphine as an adjuvant with Bupivacaine 0.5% (H) 3ml intrathecally.

Patients with history of hypersensitivity to any of the drugs, on long term analgesic therapy, those having peripheral neuropathy,

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local skin infections and spinal deformities or coagulation abnormalities were excluded from the study.

All patients underwent thorough pre anesthetic checkup and were explained about the linear visual analogue scale scoring system for pain. The multichannel monitor were applied to the patient on arrival to the operating room. A suitable peripheral vein was cannulated and I.V. Ringer solution 10 ml/kg/15 min (preload) was given to all patients before the procedure. Baseline Blood pressure, pulse rate, oxygen saturation, ECG and Respiratory rate was recorded.

Subarachnoid Block was performed under strict aseptic conditions in the sitting position at the level of L 3- L4 Intervertebral space using 23G Quincke spinal needle. Patients were placed in the supine position with 10-20 degree tilt.

Observations were made for time of drug administration, time of onset and complete sensory and motor block and recovery from the block, intraoperative sedation, time of occurrence of pain (VAS >4) and any adverse effects. The highest level of sensory block was determined in the midclavicular line bilaterally, by pinprick test using a 20-G hypodermic needle every 2minutes till the level was stabilized for four consecutive tests. Further sensory testing was performed at 20min intervals till 2 segment regression. Motor block was assessed using the modified Bromage scale, till the achievement of the highest motor level.

Intraoperatively, vitals were recorded at 5 minutes intervals for the first 20 minutes from the time of injection of spinal solution and thereafter every 20 minutes for the complete period of surgery. Side effects such as hypotension, bradycardia, nausea and vomiting, pruritus, sedation and respiratory depression were recorded and observed.

The quality of postoperative analgesia was assessed using VAS at 15min, 30min and thereafter every 30 minutes, till 2 hours postoperatively; and then every hour, till 4 hours postoperative duration.

STATISTICAL ANALYSIS

All the data were tabulated and analysed statistically. Parametric values are expressed as Mean ± standard deviation. A p value < 0.05 was considered significant. Data were analysed using the Student's unpaired 't' test and Mann Whitney U test.

RESULTS

Both groups were comparable in various demographic data like age, weight and duration of surgery and there was no significant statistical difference.

As regards the onset of sensory block, there was no statistically significant difference between group A and group B. The onset of complete motor block was more rapid with fentanyl than nalbuphine and this was statistically significant ($p<0.05$) (figure-1).

No statistically significant difference was found between both groups as regards the duration of motor block and 2 segment regression time for sensory block (figure-2).

The duration of post-operative analgesia and the effective analgesic time were more prolonged in nalbuphine group than in fentanyl group but with no statistically significant difference (figure-3).

There was no significant difference found in various hemodynamic or vital parameters intra operatively between the

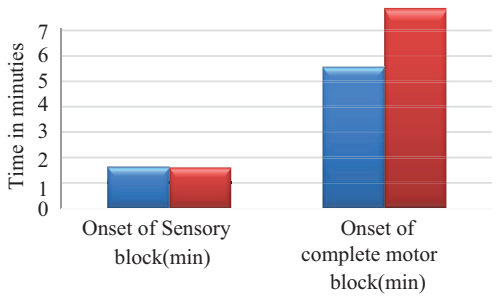

Figure-1: Compare onset of sensory and motor block

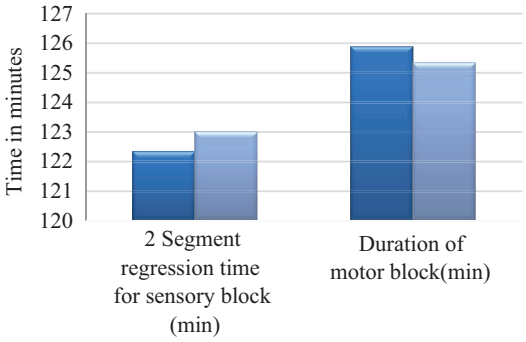

Figure-2: To compare the duration of sensory and motor block

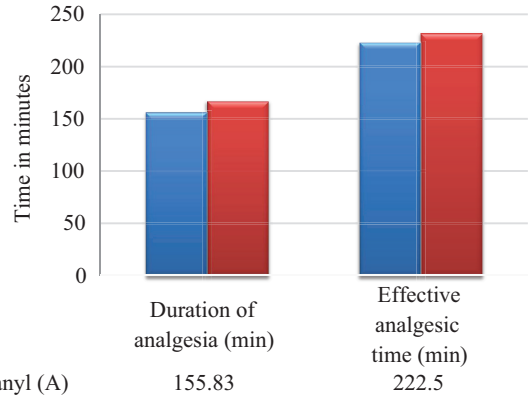

Figure-3: Duration of Analgesia (min)

Characteristics	Fentanyl n=30	Nalbuphine n=30	p value
Age (yrs)	26.33±6.08	26.97±5.40	0.671 (NS)
Weight (kg)	68.83±8.26	71.53±9.85	0.255 (NS)
Duration of surgery (min)	73.00±5.19	73.17±4.82	0.898 (NS)

Table-1: Comparition of demographic data and duration of surgery

Characteristics	Fentanyl n=30	Nalbu-phine n=30	p value
Hypotension	8 (26.7%)	6 (20%)	0.542 (NS)
Nausea and vomiting	3 (10%)	1 (3.3%)	0.301 (NS)
Pruritus	1 (3.3%)	0	0.313 (NS)
Shivering	1 (3.3%)	0	0.313 (NS)

Table-2: Adverse Effects

two groups.

As regards the onset and duration of sensory block, there was no statistically significant difference between group A and group B. The onset of complete motor block was more rapid with fentanyl than nalbuphine and this was statistically significant. This may be explained by the high lipid solubility and rapid tissue uptake of fentanyl more than nalbuphine (table-2).

Also in the present study, no statistically significant difference was found between both groups as regards the duration of motor block, hemodynamics and oxygen saturation. Neither bradycardia nor oxygen desaturation was recorded. The duration of post-operative analgesia and the effective analgesic time were more prolonged in nalbuphine group than in fentanyl group with no statistically significant difference. As regards the side effects, they were less in nalbuphine group than the fentanyl group with no statistically significant difference.

DISCUSSION

Intrathecal opioids have advantages like rapid onset of action, sympathetic and motor nerve sparing activities, technical ease of administration and simplicity of postoperative management. The major short comings of opioids are their side effects like respiratory depression and to overcome it, opioids with partial agonist-antagonist properties have been studied extensively.

Local anesthetics such as Bupivacaine act mainly by blockade of voltage gated Na+ channels in the axonal membrane and presynaptic inhibiton of calcium channels. Both Fentanyl and nalbuphine exert their action by opening K+ channels and reducing the Ca++ influx, resulting in inhibition of transmitter release. A combination of these effects may explain the observed synergism between bupivacaine and Fentanyl/nalbuphine. The synergism is characterized by enhanced somatic analgesia without an effect on the degree of level of local anesthetic induced sympathetic or motor blockade.

Fentanyl is a μ receptor agonist opioid, with a rapid onset following intrathecal injection. Nalbuphine is an opioid having agonist activity at kappa receptors and antagonistic activity at mu receptors. Nalbuphine given systemically has reduced incidence of respiratory depression and has been used to antagonize the side effects of spinal opiates.[2]

There have been a few studies of varying quality, that have supported the utility of neuraxially administered nalbuphine in managing postoperative pain. The general trend of these reports is that epidural or intrathecal delivery of nalbuphine produces a significant analgesia accompanied by minimal pruritus and respiratory depression.[3]

In our study we used 25 mcg of Fentanyl as an adjuvant with Bupivacaine 0.5% (H) 3ml intrathecally and compared its postoperative analgesic effect under spinal anaesthesia with 0.8 mg of Nalbuphine as an adjuvant with Bupivacaine 0.5% (H) 3ml intrathecally.

Xavier et al, in 2000, performed a comparative study to evaluate post operative analgesia and adverse effects after using three doses i.e. 0.2mg, 0.8mg, 1.6mg of intrathecal nalbuphine or morphine 0.2mg given for caesarean section along with bupivacaine. The longest durations of complete and effective analgesia among the nalbuphine-treated groups were provided by 0.8 mg added to bupivacaine. Neither pruritis nor PONV were observed with nalbuphine 0.2 and 0.8 mg. Intrathecal nalbuphine 0.8–1.6 mg improved the quality of intraoperative analgesia and provided a significantly faster onset of pain relief, compared with intrathecal morphine, probably because of its lipophilic properties. They concluded that 0.8mg of intrathecal nalbuphine improves intraoperative analgesia and prolongs early postoperative analgesia without increasing risk of side effects.[4]

In 2011, Mukherjee et al formulated a study to determine whether nalbuphine prolongs analgesia by comparing with control and to find out the optimum dose of intrathecal nalbuphine by comparing the 0.2, 0.4 and 0.8mg doses which prolonged post operative analgesia without increased side effects. It was observed that effective analgesia increased with increase in concentration and the ultimate observation of prolongation of analgesia was with 0.4mg of nalbuphine with 0.5% hyperbaric bupivacaine without any side effects.[5]

Mostafa et al, in 2011 compared the analgesic effects and duration of analgesia as well as the side effects of 50 mg tramadol or 2 mg nalbuphine administered via the IT route for postoperative pain relief after transurethral resection tumour of the bladder. They demonstrated that in both the groups there was similar motor block, nearly equal analgesia, delayed first analgesic request and less analgesic supplement over the first 24 hours after operation. No major postoperative complication like, itching, respiratory depression, neurological sequelae or complaints were observed among the two groups. The incidence of hemodynamic side effects like decreased blood pressure, bradycardia, respiratory depression and other side effects like somnolence and dryness of mouth were minimum and well tolerated by the patients studied. In conclusion, intrathecal administration of 50 mg tramadol and intrathecal 2 mg nalbuphine when used with 0.5% bupivacaine had a similar postoperative analgesia in the patients without producing significant related side effects like nausea, vomiting, pruritis and respiratory depression.[6]

Thus from our study it was observed that 0.8mg nalbuphine as an adjunct to spinal bupivacaine prolongs the postoperative analgesia with minimal side effects and with desirable sedation intraoperatively which helps in taking care of psychological impact of operation theatre environment.

CONCLUSION

In our study we conclude that both Nalbuphine or Fentanyl in combination with low dose hyperbaric bupivacaine (15mg) are equally efficacious and haemodynamically stable in patients undergoing lower limb surgeries. However, Nalbuphine with comparatively prolonged post operative analgesia and effective analgesia time and lesser side effects is a better adjuvant than Fentanyl for intrathecal injections of Bupivacaine 0.5% (H) in surgeries undergoing spinal anaesthesia.

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