Research Article

Comparison among intrathecal fentanyl and nalbuphine in combination with bupivacaine and plain bupivacaine for lower limb surgeries

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Abstract

Background: Nalbuphine, kappa agonist/partial mu antagonist and potent analgesic is less explored for analgesia. **Aims and Objectives:** To compare intrathecal addition of Nalbuphine verses Fentanyl to local anaesthetic on quality and duration of analgesia. **Material and Methods:** This study compared the effects of intrathecally administered, preservative-free Fentanyl and Nalbuphine in combination with bupivacaine and plain Bupivacaine in 60, ASA I or II patients of either sex who underwent lower limb surgeries with spinal anesthesia. Patients were divided into three groups (n=60). Fentanyl group (Group I) received 2.5 ml of 0.5% bupivacaine with 25mcg of fentanyl, Nalbuphine group (Group II) received 2.5 ml of 0.5% bupivacaine along with 500mcg of Nalbuphine, Control group (Group III) received 2.5ml of 0.5% bupivacaine along with 0.5 ml of CSF, Group I and II are study groups. **Results:** There is prolongation of sensory block in fentanyl and nalbuphine group as compared to control group, but there is more prolongation of sensory block duration in nalbuphine group than fentanyl group. Addition of fentanyl or nalbuphine to intrathecal bupivacaine does not prolong the motor block. The perioperative sedation was present in only nalbuphine group but all the patients were arousable and it was not associated with respiratory depression. Request for postoperative pain relief was significantly present in control group. Sedation was noticed in the Nalbuphine treated group only. **Conclusions:** Intrathecal Nalbuphine-Bupivacaine combination is better than Fentanyl-Bupivacaine combination in respect to the duration of sensory block. There was more sedation in nalbuphine treated group. Both Fentanyl and Nalbuphine reduced the analgesic requirement in the early postoperative period

Keywords: Bupivacaine, Fentanyl, Nalbuphine, Spinal.

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INTRODUCTION

Despite advances in knowledge of pathophysiology of pain, pharmacology of analgesics and development of effective techniques for postoperative pain control, many patients continue to experience considerable discomfort. Neuraxial administration of opioids in conjunction with local anesthetics improves the quality of intraoperative analgesia and prolongs the duration of postoperative analgesia[1-2]. Fentanyl (a lipophilic opioid) has a rapid onset and a shorter duration of action following intrathecal administration and it has been observed that 25 micrograms of intrathecal fentanyl prolonged the duration of bupivacaine induced sensory block (sensory regression to L1 dermatome) by 28% and reduced the analgesic requirement in the early postoperative period following bupivacaine spinal block[3-5]. Nalbuphine, although has been used for epidural analgesia but there has been very few studies in literature on the clinical characteristics after intrathecal administration of Nalbuphine[6]. We designed our study to examine and to compare the clinical effects of Fentanyl or Nalbuphine

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added to intrathecal Bupivacaine on anesthesia quality and recovery in patients undergoing lower limb surgeries.

MATERIAL AND METHODS

This observational cross sectional study was conducted with the approval of the Bharti Hospital Medical College and Hospital, Sangli, Maharashtra, ethical committee and informed written consent was obtained from all patients. Patients included for the study were all ASA physical status I or II, of either sex presenting for lower limb orthopedic surgery. On arrival in the operating room, an intravenous infusion was started in all patients with freely running Lactated Ringer's solution. All patients were monitored with automated NIBP, pulse oximetry and electrocardiogram. Patients were given midazolam 0.03mg/kg IV before turning to the lateral decubitus position for placement of the spinal block. Spinal needles used were 25 gauge pencil point needles and were introduced at L3 – 4 interspace. Patients received one of the following into the subarachnoid block: Fentanyl group (Group I) received 2.5 ml of 0.5% bupivacaine with 25mcg of fentanyl, Nalbuphine group (Group II) received 2.5 ml of 0.5% bupivacaine along with 500mcg of Nalbuphine, Control group (Group III) received 2.5ml of 0.5% bupivacaine along with 0.5 ml of CSF, Group I and II are study groups. Oxygen was administrated via a mask if the pulse oximetry reading decreased below 90%. Small boluses of intravenous (IV) ephedrine were given as needed to treat hypotension (MAP < 70 mmHg) and IV atropine was given if the heart rate fall below 60/min. Sensory testing was performed using a 20 gauge hypodermic needle, and dermatomal levels were tested every 2 minutes (min) until the level had stabilized for four consecutive tests. Testing was then conducted every 10 minutes until the point of two segment regression of the block. Further testing was performed at 20 minutes intervals until the recovery of S2 dermatome. Data related to the highest dermatomal level of sensory blockade, the time to reach this level from the time of injection, Bromage scale of motor blockade at the time of reaching peak sensory level, time to two segment regression, time to S2 sensory regression and incidence of side effects were collected. Definition of motor blockade (Bromage scale) : 0 = 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 or feet. All times were recorded from injection of the spinal anesthetic. Request for postoperative pain relief was also recorded.

RESULTS

There were 20 patients in each group, and the groups were demographically similar in all respects (Table-1).

Table 1: Demographic Characteristics of the two pretreatment groups

	Group I	Group II	Group III	P value
Age (in year)	32.0± 8.8	30.7± 9.4	33.7± 10.5	0.624
Height (in cms)	167.3± 6.6	169.1± 5.5	167.8± 3.7	0.535
Weight (in kgs)	62.9± 9.2	67.4± 7.8	65.4± 9.4	0.282
Sex (Male : Female ratio)	15:5	16:4	18:2	p>0.05
ASA I/II	18:2	16:4	16:4	p>0.05
Duration of surgery (in minutes)	94.0±20.9	90.3±23.9	96.8±25.9	p>0.05

The study results regarding the characteristics of sensory block are summarized in (Table-2).

Table 2: Characteristics of sensory block

Groups	I	II	III	P- value
Time from injection to HSL in min	7.5±1.6	7.5±1.7	6.9±1.2	>0.05
Time of two segment regression from HSL in min	95.9±8.6	97.5±10.9	82.4±9.4	<0.001
Time for sensory regression to S2 from HSL in min	158.9±11.3	166.5±11.5	137.4±9.6	<0.001

HSL- Highest sensory level, Min- minutes

There was no significant difference seen in time to reach highest level of sensory blockade in both the groups. For time of two segment regression from highest sensory level (HSL) in minutes there is statistically significant difference between all groups. It reveals that there is no difference between fentanyl and nalbuphine group, but both groups significantly different from control group. ($p < 0.05$). This means there is prolongation of sensory block in fentanyl and nalbuphine group than control group, but there is no difference among drug groups. Time for sensory regression to S2 from HSL in minutes is calculated in all three groups. It reveals that all the three groups are significantly different from each other. ($p < 0.05$). This means there is more prolongation of sensory block duration in nalbuphine group than fentanyl group and control group. Recovery parameters (Table no. 3)

from motor block were similar in all groups except a narrow statistically significant difference between fentanyl and control group for time for onset to grade IV motor block, but this is clinically insignificant. It can be well stated from our study that the addition of fentanyl (25 μg) or nalbuphine (500 μg) to intrathecal bupivacaine does not prolong the motor block.

Table 3: Characteristics of motor block

Groups	I	II	III	P - value
Onset to reach grade IV motor block (min)	6.4±1.2	6.9±1.5	7.3±1.3	0.123
Duration of grade IV motor block (min)	110.0±9.1	105.8±7.5	107.0±7.7	0.255
Duration of grade III motor block (min)	132.5±9.0	129.8±9.6	131.0±7.5	0.621
Duration of grade II motor block (min)	154.7±9.1	152.0±9.6	153.4±7.1	0.618

Times are presented in minutes (Mean + SD) rounded of the nearest whole minutes

There was no occurance of intraoperative nausea-vomitting, respiratory depression, shivering, bradycardia among all groups. There was occurance of intraoperative and postoperative hypotention in all the groups but the difference was statistically insignificant (Table no. 4 and 5).

Table 4: Postoperative parameters Characteristics of hemodynamic and other parameters

	Number of positive cases in % (sample size 20)		
Groups	I	II	III
Nausea-vomitting	5.00	0.00	5.00
Pruritus	10.00	0.00	0.00
Respiratory depression	0.00	0.00	0.00
Shivering	0.00	0.00	0.00
Bradycardia	0.00	0.00	0.00
Hypotension	25	30	25

Table 5: Intraoperative hypotention

Groups	No Hypotention	Hypotention
I	13(65.0%)	7(35.0%)
II	12(60.0%)	8(40.0%)
III	10(50.0%)	10(50.0%)

The intraoperative sedation was present in only nalbuphine group and the difference was statistically significant (Table no. 6). But all the patients were arousable and it was not associated with respiratory depression .

Table 6: Intraoperative sedation (sample size 20)

Groups	Not sedated	Sedated
I	20(100.0%)	0(0%)
II	13(65.0%)	7(35.0%)
III	20(100.0%)	0(0%)

Postoperative sedation was found in both nalbuphine and fentanyl groups but the difference is statistically insignificant (Table no. 7).

Table 7: Postoperative sedation

Groups	Not sedated	Sedated
I	18(90.0%)	2(10.0%)
II	15(75.0%)	5(25.0%)
III	20(100.0%)	0(0%)

Request for postoperative pain relief was only present in control group and the difference is found to be statistically highly significant (Table no. 8). This means there was adequate analgesia in nalbuphine and fentanyl groups.

Table 8: Request for postoperative pain relief

Groups	No Request for pain relief	Request for pain relief
I	19(95.0%)	1 (5.0%)
II	19(95.0%)	1 (5.0%)
III	10(50.0%)	10(50.0%)

There is significant linear difference in VAS Score at rest (Graph no. 1) and VAS score on movement (Graph no. 2) trends with more scores in control group indicating inadequate analgesia.

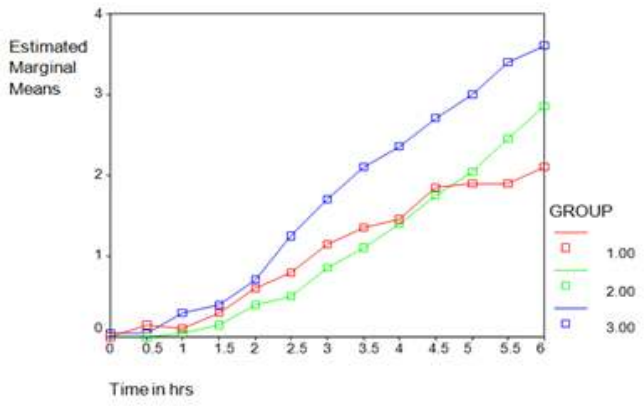

Figure 1: VAS Score at rest

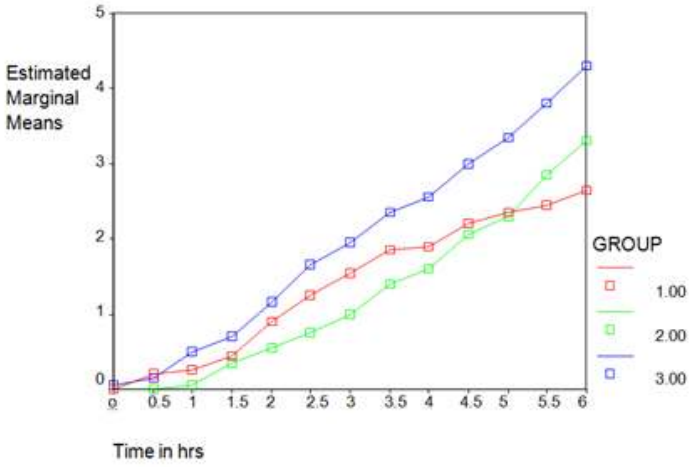

Figure 2: VAS Score on movement

DISCUSSION

Opioids and local anesthetics exert their antinociceptive effect in the spinal cord by different mechanisms. Nalbuphine hydrochloride is a potent analgesic. Its analgesic potency is essentially equivalent to that of morphine on a milligram basis. Receptor studies show that nalbuphine hydrochloride binds to mu, kappa and delta receptors, but not to sigma receptors. Nalbuphine hydrochloride is primarily a kappa agonist/partial mu antagonist analgesic[7,8,9]. Kappa-opioid receptors are distributed throughout brain and spinal cord areas involved in nociception. The greatest concentrations of kappa-receptors in nociceptive regions are in lamina I and II of Rexed in the spinal cord dorsal horn as well as in the spinal nucleus of the trigeminal nerve (substantia gelatinosa). Taken together, these data suggest that nalbuphine acts primarily at the level of the first synapse in the nociceptive system in producing analgesia[7,8,9]. The μ agonist, fentanyl exerts its action by opening K+ channels and reducing Ca++ influx, resulting in inhibition of transmitter release. The μ agonist also have a direct postsynaptic effect, causing hyperpo-larization and a reduction in neuronal activity[10,11]. Local anesthetic, bupivacaine, acts mainly by blockade of voltage gated Na+ channels in the axonal membrane, and possibly, a further effect on presynaptic inhibition of calcium channels[12]. A combination of these effects may explain the observed synergism between bupivacaine and fentanyl/nalbuphine in our study. The principal findings of this study are that the addition of 25 μg fentanyl or 500μg Nalbuphine to spinal anesthesia with hyperbaric 0.5% bupivacaine intensifies the sensory blockade and increases the duration of sensory blockade without increasing the intensity of motor block. In a previous study intrathecal addition of fentanyl to bupivacaine provided better anesthesia without prolonging recovery[4].This suggests a synergism between fentanyl and bupivacaine as reported by Wang *et al*[5]. Also Xavier Culebras *et al*[6] in their study concluded that intrathecal nalbuphine improves intraoperative analgesia and prolongs postoperative analgesia, without increasing the risk of side effects. This is consistent with our results. There is prolongation of time for two segment regression from HSL in fentanyl and nalbuphine group than control group, but there is no difference among drug groups.Time for sensory regression to S2 from HSL is significantly prolonged in group I (fentanyl) and group II (nalbuphine) than group III (control) . There is more prolongation of sensory block duration in nalbuphine group than fentanyl group. Fentanyl and nalbuphine increases intensity of sensory blockade and also prolongs its duration. This is significant both clinically and statistically. Our study demonstrated no statistically significant difference between fentanyl and nalbuphine regarding the onset and duration of motor block and which is found to be comparable to plain bupivacaine as observed in the previous study[13]. The synergism is characterized by enhanced somatic analgesia without effect on degree or level of local anesthetic induced sympathetic or motor blockade[14-17]. It can be well stated from our study that the addition of fentanyl or nalbuphine to intrathecal bupivacaine in doses of 25μg and 500 μg do not prolong the motor block. The intraoperative sedation was present in only nalbuphine group and the difference was statistically significant but all the patients were arousable and it was not associated with respiratory depression. Postoperative sedation was found in both nalbuphine and

fentanyl group but the difference is statistically insignificant. ***Alaaeldin M. Farid et al***[18] compared the effects of intrathecally administered fentanyl and nalbuphine in ASA I or II patients of either sex who underwent lower limb surgeries with spinal anesthesia and concluded that sedation was noticed in the nalbuphine treated group (20%) only. ***Eveline Faure et al***[19] compared effects of intrathecal fentanyl with nalbuphine for labour analgesia and found that nalbuphine led to slightly increased sedation ratings. Our study results were similar to both above study[18,19]. Request for postoperative pain relief was only present in control group and the difference is found to be statistically highly significant. This means there was adequate analgesia in nalbuphine and fentanyl groups. Improved perioperative analgesia following co-administration of fentanyl / nalbuphine and bupivacaine can be explained by a synergistic inhibitory action of these agents on A delta and C fiber conduction[20]. There is significant linear difference in VAS Score at rest and VAS score on movement trends with more scores in control group indicating inadequate analgesia. ***H. Singh et al***[21] in their study concluded that intrathecal Fentanyl reduced requirment of analgesic in early post operative period. ***Catherin O. Hunt et al***[22] and ***Varrasi et al***[23] found that intrathecal Fentanyl increases mean duration of postoperative analgesia. Respiratory depression is one of the major side effects of intrathecal opioid . None of our patients experienced respiratory depression and maintained SpO_2 of 98-100% in all groups. ***Varrassi G..et al***[23] in 1992 studied the ventilatory effects of different dosage of intraethecal Fentanyl on elderly patients and concluded that the patients who received 50 µg Fentanyl had respiratory depression and recommended 25 µg as only dose without respiratory depression. ***Benoit Lefevre et al***[24] Concluded that-Intravenous nalbuphine produced less respiratory depression and should be considered a suitable alternative to fentanyl for use in medically compromised patients. There was no occurance of intraoperative nausea-vomitting, respiratory depression, shivering, bradycardia among all groups. Presence of postoperative respiratory depression, shivering, bradycardia were infrequent and there was no statisticaly significant difference among all groups. In the present study hypotension (MAP<70mmhg) was noticed in 25%, 30%and 25% of the patients in groups I, II and III respectively who were treated with IV bolus of ephedrine. Animal studies have shown that fentanyl does not potentiate the effect of bupivacaine on efferent sympathetic pathways[5]. Our findings are also consistent with the author's finding as we did not encounter an increased incidence of hypotension in both of our study groups.

CONCLUSION

Intrathecal fentanyl and nalbuphine acts synergistically to potentiate bupivacaine induced sensory spinal block, which in terms reduced the analgesic requirement in the early postoperative period without prolonging motor block recovery. Nalbuphine-bupivacaine combination is better than fentanyl-bupivacaine combination in respect to the duration of sensory blockade and requirement of rescue analgesia without any significant increase in adverse effects.

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