Section: Anaesthesiology

Original Research Article

NALBUPHINE AS AN ADJUVANT IN SUBARACHNOID BLOCK IN LOWER ABDOMINAL SURGERY

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Abstract

Background: A pain-free and stress-free postoperative period reduces the morbidity and mortality associated with any surgical operation. Various methods, including epidural catheters, peripheral nerve blocks, and anaesthetic drug infiltration, have been used to reduce morbidity and mortality. **Aim:** This study aimed to determine any intrathecal changes in the onset of sensory and motor blockade by the addition of nalbuphine to levobupivacaine to determine the duration and quality of analgesia. **Material and Methods**: This randomised study included 60 patients undergoing elective operative procedures under spinal anaesthesia for lower abdominal and lower limb surgeries at the Meenakshi Medical College and Research Institute, Kanchipuram, between January 2013 and October 2014. Group L: Patients administered only local anaesthetics, Inj Levo-bupivacaine 0.5%-3 cc. Group N: Patients who were given 0.8 mg of preservative-free intrathecal nalbuphine with the local anaesthetic levobupivacaine 0.5% (3 cc). **Results**: Heart rate and mean arterial pressure at pre-OP, intra-OP OP, and post-OP showed no statistical significance. Group N had a significantly faster onset of sensory and motor blockade than group L. Group N was highly reactive to the drug and had a higher rescue analgesic requirement. The first rescue analgesic requirement was significantly later in group N. Group N had a higher mean time to attain RAM4, RAM2 regression, and maximum motor blockade, making it highly reactive to the drug. **Conclusion**: A combination of levobupivacaine 0.5% and nalbuphine in intrathecal administration enhanced analgesia duration, sedation, and postoperative analgesic requirement and minimised side effects in lower abdominal and orthopaedic surgeries.

INTRODUCTION

Pain is derived from the Latin word “poena”, which means penalty or punishment. Pain is no longer considered a penalty or a punishment. Pain relief is a primary goal of medical science. Surgical operation causes real and severe tissue damage, and surgical pain or “postoperative pain” is a universal phenomenon experienced by millions of patients worldwide. However, paradoxically, after all the efforts are taken to make the intraoperative period pain-free and stress-free, the patients are left to fend for themselves in the postoperative period. The surgical stress response peaks during the postoperative period have major effects on almost all the body systems. A pain-free and stress-free postoperative period reduces the morbidity and mortality associated with any surgical operation.

Various methods of postoperative pain relief are available, including epidural catheters, peripheral nerve blocks, and local anaesthetic drug infiltration at the surgical site. Additives such as systemic benzodiazepines and synthetic and semi-synthetic opioids are simple, effective, and commonly adopted methods for postoperative pain relief. Neural blockade is a method used to control postoperative pain. The first report on the use of intrathecal opioids (ITO) for acute pain treatment was published in 1979 by Wang et al. The use of ITO as an adjunct has a definite place in current regional anaesthesia practice. Various opioids have been used along with bupivacaine to prolong its effect, improve the quality of analgesia, and minimise the requirement of postoperative analgesics. Nalbuphine is a semisynthetic opioid with mixed mu antagonist and k agonist properties.

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Previous studies have shown that intrathecal administration of nalbuphine produces significant analgesia, accompanied by minimal pruritus and respiratory depression.

Aim

This study aimed to determine any changes in the onset of sensory and motor blockade by the addition of nalbuphine to levobupivacaine intrathecally to determine the duration and quality of analgesia and any side effects during the intra-and postoperative periods.

MATERIALS AND METHODS

This randomised study was conducted on 60 patients undergoing elective operative procedures under spinal anaesthesia for lower abdominal and lower limb surgeries at the Meenakshi Medical College and Research Institute, Kanchipuram, between January 2013 and October 2014. The study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

ASA physical status I and II of either sex and aged between 18-60 years were included.

Exclusion Criteria

Patients who underwent emergency surgery for severe respiratory, cardiovascular, renal, and endocrine disorders, allergic to local anaesthetics with coagulation disorders, and patients with local sepsis were excluded.

The spinal anaesthesia procedure was explained to the patients, and written informed consent was obtained. Routine investigations, such as complete haemogram, complete urine examination, blood sugar, electrocardiogram, chest X-ray, blood grouping, blood urea, and serum creatine, were performed. The patients were educated about the use of the visual analogue scale (VAS). The preparation of patients included a period of overnight fasting premedication with oral tablet alprazolam 0.25 mg and tablet ranitidine (150 mg) administered at night and morning on the day of surgery.

Group L: Patients administered only local anaesthetics Inj Levo-bupivacaine 0.5%-3 cc (Neon Pharmaceuticals). **Group N:** Patients who were given 0.8 mg of preservative-free intrathecal nalbuphine (Neon Pharmaceuticals) with the local anaesthetic levo bupivacaine 0.5% (3 cc). The patient explained the procedure of spinal anaesthesia after IV access was secured with an 18 G cannula. Baseline heart rate, BP, and SPO2 were recorded. Patients were also informed about the visual analogue scale (VAS) score and were taught how to express the degree of pain on the scale. Under strict aseptic precautions through a midline approach, the intrathecal block was performed between L2-L3 or L3-L4 intervertebral space using a 25 or 26 G Quincke spinal needle in the left lateral position. After the free flow of CSF, 3 cc of 0.5% Levo bupivacaine for group L patients and 3 cc of 0.5% bupivacaine with 0.8 mg of nalbuphine for group N patients were injected into subarachnoid space. The intrathecal nalbuphine dose was measured using an insulin syringe. The intrathecal injection time was recorded.

The onset of analgesia was assessed based on the time taken from the drug injection to the onset of sensory blockade (absence of pinprick sensation). Two-segment dermatomal regression of the sensory block was recorded at various intervals. The duration of analgesia was assessed using a Visual Analogue Scale (VAS) with a 0 to 10 cm score from no pain to worst pain on marked paper strips at 15, 30, and 60 min and thereafter at 4-hour intervals for a 24-hour postoperative period. Patients with a score > 3 received rescue analgesia in the form of intravenous ketorolac IM in the postoperative period. The time required for the first rescue analgesic and the VAS score at that time were recorded.

At the time of rescue analgesia administration, the patient was asked to provide a global assessment of the overall effectiveness of analgesic treatment. The quality of analgesia was assessed, as noted below, and compared between both groups. Sensory blockade was assessed using the pinprick method, and the time of onset was taken from the time of drug injection into the subarachnoid space to the loss of pinprick sensation. The time to achieve maximum sensory block was noted from the time of drug injection to the loss of pinprick sensation at the highest dermatomal level.

Motor blockade was assessed using the Bromage Scale. The time interval between the injections of the drug into the subarachnoid space and the patient's inability to lift the straight extended leg was taken as the onset time. The time to achieve maximum motor blockade was noted from the time of drug injection to the maximum degree of the motor block. The duration of analgesia was calculated from the intrathecal injection of the drug to the first analgesic demand, that is, a VAS score > 3. The patients were followed up for 24 h after surgery. The VAS score along with HR, BP, and SP02 were recorded in the recovery room, immediately after surgery, and then at 6,12, 24, and hours postoperatively. During the postoperative period, the injections of analgesics or opioids were avoided until a VAS score of > 3. Side effects, such as nausea, vomiting, pruritus, respiratory depression, urinary retention, hypotension, bradycardia, euphoria, dysphoria, pupillary changes, and altered sensorium, if any, were observed and recorded during both the intraoperative and postoperative periods.

Statistical Analysis

Descriptive statistical analyses were performed, and results of continuous measurements are presented as Mean SD (min-max), and results on categorical measurements are presented as number (%). Significance was assessed at the 5% significance level. Student's t-test (two-tailed, independent) was

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used to determine the significance of study parameters on a continuous scale between two groups (intergroup analysis). Moderately significant differences ($P < 0.05$) were strongly significant ($P < 0.01$).

RESULTS

In the age distribution of the cases, there was 1 case in both groups L and N under the age of 20, 11 cases in group L and 04 cases in group N between the ages group 21 – 30, 7 cases in group L and 11 cases in group N between the ages group 31 – 40, 8 cases in group L and 12 cases in group N between the age group 41 – 50, 3 cases in group L and 2 cases in group N above age 50 years, and the mean age for group L was 35.67 ± 19.04, and the mean age for group N was 38.05 ± 18.07, which was comparable between the two groups.

In the sex distribution of the cases, there were 17 males in Group L and 19 males in Group N. There were 13 females in Group L and 11 females in Group N.

The height distribution of the cases in both groups was predominantly in the height group 161 – 170 cm (> 40%). The mean height for group L was 164.73 ± 15.98, and the mean height for group N was 163.23 ± 14.28 and was comparable between the two groups.

In the weight distribution of the cases, both groups predominantly weighed between 51 and 60 kg (> 56%). The mean weight for group L was 56.73 ± 11.39 and the mean weight for group N was 53.12 ± 10.52, which was comparable between the two groups. [Table 1]

Heart rates and mean arterial pressure at pre-OP, intra-OP OP, and post-OP showed no statistical significance [Table 2]

The mean onset of sensory block in group N was 3.10 ± 0.803 min compared to 4.93 ± 1.143 min in group L, and the groups were statistically significant. Since Group N had a higher mean for the onset of motor blockade, Group N was highly reactive to the drug subscribed. The first rescue analgesic requirement in group N was 281.30 ± 15.300 significantly later than in group L at 203.97 ± 22.070, and the difference between the groups was statistically significant.

Since Group N had a higher mean time to attain RAM4, it was highly reactive to the drug, and the differences between groups were not statistically significant. The statistically significant Group N had a higher mean time for regression to RAM2, and Group N was highly reactive. Group N had a higher mean time for maximum motor blockade and was highly reactive; the groups were statistically significant. [Table 3]

Table 1: Demographic data of the study

		No of cases (%)	
		Group L	**Group N**
Age (years)	< 20	1 (3.3%)	1 (3.3%)
	21 – 30	11 (36.7%)	4 (13.3%)
	31 – 40	07 (23.3%)	11 (36.7%)
	41 – 50	08 (26.7%)	12 (40%)
	> 50	3 (10%)	2 (6.7%)
Gender	Male	17(56%)	19(63.3%)
	Female	13(43.3%)	11(36.7%)
Height (cm)	< 150	4 (13.33%)	05 (16.67%)
	151 – 160	11 (36.67%)	10 (33.33%)
	161 – 170	13 (43.33%)	12 (40%)
	> 170	02 (6.67%)	03 (10%)
Weight (kg)	< 50	6 (20%)	5 (16.67%)
	51 – 60	19 (63.33%)	17 (56.67%)
	61 – 70	3 (10%)	4 (13.33%)
	> 70	2 (6.67%)	4 (13.33%)

Table 2: Mean heart rate and mean arterial pressure between the groups

		Mean ± SD		P value
		Group L	**Group N**	
Heart rate	Pre-OP	88.27±9.457	87.20±8.986	0.062
	Intra OP	75.93±6.051	74.90±6.031	0.212
	Post OP	82.50±5.994	81.27±6.051	0.153
Mean arterial pressure	Pre-OP	89.70±6.675	90.20±7.788	0.004
	Intra OP	83.17±7.557	83.20±7.000	0.051
	Post OP	89.43±5.637	89.63±5.366	0.062

Table 3: The onset of sensory blockade, duration of analgesia, time of attaining ram 4, regression to the motor blockade, time for regression to ram 2 and time for maximum motor blockade between the groups

	Mean ± SD		P value
	Group L	**Group N**	
Onset of sensory blockade	4.93 ± 1.143	3.10 ± 0.803	0
The onset of motor blockade	6.73 ± 1.258	4.37 ± 1.033	0
Duration of analgesia	203.97 ± 22.070	281.30 ± 15.300	0
Time of attaining RAM 4	13.73 ± 1.098	13.13 ± 0.860	0.0572

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Regression to motor blockade	97.27 ± 17.534	142.57 ± 8.581	0.0186
Time for regression to RAM 2	92.27 ± 15.088	127.90 ± 10.626	0.0031
Time for maximum motor blockade	13.57 ± 1.794	12.90 ± 0.860	0

DISCUSSION

In our study, we used nalbuphine (preservative-free) 0.8 mg as an adjuvant to intrathecal levobupivacaine (0.5%) for various lower abdominal and lower limb surgeries and compared its postoperative analgesic effect under spinal anaesthesia using levo bupivacaine (0.5%) alone. There was no significant decrease in BP or HR in either group during the initial 30 min. Culebras et al., in 2000 evaluated the effects of different doses of intrathecal nalbuphine with bupivacaine 10mg and found no significant changes in hemodynamic status.[1] Stewart et al. reported that when levobupivacaine was given intravascularly to healthy volunteers, no changes were found in stroke index, cardiac index, heart rate, PR interval, QRS duration and QT interval.[2]

Lin ML in 1992 evaluated the effects of intrathecal nalbuphine or morphine with tetracaine and found no significant changes in hemodynamic status.3 Jeon et al., compared 2.6 ml levobupivacaine alone and 2.3 ml levobupivacaine with 15 µg fentanyl in spinal anaesthesia for TURP. There were no significant differences between the two groups regarding hemodynamic changes and motor block.4

Our results showed that the onset of sensory and motor block was faster, and the time taken to attain complete sensory and motor block was shorter in the nalbuphine group (N) than in the levobupivacaine group (L). The mean onset of sensory block in group N was 3.10 ± 0.803 min compared to 4.93 ± 1.143 min in group L. Similar results were documented by Culebras et al., found that IT nalbuphine provided a significantly faster onset of pain relief compared to IT morphine, probably because of its lipophilic nature.[1]

Compared to morphine, nalbuphine is more lipophilic, so this drug gets fixed than local anaesthetics which are not lipophilic, even though they differ in their mechanism of action. This action causes the local anaesthetic to shift away from the neural tissue and is metabolised quickly. Fournier et al., have also demonstrated that after total hip replacement, administration of nalbuphine through an indwelling IT catheter resulted in a significantly faster onset of pain relief as compared to IT morphine. They conducted their study on 40 patients posted for total hip replacement.[5]

In contrast, Tiwari et al. showed that the onset of sensory and motor blockade was not affected by intrathecal administration of nalbuphine. Seventy-five patients posted for lower limb and lower abdominal surgeries received either 0.2 mg or 0.4 mg nalbuphine or plain bupivacaine intrathecally. This disparity in the onset of blockade could be related to a lower dose of nalbuphine used in this study.[6]

We observed that the first rescue analgesic requirement in group N was 281.30 ± 15.300, which was significantly later than that in group L (203.97 ± 22.070). These results are by the study done by Mukherjee et al. who demonstrated the longest duration of postoperative analgesia in the group in which 0.8 mg nalbuphine was used as an adjuvant as compared to lower doses of nalbuphine i.e., 0.2 and 0.4 mg. 27.7 Similar results were also demonstrated by Tiwari et al., who showed a significant increase in postoperative analgesia in patients given 0.2 or 0.4mg nalbuphine intrathecally.[6]

In our study, 20 out of 30 patients in group N had an intraoperative Ramsay sedation score of 3 or 4 compared to only 3 patients in group B. Culebras et al. found comparable sedation scores in all four groups in their study which could be because they were comparing sedation scores of nalbuphine with morphine which has some sedative effects.[1]

In our study, the time to attain a score of 4 in both groups was statistically significant. The time for attaining ram 4 in group N was 13.13 ± 0.860 and in group L it was 13.73 ± 1.098. None of the patients in either group experienced any significant side effects, such as respiratory depression or pruritus. The side effects noted in group N were nausea, vomiting, and urinary retention in one patient each. In group L two patients experienced nausea and urinary retention.

Culebras et al., the longest durations of complete and effective analgesia among the nalbuphine-treated groups were provided by 0.8 mg added to bupivacaine. Neither pruritus nor PONV was 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 the risk of side effects.[1]

Mukherjee et al., to find out the optimum dose of intrathecal nalbuphine by comparing the 0.2, 0.4 and 0.8mg doses which prolonged postoperative analgesia without increased side effects. It was observed that effective analgesia increased with an 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.[7]

Mostafa et al. demonstrated that in both groups, there was a similar motor block, nearly equal analgesia, delayed first analgesic request, and less analgesic supplement over the first 24 h after the operation. Intrathecal administration of 50 mg tramadol and intrathecal 2 mg nalbuphine when used with 0.5% bupivacaine had similar

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postoperative analgesia in the patients without producing significant related side effects like nausea, vomiting, pruritis and respiratory depression.[8] Lin ML in 1992 found fewer side effects with nalbuphine than with morphine.[3]

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

CONCLUSION

We conclude that intrathecal administration of 3 ml of levobupivacaine 0.5% with nalbuphine 0.8 mg produces a longer duration of analgesia and better sedation than levobupivacaine 0.5% alone in lower abdominal and orthopaedic surgeries, with advantages such as longer duration of analgesia, better sedation, reduced postoperative analgesic requirement, and minimal side effects.

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