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Original Research Article

A COMPARATIVE STUDY ON EFFECT OF ADDITION OF NALBUPHINE TO 0.5% BUPIVACAINE IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERY AT A TERTIARY CARE CENTRE

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ABSTRACT

Background: Local anesthetic agents like bupivacaine alone may not be enough for effective analgesia. They need some addition of adjuvants. Hence to achieve the block early as well as to sustain it for sufficiently longer time, various adjuvants have been tried. The objective is to compare the effect of addition of nalbuphine to 0.5% bupivacaine to plain 0.5% bupivacaine in patients undergoing lower abdominal surgery.

Materials and Methods: Hospital based prospective comparative study was carried out among those undergoing lower abdominal surgeries under spinal anesthesia. Patients were divided in two groups of 30 each. First group i.e. control group received 3.5 mL of 0.5% Bupivacaine in subarachnoid block (SAB) and the second group i.e. the Study group received 3.5 mL of 0.5% Bupivacaine and 0.1 mL of Nalbuphine (10 mg/ml ampule). Both the groups were compared for sensory and motor effects including hemodynamic parameters as well as side effects.

Results: Both groups were comparable for baseline characteristics. Onset of sensory blockade, motor blockade was significantly quicker in nalbuphine group compared to controls. Two segment regression, time to rescue analgesic was significantly more in nalbuphine group. Total dose of analgesic required was significantly lesser for patients from nalbuphine group ($p<0.05$). All hemodynamic parameters at baseline, 0, 10, 30, 60 and 120 min was comparable in two groups ($p>0.05$). Very few cases had side effects in both groups.

Conclusion: Nalbuphine was found initiate quick onset of anesthesia and maintain analgesia for longer period. Thus, it reduced the requirement of analgesics. At the same time, it was safe. Hence, we recommend use of nalbuphine as additive to Bupivacaine in patients undergoing lower abdominal surgeries under spinal anesthesia.

Keywords: Nalbuphine, bupivacaine, analgesia, effect.

INTRODUCTION

For lower limb and abdominal surgeries, spinal anesthesia is the technique of choice. It is popular. It is regional anesthesia that is effective. Bupivacaine is one of the most commonly used anesthetic agent for spinal anesthesia.[1] However, local anesthetic agents like bupivacaine alone may not be enough for effective analgesia. They need some addition of adjuvants. Hence to achieve the block early as well as to sustain it for sufficiently longer time, various adjuvants have been tried. First one in this series was Morphine. Nalbuphine is one such adjuvant. It is opioid antagonist as well as opioid agonist. It can prove very much useful. It can enhance the action of analgesia that is opioid based. At the same time, it encounters the side effects of opioids.[3-4]

In one study, the nalbuphine has been found to be effective in a dose of 0.4 mg when given intrathecally when given in addition to bupivacaine in the dose of 0.5% bupivacaine.[5] Another study compared the

traditional morphine with nalbuphine in different doses and observed that nalbuphine was effective in the dose of 0.8 mg.[6]

The quality of analgesia before and after surgery is found to be very much improved and of good quality when nalbuphine was added to bupivacaine. The adverse effects were also very few as documented elsewhere. The μ-opioid effects are attenuated by nalbuphine. At the same time it is also found to be very much responsible for the enhancing the effects of κ-opioid. Thus, it is a mixed synthetic adjuvant that can be used in the spinal anesthesia as an adjuvant to bupivacaine or other local anesthetics. Till date, there are no reports related to the neurotoxicity of the nalbuphine. In addition to nalbuphine, we have other adjuvants like fentanyl, morphine etc. But, the problem with these adjuvants is that they are listed under the Narcotics Act. Due to this, there is limited availability of these drugs. But, this is not the case with nalbuphine. Because of this, nalbuphine can be available easily without much trouble. At the same time it is effective and is not associated with serious side effects.[7] In one such study 8 when nalbuphine in the dose of 0.8 mg was compared with fentanyl in the dose of 25 μg as adjuvants to bupivacaine, both the drugs were found out to be equally effective. As mentioned above, fentanyl is listed under Narcotics Act making its availability limited. This is not the case with nalbuphine, making it easily available.

More studies in different populations are required to prove the effectiveness of nalbuphine as an adjuvant to bupivacaine in the lower abdominal and lower limb surgeries. Hence present study was carried out to compare the effect addition of nalbuphine to 0.5% bupivacaine to plain 0.5% bupivacaine in patients undergoing lower abdominal surgery.

MATERIALS AND METHODS

We carried out a hospital-based, prospective comparative study at a single centre. The study was carried out over a period of one year at the Department of Anesthesiology of a teaching hospital. Institutional Ethics Committee permission was obtained. Written informed consent was taken from all eligible study participants before enrolling them in the study. Randomization was not done.

Adults of age more than 18 years of age belonging to either gender, undergoing the lower abdominal surgeries at the study centre and willing to participate were included in the present study. Those with severe morbid conditions, allergic to any drugs under the present study, were excluded.[8]

Jyothi B et al,[9] compared the 0.8 mg nalbuphine as an adjuvant to 3 mL of 0.5% heavy bupivacaine 15 mg with that of 0.5 mL of 0.9% normal saline to a total volume of 3.5 mL as an adjuvant to 3 mL of 0.5% heavy bupivacaine 15 mg. They found that the mean duration of analgesia was 322.4 min in the nalbuphine group, compared to 190.4 min in the control group. Based on these findings of mean values with 80% power and 95% of confidence level, the sample size of the present study came out to be one in each group. But, to satisfy the statistical equations, we took 60 patients undergoing lower abdominal surgeries.

These 60 patients were eligible and consenting. They were randomly allocated to one of the two groups. First group i.e. control group received 3.5 mL of 0.5% Bupivacaine in subarachnoid block (SAB) and the second group i.e. the Study group received 3.5 mL of 0.5% Bupivacaine and 0.1 mL of Nalbuphine (10 mg/ml ampule). Each group was having 30 cases each.

Before the surgery, baseline characteristics like age, sex, height, weight, ASA grades were noted in the pre-designed, pre-tested, semi-structured study questionnaire. After ascertaining the fitness for surgery patients were taken to operation theatre. All routine protocols were followed as per the standard guidelines and the operative procedures of the hospital. In the operation theatre, the patient was connected to the monitor and the baseline parameters were recorded. The hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were recorded at baseline, zero min, 10, 30, 60 and 120 min.

Other parameters like onset of sensory block at T-10, onset of motor block, two segment regression, complete motor recovery, time to rescue analgesia and total dose of analgesic (tramadol for the first 24 hours) required were noted. Visual analogue score (VAS) more than three was considered as requirement for analgesic. Adverse effects like nausea, vomiting, hypotension, shievering and pruritus were monitored and noted if occurred at all.

Microsoft Excel worksheet was used to enter the data. The data was expressed as proportion in case of categorical variables and mean or median in case of continuous variables depending upon the normal distribution. For comparison of proportion chi square test or the Fischer exact test was used as the case may be. For comparison of mean or median values either independent samples t test or the Mann-Whitney U test was used. P value of less than 0.05 was taken as statistically significant.

RESULTS

Table 1: Comparison of baseline characteristics in two groups

Characteristics		Nalbuphine group (N=30)	Control group (N=30)	P value
Sex	Male	17 (48.6%)	18 (51.4%)	0.069
	Female	13 (52%)	12 (48%)	
Age (years)		45.5+18.4	44.1+13.4	0.743

Height (cm)	161.9+9.5	157.3+13.2	0.132
Weight (kg)	61.1+11.1	62.4+13.6	0.694

Both the groups were comparable for baseline characteristics like age, sex, height, weight (p>0.05).

Table 2: Comparison of sensory and motor parameters in two groups

Parameters	Nalbuphine group (N=30)	Control group (N=30)	P value
Onset of sensory block (min)	3.53+1.2	4.73+2.03	0.007
Onset of motor block (min)	3.53+1.66	4.7+2.03	0.0176
Two segment regression (min)	106.5+18.6	89.5+19.8	0.001097
Complete motor recovery (min)	221.93+65.4	216.03+92.8	0.777
Time to rescue analgesic (min)	317.9+76.8	274.4+52.1	0.01285
Total dose of analgesic required (mg)	160.0+16.3	173.3+13.9	0.00122

The onset of sensory blockade, motor blockade was significantly quicker in nalbuphine group compared to control group. Two segment regression, time to rescue analgesic was significantly more in the nalbuphine group compared to controls. The total dose of analgesic required was significantly lesser for patients from the nalbuphine group compared to the control (p<0.05).

Table 3: Comparison of hemodynamic parameters in two groups

Parameters	Time (min)	Nalbuphine group (N=30)	Control group (N=30)	P value
Heart rate (per min)	Baseline	81.6+16.5	80.8+16.6	0.841
	Zero min	82.6+19.5	83.6+16.5	0.825
	10 min	74.9+16.2	74.7+14.4	0.973
	30 min	70.4+16.9	69.5+13.2	0.812
	60 min	66.3+15.8	69.8+11.6	0.333
	120 min	68.2+14.5	72.1+11.8	0.261
Systolic blood pressure (mmHg)	Baseline	134.9+17.2	137.8+14.4	0.481
	Zero min	133.3+19.1	134.3+15.38	0.826
	10 min	116.6+16.4	113.2+16.9	0.442
	30 min	115.3+16.3	112+15.9	0.427
	60 min	116.5+17.1	111.7+26.9	0.410
	120 min	113.7+19.1	123.6+16.2	0.342
Diastolic blood pressure (mmHg)	Baseline	80.7+11.4	83.7+10.03	0.284
	Zero min	77.3+15.2	82.2+12.7	0.181
	10 min	66.5+12.7	67.5+13.1	0.758
	30 min	67.2+10.8	67.4+13.9	0.942
	60 min	66.4+9.4	69+13.2	0.388
	120 min	67.2+8.2	72.4+13.4	0.076
Mean arterial pressure (mmHg)	Baseline	96.7+14.7	99.9+12.6	0.355
	Zero min	95.1+12.8	95.8+13.7	0.832
	10 min	80.3+11.7	82.3+15.9	0.585
	30 min	79.5+12.2	80.7+13.6	0.728
	60 min	80.1+11.9	81.1+13.3	0.761
	120 min	79.7+11.5	85.5+14.9	0.0961

All the hemodynamic parameters like heart rate, mean systolic blood pressure, mean diastolic blood pressure, mean arterial pressure at baseline, 0, 10, 30, 60 and 120 min was comparable in two groups (p>0.05).

Table 4: Comparison of side effects

Side effects		Nalbuphine group (N=30)	Control group (N=30)	P value
Nausea	No	30	30	1
Vomiting	Yes	3	3	1
Hypotension	Yes	5	8	0.347
Shivering	Yes	1	1	1
Pruritus	No	30	30	1

Very few cases had side effects in both the groups and the comparison was not found to be statistically significant (p>0.05).

DISCUSSION

In the present study both the groups were comparable for baseline characteristics like age, sex, height, weight (p>0.05). The onset of sensory blockade, motor blockade was significantly quicker in nalbuphine group compared to control group. Two segment regression, time to rescue analgesic was significantly more in the nalbuphine group compared to controls. The total dose of analgesic required was significantly lesser for patients from the nalbuphine group compared to the control (p<0.05). All the

hemodynamic parameters like heart rate, mean systolic blood pressure, mean diastolic blood pressure, mean arterial pressure at baseline, 0, 10, 30, 60 and 120 min was comparable in two groups ($p>0.05$). Very few cases had side effects in both the groups and the comparison was not found to be statistically significant ($p>0.05$).

Borah TJ et al,[10] had in their study 25 cases scheduled for lower limb surgery in four groups. First was control group and remaining three received nalbuphine in the dose of 0.4, 0.8 and 1.6 mg respectively. Patients in the nalbuphine group experienced faster onset of sensory and motor block. They also had significantly highest two segment regression. Total analgesia duration was also prolonged. These findings are similar to the findings of the present study. Just like present study, the hemodynamic parameters were also similar showing no statistical difference. The authors felt that instead of other opioids, nalbuphine is better as it has minimal amount of side effects.

Vengadessane A,[11] carried out a double blind randomized study. It was prospective in nature. The patient were operative under the supraclavicular block. They had two groups of 30 each in their study. First group had nalbuphine given and the second group had morphine given. Onset of sensory block was quick in nalbuphine group and the difference was observed to be statistically significant. We also found quick onset of action due to nalbuphine. Same thing was noted even for motor block also. The authors reported that the duration of analgesia was similar in two groups. In the present study, we found that nalbuphine group was having more duration of analgesia. However, in our study, the comparison was with normal saline and this author study, it was with morphine. They like the present study concluded that nalbuphine acts very fast and has prolonged period of action and at the same time, safe also.

Bindra TK et al,[12] had 150 cases in their study who were aged 20-45 years of age. All underwent the spinal anesthesia. It was randomized controlled study. The patients and the anesthesiologists were blinded for the procedure. They had random allocation in three groups of 50 each. First group was given nalbuphine, second group was given fentanyl and third group was given normal saline. They found that the first group who was given nalbuphine had the longest duration of analgesia compared to fentanyl and normal saline group. Even the number of rescue analgesics required was significantly lowest in those who were given nalbuphine than other two groups. These findings are well in accordance with the findings of the present study. Thus, the authors concluded that the nalbuphine as well as fentanyl are both effective than the control group. But, nalbuphine is better than fentanyl.

Nagaraj B et al,[13] also conducted one randomized controlled trial. It was also doubly blinded in nature. They had three groups of 20 each. They used the random allocation software for allocation of the participants in three groups. First group was given nalbuphine. Second group was given dexmedetomidine and the third group was given normal saline. The authors observed that the onset of sensory as well as motor block was comparable in three groups. This was not in accordance with the present study as we found that the onset of sensory as well as motor block was very quick with nalbuphine. This difference may be due to the settings where the study was carried out and the dose of each adjuvant used. Again they stated that dexmedetomidine group experienced the longer time for two segment regression than the nalbuphine and control group. We compared only with normal saline and these authors had dexmedetomidine also in their study.

Shi W et al,[14] carried out a meta analysis. Objective was to find out what is the benefit of analgesia offered by nalbuphine when it is mixed with local anesthetic drug in brachial plexus block. They included 17 randomized controlled trials which had 1104 patients. They found that analgesia duration was better in nalbuphine group compared to control. The onset of motor and the sensory block was quick with nalbuphine when it was compared with control. We also found similar results. The side effects in the control group and the nalbuphine group were not different. We also observed similar reports. The authors from their meta-analysis concluded that the effectiveness of nalbuphine was of moderate quality evidence.

Gupta K et al,[15] assessed not only the safety but also the effectiveness of nalbuphine when it was added to bupivacaine. They had included 60 cases in their study. Later they created two groups and each group had 30 cases by using random allocation technique. One group i.e. control group with normal saline and the other group i.e. nalbuphine group were there. The authors observed that the nalbuphine was not found to be affecting the onset of either the motor or the sensory block. However, it was found out to be effective in prolonging the duration of the block of both the kinds. In the present study we found that nalbuphine not only was quick in action but also sustained it for longer duration. The authors stated that nalbuphine did not alter the hemodynamics and also found to be safe which is in accordance with the results of the present study.

Shah MS et al,[16] conducted a triple arm study which was randomized. 20 patients each in three groups were placed. First group was given plain bupivacaine. Second group was given 1.6 mg of nalbuphine along with bupivacaine and the third group was given a dose of 2.4 mg instead of 1.6 mg of the second group. All three groups showed that they had almost all similar onset of motor and the sensor block and the difference was not found out to be statistically significant. Analgesia duration increased progressively from group one to three showing the more dose of nalbuphine is directly correlated with total analgesia duration. Side effects were minimal and easily manageable. The authors stated that nalbuphine even in the low dose of 1.6 mg can be used as an effective and safe adjuvant to bupivacaine.

Gurunath BB et al,[17] had two groups in their study. They compared the effects of nalbuphine with that of fentanyl when given in combination with bupivacaine. The authors found that even though it took time for nalbuphine to act for sensory block, but its action remained prolonged compared to fentanyl.

CONCLUSION

Nalbuphine was found to initiate quick onset of anesthesia and maintain analgesia for longer period. Thus, it reduced the requirement of analgesics in the postoperative period. At the same time, it was safe. Hence, we recommend use of nalbuphine as additive to local anesthetics in patients undergoing surgery under spinal anesthesia.

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