Section : Anaesthesology

Original Research Article

A COMPARATIVE STUDY OF EPIDURAL NALBUPHINE WITH 0.5% BUPIVACAINE VS 0.5% BUPIVACAINE ALONE IN INFRAUMBILICAL SURGERIES

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ABSTRACT

Background: Epidural anesthesia offers a wide range of applications. It is widely used for operative anesthesia, obstetric analgesia, postoperative pain control, and chronic pain management. A local anaesthetic–opioid combination provides superior analgesia during perioperative and postoperative period. Epidural opioids have fewer respiratory complications and can be mobilized sooner in the postoperative period. The main aim is to compare the sensory and motor blockade characteristics of epidural Nalbuphine mixed with 0.5% Bupivacaine with that of 0.5% Bupivacaine alone in infra umbilical surgeries. **Materials and Methods:** A prospective randomized double-blinded study was done in 60 patients divided into two group with 30 in each group as group A and group B by computer generated random numbers. Group A: Received 15 ml of 0.5% bupivacaine with 1 ml of nalbuphine (10mg); Group B: Received 15 ml of 0.5% bupivacaine with 1 ml of normal saline. The differences between the groups were statistically analyzed with the Independent t-test for continuous variables and Pearson's chi-square test for categorical variables. **Result:** The time of onset of sensory blockade (5.16 ± 1.39 mins vs 9.03± 1.63 mins) , time taken for peak sensory blockade (12.66 ± 2.31 mins vs 17.13 ± 2.08 mins) and the duration of sensory blockade (285.33 ± 27.76 mins vs 247 ± 19.68mins) respectively were significantly faster in group A when compared with group B. The time of onset of motor blockade, the time taken for peak motor blockade and the duration of motor blockade were statistically not significant between both groups. **Conclusion:** Epidural Nalbuphine as an aduvant to bupivacaine hastens the onset of sensory blockade and significantly prolonged the duration of anaesthesia and postoperative analgesia, with stable haemodynamics.

INTRODUCTION

In 1947, Manuel Martinez Curbelo (1906–1962) was the first to describe placement of a lumbar epidural catheter.[1] Deposition of drugs in the epidural and subarachnoid space paved a new era for pain relief. Epidural anesthesia offers a wide range of applications than the typical all-or-nothing spinal anesthetic. An epidural block can be performed at the lumbar, thoracic or cervical level. Epidural techniques are widely used for operative anesthesia, obstetric analgesia, postoperative pain control, and chronic pain management. It can be used as a single shot technique or with a catheter that allows intermittent boluses and/or continuous infusion. The role of epidural anaesthesia and analgesia in reducing the incidence and severity of perioperative physiologic derangements, in addition to relieving pain has been reported in several studies.[2,3]

Drugs commonly used for epidural based analgesia techniques include local anesthetics,[4] Opioids,[5] local anesthetic-opioid combinations.[6] The advantage of local anaesthetic and opioid combination eliminates the pain at the nerve axon and spinal cord respectively.

Nalbuphine is an opioid agonist-antagonist that binds to the μ, K and δ- receptors. At the k -receptor, nalbuphine functions as an antagonist, and at the μ -receptor in the dorsal horn of the spinal cord, it functions as an agonist.[7,8] Mild analgesia, respiratory depression, and sedation are brought on by the activation of the spinal and supraspinal μ-receptors. Like other agonist-antagonists, nalbuphine interferes with the analgesia brought on by pure μ -agonists. The action on kappa receptors produce analgesia with a lower incidence and severity of mu receptor side effects. It also has a low potential for addiction and little effect on respiratory depression.

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Despite the rising popularity of regional anesthesia, adjuvants like nalbuphine are used far less frequently than fentanyl. In this study, we have examined the onset, duration, need for postoperative analgesia, and side effects of nalbuphine when added to 0.5% isobaric bupivacaine as an adjuvant in epidural blockade.

Aim and Objectives

The main aim is to differentiate the potency of Nalbuphine as adjuvant when combined with 0.5% bupivacaine in patients undergoing elective infraumbilical surgical intervention under epidural blockade in terms of the onset and duration of sensory and motor blockade. The secondary objective was to evaluate the hemodynamic parameters, duration of postoperative analgesia, and complications or side effects between the two groups.

MATERIALS AND METHODS

The present study was done at Gandhi Medical College/Hospital, Secunderabad, during 2022- 2024. After obtaining approval for the study from Institutional ethics Committee, written consent was obtained from all the patients.

To achieve optimal randomization, 60 patients were divided into two groups of 30 each, and then randomly assigned by computer-generated random numbers to one of the two groups listed below: the bupivacaine with nalbuphine group (Group A; n=30) or the bupivacaine group (Group B; n=30). A sequentially numbered opaque sealed envelope was used to ensure confidentiality. Group A: Received 15 ml of 0.5% bupivacaine with 1 ml of nalbuphine (10mg); Group B: Received 15 ml of 0.5% bupivacaine with 1 ml of normal saline.

Inclusion Criteria

All patients posted for elective infra-umbilical surgeries under ASA Grade I and II including both males and females.

Exclusion Criteria

Patients who are unwilling to give consent; ASA Grade III, IV, V or E; Obese patients, Patients with severe CVS abnormalities, renal or hepatic failure; Patients with H/O neurological surgeries or spine deformities, Patients with coagulation defects or those on anti-coagulants.

Informed consent was obtained after explaining the procedure. All patients were subjected to pre anaesthetic checkup on the day before surgery to find out systemic illness complicating anaesthesia. On the day of surgery, the patients were shifted to the operation theatre and baseline vital hemodynamic parameters such as heart rate, non-invasive arterial blood pressure, oxygen saturation and ECG were noted. Intravenous line was secured with an 18G intravenous catheter and preloading was done with 500ml of Ringer's Lactate. No narcotic premedication was given. The patients were explained about the 10 point visual analogue of pain scale.

Technique: After thorough aseptic precautions L1-L2 or L2-L3 Space located and using a16 gauge Huber point Tuohy needle epidural space was identified with loss of resistance technique. Epidural catheter was inserted and aspirated to rule out subarachnoid or intravascular placement of the catheter. The placement was confirmed by 3ml of 2% lidocaine with adrenaline 1: 2 00,000 and fixed. On confirmation, Group A patients were given 15 ml of 0.5% bupivacaine with 1 ml of nalbuphine (10mg) into the epidural catheter as a single bolus dose and Group B patients were given 15 ml of 0.5% bupivacaine with 1 ml of sterile water into the epidural catheter as a single bolus dose and the patients were positioned for the surgery.

The following parameters were observed in the study

- Onset of sensory blockade
- Onset of motor blockade
- Maximum time for maximum level of sensory blockade.
- Time taken for maximum motor blockade according to modified Bromage scale
- 2 segment regression time.
- Total duration of sensory blockade
- Total duration of motor blockade.
- Quality and duration of analgesia.
- Pulse rate, blood pressure, respiratory rate, Spo2 every 5mins.

Surgeons were asked to proceed with the surgery only after the maximum level of blockade was established.

Intraoperatively, complications like bradycardia were dealt with I.V. atropine (12-20μg/kg). A fall in systolic blood pressure by 20% from the baseline value was considered as hypotension and managed with IV fluids, oxygen and inj. Mephentermine I.V (6mg boluses). Any episodes of desaturation (SpO2<90%) or respiratory depression (< 10 breaths per minute) were noted. At the end of surgery patients were observed in the recovery room for further two hours and sent to postoperative ward.

Patients were asked to mark a point scale on the 10 point visual analogue scale of pain according to the intensity of pain. The observation was done every 30minutes. Supplementary analgesia was given when VAPS more than 4. The total number of rescue analgesics (inj. Diclofenac 75 mg IM) in the first 24 hours were noted down to assess the quality of analgesia.

The side effects due to Nalbuphine like nausea, vomiting, pruritis, urinary retention were noted down.

Statistical Analysis: All the data were entered in Excel 2019 and statistical analysis was performed using the statistical software, SPSS 25.0.0.0. Data were expressed in percentages and mean values (with standard deviation). Differences between the groups were analyzed using Pearson's chi-square test is used for categorical variables and the independent t-test for continuous variables. In cases where the p-value

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was less than 0.05, the results were deemed statistically significant.

RESULTS

Majority of the study participants were in the age group between 20 and 60 years with mean age of 38.43 ± 9.56 in group A and 39.06 ± 9.83 in group B. Other demographic parameters like sex distribution of the individual, weight, and ASA grades were comparable among both the groups (Table 1). There were statistically no significant difference between mean age, weight, gender and ASA grading in both groups.

Table 1: Demographic details between Group A and Group B.

Parameters		Group A	Group B	p-Value
Age	Mean in yrs. ± S. D	38.43 ± 9.56	39.06 ± 9.83	0.802
Weight	Mean in kg ± S. D	63.03 ± 9.44	62.7 ± 9.59	0.894
Sex	Male	22 (73%)	23 (77%)	
	Female	8 (27%)	7 (23%)	
ASA	Grade 1	12 (40 %)	12 (40 %)	
	Grade 2	18 (60 %)	18 (60 %)	

When comparing group A to group B, The time of onset of sensory blockade was highly significant (p< 0.01). In group A the minimum time was 3 minutes and maximum 8 minutes with a meantime of 5.16 ± 1.39 minutes. In group B the minimum time was 6 minutes and maximum 12 minutes with a mean time of 9.03± 1.63 minutes. The time of onset of motor blockade was statistically not significant (p > 0.05). In group A the minimum time was 10 minutes and maximum 15 minutes with a meantime of 12.6 ± 1.49 minutes. In group B the minimum time was 10 minutes and maximum 15 minutes with a mean time of 13.3± 1.41 minutes. The time taken for peak sensory blockade was highly significant (p<0.01). In group A the minimum time was 10 minutes and maximum 18 minutes with a meantime of 12.66 ± 2.31 minutes. In group B the minimum time was 14 minutes and maximum 20 minutes with a mean time of 17.13 ± 2.08 minutes. The time taken for peak motor blockade was statistically not significant (p > 0.05). In group A the minimum time was 18 minutes and maximum 26 minutes with a meantime of 21.86 ± 2.37 minutes. In group B the minimum time was 18 minutes and maximum 30 minutes with a mean time of 22.93 ± 2.88 minutes.

The time taken for two segment regression was significant (p< 0.05). In group A the minimum time was 60 minutes and maximum 90 minutes with a meantime of 72.33 ± 9.35 minutes. In group B the minimum time was 50 minutes and maximum 80 minutes with a mean time of 67.33 ± 9.89 minutes

The duration of surgery was statistically not significant in the two groups (p > 0.05).The duration of sensory blockade was highly significant (p < 0.01). In group A the minimum time was 240 minutes and maximum 320 minutes with a meantime of 285.33 ± 27.76 minutes. In group B the minimum time was 200 minutes and maximum 280 minutes with a mean time of 247 ± 19.68 minutes. The duration of motor blockade was statistically not significant (p > 0.05). In group A the minimum time was 150 minutes and maximum 200 minutes with a meantime of 170.4 ± 13.23 minutes. In group B the minimum time was 140 minutes and maximum 200 minutes with a mean time of 163 ± 16.64 minutes.

[Table 2] shows the association of onset, duration of sensory, motor blockade, time taken blockade and two segment regression with study participants.

Table 2: Association of onset, duration of sensory, motor blockade, time taken blockade and two segment regression with study participants

Parameters (mins)	Group A (n=30)	Group B (n=30)	p-Value
Onset of sensory block	5.16 ± 1.39	9.03 ± 1.63	< 0.01
Onset of motor blockade	12.6 ± 1.49	13.3 ± 1.41	0.066
Time taken for P.S.B	12.66 ± 2.31	17.13 ± 2.08	< 0.01
Time taken for P.M.B.	21.86 ± 2.37	22.93 ± 2.88	0.118
Two segment regression time	72.33 ± 9.35	67.33 ± 9.89	0.04
Duration of surgery	65.16 ± 11.56	67.83 ± 11.19	0.367
Duration of sensory blockade	285.33 ± 27.76	247 ± 19.68	< 0.01
Duration of motor blockade	170.4 ± 13.23	163 ± 16.64	0.0616

P.S.B= peak sensory blockade; P.M.B= peak motor blockade

There was statistically no significant difference in the baseline parameters between the two groups [Table 3].

Table 3: Comparison of baseline variables

Baseline Parameters	Group A (Mean ± S.D.)	Group B (Mean ± S.D.)	p value
Heart rate	81.73 ± 9.34	81.23 ± 8.98	0.8333
Systolic blood pressure	127.6 ± 7.96	125.76 ± 7.49	0.3603
Diastolic blood pressure	83.23 ± 5.36	80.1 ± 7.78	0.07475
Mean arterial pressure	98.1 ± 5.1	95.13 ± 6.92	0.06344

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Mean heart rates in both the groups were compared and it was observed that p-value was significant only at 6th, 7th, 8th, 9th and 10th hours and at rest of the times, the p-values were insignificant [Figure 1].

Mean arterial pressures in both the groups were compared and it was observed that P-value was significant only at 3rd, 6th, 7th, 8th, 9th and 10th hours and at rest of the times, the P-values were insignificant [Figure 2].

There was statistically no significant difference in respiratory rates between the two groups [Figure 3].

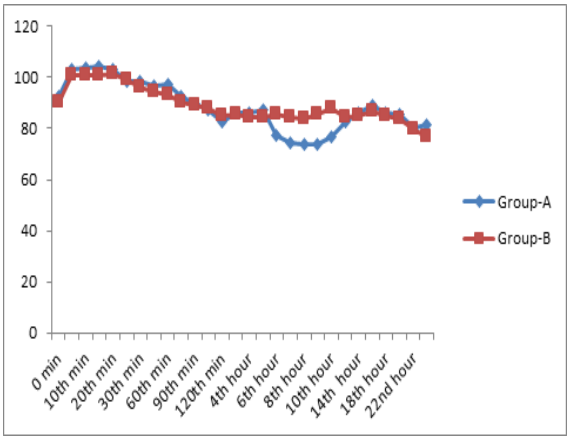

Figure 1: Comparison of heart rates between the two groups

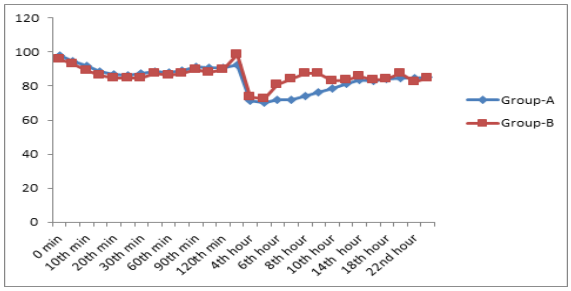

Figure 2: Comparison of Mean arterial pressures between the two groups

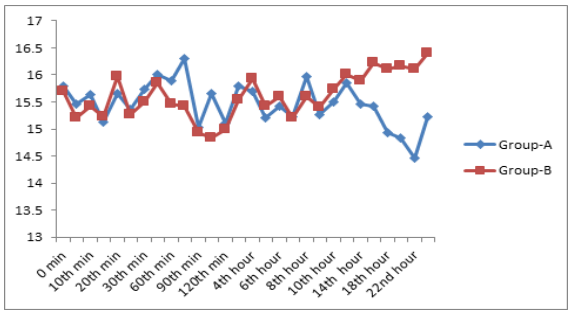

Figure 3: Comparison of respiratory rates between the two groups

Table 4: Comparision of vas scores between the two groups

Time		VAS score	
		0-4	5-10
0–6 Hours	Group A	30(100%)	0
	Group B	24(80%)	6 (20 %)
6–12 hours	Group A	21 (70%)	9 (30%)
	Group B	6 (20 %)	24 (80%)
12–24 hours	Group A	2 (7%)	28 (93%)
	Group B	0	30(100%)

30% of patients in group A had a pain score more than 4 during 6- 12 hours of postoperative period as compared to 80 % in group B [Table 4]. The pain scores were similar in both the groups in the first six hours of postoperative period. Rescue analgesic (inj. Diclofenac) was given when VAS score was more than 4.

[Table 5] shows that the number of rescue analgesics required in the first 24 hrs of post operative period in group B were significantly higher ($p < 0.01$) when compared with group A.

Table 5. No. of rescue analgesics required in both groups

No. of rescue analgesics	Mean	S.D.	S.E.	p value
Group A	1.67	0.48	0.087	< 0.01
Group B	2.57	0.50	0.092	

Side Effects in Both Groups [Table 6]

Table 6. Comparision of side effects in between both the groups

Side Effects	Group- A		Group- B	
	n	%	n	%
Nausea and vomiting	1	3.3 %	2	6.6 %
Respiratory depression	-	-	-	-
Urinary retention	-	-	-	-
Pruritus	-	-	-	-
Hypotension	2	6.6 %	3	10 %
Bradycardia	1	3.3 %	2	6.6%
Shivering	1	3.3 %	2	6.6 %

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The side effects in both groups find that 1 patient in Group A (3.33%) and 2 patients (6.67%) in Group B experienced nausea and vomiting which were not significant statistically. 2 patients in Group A (6.67%) and 3 patients in Group B (10%) had hypotension which was not significant statistically. 1 patient in Group A (3.33%) and 2 patients in Group B (6.67%) experienced bradycardia which were not significant statistically. 1 patient in Group A (3.33%) and 2 patients in Group B (6.67%) had shivering which were not significant statistically. All the side effects were treated immediately.

DISCUSSION

Epidural anaesthesia is superior to Spinal anaesthesia as the desired block levels can be achieved without significant haemodynamic disturbances and top-up doses of anaesthetics & analgesics can be given. Epidural administration of narcotics for postsurgical analgesia gained increasing popularity following the discovery of opioid receptors in the spinal cord capable of producing potent analgesia as reported by Yaksh and Rudy in 1976. It is now clear that epidural administration of opioids is superior to traditional intravenous and intramuscular injections of opioids because this modality of analgesia has unique advantages over conventional, intermittent IV/IM administration of narcotics. Patients given epidural narcotics have fewer respiratory complications and can be mobilized sooner in the postoperative period.

Several narcotics have been evaluated in order to identify a drug that affords as efficient analgesia but causes much less respiratory depression when given epidurally for epidural use. The agonist/ antagonist narcotic agents like nalbuphine can be expected to offer some scope in this respect, since the respiratory depression reaches ceiling level with higher receptor occupancy at higher dose of the drug. There are very few studies comparing the effect of addition of epidural nalbuphine to bupivacaine. Most of the studies on nalbuphine were comparing it with other drugs intravenously or intrathecally. Hence the need for this study.

In the present study, the meantime for onset of sensory blockade was significantly faster (5.16 ± 1.39 mins) in group A when compared to group B (9.03± 1.63 mins). The time taken for peak sensory blockade was significantly faster ($p<0.01$) in group A (12.66 ± 2.31 mins) when compared to group B (17.13 ± 2.08 mins). The time taken for two segment regression was also significantly prolonged ($p< 0.05$) in group A (72.33 ± 9.35 mins) when compared to group B (67.33 ± 9.89 mins). The duration of sensory blockade was also significantly prolonged ($p < 0.01$) in group A (285.33 ± 27.76 mins) when compared to group B (247 ± 19.68 mins).

All the motor blockade parameters like the time of onset of motor blockade (12.6 ± 1.49 mins vs 13.3± 1.41 mins), the time taken for peak motor blockade (21.86 ± 2.37 mins vs 22.93 ± 2.88 mins), the duration of motor blockade (170.4 ± 13.23 mins vs 163 ± 16.64 mins) was statistically not significant ($p > 0.05$) between both the groups.

In the present study, it was observed that addition of Nalbuphine to bupivacaine epidurally has significantly prolonged the sensory blockade characteristics whereas the motor blockade characteristics remain not changed significantly.

Chatrath et al,[9] compared nalbuphine versus tramadol added to bupivacaine for postoperative analgesia in lower limb orthopedic surgeries under CSE. The mean duration of analgesia in group A was 380 ± 11.49 min and in group B was 380 ± 9.8 min. The mean sedation score was found to be more in tramadol group than nalbuphine group. The mean patient satisfaction score in nalbuphine group was 4.40 ± 0.871 and in tramadol group was 3.90 ± 1.150 which was found to be statistically significant ($P < 0.05$). They concluded that the addition of nalbuphine with bupivacaine was effective for postoperative analgesia in terms of quality of analgesia and patient satisfaction score as compared to tramadol.

Mukesh Kumar et al,[10] in their study, Comparative Evaluation of Butorphanol Versus Nalbuphine for Postoperative Epidural Analgesia in Lower Limb Orthopaedic Surgeries found that Onset of analgesia was earliest in Nalbuphine group (1.45±0.51 min) followed by butorphanol group (4.45±0.61 min) and maximum in ropivacaine plain group (8.30±0.97 min). The duration of analgesia was significantly prolonged in Nalbuphine group (6.40±0.821 hr) followed by butorphanol group (4.45±0.605 hr) and shortest in plain group (2.30±0.470 hr). They have concluded that Butorphanol and Nalbuphine as epidural adjuvants are equally safe and provide comparable stable hemodynamics, early onset and establishment of sensory anesthesia. Nalbuphine provides a significantly prolonged post-operative analgesia with less sedation and stable haemodynamics.

Harichandan et al,[11] compared epidural ropivacaine 0.2% with fentanyl or nalbuphine as adjuvants for post-operative analgesia in lower limb surgeries. they hve concluded that epidural nalbuphine in a dose of 2.5 mg with 0.2% ropivacaine provided a longer duration of analgesia (398.45 vs. 222.88 min) with better pain score and lesser sedation which was useful for post-operative patient compliance and satisfaction when compared to 25 mcg of fentanyl.

Swarna Banerjee et al,[12] observed that the addition of fentanyl produced faster onset of analgesia with adverse effects like sedation and pruritus than butorphanol and nalbuphine when given epidurally along with 0.125% bupivacaine. Butorphanol administered epidurally has advantage of longer duration of analgesia than fentanyl or epidural nalbuphine with side effects like nausea vomiting and sedation. Nalbuphine had better duration of analgesia with fewer side effects.

S Manojprabhakar et al,[13] observed that the mean duration of analgesia was longer in Nalbuphine group

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(387.83 + 38.32mins) when compared to Fentanyl group (343.60 + 25.64 min). They have concluded that Nalbuphine as an epidural adjuvant to bupivacaine provides better postoperative analgesia with lesser hemodynamic alterations and very minimal side effects for patients undergoing lower limb surgeries.

Babu S et al,[14] in their study compared thoracic Epidural Ropivacaine with Nalbuphine and Ropivacaine with Butorphanol for Post-Operative Analgesia in the Emergency Laparotomies. Nalbuphine group had good quality of analgesia and stable cardiorespiratory parameters for the initial 6 h of postoperative period, after which they were comparable in both groups. Furthermore, the need of rescue analgesia was higher (20%) in the Butorphanol group during the first 6 h. The side-effect profile was comparable with a little higher incidence of nausea in both groups.

Kaushal et al,[15] compared intrathecal nalbuphine with buprenorphine as adjuvants in lower limb orthopedic procedures and discovered that neither group experienced many adverse effects. For lower limb orthopedic procedures, intrathecal buprenorphine is a better adjuvant to 0.5% bupivacaine because it prolongs the sensory block and delays the delivery of the first dose of rescue analgesia.A statistically significant difference (p=0.001) was observed in the mean duration of the sensory block between the buprenorphine group (269.01 ± 9.77 minutes) and the nalbuphine group (186.30 ± 4.34 minutes). Likewise, there was a statistically significant difference in the mean duration of the motor block between the buprenorphine (194.03 ± 6.29) and nalbuphine (184.08 ± 4.14) groups (p=0.001).

Fornier et al,[16] discovered that when 400 mg of nalbuphine or 160 mg of morphine were injected intrathecally and dissolved in 4 ml of normal saline, nalbuphine exhibited a significantly quicker onset of sensory blockade and a shorter duration of analgesia compared to morphine.

The limitations in our study: There are very few studies comparing nalbuphine epidurally with other drugs and these studies evaluated only the duration of post operative analgesia and the incidence of side effects with nalbuphine. Most of the studies on nalbuphine which evaluated the sensory and motor blockade were done in intrathecal route of administration. So few parameters like onset and duration of sensory blockade evaluated in this study were not in agreement with other studies where nalbuphine was given intrathecally.

CONCLUSION

This prospective, randomized, single blind study, where in Nalbuphine in a dose of 10mg was added epidurally to 0.5% Bupivacaine for infra umbilical surgeries concludes that Epidural Nalbuphine hastens the onset of sensory blockade and significantly prolonged the duration of anaesthesia and postoperative analgesia, with stable haemodynamics.

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