

Original Research Article


A comparative study of epidural 0.5% bupivacaine with nalbuphine and 0.5% bupivacaine with fentanyl in lower abdominal and lower limb surgeries

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Abstract

Background: Epidural opioids have unique advantages over conventional, intermittent IV/ IM administration, in that patients given epidural opioids have fewer respiratory complications and can be mobilized sooner in the postoperative period.

Aim: To compare the effects of epidural 0.5% Bupivacaine with nalbuphine and 0.5% bupivacaine with fentanyl in lower abdominal and lower limb surgeries.

Materials and methods: This prospective, randomized, single blind study, where in Epidural Nalbuphine (10 mg) with 0.5% bupivacaine and epidural fentanyl (50 µg) with 0.5% bupivacaine in lower abdominal and lower limb surgeries.

Results: There were statistically no significant difference between mean age, weight, gender, ASA grading, types of surgeries and baseline parameters in both groups. The duration of surgery and time of onset of sensory blockade, motor blockade and peak motor blockade were not statistically significant ($p > 0.05$). The duration of sensory blockade was highly significant ($p < 0.01$). Duration of motor blockade was not statistically significant ($p > 0.05$). Mean heart rates in both the groups were significant only at 6th, 7th, 8th, 9th and 10th hours. Mean arterial pressures in both the groups were significant only at 3rd, 6th, 7th, 8th, 9th and 10th hours. 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. The pain scores were similar in both the groups in the first six hours of postoperative period. Number of rescue

analgesics required in the first 24 hours of post-operative period in group B were significantly higher ($p < 0.01$) when compared with group A. 4 patients (13.2%) in Group B experienced respiratory depression which is significant statistically.

Conclusions: Epidural Nalbuphine with 0.5% bupivacaine significantly prolongs the total duration of sensory blockade with better postoperative analgesia when compared to epidural fentanyl with 0.5% bupivacaine, with stable hemodynamics and less side effects.

Key words

Epidural Fentanyl, Nalbuphine, Bupivacaine.

Introduction

Analgesia, one of the components of triad of anaesthesia, has now extended to relief of postoperative pain, chronic pain and cancer pain. The spinal cord has taken the center stage in analgesia practice following the demonstration of analgesia with intrathecal morphine by Yaksh and Rudy (1977) [1]. In 1947, Manuel Martínez Curbelo (1906–1962) was the first to describe placement of a lumbar epidural catheter [2]. Deposition of drugs in the epidural and subarachnoid space paved a new era for pain relief.

Epidural anesthesia [3, 4] offers a wide range of applications than the spinal anaesthesia. 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 knowledge of specific opiate receptors in the substantia gelatinosa of the posterior horn of spinal cord resulted in wide spread use of epidural opiates in the treatment of acute and chronic pain (Pert and Snyder, 1973) [5]. A local anaesthetic – opioid combination provides superior analgesia during perioperative and postoperative period.

Epidural opioids have unique advantages over conventional, intermittent IV/ IM administration, in that patients given epidural opioids have fewer respiratory complications and can be mobilized

sooner in the postoperative period. Though pure opioid agonists like morphine and fentanyl has already established its role in epidural administration for pain relief, its side effects like respiratory depression, nausea, vomiting, urinary retention etc., has made physician to search for a better drug for epidural employment. The agonist/antagonist opioid agent Nalbuphine can be expected to offer some scope in this respect, since the respiratory depression reaches ceiling level at higher dose of this drug.

This study was designed to evaluate the effectiveness of relief of pain, onset of pain relief and side effects due to epidural administration of bupivacaine with nalbuphine mixture and bupivacaine with fentanyl in patients who had undergone lower abdominal and lower limb surgeries.

Materials and methods

The present study was done at Gandhi Medical College, Secunderabad during 2015- 2017 on 60 patients in between age group of 20-60 years of ASA grade I and II undergoing elective infra-umbilical surgeries after obtaining approval for the study from Institutional Ethics Committee. Written consent was obtained from all the patients.

Inclusion criteria: Patients posted for elective infra-umbilical surgeries under ASA Grade I and II including both males and females.

Exclusion criteria: Obese patients, uncontrollable hypertension, uncontrollable diabetes mellitus, severe CVS abnormalities, renal or hepatic failure, with history of

continuous measurements were presented on Mean \pm SD and results on categorical measurements were presented in Number (%). Significance was assessed at 5 % level of significance. Significant (P value: 0.01<P< 0.05) and highly significant (P value: P<0.01) were considered.

Results

There were statistically no significant difference between mean age, weight, gender and ASA grading in both groups (**Table – 1**). There was statistically no significant difference in the types

of surgeries between the two groups (**Table – 2**). There was statistically no significant difference in the baseline parameters between the two groups (**Table – 3**).

The duration of surgery and time of onset of sensory blockade, motor blockade and peak motor blockade are not statistically significant (p> 0.05) (**Table – 4**). The duration of sensory blockade was highly significant (p < 0.01). The duration of motor blockade was not statistically significant (p > 0.05) (**Table – 5**).

Table - 1: Comparison of demographic data in both groups.

Demographic Parameters		Group A (n=30)	Group B (n=30)	p value
Age in years (Mean \pm S.D)		38.43 \pm 9.56	39.06 \pm 9.83	0.802
Weight in kg (Mean \pm S.D)		63.03 \pm 9.44	62.7 \pm 9.59	0.894
Sex	Male	22 (73%)	23 (77%)	0.72
	Female	8 (27%)	7 (23%)	0.72
ASA	Grade 1	12 (40%)	12 (40%)	1.0
	Grade 2	18 (60%)	18 (60%)	1.0

Table - 2: Types of surgeries performed.

Type of surgery	Group –A		Group –B	
	Frequency	Percentage	Frequency	Percentage
TVH	3	10	3	10
Herniorrhaphy/ plasty	15	50	14	47
Varicose veins	4	13	5	17
Appendicectomy	5	17	4	13
Below knee Amputation	3	10	4	13
Total	30	100	30	100

Table - 3: Comparison of baseline variables.

Baseline Parameters	Group A (Mean \pm S.D.)	Group B (Mean \pm S.D.)	p value
Heart rate	81.73 \pm 9.34	81.23 \pm 8.98	0.8333
Systolic blood pressure	127.6 \pm 7.96	125.76 \pm 7.49	0.3603
Diastolic blood pressure	83.23 \pm 5.36	80.1 \pm 7.78	0.07475
Mean arterial pressure	98.1 \pm 5.1	95.13 \pm 6.92	0.06344
Respiratory rate	15.8 \pm 0.80	15.9 \pm 1.047	0.7446

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 – 2**).

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 – 3**).

Table - 4: Comparison of variables in both groups.

		Mean	S.D	p value
Duration of surgery in mins	Group A	65.16	11.56	0.3667
	Group B	67.83	11.19	
Onset of sensory block in mins	Group A	5.76	1.61	0.92
	Group B	5.80	1.47	
Onset of motor blockade in mins	Group A	12.6	1.49	0.066
	Group B	13.3	1.41	
Time taken for peak motor blockade in mins	Group A	21.86	2.37	0.118
	Group B	22.93	2.88	

Table - 5: Duration of sensory and motor blockades between the two groups.

Variable		Mean	S.D	S.E.	p value
Duration of sensory blockade	Group A	285.33	27.76	5.06	< 0.01
	Group B	247	19.68	3.59	
Duration of motor blockade	Group A	170.4	13.23	2.41	0.0616
	Group B	163	16.64	3.03	

Figure - 2: Comparison of heart rates between the two groups.

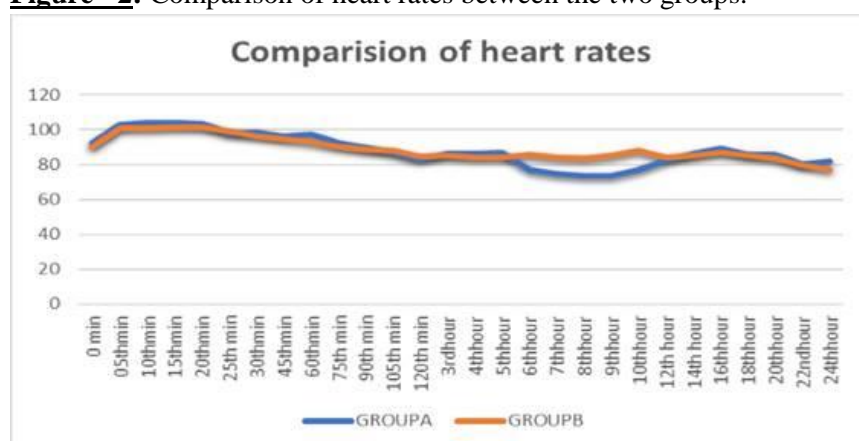


Figure - 3: Comparison of Mean arterial pressures between the two groups.

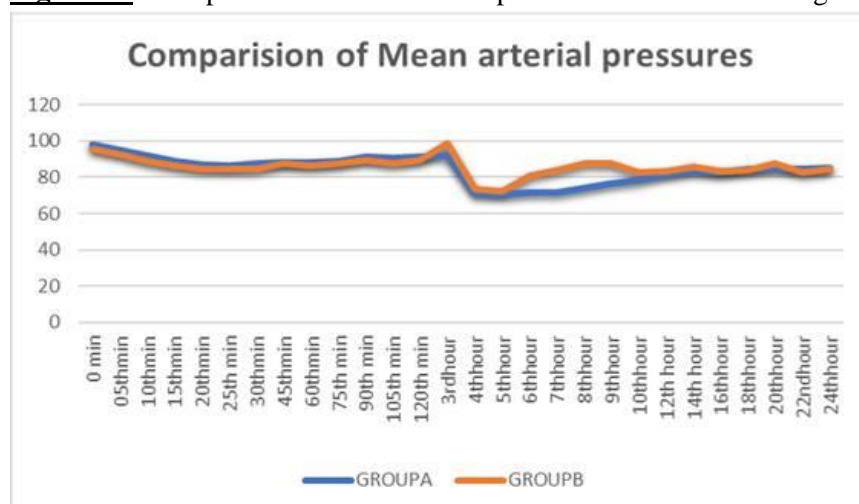


Figure - 4: Comparison of respiratory rates between the two groups.

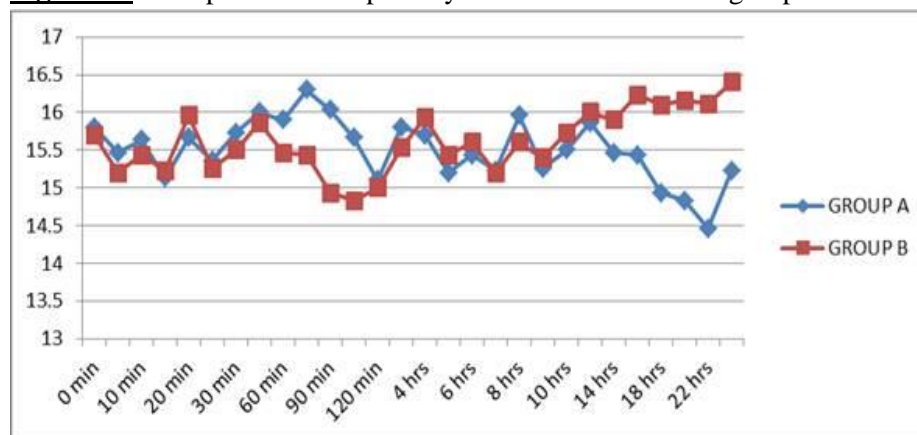


Table - 6: Comparison of vas scores between the two groups.

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%)

Table - 7: Comparison of side effects in between both the groups.

Side effects	Group- A		Group- B		p value
	n	%	n	%	
Nausea and vomiting	1	3.3 %	3	10 %	0.3
Respiratory depression	-	-	4	13.3%	0.04 (p<0.05)
Urinary retention	-	-	-	-	
Pruritus	-	-	3	10%	0.07
Hypotension	2	6.6 %	3	10 %	0.63
Bradycardia	1	3.3 %	2	6.6%	0.5
Shivering	1	3.3 %	2	6.6%	0.5

There was statistically no significant difference in respiratory rates between the two groups (**Figure - 4**).

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. 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. Number of rescue analgesics required in the first 24 hours of postoperative period in group B were significantly

higher ($p < 0.01$) when compared with group A (**Table - 6**).

4 patients (13.2%) in Group B experienced respiratory depression which is significant statistically. All the side effects were treated immediately (**Table - 7**).

Discussion

In present study Demographic data comparing age, sex, weight shows no statistically significant difference among both the groups.

Onset of sensory blockade is taken as the time from the completion of the injection of the study drug till the patient does not feel the pin prick at T12 level on the dependent side. Mean time of sensory blockade in our study was Group- A was 5.76 min and Group- B - 5.80 min. The time of onset of sensory blockade was not significant ($p > 0.05$). In group A the minimum time was 3 minutes and maximum 8 minutes. In group B the minimum time was 4 minutes and maximum 9 minutes.

Kamel HS, et al. [6] compared the effects of epidural nalbuphine and clonidine added as adjuvants to bupivacaine for full term primigravida in labor. The shortest onset time of analgesia was recorded in the bupivacaine and nalbuphine group. H.M. Santosh Kumar, et al. [8] compared the effects of epidural bupivacaine with buprenorphine over epidural bupivacaine with fentanyl for lower limb surgeries. Onset of analgesia in bupivacaine with fentanyl group was 6.6 min, which is comparable to our study. Suraj Dhale and Vaishali Shelgaonkar [9] in 2000, studied different doses of epidural fentanyl (25 μg , 50 μg , 75 μg) with 0.5% bupivacaine for perioperative analgesia found that 50 μg had a quicker onset of analgesia within which is close to our observation.

In this study also, rapid onset in group A and group B patients is due to synergistic effect of nalbuphine and fentanyl with bupivacaine. High lipid solubility and high potency may explain the faster onset of pain relief. High lipid solubility results in fast distribution to opioid receptors present in spinal cord and CNS and increases its final concentration there.

R. Fournier, et al. [10] studied and reported the administration of intrathecal nalbuphine resulting in a significantly faster onset of sensory blockade. 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 minutes. In group B the minimum time was 10 minutes and maximum 15 minutes with a

meantime of 13.3 minutes. This is in agreement with other studies.

Tiwari AK, Tomar GS [11] evaluated the effects of addition of 2 different doses of intrathecal nalbuphine to intrathecal hyperbaric 0.5% bupivacaine in infra umbilical surgeries. The onset of motor blockade was similar in all groups.

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 minutes. In group B the minimum time was 18 minutes and maximum 30 minutes with a mean time of 22.93 minutes.

Santosh Kumar, et al. [8] compared the effects of epidural bupivacaine with buprenorphine over epidural bupivacaine with fentanyl for lower limb surgeries. The mean time to achieve complete motor blockade was 18.9 min in bupivacaine with buprenorphine group and 18.63 in bupivacaine with fentanyl group which was statistically insignificant in both the groups which is comparable to our study.

The duration of sensory blockade was statistically highly significant ($p < 0.01$). In group A the minimum time was 240 minutes and maximum 320 minutes with a meantime of 285.33 minutes. In group B the minimum time was 200 minutes and maximum 280 minutes with a mean time of 247 minutes. The findings in the present study were consistent with those of other studies.

Manisha Sapate, et al. [11] compared the effects of addition of nalbuphine to intrathecal bupivacaine. The duration of sensory blockade was significantly prolonged in nalbuphine group compared to bupivacaine group. Tiwari AK, Tomar GS [12] evaluated the effects of addition of 2 different doses of intrathecal nalbuphine to intrathecal hyperbaric 0.5% bupivacaine in infra umbilical surgeries. The duration of sensory blockade were significantly prolonged in

nalbuphine groups when compared with bupivacaine group. Arghya Mukherjee, et al. [13] compared intrathecal bupivacaine alone with three different doses of nalbuphine added to bupivacaine. The duration of sensory blockade was significantly and progressively prolonged in all the three groups of nalbuphine when compared with bupivacaine group.

The duration of motor blockade was not significant ($p > 0.05$). In group A the minimum time was 150 minutes and maximum 200 minutes with a meantime of 170.4 minutes. In group B the minimum time was 140 minutes and maximum 200 minutes with a mean time of 163 minutes. This is in comparison with other studies.

Kamel HS, et al. [6] compared the effects of epidural nalbuphine and clonidine added as adjuvants to bupivacaine for full term primigravida in labor. The duration of motor blockade was similar in both groups. Manisha Sapate, et al. [11] compared the effects of addition of nalbuphine to intrathecal bupivacaine. Mean duration of motor blockade was similar in both groups. Tiwari AK, Tomar GS [12] evaluated the effects of addition of 2 different doses of intrathecal nalbuphine to intrathecal hyperbaric 0.5% bupivacaine in infra umbilical surgeries. The duration of motor blockade was comparable in both groups.

It was one of the explicit aims in the present study to measure the quality of analgesia. The duration of analgesia was taken as the time from the administration of epidural anaesthesia till the requirement of first rescue analgesic. It was measured using VAS at every 5mins in first half an hour then at 15 min up to two hours and there afterwards every 1 hour for 24 hours. Rescue analgesics were given when the VAS score was 5 or more. Quality of analgesia is taken as number of rescue doses in first 24 hours.

In the present study, VAS scores in the first 6 hours were less than 5 in all patients in group A (100%) whereas only 24 (80%) of patients had

scores less than 5 in group B. During 6 to 12 hrs in the post-operative period, 9 patients in group A (30 %) had VAS scores 5 or more whereas 24 patients in group B (30%) had VAS scores more than 5. After 12 hours up to 24 hours in the post-operative period, 28 patients in group A (93 %) had VAS scores 5 or more whereas all patients in group B (100%) had VAS scores more than 5.

The total number of rescue analgesics required in the first 24 hours in the post-operative period was statistically significant. ($p < 0.01$). In group A, the minimum number of rescue analgesics required was 1 and maximum were 2 with a mean of 1.67. In group B, the minimum number of rescue analgesics required was 2 and maximum were 3 with a mean of 2.57. These findings were in agreement with other studies.

Manisha Sapate, et al. [11] compared the effects of addition of nalbuphine to intrathecal bupivacaine. Duration of postoperative analgesia was 8 to 9 hours (566 ± 15.5 min) in bupivacaine and nalbuphine group compared to 2 to 3 hours (159.5 ± 18.42 min) in bupivacaine group. Tiwari Ak, Tomar GS [12] evaluated the effects of addition of 2 different doses of intrathecal nalbuphine to hyperbaric 0.5% bupivacaine in infra umbilical surgeries. They concluded that nalbuphine hydrochloride (400 μ g) significantly prolongs the duration of sensory blockade and postoperative analgesia. H.M. Gomaa, et al. [14] Compared intrathecal nalbuphine with intrathecal fentanyl as an adjuvant to hyperbaric bupivacaine in cesarean section. They concluded that the duration of post-operative analgesia was more prolonged in nalbuphine group. Arghya Mukherjee, et al. [13] compared intrathecal bupivacaine alone with three different doses of nalbuphine added to bupivacaine, the duration of analgesia was significantly and progressively prolonged in nalbuphine groups when compared with control group.

In the present study, 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. 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. The mean arterial pressures were more in group B when compared with group A. More stable hemodynamic pattern was seen in group A. This difference in hemodynamics could be due to poor post-operative analgesia in group B when compared with group A.

The findings are in agreement with other studies. Santosh Kumar, et al. [8] compared the effects of epidural bupivacaine with buprenorphine over epidural bupivacaine with fentanyl for lower limb surgeries. In bupivacaine with fentanyl group, MAP from baseline 98.97 mmHg fell to 87.90 mmHg at 45 min then picking up slowly to 93.7 mmHg at 120 min thereafter remained significantly high throughout the study which is comparable to our study. Manisha Sapate, et al. [11] compared the effects of addition of nalbuphine to intrathecal bupivacaine. There was statistically significant difference in hemodynamic parameters like heart rate, mean, systolic and diastolic BP, but clinically these parameters were within normal limits and did not require any intervention.

Tiwari AK, Tomar GS [12] evaluated the effects of addition of 2 different doses of intrathecal nalbuphine to hyperbaric 0.5% bupivacaine in infra umbilical surgeries. There were statistically no significant differences hemodynamically. H.M. Gooma, et al. [14] Compared intrathecal nalbuphine with intrathecal fentanyl as an adjuvant to hyperbaric bupivacaine in cesarean section. Both groups were comparable in providing hemodynamic stability. Kamel HS, et al. [6] compared the effects of epidural nalbuphine and clonidine added as adjuvants to bupivacaine for labor analgesia. Only nalbuphine group showed stable hemodynamics throughout the whole study. Vandenberg, et al. [15] Compared equipotent doses of nalbuphine, tramadol, pethidine and placebo in reducing the hemodynamic stress response to laryngoscopy

and tracheal intubation. Only nalbuphine group showed decreased hemodynamic stress response when compared with other three groups.

The respiratory depression was monitored by observing the respiratory rate and Oxygen saturation (SpO₂). A fall in respiratory rate below 10 breaths per min or fall in SpO₂ less than 95 % were considered suggestive of respiratory depression. There was statistically significant difference in respiratory depression between the two groups. There was no decrease in respiratory rate or SpO₂ in nalbuphine group as seen with fentanyl which is pure opioid agonists. The findings in this study were in correlation with many other studies.

Kamel HS, et al. [6] compared the effects of epidural nalbuphine and clonidine added as adjuvants to bupivacaine for labor analgesia. There was no significant respiratory depression in the mothers in all groups. There were no significant changes in the fetal arterial blood gas analysis indicating no fetal depression in all groups. Tiwari AK, Tomar GS [12] evaluated the effects of addition of 2 different doses of intrathecal nalbuphine to hyperbaric 0.5% bupivacaine in infra umbilical surgeries. There was no significant respiratory depression in both nalbuphine groups and bupivacaine group. Culebras, et al. [16] compared the analgesic efficacy and adverse effects of intrathecal nalbuphine, at three different doses, and intrathecal morphine for postoperative pain relief after cesarean deliveries. There was no maternal or newborn respiratory depression in both groups. Neonatal conditions (Apgar scores and umbilical vein and artery blood gas values) were similar for all groups.

Arghya Mukherjee, et al. [13] compared intrathecal bupivacaine alone with three different doses of nalbuphine added to bupivacaine. There was no statistically significant difference in the intraoperative respiratory rate and SpO₂ between the groups.

Santosh Kumar, et al. [8] compared the effects of epidural bupivacaine with buprenorphine over epidural bupivacaine with fentanyl for lower limb surgeries. In bupivacaine with fentanyl Group, mean basal respiratory rate which was 18.4/ min fell to 16.43 at 30th min, which is comparable to our study. Shaila S Kamath, et al. [7] compared the analgesic effect of intravenous nalbuphine and tramadol in patients with post-operative pain. The mean changes in respiratory rate and oxygen saturation were not statistically significant in both groups.

No patient developed respiratory depression as measured by sequential arterial PaCO₂ measurements for 24 hours. Nalbuphine may be an alternative to meperidine for treating post anesthetic shivering.

Conclusion

This prospective, randomized, single blind study, where in Epidural Nalbuphine (10 mg) with 0.5% bupivacaine and Epidural Fentanyl (50 µg) with 0.5% bupivacaine in lower abdominal and lower limb surgeries concludes that Nalbuphine and fentanyl when used with Bupivacaine has comparable onset of time for sensory blockade and comparable motor blockade properties. Epidural Nalbuphine with 0.5% bupivacaine significantly prolongs the total duration of sensory blockade with better postoperative analgesia when compared to Epidural Fentanyl with 0.5% bupivacaine, with stable hemodynamics and less side effects.

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