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Clinical Study of Epidural Nalbuphine vs Tramadol for Postoperative Pain Relief in Lower Limb Orthopedic Surgeries

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Abstract

Context: Achieving satisfactory postoperative analgesia with epidural opioids has been the subject of research many times. *Aims:* To evaluate postoperative pain relief in patients administered with epidural nalbuphine or tramadol for lower-limb surgery under combined spinal-epidural anesthesia. *Settings:* Tertiary hospital, Kanchipuram Dist, Tamil Nadu. *Design:*Prospective observational study. *Materials and Methods:* The study was done on patients undergoing lower-limb orthopedic procedures. The patients were assigned to either epidural nalbuphine (N) Group or epidural tramadol (T) Group. The convenience sampling technique was used until each group had 40 subjects. Group N received epidural 0.125 % bupivacaine with nalbuphine 0.2 mg/ml infusion@6ml/hr and Group T with epidural 0.125 % bupivacaine with tramadol2mg/ml infusion@6ml/hr started at sensory regression to T10 for postop analgesia. The pain severity was assessed using Visual Analog Scale (VAS) and sedation was assessed using Pasero Opioid-induced Sedation Scale (POSS). Intravenous paracetamol was used as rescue medication. *Statistical analysis used:* Chi-square test and unpaired *t*-test. *Results:* The mean sedation at 2 hrs was 1.65 ± 0.8 in tramadol and 2.8 ± 0.41 in the nalbuphine group. The difference was statistically significant (p - value < 0.001). The mean VAS at 12 hrs was 1.06 ± 0.4 in tramadol and 1.26 ± 0.44 in nalbuphine. At 24 hrs it was 0.86 ± 0.41 in tramadol and 1.05 ± 0.34 in nalbuphine group, with statistically significant differences (p - value < 0.05). In the tramadol group, 5 (12.5%) had vomiting and 6 (15%) were administered with IV paracetamol. *Conclusions:* Nalbuphine was more effective in providing postoperative pain relief compared to Tramadol. Tramadol was associated with a higher incidence of nausea and vomiting.

Keywords: Nalbuphine; Tramadol; Postoperative Analgesia; Sedation; Nausea; VAS.

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Introduction

Spinal anesthesia is a well-known technique used for lower-limb orthopedic surgeries. It is known for its rapid onset of action, simplicity to perform and good muscle relaxation while requiring lower drug dosage and lower incidence of the failed block.[1,2] However, the duration of spinal anesthesia is shorter which in turn shortens postoperative analgesia. Due to this, various adjuvants are added to improve the quality and duration of spinal blockage.[1] A combined spinal-epidural technique is another option where the local anesthetic opioid combination can be used as an intermittent or continuous epidural infusion to provide postop analgesia.

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Opioids are one of the commonly added adjuvants to the local anesthesia. Tramadol, a centrally acting analgesic, is commonly used for the control of postoperative analgesia.[3] Tramadol has a dual mechanism of action. It acts on opioid receptors as well as inhibits neuronal uptake of norepinephrine and serotonin. Due to this nonopioid action, tramadol has a lesser risk of producing respiratory depression than other opioids.[4] However, a higher incidence of nausea and vomiting is one of the concerns for the use of tramadol in postoperative patients.[5,6]

Nalbuphine is a synthetic opioid analgesic with agonist-antagonist activity and acts as an antagonist at μ-receptors and agonists at *k*-receptors to provide reasonably potent analgesia.[7] Studies have shown that nalbuphine was associated with lesser incidence of nausea and vomiting as compared to tramadol during the postoperative period.[5] However, it was associated with complications like respiratory depression, undesirable sedation, and urinary retention.[1]

Evaluation of postoperative analgesic effect of various adjuvants is of great importance to anesthesia practice and its effectiveness is an essential step toward identifying better pain management strategies and developing guidelines for better practice.[8] Moreover, there are a lack of well-designed Indian studies comparing nalbuphine and tramadol. Hence, the study was done to evaluate and compare the efficacy and safety of epidural infusion of 0.125% bupivacaine with either nabuphine or tramadol.

Subjects and Methods

The study was a prospective observational study conducted among 80 participants admitted in our tertiary care hospital. Adult patients (18–70 years of age) with the American Society of Anesthesiologists physical status class I and II undergoing elective lower limb orthopedic procedures performed under combined spinal-epidural anesthesia were included in the study.

Patients not willing to give consent, patients with bleeding diathesis or on anticoagulant therapy, morbidly obese patients and patients with cardiac, renal, hepatic & neurological disorders were excluded from the study. Convenience sampling was done to recruit the study participants in either epidural nalbuphine or epidural tramadol group. Participants were serially included in the study till both groups had 40 patients each. The study commenced after obtaining institutional ethics committee approval and written informed consent from the patients.

After connecting monitors, the Intravenous line was started. Preanesthetic medications included intravenous glycopyrrolate (4 μg/kg) and ondansetron (0.1 mg/kg). Coloading was done with 500 ml of ringer lactate. Under aseptic precautions first, the epidural catheter was placed in L1-L2 space using the Loss of Resistance technique. Then spinal anesthesia was given with 3.5 ml of 0.5% bupivacaine heavy at L3-L4 space using a 25 g quincke needle.

The patients randomly received either bupivacaine nalbuphine or bupivacaine tramadol epidural infusion for postoperative pain relief. The epideural infusion was started after sensory regression to T11 level.

Group N - 0.125 % bupivacaine with nalbuphine, 0.2 mg/ml infusion@6ml/hr

Group T- 0.125 % bupivacaine with tramadol, 2 mg/ml infusion@6ml/hr

Pain severity was assessed by the Visual Analog Scale (VAS). The score was assessed as 0, no pain and 10, worst imaginable pain. Intravenous paracetamol was administered as rescue medication on patients demand.

Sedation was assessed by Pasero Opioid-induced Sedation Scale (POSS).[9] The scores were as follows: 1 awake and alert; 2, slightly drowsy, easily aroused; 3, frequently drowsy, arousable, drifts off to sleep during the conversation; and 4, somnolent, minimal or no response to verbal or physical stimulation.

Nausea and vomiting were assessed on a 5-point scale: 0, no nausea or vomiting; 1, mild nausea, no treatment required; 2, nausea only, antiemetic prescribed until resolution; 3, vomiting, antiemetic prescribed until resolution; and 4, nausea/vomiting that did not respond to antiemetic. Ondansetron was used as an antiemetic for the control of vomiting. Assessment of all scores was performed every 2 hours after surgery till 24 hours.

Sample size calculation

The sample size was calculated assuming the expected mean and standard deviation of the sedation score in the nalbuphine as μ_1, σ_1 (1.3, 0.3) and in the tramadol as μ_0, σ_0 (1.5,0.3), as per the pervious study by Chatrath V et al.[10] The other parameters considered for sample size calculation included were 80% power of study and 5% two sided alpha error. The required sample size was calculated using the following formula as proposed

by Kirkwood BR et al.[11]

Formula used for sample size calculation

$$N = \frac{(u+v)^2\,(\sigma_1^2+\sigma_0^2)}{(\mu_1-\mu_0)^2}$$

N = Sample size

σ_1, σ_0 = Standard deviations (σ_1 = 0.3 and σ_0 = 0.3)

u = Two sided percentage point of the normal distribution corresponding to 100% - the power = 80%, u = 0.84

v = Percentage point of the normal distribution corresponding to the (two sided) significance level for significance level = 5%, v = 1.960.

The required sample size as per the above-mentioned calculation was 35 in each group. To account for a nonparticipation rate/loss to follow up rate of a about 10%, another 4 subjects will be added to the sample size. Hence, the final required sample size was rounded off to 40 subjects in each group.

Statistical Methods

Sedation and VAS were considered as primary outcome variables. Postoperative complications and use of rescue analgesia was considered as secondary outcome variables.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Data was also represented using appropriate diagrams like a bar diagram, pie diagram and box plots.

All Quantitative variables were checked for normal distribution within each category of explanatory variables by using visual inspection of histograms and normality Q-Q plots. Shapiro-Wilk test was also conducted to assess normal distribution. Shapiro-Wilk test p - value of > 0.05 was considered as a normal distribution.

For normally distributed Quantitative parameters the mean values were compared between study groups using Independent sample t-test (2 groups). Categorical outcomes were compared between study groups using Chi-square test. p - value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.[12]

Results

A total of 80 subjects were included in the final analysis. Most participants were aged between 61 and 70 years. In the tramadol group, 30 (75%) participants were males and 10 (25%) were females. In the nalbuphine group, 28 (70%) were males and 12 (30%) were females. The age and gender were comparable between the groups. (p - value > 0.05), (Table 1).

Table 1: Comparison of gender between group (N = 80)

Age Group	Group		Chi-square	p - value
	Tramadol (N = 40)	Nalbuphine (N = 40)		
< 20	2 (5%)	2 (5%)	0.784	0.978
21–30	9 (22.5%)	6 (15%)		
31–40	7 (17.5%)	8 (20%)		
41–50	6 (15%)	7 (17.5%)		
51–60	4 (10%)	4 (10%)		
61–70	12 (30%)	13 (32.5%)		
Gender				
Male	30 (75%)	28 (70%)	0.251	0.617
Female	10 (25%)	12 (30%)		

Among the tramadol, Proximal Femoral Nailing (PFN), Intramedullary Nailing (IMNL), Anterior Cruciate Ligament **(**ACL) repair, hemiarthroplasty and plating were more common surgeries performed. In patients receiving nalbuphine,

Table 2: Comparison of procedure between group (N = 40)

Procedure	Group	
	Tramadol (N = 40)	Nalbuphine (N = 40)
Anterior Cruciate Ligament Repair	7 (17.5%)	3 (7.5%)

Procedure	Group	
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)
Dynamic Hip Screw (DHS)	1 (2.5%)	5 (12.5%)
External Fixation (Ex Fix)	0 (0%)	3 (7.5%)
Plating	4 (10%)	0 (0%)
Hemiarthroplasty	5 (12.5%)	2 (5%)
Ilizarov	2 (5%)	0 (0%)
Intramedullary Nailing (IMNL)	6 (15%)	6 (15%)
Proximal Femoral Nailing (PFN)	14 (35%)	18 (45%)
Total Hip Replacement (THR)	1 (2.5%)	3 (7.5%)

*No statistical test was applied-due to 0 subjects in the cells.

Proximal Femoral Nailing (PFN), Intramedullary Nailing (IMNL) and Dynamic Hip Screw (DHS) was more commonly performed, (Table 2).

The mean sedation score (SED) at 2 hours was 1.65 ± 0.8 in tramadol group and it was 2.8 ± 0.41 in nalbupine group. The difference in the SED at 2 hrs between the group was statistically significant (*p* - value < 0.001). The differences were insignificant at 4, 6, 8 12 and 24 hours, (Table 3).

Table 3: Comparison of sedation between the two groups at different follow-up time periods (*N* = 80)

Parameter	(Mean ± SD)		*p* - value
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)	
Sedation 2 hrs	1.65 ± 0.8	2.8 ± 0.41	< 0.001
4 hrs	2.78 ± 0.42	2.83 ± 0.38	0.582
6 hrs	2.95 ± 0.22	3 ± 0	0.156
8 hrs	3 ± 0	3.38 ± 1.33	0.079
12 hrs	3 ± 0	3 ± 0	*
24 hrs	3 ± 0	3 ± 0	*

The mean VAS at 12 hrs was 1.06 ± 0.4 in tramadol group and it was 1.26 ± 0.44 in nalbupine group. The difference in the VAS at 12 hrs between the group was statistically significant (*p* - value 0.035). The mean VAS at 24 hrs was 0.86 ± 0.41 in tramadol group and it was 1.05 ± 0.34 in nalbupine group. The difference in the VAS at 24 hrs between the nalbupine group was statistically significant (*p* - value 0.028). Whereas, at 2, 4, 6 and 8 hours, the difference was not significant, (Table 4).

Table 4: Comparison of mean of VAS between the two groups at different follow-up time periods (*N* = 80)

Parameter	(Mean ± SD)		*p* - value
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)	
VAS 2 hrs	2.5 ± 0.99	2.2 ± 0.41	0.079
4 hrs	1.83 ± 0.55	1.79 ± 0.47	0.743
6 hrs	1.66 ± 0.57	1.6 ± 0.44	0.585
8 hrs	1.41 ± 0.48	1.3 ± 0.46	0.289
12 hrs	1.06 ± 0.4	1.26 ± 0.44	0.035
24 hrs	0.86 ± 0.41	1.05 ± 0.34	0.028

Tramadol was associated with a higher incidence of vomiting and about 6 (15%) participants in tramadol group required rescue analgesic (IV

Table 5: Comparison of complications and rescue analgesic between group (*N* = 80)

Complications	Group	
	Tramadol (*N* = 40)	Nalbuphine (*N* = 40)
Vomiting	5 (12.5%)	0 (0%)
Rescue Analgesic (IV paracetamol)	6 (15%)	0 (0%)

*No statistical test was applied-due to 0 subjects in the cells.

paracetamol). One participant needed 2 doses and 5 participants needed 1 dose of rescue analgesis (Table 5).

Discussion

The postoperative pain is a concern among most of the patients undergoing orthopedic surgical procedures. Insufficient pain relief is a common concern among these patients, which may adversely affect their quality of life and functions.[5,13] Opioid analgesics such as tramadol and nalbuphine are commonly used for the management of postoperative pain. In the present study, most participants belonged to the higher age group of 61–70 years. This was in accordance to many other previous studies.[6,14]

In the present study, the mean sedation score was significantly higher in the nalbuphine group compared to the tramadol group at 2 hrs. Gupta, KL et al.[1], in their study concluded that nalbuphine is a good sedative and provides good postoperative pain relief. Saxena, D et al.[15], in their study determined tramadol to be a safe and effective adjuvant to epidural bupivacaine for prolongation of the total duration of analgesia in lower-limb surgeries. Chatrath, V et al.[10], found 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. Solanki, RN et al.[6], concluded in their study that nalbuphine produces better pain relief and hemodynamic stability in the postoperative period in patients undergoing orthopedic surgeries when compared to tramadol. However, many comparative studies conducted in the past have concluded that the mean sedation scores did not differ between the groups for lower-limb surgery unlike the current study.[5,6]

In the present study, the mean VAS score was significantly higher in the nalbuphine group at 12 hrs and 24 hrs postsurgery. Chatrath, V et al.[10], also found that the mean VAS score in the nalbuphine group was found to be significantly lesser compared to the tramadol group. The quality of surgical analgesia was excellent in 40 (100%) patients in the nalbuphine group, which was seen only in 36 (90%) patients in the tramadol group. Solanki RN et al.[6], found similar results in their study.

In the present study, the tramadol group was associated with a higher incidence of nausea and vomiting 5 participants and 6 participants needed rescue analgesics. In the study by Solanki, RN et al.[6], Vyas, V et al.[5], Chatrath, V et al.[10], it was found that tramadol resulted in early pain relief but a higher incidence of nausea and vomiting. Sharma, K et al.[16], in their study found that mild respiratory depression and sedation was reported with Nalbuphine. Nausea vomiting was significantly high with Tramadol. A number of rescue analgesic doses were also found lesser in the other comparative studies.[5,6,10]

Conclusion

Epidural nalbuphine was a better choice in providing postoperative pain relief in patients undergoing orthopedic surgical procedures under combined spinal-epidural anesthesia. Tramadol was associated with a higher incidence of nausea and vomiting.

Key Messages

Epidural nalbuphine as well as epidural tramadol provide good postoperative pain relief. The nalbuphine is a superior drug in patients undergoing orthopedic surgical procedures under combined spinal-epidural anesthesia in terms of slightly better VAS and sedation scores.

Tramadol is associated with higher incidence of postoperative complication such as nausea, vomiting and use of rescue medication as compared to nalbuphine.

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Declarations

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