

**ORIGINAL RESEARCH ARTICLE****EPIDURAL BUTORPHANOL FOR POST OPERATIVE ANALGESIA IN LOWER LIMB SURGERIES:
A COMPARATIVE STUDY WITH EPIDURAL TRAMADOL**GP Deo^{1*}, SK Shrestha¹, IN Shrestha¹¹ Department of Anaesthesiology & Critical Care, Chitwan Medical College, Bharatpur, Nepal***Correspondence to:** Dr Gopendra Prasad Deo, Department of Anaesthesiology & Critical Care, Chitwan Medical College, Bharatpur, Nepal.Email: gopendradeo@gmail.com**ABSTRACT**

To compare the efficacy of epidural butorphanol and tramadol for post operative analgesia in lower limb surgeries. Randomized, controlled, double blind, prospective study conducted at Department of Anaesthesia and Critical Care, Chitwan Medical College from September 1st 2015 to August 31st 2016. 60 patients of ASA Grade I and II of either sex, aged between 18-65 years willing for epidural analgesia for post operative analgesia were included in the study. They were divided into two groups: Group B- Butorphanol group and Group T- Tramadol group. Subjects of Group B received 2mg of Butorphanol and 0.25% Bupivacaine making a total volume of 10 ml and that of Group T received 100mg of Tramadol and 0.25% Bupivacaine also making a total volume of 10 ml. Analgesic efficacy was assessed by Visual Analogue Scale (VAS). The onset and duration of analgesia along with side effects were also assessed. The quality of analgesia was studied using time to independent mobilization and overall patient satisfaction. Total number of patients was 60, of ASA Grade I and II, aged between 18-65 years. The mean age of patients in Group B was 42.6±11.7 years and 46.1±11.2 years in Group T. Time of onset of analgesia after epidural injection was 7.4±0.9 minutes in Group B and 12.7±1.5 minutes in Group T and the difference was found to be statistically significant. Duration of analgesia was 317.1±99.1 minutes and 438.8±136.6 minutes in Butorphanol and Tramadol groups respectively which was also statistically significant. Sedation was significantly higher in butorphanol group whereas nausea and vomiting was higher in tramadol group. Quality of analgesia in terms of patient satisfaction was better with epidural butorphanol. Both epidural tramadol and butorphanol were effective in relieving post operative pain however butorphanol had lesser side effects and greater patient satisfaction compared to tramadol but the duration of action was relatively short.

Key words: Butorphanol, Epidural analgesia, Post-operative analgesia, Tramadol.**INTRODUCTION**

Adequate postoperative pain management is an integral part of the management of all surgeries. Postoperative pain gives rise to various physiological and psychological phenomenon and can be detrimental to health and recovery of patients. The provision of good quality post operative analgesia is important not only to ease patients suffering and induce sense of well being, but also vital for early mobilization, less post operative complications and early discharge¹.

Epidural analgesia remains superior route for thoraco-abdominal and lower limb surgeries since it preserves the pulmonary function and provides early mobilization with lesser risk of deep vein thrombosis. Epidural administration of local anesthetics produces

adequate analgesia albeit of a shorter duration and so, to prolong it, opioids are added. Epidural morphine provides good post operative analgesia but is associated with undesirable side effects like respiratory depression, urinary retention, nausea, vomiting and pruritus².

Both butorphanol, a mixed agonist antagonist opioid and tramadol, a moderately potent opioid agonist has been used for postoperative analgesia. So, this prospective, randomized, controlled, double blind study was designed to compare the efficacy of epidural butorphanol and tramadol as post operative analgesics.

MATERIAL AND METHODS

After obtaining approval of CMC-IRC and informed consent, 60 patients with ASA physical status I and II of either sex between 18 to 65 years undergoing lower limb surgeries were included. Exclusion criteria included were patient's refusal for epidural analgesia or subarachnoid block, ASA physical status III or more, age less than 18 years and more than 65 years, failed or partial effect of subarachnoid block, history of hypersensitivity to butorphanol or local anesthetics, uncontrolled hypertension, known coronary artery disease and patient requiring general anaesthesia. Patients were familiarized with visual analogue scale (VAS) scoring pre-operatively and taught to grade their pain on scale.

All patients were premedicated with tablet Diazepam (0.2 mg/kg body weight), the night before and Ranitidine 150 mg and Alprazolam 0.25 mg orally as premedicants 2 hours before surgery. In the operation theatre, an intravenous line was secured and was connected to multichannel monitor showing electrocardiography, noninvasive blood pressure (NIBP), respiratory rate and pulse oximeter. The patients were preloaded with lactated ringer solution 15ml/kg over 15 to 30 minutes. All the patients were planned under combined spinal epidural anaesthesia.

After proper positioning, with all aseptic precautions, local anaesthesia was infiltrated. Then epidural space was identified in L₂-L₃ or L₃-L₄ space using 18G Tuohy's needle using loss of resistance to air technique. An epidural catheter was introduced through the Tuohy's needle and was advanced 3-4 cm in the epidural space. Correct placement of catheter was checked with a test dose of 3 ml of 2% lidocaine with epinephrine (1: 200000) given through epidural catheter. Following insertion of the epidural catheter, subarachnoid block was given to all the patients, using a 25 gauge Quincke Babcock needle, through an intervertebral space below the epidural catheter insertion. After free flow of clear cerebrospinal fluid, a dose of 0.3mg/kg body weight of hyperbaric 0.5% bupivacaine was injected. Patient was then positioned as needed for the surgery. No opioids or sedatives were given via any route to any of the patients in perioperative period.

During resolution of subarachnoid block, post-

operative pain was evaluated using a 100 mm visual analogue scale (VAS) which consists of 100mm line drawn on a 3x5 inch card with 0 indicating no pain while 100 represents worst imaginable pain. The post operative pain assessment was done by an observer unaware of assigned medication group. Each patient was instructed to mark the scale at the point which he or she felt was representative of level of pain. When the patient indicated that pain was 40mm or more or asked for pain relief, study medication was given via epidural catheter according to their assigned group in a double blind fashion.

The groups were:

Group B - Bupivacaine 0.125% + Butorphanol 2 mg (total volume=10ml)

Group T - Bupivacaine 0.125% + Tramadol 100 mg (total volume=10ml)

The study drugs were prepared by a doctor who was not a part of the team. Patients were randomly allocated into 2 groups of 30 patients each by computer generated randomization. The study was carried out in double blind fashion by making 60 coded slips. The person performing the procedure and carrying out the observation was blinded to the drug solution injected. Each medication was diluted to a total of 10 ml with sterile preservative free saline injection. The 10 ml syringe containing the study drug was labeled with patient's code number. Each patient was instructed that he or she could request for supplemental medication at any time during the study.

Baseline visual analogue score (VAS) along with blood pressure, respiratory rate, pulse rate was recorded at the time of epidural drug administration and was then monitored continuously for one hour in post operative care unit for onset of analgesia (VAS reduction by 10 mm), time to VAS score <10mm if achieved and lowest VAS score (VAS_{min}) and corresponding physiological parameters. The patients were then monitored half hourly until VAS is more than 40 mm or asked for pain relief. Once patient asked for pain relief or VAS was more than 40, the allocated medication was given epidurally and this was used as end of patient's participation in the study.

The following pain variables were determined:

- The onset of analgesia was defined as the time in minutes from full injection of the study medication to initial reduction in pain intensity (using VAS) of at least 10 mm on two consecutive evaluations³.
- Time to VAS score < 10 mm³
- Lowest VAS score (VAS_{min})³
- The duration of analgesia was defined as the time between onset of analgesia and either a return to baseline VAS or the time when additional pain medication was requested (whichever occurs first)³.
- VAS pain scores when the patient received the study medication (VAS baseline) and VAS scores when patient requested additional medication (VASend)³.

Patient who reported no decrease in VAS for 30 minutes and requested for additional analgesics within 30 minutes was given injection Pethidine intravenously as rescue medication and assuming epidural catheter not in proper place, the patient was excluded from the study.

When a patient requested for analgesia after cessation of the effect of first dose of study medication, the time interval immediately preceding the request was used as the end point of study duration and second dose of study drug was injected. No patient was withheld of analgesic at any time for the purpose of the study. The quality of analgesia was assessed by patient satisfaction and time to independent mobilization (the time patient started sitting independently from supine position). Overall satisfaction of the patient was assessed by using 100 points visual analogue scale (0 no satisfaction, 100 best satisfaction)⁴.

Side effects and complication;

Patients were monitored closely to observe and treat any complications.

Each patient was evaluated 4 hourly for the next 24 hours for side effects like sedation, nausea, vomiting, pruritus and hallucination. On occurrence of any of the side effect, it was treated accordingly when

needed.

Sedation Score⁵

0. Awake and oriented
1. Dozing intermittently but easily arousable
2. Sedated, sleeping but arousable
3. Difficult to arouse or unarousable

Nausea Vomiting Score⁶

0. No nausea, no vomiting
1. Light nausea, one episode of vomiting
2. Moderate nausea, two vomiting episode
3. Severe nausea, three or more vomiting episodes

Respiratory Depression Score⁷

1. Normal rate
2. 8-12 breaths/min
3. < 8 breaths/min

Pruritus Score⁸

0. No pruritis
1. Mild pruritis, no treatment required
2. Moderate pruritis, treatment required

Statistical analysis:

After the study was completed, the data were coded and decoded and patients were sorted into two groups on the basis of drug administered. Data were analysed on the basis of numerical or categorical variable. In numerical variable, Parametric test as independent t test was applied and in categorical variable, nonparametric test as Chi square test was applied to identify whether the data was statistically significant or not. Data were entered in a master chart in MS Excel 2007 and analyzed by Statistical Package for Social Science (IBM SPSS) version 20. Findings were considered statistically significant when p-value was less than 0.05 and were considered highly significant when p-value was less than 0.001.

RESULTS

Sixty cases were taken in the study, having ASA physical status Grade I and II, aged between 18-65 years willing for epidural analgesia for post-operative analgesia in the duration from 1st Sept. 2015 to 31st Aug. 2016 in Department of Anaesthesia and Critical Care, Chitwan Medical College and Teaching

Hospital. They were divided into 2 equal groups. All 60 patients enrolled completed the study. No technical difficulty or inadvertent dural puncture was encountered. Both groups were comparable with regards to age, sex, weight, duration of surgery and time from end of surgery to epidural administration of study medication (table 1).

Table 1: Distribution of demographic data of patients

Parameters		Group B	Group T	P value
Age (years)	Mean±SD	42.6±11.7	46.1±11.2	0.245 ^Δ
Sex	Male	12(40%)	13(43.3%)	0.793 ^Ψ
	Female	18(60%)	17(56.7%)	
Weight	Mean±SD	54.6±11.3	53.6±6.3	0.695 ^τ
Duration of Surgery (minutes)	Mean±SD	87.0±20.8	85.8±25.7	0.847 ^Δ
Time to study medication (minutes)	Mean±SD	50.7±14.1	52.3±19.3	0.673 ^Δ

^Δ P-value computed by equal variance assumed by independent t test, ^Ψ p-value computed by chi square test, ^τ P-value computed by unequal variance assumed by independent t test.

All the baseline parameters at the time of study medication including VAS_{baseline} were comparable. (Table 2)

Table 2: Baseline parameters at the time of administration of study medication among the groups

Parameters	Group B	Group T	P value
Vas Baseline (mm)	42.0±4.1	42.3±6.3	0.808
HR (bpm)	82.8±11.2	85.7±9.9	0.299
SBP (mmHg)	124.6±13.1	126.2±10.3	0.601
DBP (mmHg)	80.8±9.4	81.8±8.0	0.669
RR (per min)	16.7±2.6	18.5±2.9	0.014

P-value computed by equal variance assumed by independent t test, p-value <0.05 is considered to be significant.

The onset of analgesia was faster with butorphanol but the duration of analgesia was longer with tramadol (Table 3).

Table 3: Pharmacokinetic Profile: Onset of analgesia

Parameters	Group B	Group T	P value
Onset time (min)	7.4±0.9	12.7±1.5	<0.001
Duration of analgesia (min)	317.1±99.1	438.8±136.6	<0.001

P-value computed by unequal variance assumed by independent t test, p-value <0.05 is considered to be significant.

Table 4 shows sedation was higher in Butorphanol Group however nausea & vomiting was seen in Tramadol Group .

Table 4: Side Effects

Parameters	Group B	Group T	P-Value
Sedation	28 (93.3%)	13 (43.33%)	<0.001
Nausea & Vomiting	0	4 (13.33%)	0.002
Pruritus	0	1	
Respiratory Depression	0	0	
Bradycardia	0	0	
Dry Mouth	0	0	
Hallucination	0	0	

Table 5 shows even though there was no statistically significant difference between two groups in terms of time to independent mobilization, satisfaction was better with Butorphanol.

Table 5: Quality of analgesia

Parameters	Group B	Group T	P-value
Time to independent mobilization (hrs)	30.6±6.4	31.7±5.6	0.453
Satisfaction	85.3±7.8	78.0±9.6	0.002

P-value computed by equal variance assumed by independent t test, p-value <0.05 is considered to be significant

DISCUSSION

Effective postoperative pain control is an important component of postoperative recovery and a prime concern for anaesthesiologists. The goal of modern postoperative pain management is to minimize suffering and enhance recovery and rehabilitation through blunting maladaptive reflexes³. Epidural route is being used extensively for post operative pain control. The advantages of epidural route include the use of lower doses, longer duration of effects and lower incidence of side effects⁹. Combined spinal epidural anaesthesia finds a common place for perioperative management of lower limb surgeries, having advantages of both spinal anaesthesia and epidural analgesia, initially providing an intense sensory and motor blockade of rapid onset, followed by post operative pain management by epidural analgesia, after regression of spinal analgesia.

Epidural injection of local anesthetics provides good analgesia at the cost of motor block and sympathetic block. Motor block is quite distressing as it delays mobilization and sympathetic block may cause hypotension. In addition, it has shorter duration of action⁹. Epidural morphine is effective in relieving post operative pain for longer duration but is associated with delayed respiratory depression, urinary retention, nausea & vomiting along with pruritus¹⁰. So, this prospective, randomized, double blind dose response study was designed to compare the efficacy of epidural butorphanol and tramadol as post operative analgesics.

This study involved 60 patients randomized in 2 equal groups. All the patients had received total of 10 ml of 0.125% of plain bupivacaine with either 2 mg of butorphanol in group B or 100 mg of tramadol in group T. The mean time of onset of analgesia was 7.4±0.9 minutes in group B and 12.7±1.5 minutes in group T suggesting onset was faster with epidural butorphanol. The results were comparable with the study done by Swathi et al¹¹ which also showed that onset of action was faster with butorphanol. Our study shows that tramadol had a longer duration of analgesia compared to butorphanol for postoperative epidural analgesia and the results were statistically significant. Mean duration of action of epidural butorphanol was 317±99.1 minutes and that of epidural tramadol was 438.8±136.6. Similar results were found in the study done by Swathi et al¹¹ and Gupta et al¹².

Comparing VAS scores, it was found that VAS score was not statistically significant between two groups before giving drugs. After 30 minutes, it was found that VAS score was significantly lower in both groups. VAS scores were significantly lower in Butorphanol group than Tramadol group at various time intervals suggesting that pain relief was significantly better in Butorphanol group. Significant reduction in VAS scores were also observed by Swathi¹¹ et al, Pokharel et al¹³, Bharti et al¹⁴, Palacios et al¹⁵ and Rawal et al¹⁶.

Nausea and vomiting was observed in none of the patients in Group B and 4 patients in group T which is statistically significant. Tramadol is known to cause higher incidence of nausea and vomiting¹⁷. So drugs to control nausea and vomiting should be given when tramadol is used. Sedation was seen in 28 out of 30 patients of Group B and 13 out of 30 patients in group T which was highly significant (p<0.001). Mild sedation is desirable in the post operative period. Higher incidence of sedation in Butorphanol group and higher incidence of nausea and vomiting in Tramadol group were also seen in study done by Abboud et al¹⁰ and Gupta et al¹². Patients who received epidural butorphanol reported significantly higher level of somnolence in a similar study done by Gambling et al.¹⁸ Similarly, in the study done by Bailey et al¹⁹ sedation was seen more frequently in the groups receiving butorphanol. Pruritis was observed in 1 of the patient who received tramadol.

None of our patients ever had a respiratory rate of less than 12 breaths/min. The finding was similar with the studies done by Abboud et al¹⁰ and Palacios et al¹⁵. All the patients maintained a respiratory rate greater than 12 throughout the study period in the similar study done by Hunt et al²⁰.

We have used time to independent mobilization and patient's satisfaction to assess quality of analgesia and have inferred that quality of analgesia is better with butorphanol. Though there was no statistically significant difference in time to independent mobilization, overall satisfaction was better with butorphanol and the results were found to be statistically significant ($p= 0.002$)[Table 5].

There are some obvious limitations of our study. First, although epidural administration of tramadol has been extensively used for analgesia by numerous investigators in clinical studies, more studies are needed to assess the safety of its intrathecal administration for post operative analgesia. Second, clinically significant respiratory depression was not observed in our study but respiratory rate being less sensitive, it is better to measure PaCO₂. Not measuring PaCO₂ was a limiting factor in our study. Third, the result of our study could have been more precise if the sample size of study group would have been large, but the patients who gave consent for epidural analgesia were limited in our institution.

Thus it can be concluded from this study that epidural Butorphanol is a safe and effective method of providing post operative pain relief with lesser side effects and greater patient satisfaction compared to tramadol but of relatively shorter duration.

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