

## A comparison between epidural Butorphanol and Tramadol for postoperative analgesia, sedation and side effects using CSEA technique for surgeries below the level of umbilicus

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### Abstract

**Background and Aims:** Epidural analgesia using low doses of local anesthetic agent with or without adjuvants like opioids is a popular, simple, effective and economical way of providing postoperative analgesia. We proposed to evaluate and compare the efficacy of epidural opioids, Butorphanol and Tramadol using Combined Spinal Epidural Analgesia (CSEA) technique for surgeries below the level of umbilicus for postoperative analgesia, sedation and side effects.

**Methods:** In this prospective, double blind, randomized controlled clinical trial, 60 patients aged 18 to 60 years, ASA grade 1 or 2 posted for planned elective surgery below the level of umbilicus were selected.

**Study Design:** The patients were randomly allocated into 2 groups to receive postoperatively either 1 mg of inj. Butorphanol (dissolved in 10 ml of normal saline) (**Group B**) or 50 mg of inj. Tramadol (dissolved in 10 ml of normal saline) (**Group T**) epidurally as a bolus dose when the VAS score for pain was more than 4 after the conclusion of surgical procedure as the effect of spinal anaesthesia started wearing off.

**Statistics and Results:** The mean duration of analgesia with tramadol (group T) 6.481 ( $\pm$  0.86842) hrs. was significantly higher than with butorphanol (group B) i.e., 5.352 ( $\pm$ 0.33258) hrs with a p value of 0.0001. Pain scores were also significantly lower statistically in group B as compared to group T. Sedation scores were significantly higher in group B than group T, which was statistically highly significant (p= 0.0001)

**Conclusion:** Both epidural, butorphanol and tramadol provided good postoperative analgesia. The duration of analgesia was longer with tramadol, quality of analgesia was better with butorphanol, sedation more with butorphanol as compared to tramadol and other side effects were comparable

**Keywords:** Epidural, tramadol, butorphanol, postoperative analgesia.

### 1. Introduction

Combined spinal and epidural anaesthesia technique (CSEA) [1] is a regional anaesthetic technique which combines benefits of spinal anaesthesia and epidural anaesthesia and analgesia. Postoperative analgesia is very essential for immediate postoperative pain relief using systemic analgesics, oral or parental, epidural analgesia, local infiltration at site of surgery and local nerve blocks. Epidural analgesia using local anesthetic agents is a popular, simple, effective and economical way of providing postoperative analgesia. Due to short duration of local anesthetics, opioids have been added, so that even small doses can provide profound analgesia of good duration with few side effects [2] Several combinations of local anaesthetics ( LA's) and adjuvants such as tramadol, sufentanyl, clonidine and

fentanyl have been employed in the search for near ideal agent, which remains elusive[3] Butorphanol tartrate, a synthetic morphinian derivative is a mixed agonist-antagonist non narcotic analgesic of the phenanthrene series while tramadol is a centrally acting opioid agonist of aminocyclohexanol group. Both butorphanol, a mixed agonist antagonist opioid and tramadol hydrochloride a moderately potent opioid agonist have been used for this purpose separately in few studies [3,4] We conducted this study, to compare epidural Butorphanol and Tramadol for postoperative analgesia, sedation and side effects using CSEA technique for surgeries below the level of umbilicus

### 2. Materials and Methods

With institutional ethics committee approval[IEC/ IRB No: 12/ 2011(D)]a randomized, double blind,

prospective study was done on 60 patients of ASA status (1 or 2) aged between 18- 60 years for planned elective surgery below the level of umbilicus under combined spinal epidural anaesthesia

Patients were randomly allocated into 2 groups, Group B (Butorphanol) who received 2 mg of inj. Butorphanol diluted in normal saline (total volume 10 ml) postoperatively through epidural catheter followed by 1mg top up doses, Group T (Tramadol) who received 100 mg of Inj. Tramadol, diluted in normal saline (total volume 10 ml) postoperatively through epidural catheter followed by 50 mg top up doses.

Patients with skin infection at the puncture site, coagulopathy, hypersensitivity to local anesthetics, asthma, cardiac, renal, hepatic or CNS disorders, and pregnant females were excluded from the study

Detailed preanaesthetic checkup was done and patients were explained about linear visual analogue score (VAS) using 11 markings on a 10 centimeter line, where “0”denotes “no pain” while “10” denotes “worst pain imaginable”. The nature and safety of the procedure was explained and written, valid, informed consent was obtained. Randomisation of the 2 groups of 30 patients each was done in a double blind manner by making 60 coded slips. Person performing the procedure and carrying out observations was blinded to the drug solution injected. The drug solutions were prepared in 2 separate syringes of 10ml, one for bolus and other for top up doses.

In the operation theatre, adequate starvation status was confirmed. Patient’s baseline heart rate (HR), blood pressure (B.P), electrocardiogram and peripheral arterial oxygen saturation (SpO<sub>2</sub>) were obtained. Intravenous line was secured and an infusion of ringer’s lactate was started.

Under all the aseptic precautions, CSE was initiated with double puncture technique, epidural was given at L<sub>2-3</sub>, L<sub>3-4</sub>, with loss of resistance technique and catheter was inserted and spinal was given one space lower using 25 G spinal needle with 2.5 to 3 ml of 0.5% bupivacaine. Sensory and motor levels of block were assessed with constant monitoring of all the vital parameters all through the surgery.

At the end of surgery, the levels of sensory and motor block were noted. When VAS for pain reached 4, then epidural bolus from 10 ml syringe was given to all patients depending upon the group allocated. Group B (n=30) received 2 mg of inj. Butorphanol dissolved in normal saline (total volume 10 ml) and Group T (n=30) received 100 mg of inj. Tramadol dissolved in normal saline (total volume 10 ml) Further, epidural top up doses of 1mg inj. Butorphanol dissolved in normal saline (total volume 10 ml) and 50 mg of inj. Tramadol dissolved in normal saline (total volume 10 ml) were given when pain of VAS >4. In case more doses were required, the supervisor provided additional doses filled in 10 ml syringe according to the group.

Patients were assessed at half hourly interval for first 2 hrs, then 4, 8, 12, 24 hours after giving 1<sup>st</sup> dose of epidural opioid. Visual Analogue Scale (VAS) {0 = No pain,1-3 = Mild pain, 4-7 = Moderate pain,8-10 = Severe pain} Sedation Score ( 0 = Fully awake,1 = Slightly drowsy, 2 = Asleep but easily arousable, 3 = Fully asleep and not arousable, vital parameters (HR, BP, RR and SpO<sub>2</sub>)Side effects (nausea, vomiting, retention of urine, pruritis and respiratory depression, hypotension, bradycardia) were assessed

Rescue Analgesia was decided depending on timing of incremental doses, interval between injections and total dose given in 24 hours. If analgesia was poor even after two consecutive epidural doses given 20-30 minutes apart, patients were given inj. diclofenac 75 mg intramuscularly as rescue analgesia.

At the end of the study decoding of groups was done and to analyse the results, means ± standard deviation (SD) range of all the monitored parameters were calculated. The results were analysed using student’s t-test for testing the significance of postoperative pain score and duration of analgesia between the groups. The chi –square test was used to test the demographic variables, number of epidural dosages required over 24 hrs and postoperative side effects. p value was calculated. A p value of <0.05 was considered statistically significant

### 3. Observations and Results

All 60 patients enrolled in the study, completed the study according to the protocol and were included in the analysis. The demographic criteria like age, sex, ASA status, duration of surgery and the sensory level achieved were comparable in both groups and there was no statistically significant difference between two groups (p > 0.05) (Table- 1 A,B,C,D)

**Table 1A: Demographic Data (Age and Sex)**

	<b>Group B (mean ±S.D)</b>	<b>Group T (mean ±S.D)</b>	<b>P Value</b>
<b>Age (years)</b>	36.17 ± 6.634	38.2±5.027	0.186
<b>Sex (F:M)</b>	7:23	5:25	0.519

From Table 1A, it can be seen that the mean age in Group B was 36.17 (± 6.634) years and group T, was 38.2 (± 5.027) years. Difference in age between the two groups was statistically not significant (p value of 0.186) Out of 30 patients in groups B, 23 were male (76.7%) and 7 were female (23.3%). Out of 30 patients in group T, 25 were male (83.3%) and 5 were female (16.7%). Difference in sex between two groups was statistically not significant (p value of 0.519). That means that the age and sex were comparable in both the groups.

**Table 1B: ASA Grading**

		Group B		Group T		p value
		No. of patients	% of patients	No. of patients	% of patients	
ASA grade	Grade I	28	93.3%	28	93.3%	1.0
	Grade II	2	6.7%	2	6.7%	
	Total	30	100.0%	30	100.0%	

Table 1B shows that out of 30 patients in group B, 28 were ASA grade I and 2 were ASA grade II, similarly in group T also, 28 were ASA grade I and 2 were ASA grade II, with a p value of 1.0 which shows that there was no statistical difference between the two groups regarding ASA status

**Table 1C: Duration of Surgery**

	Group B (mean ±S.D)	Group T (mean ±S.D)	P Value
Duration of surgery (hrs)	2.389± 0.1965	2.358± 0.1320	0.486

Table 1C shows that the duration of surgery in group B was 2.389 (±0.1965) hrs. and in group T it was 2.358 (±0.1320) hrs, with a p value of 0.486 which was comparable.

**Table 1D: Sensory Level Achieved**

Sensory Level	Group B		Group T	
	No. of Pt.	% of Pt.	No. of Pt.	% of Pt.
T6	0	0%	1	3.3%
T7	2	6.7%	5	16.7%
T8	10	33.3%	5	16.7%
T9	13	43.3%	14	46.7%
T10	4	13.3%	2	6.7%
T11	1	3.3%	3	10.0%
Total	30	100.0%	30	100.0%

Also Table 1D shows that the highest sensory level achieved in group B was T<sub>7</sub> (6.7%) and in group T it was T<sub>6</sub> (3.3%) 15 patients in group B achieved T<sub>9</sub> sensory level (43.3%) whereas 14 patients in group T achieved T<sub>9</sub> sensory level (46.7%) which is nearly comparable.

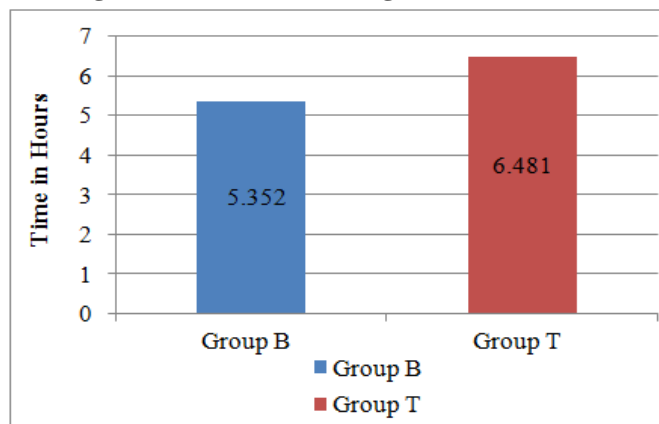
Mean baseline values of pulse rate, blood pressure and oxygen saturation (SpO<sub>2</sub>) were comparable in both the groups. There were no significant changes in these parameters within the group as well as between the two groups at different time intervals throughout the 24 hrs study period (p> 0.05) Mean interval between the time of spinal anaesthesia and time of first bolus epidural analgesic dose was comparable in two groups.

**Table 2: Duration of Analgesia after 1<sup>st</sup> Dose**

Duration of analgesia (hrs.)	Group B (mean ±S.D)	Group T (mean ±S.D)	P Value
	5.3520 ± 0.33258	6.4810 ± 0.86842	0.0001%

Mean duration of analgesia (taken from bolus injection given epidurally to the requirement of 1<sup>st</sup> top up) in group T was 6.481 (±0.86842) hrs which was significantly higher than group B, i.e., 5.352 (±0.33258) hrs. with a p value of 0.0001 (Table 2). This clearly shows that in our study Tramadol gave longer duration of analgesia than Butorphanol which was statistically highly significant (Figure 1).

**Figure 1: Duration of Analgesia after 1st Dose**



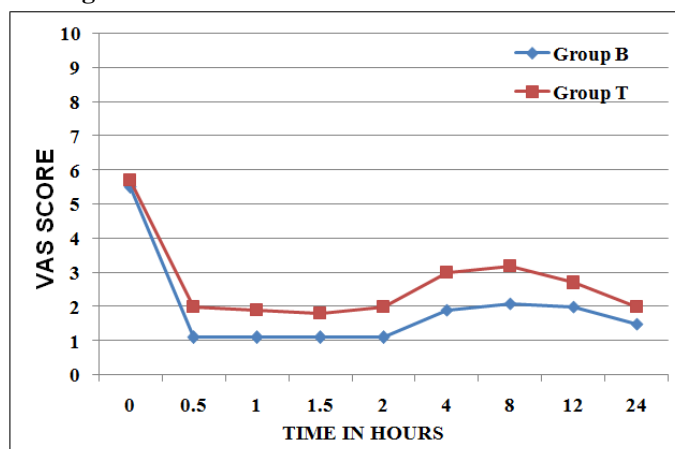
**Table 3: Visual Analogue Score Over 24 Hrs**

Interval in Hours	Group	No. of patients	Mean VAS score	Std. Deviation	P value
0	B	30	5.50	0.509	0.118
	T	30	5.70	0.466	
0.5	B	30	1.10	0.305	0.0001
	T	30	2.00	0.000	
1	B	30	1.10	0.305	0.0001
	T	30	1.90	0.305	
1.5	B	30	1.10	0.305	0.0001
	T	30	1.80	0.407	
2	B	30	1.10	0.305	0.0001
	T	30	2.00	0.000	
4	B	30	1.90	0.305	0.0001
	T	30	3.00	0.000	
8	B	30	2.10	0.305	0.0001
	T	30	3.20	0.407	
12	B	30	2.00	0.000	0.0001
	T	30	2.70	0.466	
24	B	30	1.50	0.509	0.0001
	T	30	2.00	0	

Patients were assessed for pain by evaluating Visual Analogue Score (VAS) after the 1<sup>st</sup> dose of epidural opioid, at half hourly intervals for 1<sup>st</sup> 2 hrs., then at 4, 8, 12 and 24 hours respectively. It can be seen from (Table 3) that at the time of giving the 1<sup>st</sup> dose, mean VAS score in group B was 5.5 (± 0.509 S.D.) and in group T was 5.7 (± 0.466) having a p value of 0.118. This means that there was no statistical difference between the two groups at the beginning of the study. Also at ½ hr. interval and thereafter for every interval, VAS score in group T was always higher than group B

throughout till 24hrs and the p value of 0.0001 at every interval was statistically highly significant (Figure 2).

**Figure 2: VAS Score Over 24 Hrs. After 1<sup>st</sup> Dose**



**Table 4: Sedation Score Over 24 Hrs**

Interval in Hours	Group	Number of patients	Mean Sedation Score	Std. Deviation	P value
0	B	30	0	0	0.0001
	T	30	0	0	
0.5	B	30	1.57	0.504	0.0001
	T	30	0.43	0.504	
1	B	30	1.53	0.507	0.0001
	T	30	0	0.000	
1.5	B	30	0.83	0.379	0.0001
	T	30	0	0.000	
2	B	30	0.80	0.407	0.0001
	T	30	0	0.000	
4	B	30	0.83	0.379	0.0001
	T	30	0	0	
8	B	30	0.73	0.450	0.0001
	T	30	0.00	0	
12	B	30	0.87	0.346	0.001
	T	30	0.00	0	
24	B	30	0.10	0.305	0.078
	T	30	0	0	

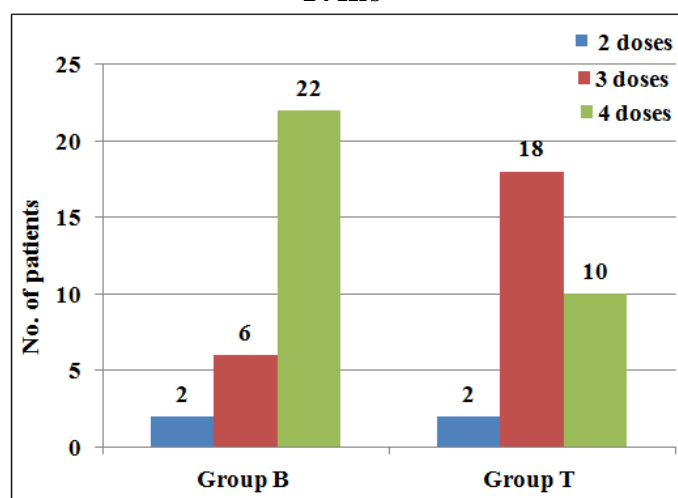
Patients were assessed for sedation score after the 1<sup>st</sup> dose of epidural opioid, at half hourly intervals for 1<sup>st</sup> 2 hrs., then at 4, 8, 12 and 24 hours respectively. It can be seen from Table 4 that at the time of giving the 1<sup>st</sup> dose, mean sedation score in group B and group T was 0. This means that the two groups were comparable. At ½ hr. and thereafter every interval the Sedation Score in group B was always higher than group T upto 12 hrs. and found to be statistically highly significant (p value of 0.001) At 24 hrs, mean sedation score between group B and group T wasn't found statistically significant (p value 0.078).

**Table 5: Epidural Dosages Required for Analgesia Over 24 Hrs**

	No. of pt.	% of pt.	No. of pt.	% of pt.	0.005
Epidural doses	2	6.7%	2	6.7%	
	3	20.0%	18	60.0%	
	4	73.3%	10	33.3%	
	<b>Total</b>	<b>30</b>	<b>100.0%</b>	<b>30</b>	

From Table 5 it can be seen that in group B, 2 patients (6.7%) required 2 epidural doses, 6 patients (20.0%) required 3 doses and 22 patients (73.3%) required 4 doses. In group T 2 patients (6.7%) required 2 doses, 18 patients (60.0%) required 3 doses and 10 patients (33.3%) required 4 doses which is statistically significant (P value of 0.005) (Figure 3).

**Figure 3: Epidural Dosages Required for Analgesia Over 24 Hrs**



**Table 6: Rescue Analgesia Required Over 24 Hrs**

No. of Rescue Analgesia	Group B		Group T		P value
	No. of pt.	% of pt.	No. of pt.	% of pt.	
0	30	100.0%	28	93.3%	0.355
2	0	0%	1	3.3%	
3	0	0%	1	3.3%	
<b>Total</b>	<b>30</b>	<b>100.0%</b>	<b>30</b>	<b>100.0%</b>	

If analgesia was found to be inadequate even after two consecutive epidural doses given 20-30 minutes apart, patients were given injection diclofenac 75 mg intramuscularly as rescue analgesia. It can be seen from (Table 6) that in group T, 2 patient required rescue analgesia wherein no patient in group B required rescue analgesia. The difference between the two groups, however, was statistically insignificant (p value of 0.355).

**Table 10: Postoperative Side Effects Over 24 Hrs**

Side effects	Group B	Group T	P Value
Nausea and vomiting	0(0%)	4(13.3%)	0.112
Bradycardia	0	0	
Hypotension	0	0	
Pruritis	0	0	
Respiratory depression	0	0	

Table 7 shows side effects in postoperative period up to 24 hours in two groups. Nausea and vomiting was seen in 4 patients in group T, whereas none of the patients in group B had nausea and vomiting. However, it was statistically not significant ( $p = 0.112$ ). Other side effects like bradycardia, hypotension, pruritis and respiratory depression were not found in either group.

#### 4. Discussion

Pain is 5<sup>th</sup> vital sign. Postoperative pain is acute pain, mostly nociceptive in nature and can progress to chronic pain. Combined spinal and epidural anaesthesia combines the advantages of both spinal and epidural technique by initially providing an intense sensory and motor block of rapid onset [3,4]. After the surgical procedure and regression of spinal analgesia, the epidural catheter can be used to provide postoperative pain relief [5] Opioids like morphine, fentanyl, tramadol and butorphanol provide effective analgesia and epidural administration has advantages over systemic administration as it provides more analgesia and less sedation as well as less systemic side effects.

In our study we compared two opioids - Butorphanol and Tramadol for epidural analgesia. The characteristics which distinguish Butorphanol and Tramadol are related to their opioid receptor spectra. Butorphanol has low affinity for  $\mu$  receptors to produce antagonism, moderate affinity for kappa receptors and minimal affinity of sigma receptors. Tramadol has moderate affinity for  $\mu$  receptors and weak affinity for kappa and delta receptors [6-9].

The purpose of our study was to compare equipotent doses of Butorphanol and Tramadol given epidurally for postoperative analgesia, sedation and side effects. The mean duration of analgesia was calculated from the time of bolus injection given epidurally to the requirement of first top up. In group T, it was 6.481 ( $\pm 0.86842$ ) hrs which was significantly higher than group B, i.e., 5.352 ( $\pm 0.33258$ ) hrs. with a p value of 0.0001 (Table 2 and Figure 1). This showed that tramadol gave longer duration of analgesia than Butorphanol which was statistically highly significant

Sayyid *et al*[10] in their study on epidural Tramadol (100 mg) for postoperative pain relief after caesarean section found the duration of analgesia to be 4.5 $\pm$ 3.1 hours. These results were different from our study (Table 2) may be because of difference in type of surgery and also because patients

received epidural anesthesia only while in our study patients were given spinal anesthesia.

Gupta *et al*[11] in their study found duration of analgesia with Butorphanol of 5.35 $\pm$ 0.29 hrs and 6.25 $\pm$ 1.58 hrs with Tramadol, which is comparable with our study

Abboud *et al* [12] found an analgesia lasting 8 hours postoperatively with 4 mg of epidural Butorphanol in patients undergoing cesarean section under epidural anaesthesia. This result was different from our study (Table 2). The probable reason may be that they gave 4 mg of Butorphanol epidurally whereas we gave 2mg and they gave along with local anaesthetic for cesarean section under epidural anesthesia

As per Table 3 and Figure 2 at the time of giving the 1st dose, mean VAS score in group B was 5.5 ( $\pm 0.509$  S.D.) and in group T was 5.7 ( $\pm 0.466$ ) having no statistical difference between the two groups at the beginning of the study (p value of 0.118) It can also be seen from Table 3 and Figure 2 that at  $\frac{1}{2}$  hr. interval and thereafter for every interval, VAS score in group T was always higher than group B throughout till 24 hrs. and the p value of 0.0001 at every interval was statistically highly significant

Palacios *et al* [13] found decreased VAS with epidural Butorphanol, their results are similar to our study whereas Rawal *et al* [1] found lower VAS scores with epidural Tramadol 100 mg when compared to our study The probable reason may be that they gave bolus Tramadol by lumbar epidural catheter and infusion of Tramadol by thoracic epidural catheter giving results different than our study.

Patients were observed for sedation score over 24 hrs postoperatively. At the time of giving the 1st dose, mean Sedation Score in group B and group T was 0 (Table 4) This means that two groups were comparable and there was no sedation present at the time of giving 1<sup>st</sup> bolus dose of either drug. At  $\frac{1}{2}$  hr. and thereafter the Sedation Score with Butorphanol was always higher than with Tramadol up to 12 hrs and found to be statistically highly significant (p value of 0.001). At 24 hrs, mean sedation score between Butorphanol group and Tramadol group wasn't found statistically significant (p value 0.078). Our study showed that Butorphanol caused more sedation than Tramadol.

Gupta *et al*[11] in their study also found that sedation was more in group of patients who received Butorphanol than Tramadol. They found sedation in 28 patients out of 30 patients with epidural Butorphanol and in 14 patients out of 30 with Tramadol which was statistically significant like in our study. This proved that Butorphanol causes more sedation than Tramadol when given epidurally.

In Butorphanol group, majority of patients required 4 epidural doses over 24 hrs postoperatively while in Tramadol group, majority of patients required 3 doses. This difference was found to be statistically significant with p value of 0.005 (Table 5 and Figure 3).

As per Table 6 and Figure 9, it can be seen that no patient in group Butorphanol required rescue analgesia by inj. Diclofenac while 2 patients in group Tramadol required rescue analgesia in 24 hrs postoperative which was statistically not significant (p value 0.355). Gupta *et al*[8] found similar results with respect to epidural doses required over 24 hrs and rescue analgesia. Gupta *et al*[11] also found that the rescue analgesia required in Butorphanol group was less than in Tramadol group

Table 10 shows side effects in postoperative period up to 24 hours in two groups. Nausea and vomiting was seen in 4 patients in Tramadol group, whereas none of the patients in Butorphanol group had nausea and vomiting. However, it was statistically not significant (p value of 0.112)

Gupta *et al* [11,14] in their study found no nausea and vomiting in Butorphanol group while few patients of Tramadol group reported nausea and vomiting which was statistically not significant. Our results are comparable. They found no respiratory depression, hypotension and bradycardia in their study. Similarly in our study, other side effects like bradycardia, hypotension, pruritis and respiratory depression were not found in either group.

Singh *et al* [15] in their study found that onset of action was faster in patients receiving Butorphanol, (78%) had onset of analgesia in 8-10 mins while 68% had onset of analgesia in 11-15 mins. in patients receiving Tramadol. Duration of analgesia was longer with Tramadol. Quality of analgesia by using VAS score was better in group 'Butorphanol' ( $0.53 \pm 0.5$ ) than group Tramadol ( $0.92 \pm 0.70$ ). There were no significant effects on blood pressure, heart rate, respiratory rate, and SPO<sub>2</sub> in both groups. The side effects associated with 'Butorphanol' group was sedation (80%), nausea and urinary retention was seen only in 1 patient in each group. In group 'Tramadol' only nausea was noted. These findings were comparable to our study.

We conclude that Butorphanol and Tramadol, both synthetic nonnarcotic opioid analgesics, provide good postoperative analgesia when given epidurally as sole agents. The duration of analgesia was longer with Tramadol as compared to Butorphanol, but the quality of analgesia was better with Butorphanol as compared to Tramadol. However, both the drugs are comparable with respect to side effects except sedation, which is more with Butorphanol.

## References

- [1] Rawal N, Holmstrom B, Crowhurst JA, Van Zundert A., The combined spinal-epidural technique. *Anesthesiology clinics of North America*, 2000; 18(2):267 - 95.
- [2] Kaur Haramritpal, Singh, Gurpreet RaniSunita, GuptaKewal Krishan *et al*. Effect of dexmedetomidine as an adjuvant to levobupivacaine in supraclavicular brachial plexus block: A randomized double-blind prospective study. *JOACP*, 2015; 31(3): 333-8.
- [3] Malik P, Manchanda C, Malhotra N. Comparative evaluation of epidural fentanyl and butorphanol for postoperative analgesia. *J Anaesth Clin Pharmacol* 2006; 22(4): 377-82.
- [4] Lakhotiya R, Tanwar GL, Jain S, Vyas KP. Epidural tramadol for postoperative pain relief. *Indian J Anaesth* 1998; 42(1): 38-42.
- [5] Wu CL. Acute postoperative pain. Miller RD. *Anesthesia*. 6<sup>th</sup>ed. Pennsylvania: Churchill Livingstone; 2005. p.2764-5.
- [6] Robert Stoelting, Simon Hillier, *Pharmacology and physiology in Anesthetic Practice* 2006; 4: 118-119.
- [7] Bowdle T. Pharmacology of analgesia. In Wylie and Churchill-Devidson's *A Practice of Anaesthesia*, Thomas EJ Healy, Paul R Knight (Ed), Arnold Publishers, London, Seventh Edition, 2003:543-563.
- [8] Gutstein HB, Akil H, *Opioid Analgesic*, Goodman and Gillman's *The Pharmacological Basis of Theurapeutic*, 2001, 10<sup>th</sup>edition; 569-619.
- [9] Fukuda K. Intravenous opioid Anaesthetics, *Miller's Anaesthesia* 2005; (6): 379-435.
- [10] Sayyid SS, Maroun MA, Sleiman D, Sfeir M, Baraka A. Epidural Tramadol for postoperative pain after cesarean section. *Candian Journal of Anaesthesia* 1999; 46(8):731-735.
- [11] Ruchi Gupta, SimmerpreetKaur, Saru Singh, K.S.Aujla. A Comparison of Epidural Butorphanol and Tramadol for Postoperative Analgesia Using CSEA Technique *J Anaesth Clin Pharmacol* 2011; 27(1): 35-38.
- [12] Abboud TK, Moore M, Zhu J, Murakawa K, Minehart M, Longhitano M, *et al*. Epidural Butorphanol or morphine for the relief of post-cesarean section pain: ventilatory responses to carbon dioxide. *Anesth Analg*. 1987; 66:887-93.
- [13] Palacios TQ, Jones MM, Hawkins JL, Adenwala JN, Longmire S, Hess KR, *et al*. Post- Cesarean section analgesia. A comparison of epidural Butorphanol and morphine. *Can J Anaesth*. 1991; 38: 24-30.
- [14] Gupta Neru, Smriti Anand, Gulati Smriti, Gupta Styadev, B B Kapoor, Comparison of Tramadol and Butorphanol for Analgesic Efficacy and Safety, *JK Science*, 2008; 10(3): 132-134.
- [15] Singh Bhagwat, Nihlani Sanjay, and Postoperative Analgesia: A Comparative Study Of epidural Butorphanol and Epidural Tramadol, *Journal of Advance Researches in Biological Sciences*, 2011; 3 (2): 86-89.