

Original Research Article

Comparative study of duration of analgesia with epidural bupivacaine and bupivacaine with tramadol in lower limb surgeries

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ABSTRACT

Background: The administration of local anaesthetic and opioid mixture via epidural route is excellent for post-operative pain during lower limb surgeries. This combination provides better quality of analgesia, lower side effects and high level of patient satisfaction. Therefore, this study was taken up to evaluate the efficacy safety, tolerance and side effects for the combination of tramadol and bupivacaine in the management of post-operative pain.

Methods: This was a prospective study where a total of 40 patients; 20 each in group I and II were selected. Patients who were admitted for lower limb surgeries in age range of 18-50yrs and belonged to ASA grade I & II. Group A was given epidural bupivacaine 0.5% and group B was given epidural bupivacaine 0.5% with tramadol 50mg. The parameters studied were onset of action, quality of anesthesia, degree of motor blockade, duration of analgesia, hemodynamic alterations, intraoperative and postoperative complications. Pain was evaluated with verbal score. Results were evaluated statistically.

Results: The mean duration of analgesia was significantly longer in patients with tramadol. The quality of analgesia and pain scores were better in patients who were administered tramadol. The number of drug doses required was significantly reduced by addition of tramadol.

Conclusions: Tramadol is a safe and effective adjuvant to epidural bupivacaine for prolongation of total duration of analgesia in lower limb surgeries.

Keywords: Analgesia, Bupivacaine, Epidural, Lower limb surgery, Tramadol

INTRODUCTION

Regional anaesthesia has proved to be safe and beneficial for lower limb surgeries. Among various regional anaesthesia techniques epidural anaesthesia has become increasingly widespread and popular in recent years because of its less side effects and better postoperative analgesia. Local anaesthetics are the drugs that cause neural blockade and thus inhibit transmission of impulse. Bupivacaine 0.25%, 0.5% solution was found to be excellent drug giving rapid onset and a profound degree of analgesia. Opioids produce analgesia by binding to opioid receptors in substantia gelatinosa of spinal cord

whereas local anaesthetics provide analgesia by blocking pain transmission at nerve roots and dorsal root ganglion.¹ Even if an extremely low concentration of local anaesthetic is added to an opioid, quality of analgesia may be superior. The administration of local anaesthetic opioid mixtures via epidural route is excellent for post-operative pain following abdominal, pelvic or orthopaedic procedures on lower extremities. Patients are found to have better preservation of pulmonary function and can ambulate early. Epidural administration of opioids in combination with local anaesthetic agents in low dose offers new dimensions in the management of post-operative pain.² The rationale for this technique in

post-operative pain management is a better quality of analgesia that can be achieved by systemically administered analgesics, a lower incidence of side effects, improved surgical outcome and high levels of patient satisfaction.²

METHODS

This study was conducted on 40 patients undergoing lower limb surgery at a tertiary level hospital in central India in 1 year. Patients of either sex in age range of 18-50 years and belonging to ASA grade I and II were selected randomly for the study. The patients weighed between 50-80 kilograms and were scheduled to undergo elective surgery. Patients with absolute contra indication for epidural block like bleeding disorder or receiving drugs like anticoagulants or Mono Amine Oxidase (MAO) inhibitors were not selected. Those patients who presented with raised intra-cranial pressure, infection at the site of injection, neurological deficit and psychiatric diseases were excluded from the study. Similarly, Patients who were chronic abusers of analgesics and benzodiazepines were also not included in the study.

A detailed preoperative assessment was done before selecting the patients for epidural analgesia by thorough history taking and clinical examination. All patients were informed about the nature and technique of the study and an informed consent was obtained from each patient. A thorough general physical examination and systemic examination was carried out. Age, Sex, height, weight and vital parameters including pulse rate (PR), blood pressure (BP) and respiratory rate (RR) were recorded. Electrocardiogram, chest X-ray, complete blood count, Prothrombin time (PT), random blood sugar and renal function tests were done and Xylocaine sensitivity was recorded. Patients were randomly allocated in two groups by picking up lots on the day of surgery. They were grouped according to the drug employed for epidural block as under:

Group-I: consisted of 20 patients who received 0.5% Bupivacaine (20ml) + (1ml) normal saline.

Group-II: consisted of 20 patients who received 0.5% Bupivacaine (20ml) + Tramadol 50mg (1ml).

Total volume administered through epidural route was 21ml. Patients in either group did not receive any other drug preoperatively for sedation or analgesia. Narcotic pre-medication was avoided so that analgesia could be attributed to bupivacaine or tramadol only. Similarly, benzodiazepine was avoided for sedation and amnesia.

All the patients were pre-loaded with 15ml/kg body weight Ringer lactate. Standard procedure was adopted for epidural block with all aseptic precautions and the drugs aforementioned were administered according to respective group. After the drug was injected following observations were recorded:

Assessment of sensory block

The cephalad spread was assessed by pinprick using a short bevel 25 gauge needle every 10 min intervals for one hour after injection of local anaesthesia and then every 30 min until the sensory level was below the inguinal ligament.

Assessment of motor block

It was assessed at the same time intervals using modified Bromage scale as follows:

Table 1: Modified Bromage Scale.

Modified Bromage Scale	
Activity	Score
Able to lift legs against gravity	0
Able to flex knee but unable to flex legs	1
Able to move feet but unable to flex knee	2
Unable to move any joints	3

Monitoring and management

Pulse rate, Blood pressure and respiratory rate were recorded every 5 min till 15 min, then every 15 min till 1 hr. After 1st hours recordings were made at 2nd, 4th, 8th, 12th and 24th hr. Thus, patient follow up was done for 24 hours.

Pulse rate

PR < 60/min was graded as bradycardia, PR > 120/min was graded as tachycardia. 0.6mg Atropine was kept ready if needed in any episode of bradycardia.

Blood pressure (BP)

Variation in BP was observed and hypotension was recorded. If systolic B.P. fell more than one third of pre-operative value, it was treated by injection mephentermine sulphate.

Respiratory rate

This was monitored intra-operatively in all the patients and any variations from the preoperative reading were recorded. All the parameters PR, B.P and RR, recorded after epidural injection and during surgery and for the first 24 hours were compared with baseline. Changes in following parameters were recorded for inter-group comparison.

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Changes in following parameters were recorded for inter-group comparison.

Duration of surgery

In this study surgeons were allowed to start the operation once pain at the operative site was absent. Duration of surgery was taken as time from the incision to skin closure.

Intra operative medication

No analgesic or preoperative medication that might influence analgesia or cause sedation was given. Patients, in whom any such medication was given, were excluded from the study.

Sedation score

Degree of sedation was closely monitored using score as suggested by Fukuda et al.³

Table 2: Sedation score.

Sedation score	
Very excited	0
Alert and tense =1	1
Sedated and sleepy with opened eyes	2
Objectively sleepy but subjectively not	3
Patient complaining of feeling sleepy	4
Drowsy and almost no response to verbal commands	5

Post-operative pain assessment

Pain assessment was done by verbal rating score. Patients were informed about this pre-operatively.

Table 3: Verbal rating Score for pain.

Verbal rating score for pain	
No pain	0
Mild pain	1 (analgesia not needed)
Moderate pain	2 (need analgesia)
Severe pain	3 (need analgesia immediately)

In the first 24 hours during follow up of the patients, analgesia was given by epidural catheter when required by the patients in the form of tramadol 100 mg (2ml) completed to 10 ml by 0.9% saline. If this was not

sufficient to control pain within 30 min, additional dose was given maximally 200 mg in one hour. If the patient was still complaining after 30 min Diclofenac sodium was given intramuscularly.

Duration of analgesia

This was calculated in both the groups from the time of onset of analgesia to the time of first analgesic requirement.

Side effects

Patients were closely observed postoperatively for 24 hours to note any side effects like sedation, shivering, micturition difficulties, pruritus, nausea and vomiting, seizures.

Statistical analysis

All the relevant data were recorded and the result thus obtained were subjected to statistical analysis. Paired and unpaired student t test were used. A significant value was considered when $P < 0.05$.

RESULTS

A total of 40 patients were studied and divided into two groups as aforementioned. Both the groups were contrasted under various parameters and statistical evaluation was done.

Demographic data

For Group 1 patients the mean age, mean weight and mean height was 29.65(+7.86), 62.75 (+7.92) and 158.4(+7.24) respectively while for Group 2 patients the respective findings were 35.1 (+8.94), 63(+7.14) and 159.3(+6.71). No statistically significant difference was observed between the two groups with regard to age, weight and height of patients and the groups were properly matched.

Sensory blockade

The time required for onset of sensory blockade, to reach maximum level and then regression to L1 level was noted.

Table 4: Time of sensory blockade (Mean + Sd)

Characteristics	Group I Mean(+SD)	Group II Mean(+SD)	P Value
Time for onset of sensory block (min)	10.55 (± 1.6)	10.35 (± 1.32)	$P > 0.05$
Time to reach max level (min)	24.95 (± 2.5)	22.75 (± 2.35)	$P > 0.05$

The maximum level of blockade was achieved between thoracic spine levels 7 to 10. No statistically significant difference between the two groups while comparing sensory block (Table 4).

Motor blockade

The time required for motor blockade for both the groups was calculated. None of them had any patient scoring Bromage scale 2. Time of regression of motor blockade from Bromage scale 1 to 0 were calculated and contrasted for each group and no statistically significant difference

between the two groups could be observed in this regard (Table 5).

Duration of analgesia

This was found out to be 194.05 (+4.55) minutes for group 1 patients. For Group 2 patients, the observed duration was 264.5(+3.41) minutes. The difference between two was highly significant (p<0.005). This indicates that tramadol increases the duration of Bupivacaine anaesthesia thereby prolonging the time to first request of any analgesic.

Table 5: Time of motor blockade (Mean + SD)

Characteristics (min)	Group I Mean(+SD)	Group II Mean(+SD)	P Value
Time for reach Bromage scale-1	32.25(+2.65)	31.75(+1.32)	P>0.05
Time to reach Bromage scale-0 level (min)	142.10(±4.587)	145.65(±2.81)	P>0.05

Variations in vital parameters

Vital parameters like pulse rate (PR), mean blood pressure (MBP) and respiratory rate (RR) were recorded for every patient of each group at serial intervals. These parameters were recorded at baseline before induction and then at 5,10,15,30 and 45 minutes after inducing the patient. Subsequently, the recordings were done at 1, 2, 4,8,12 and 24 hours after induction and following observations were made

Pulse rate

In both the groups the mean values of PR increased significantly at 4, 8 and 12 hrs in comparison with baseline values (p<0.05). There was significant difference between the two groups at 4th hour (p<0.05) (Figure 1).

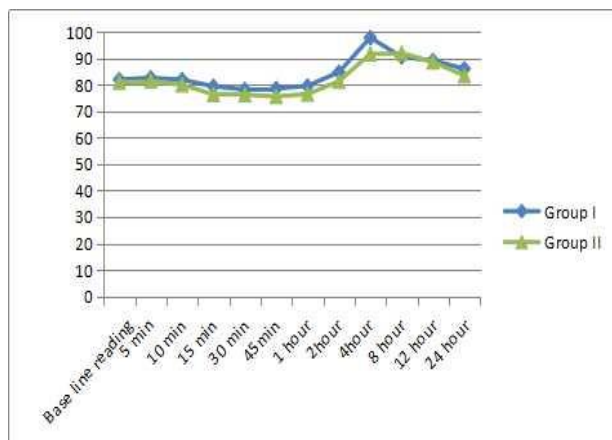


Figure 1: Comparison of variations in pulse rate between two groups.

Mean blood pressure

The values of MBP decreased significantly in the first hour after induction. The mean B.P. increased at the 4th hour in both the groups but the rise noticed in group I was significantly more than group 2. It is also noteworthy, that the decrease of MBP in group 2 after 4 hours was also significantly more as compared to group 1 (Figure 2).

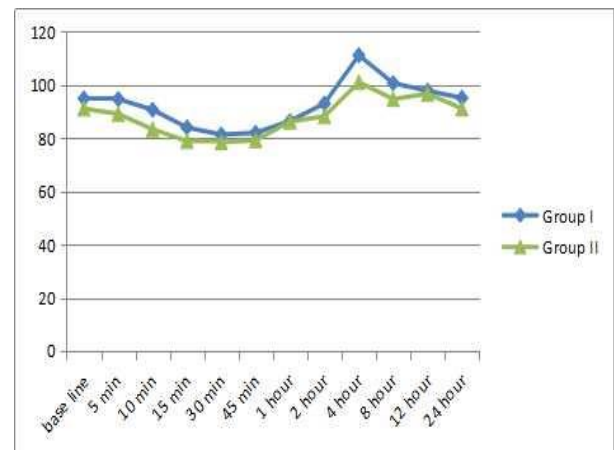


Figure 2: Comparison of variations in mean blood pressure in two groups.

Respiratory rate

The respiratory rates were near to baseline values in both the groups up to 4 hours of induction. No significant alteration in RR was found between the two groups. However, at 4th hour RR was significantly increased in both groups in comparison to the baseline values. Also, RR at 4th hour in group 1 was more than

that in group 2 and the difference was statistically significant($p < 0.05$) (Figure 3).

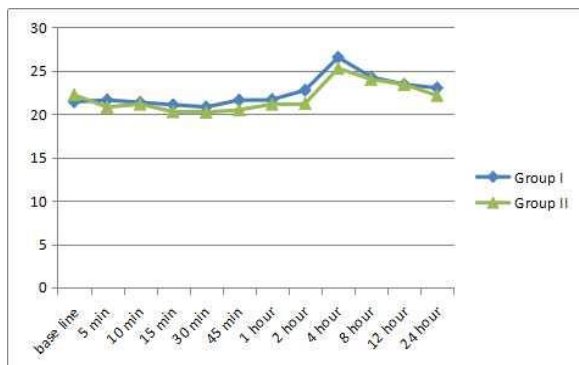


Figure 3: Comparison of variation in respiratory rate between two groups

Side-effects

Various side effects were observed among patients of both the groups. Majority of side effects were observed more among group 1 patients. No side effect was observed intra-operatively except shivering which was observed exclusively in group 1. Post operatively nausea and vomiting were the most frequent side effects seen. Both were seen more commonly in group 1 and the difference was statistically significant. No patient required metoclopramide as their frequency and severity Frequency of drug doses:

On comparing the mean number of doses of analgesic drug in each group it was found that the patients in group I required 5.05(+0.89) doses as compared to 2.05(+0.61) doses required by patients in group II. This difference was statistically significant and suggested that patients with tramadol required less doses of drug for analgesia were mild. Sedation was more commonly

observed amongst group 2 patients although the findings were not statistically significant (Figure 4).

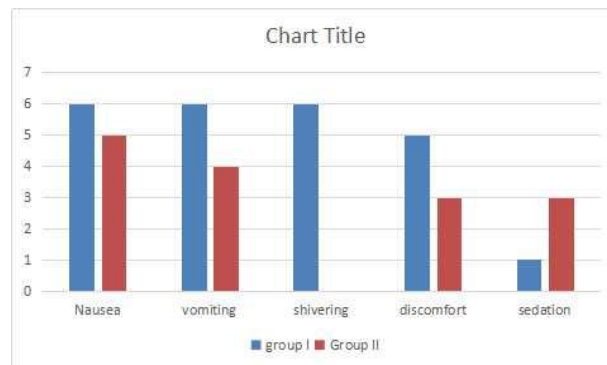


Figure 4: Comparison of side effects between two groups.

Verbal rating score for pain

This was recorded for each patient in both the groups. Lower pain scores were noticed in group II as compared to group I indicating better pain control in patients where tramadol was used. The difference, however, was statistically significant only at 2.5, 3 and 4 hours after anaesthesia (Table 6).

Frequency of drug doses:

On comparing the mean number of doses of analgesic drug in each group it was found that the patients in group I required 5.05(+0.89) doses as compared to 2.05(+0.61) doses required by patients in group II. This difference was statistically significant and suggested that patients with tramadol required less doses of drug for analgesia.

Table 6: verbal rating scores for pain.

Verbal rating score at	Group I (Mean±SD)	Group II (Mean±SD)	P value
2.5 hours	2.45 ±0.51	0.5 ±0.51	P<0.05*
3 hours	2.35 ±0.58	1.45 ±0.51	P<0.05*
4 hours	2.15 ±0.67	1.5 ±0.61	P<0.05*
8 hours	1.45 ±0.51	1.2 ±0.83	p>0.05
12 hours	1.5 ±0.51	1.1±0.55	p>0.05
24 hours	1.3 ±0.47	1.4 ±0.5	p>0.05

DISCUSSION

A wide range of option exists to combat pain, each having its own set of advantages and disadvantages. Tramadol, a synthetic 4-phenyl-piperidine analog of codeine, is a racemic mixture of two enantiomers, with synergistic anti-nociceptive interaction.⁴ The (+)

enantiomer has moderate affinity for the opioids μ receptor and inhibits serotonin uptake, and the (-) enantiomer is a potent norepinephrine synaptic release inhibitor. The result is an opioid with a lack of respiratory depressant effects despite an analgesic potency that has been shown to be approximately equal to that of pethidine in some studies.^{5,6,7} Tramadol inhibits nor-adrenaline and serotonin reuptake and

simulate serotonin release both of which act as transmitters in the descending inhibitory pathways, which enhance analgesia. Various studies have shown that the combination of an opioid and an alpha-2 adrenergic agonist may act synergistically for the analgesic response without potentiating respiratory depression.

Multiple trials have been conducted to establish the optimum dose and route of administration of tramadol. The inference which could be drawn was that, in adults, the optimal initial dose of tramadol is 3mg/kg for acute pain of moderate to severe intensity. Amongst various routes of administration, intravenous route results in most rapid action but the epidural route has the advantages of longer duration of action with less side effects especially if used with local anaesthetic agent.

Analgesia

Various studies have shown that epidural route of administration produces prolonged post-operative analgesia. De Witte et al. concluded that under clinical circumstances, much of the opioid activity of tramadol resulted from its main metabolite which binds to mu-opioid receptor better than the parent compound.⁸ Fu et al reported 12 hrs. of analgesia with tramadol 50 mg & 11.5 hours with 75 mg tramadol with low VAS scores.⁹ Delilkan et al in their study found that epidural tramadol 50 and 100mg produced good pain relief in the postoperative period in abdominal surgery. Tramadol 100mg patients required fewer doses of analgesic drug and each dose gave longer duration and better quality of pain relief than epidural bupivacaine as seen in the significantly lower pain scores at 3,12 and 24 hours.¹⁰ Siddik-Sayyid et al in another study compared the postoperative analgesic effect of 100mg versus 200mg epidural tramadol and saline.¹¹ They concluded that the mean time to first analgesic administration was longer in patients who received 100mg tramadol (4.5+3.1hour) and 200mg tramadol (6.6+3.4hour) than in those who received placebo (2.8+2hour). The mean cumulative doses of meperidine and diclofenac, as analgesic drugs over 24 hours were less in the 100mg and 200mg tramadol groups than in the control group.¹¹ Senel et al studied sixty boys between 12-84 months of age, undergoing unilateral herniotomy and found that caudal administration of 0.25% bupivacaine 1ml/kg with the addition of tramadol 1.5mg/kg resulted in superior analgesia with a longer period without demand for additional analgesics compared with caudal bupivacaine or tramadol alone.¹² Choudhary and colleagues compared caudal 0.5 ml/kg bupivacaine 0.25% plus ketamine and bupivacaine 0.25% plus tramadol and showed significant long duration of analgesia without increase in adverse effects when compared with bupivacaine alone.¹³

Clinico-pharmacological studies have shown that the combination of epidural local anaesthetic and opioid

drugs can provide superior analgesia compared with that of epidural local anaesthetic alone or opioid drugs alone. Local anaesthetic agents potentiate epidural intra-thecal opioid analgesia via a poorly defined mechanism. Hirota et al suggested that clinical concentrations of local anaesthetics interact with mu and kappa but not delta opioid receptors. This may explain why in the tramadol group, the analgesic effect of the drug was prolonged than that of bupivacaine alone.¹⁴

The present study showed that 100mg epidural tramadol provide adequate postoperative pain relief following lower limb orthopedic procedures as evidenced by lower pain scores, longer mean time to the first analgesia request, and less requirement for supplementary analgesics than in patients receiving epidural bupivacaine alone, postoperative. The delayed onset of the analgesic action of tramadol was only observed in the control group. They needed longer time to be satisfied with fair pain relief. That was not observed in the group, which received tramadol preoperatively. This could be explained on the basis of the pharmacokinetic properties of the drug. The data derived from our study was closely related to the above-mentioned studies and were found to be statistically significant ($p < 0.001$) when compared between the two groups.

Duration of analgesia

In the study by Singh et al the mean duration of analgesia in Group A patients was found to be 180.00 ± 15.19 minutes, whereas in Group B patients it was 300.88 ± 22.07 minutes.² In present study was found out to be $194.05 (+4.55)$ minutes for group I patients. For Group II patients, the observed duration was $264.5(+3.41)$ minutes. The difference between two was highly significant ($p < 0.005$). This indicates that tramadol increases the duration of Bupivacaine anaesthesia thereby prolonging the time to first request of any analgesic.

Pain score

Anis Aribogan and Colleagues found lower VAS score in the group receiving bupivacaine with tramadol epidurally ($p < 0.05$).¹⁵ Similar observations were made by Singh et al. and Lin WQ et al in their respective studies.^{2,16} In present study verbal rating score for used for assessment of pain. In accordance with other similar studies our study also observed, lower pain scores in group II (bupivacaine with tramadol) as compared to group I (bupivacaine alone). Iqbal et al showed that the pain scores were similar to the other group up to 1 hour post operatively. But group II (Bupivacaine Tramadol) had significantly better pain scores than group I (Bupivacaine) after 2nd, 3rd, 4th & 5th hours post operatively.¹ Similar findings were observed in our study as well.

Cardiovascular effects

Vogel et al concluded that tramadol may be given to patients with pain due to myocardial infarction as it has no effect on hemodynamic parameters.¹⁷ Lebedeva et al while using tramadol in the early postoperative period have remarked on the stability of the hemodynamic parameters.¹⁸ Hackl et al while comparing fentanyl and tramadol found that while heart rate increased likely with both opioids, mean arterial pressure remain unchanged with tramadol.¹⁹ In a recent study, by Singh et al, no statistically significant difference was observed in relation to heart rate and blood pressure between the two groups which were serially monitored up to 24 hours.² These findings corroborated to the study of Baraka and colleagues.²⁰ The haemodynamic parameters monitored in present study have shown that tramadol has only a negligible effect on the systemic and pulmonary circulation and shows a stable cardiovascular profile.

Degree of motor blockade

In their study, Iqbal and colleagues detected that all the patients in group I (Bupivacaine) reached Bromage grade I i.e. inability to move feet. Similarly, all the patients in group II (Bupivacaine+Tramadol) also, reached Bromage grade I. Likewise, in present study all the patients in both the groups reached Bromage grade I. The present study correlates with those of Dunne et al (1991) who used 0.5% Bupivacaine through epidural route and reported that all the patients reached Bromage grade I.³

Adverse effects

Various adverse effects like respiratory depression, pruritus, nausea, vomiting and urinary retention have been reported after administration of opioid drugs. Tramadol has been recommended as an analgesic without respiratory depression. Nausea and vomiting can occur reflecting its opioid activity, although constipation appears to be less of a problem with tramadol than with other opioids. Tramadol has relatively low addiction potential.

Dellikan et al showed that respiratory depression is not significant with epidural tramadol.¹⁰ In our study as well no evidence of respiratory depression even with subsequent administration of epidural tramadol was observed. The absence of respiratory depression following epidural or parenteral tramadol compared with epidural parenteral morphine may be attributed to the different mechanism of their analgesic actions. Morphine acts selectively as an agonist, which can produce analgesia as well as respiratory depression. It is μ (μ) and kappa(κ) agonist. Tramadol is a weak μ receptors agonist. μ -receptors mediate analgesia and respiratory depression, while kappa receptors mediate

analgesia and sedation. Whether kappa agonist activity contributes to respiratory depression is uncertain.

The most frequently reported side effect with tramadol is nausea and vomiting. This can be explained by the 5-HT release action of the drug. In their study, Singh et al found about 10% patients who were administered tramadol by epidural route complained of nausea.² Baraka and Colleagues reported nausea and vomiting in 20% of patient with epidural tramadol.²⁰ This result is similar to Siddik-Sayyid et al where nausea and vomiting were reported more in patients who were given tramadol.¹¹ In our study, nausea and vomiting were not reported intra-operatively. In post-operative period nausea and vomiting were reported in 25% patients in whom epidural tramadol was used. This high incidence of nausea and vomiting is explained by the frequent epidural tramadol administration.

Tramadol has been shown to be effective in the treatment of post-operative shivering and for the treatment of shivering under regional anaesthesia (epidural or subarachnoid). In our study eight cases of intra-operative shivering were reported in the bupivacaine only group while no patient in the tramadol group suffered from this side effect. Tramadol has mu-receptor activity and minimal kappa receptor activity. Pure mu agonists such as morphine and fentanyl do not have significant anti-shivering effect, thus it is highly likely that anti-shivering effect of tramadol may be mediated via its serotonergic or noradrenergic activity or both. Tramadol has also shown good effect on treatment of shivering after epidural, but repeated doses in the postoperative period elevated the incidence of side effects, as nausea, vomiting and urinary difficulties. Vickers and Colleagues reported sedation potential of tramadol to be 1.1%.²¹ In the study by Singh et al somnolence was noticed in 12.5% patients who were administered tramadol.² In our study the sedation was noted in 20 % patient in tramadol group which is slightly higher than other studies. Baraka and Colleagues found itching in 10% of tramadol treated patient.²⁰ In studies conducted by Singh et al and Iqbal et al no patient from either group was reported to have pruritus.^{1,2} Similarly no patient in our study complained of pruritus which is in accordance with other studies. Singh et al observed urinary retention in only one patient 2.5% with tramadol.² In our study none of the patient suffered from urinary difficulty or urinary retention in either group as was observed by Iqbal et al.¹

CONCLUSION

Epidural administration of local anaesthetic with opioids can provide very good analgesia during and after surgical procedures of lower extremity. The mean duration of analgesia was significantly longer in patients with tramadol than those who received 0.5% bupivacaine only through the same route. The quality of analgesia and pain scores are better in patients who

were administered tramadol. There was no significant difference regarding the mean onset of analgesia between the two groups but number of drug doses required was significantly reduced by addition of tramadol. Tramadol is a safe and effective adjuvant to epidural bupivacaine for prolongation of total duration of analgesia in lower limb surgeries.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Iqbal J, Manhas A, Ahmed I, Abeeda S, Habib M, Ahmed H. Epidural Anesthesia in Lower Limb Surgeries: A Comparison between Bupivacaine Alone and Bupivacaine with Tramadol. *Br J Med Health Res.* 2015;2(10):14-23.
- Singh A, Prasad H. Comparative study of duration of analgesia with epidural bupivacaine & bupivacaine with tramadol in lower limb and lower abdominal surgeries. *Int J Drug Del.* 2013;5(2):239-44.
- Fukuda T, Dohi S, Naito H. Comparisons tetracaine spinal anaesthesia with clonidine or phenylephrine in normotensive and hypertensive humans. *Anaesth analg.* 1994;78(1):106-11.
- Raffa RB, Friderichs E, Reimann W, Shank RP, Codd EE, Vaught JL et al. Complementary and synergistic antinociceptive interaction between the enantiomers of tramadol. *J Pharmacol Exp Ther.* 1993;267:331-40.
- Vickers MD, O'Flaherty D, Szekely SM, Read M, Yoshizumi J. Tramadol: Pain relief by an opioid without depression of respiration. *Anaesthesia.* 1992;47:291-6.
- O'Flaherty D, Szekely S, Vickers MD. Tramadol versus pethidine analgesia in postoperative pain. *Pain* 1990;5:179.
- Lehman KA, Jung C, Hoeckle W. Tramadol and pethidine in postoperative pain therapy: A randomised double-blind trial with intravenous on-demand analgesia. *Schmerz Pain Douleur.* 1985;6:88-100.
- De Witte J, Sessler DI. Perioperative shivering: physiology and pharmacology. *Anesthesiology.* 2002;96(2):467-84.
- Fu YP, Chan KH, Lee TK, Chang JC, Dai YP, Lee TY. Epidural tramadol for postoperative pain relief. *Ma Zui Xue Za Zhi.* 1991;29:648-52.
- Delilkan AE, Vijayan R. Epidural tramadol for postoperative pain relief. *Anaesthesia* 1993;48:328-31.
- Siddik-Sayyid S, Aouad-Maroun M, Sleiman D, Sfeir M, Baraka A. Epidural tramadol for postoperative pain after Cesarean section. *Can J Anaesth.* 1999;46:731-5.
- Senel A C, Akyol A, Dohman D. Caudal Bupivacaine, Tramadol combination for postoperative analgesia in paediatric herniorrhaphy. *Acta Anaesthesia Scand.* 2001;45:786-9.
- Choudhary AH, Dharmani P, Prakash N. Comparison of caudal epidural, bupivacaine with bupivacaine plus tramadol & bupivacaine plus ketamine for post operative analgesia in Children. *Anaesth. Intensive Care.* 2008;36(2):174-9.
- Hirota K, Okawa H, Appadu BL. Interaction of local anaesthetics with recombinant mu, kappa and delta opioids receptors expressed in Chinese hamster ovary cells *Br. J. Anaesthe.* 2000;85(5); 740-6.
- Anis Airbogan and Colleagues: comparison of tramadol with or without bupivacaine after major urologic studies. *Uro Int.* 2003;71:168-75.
- Lin WQ, Zing WA. comparison of post-operative analgesia with tramadol, morphine versus their combination undergoing abdominal cancer surgery. *Ai Zheng.* 2002;21(7)794-6.
- Vogel W, Burchardi H, Sihler K, Valic L. The effect of tramadol, a new analgesic, on respiration and cardiovascular function. *Arzneimittel for schung.* 1978;28(1a):183-6.
- Lebedeva RN, Bondarenko AV, Nikoda VV, Chaus NI, Tugarinov SA. Clinical aspects of the use of nubain, tramal and moradol in patients in the early postoperative period. *Anesteziol Reanimatol.* 1992;(2):3-7.
- Hackl W, Fitzal S, Lackner F, Weindlmayr-Goettel M. Comparison of fentanyl and tramadol in pain therapy with an on-demand analgesia computer in the early postoperative phase. *Anaesthesist.* 1986;35(11):665-71.
- Baraka A, Jabbour S, Ghabash M, Nader A, khoury G, Sibai A. Comparison of epidural tramadol & epidural morphine for post-operative analgesia. *Can J Anesth.* 1995;40:308-13.
- Vickers MD, Parvinic D. comparison of tramadol with morphine for abdominal Surg. *Eur J Anesth.* 1995;12:268-7.

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