Original Research Article

Comparative study between epidural tramadol vs buprenorphine for postoperative analgesia

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Abstract

Aim: This study was designed to compare the postoperative analgesia between tramadol and Buprenorphine through an epidural technique in patients undergoing lower abdominal surgeries based on the onset of analgesia, its duration, degree of analgesia, haemodynamic parameters, respiratory rate and side-effects over a period of 24 hrs postoperatively. **Method:** A total of 60 patients undergoing lower abdominal surgeries with 30 in each group were randomized to receive either single dose of tramadol 1-2mg/kg diluted with 10cc Normal saline or single dose of buprenorphine 2-3 µg/ kg diluted with 10 cc normal saline. **Results:** Epidural tramadol produced faster onset of analgesia (13.79±2.07minutes) compared to epidural buprenorphine (18.96 ±2.984 minutes) as buprenorphine has slow rate of association and disassociation with the opioid receptor. The duration of analgesia in the group which received buprenorphine (14.06 ±3.14 hours) and the group which received tramadol (12.9 ±3.009 hours) were not statistically significant as Z value = 1.462 (<2). Degree of analgesia was equal in both the groups and the difference is not statistically significant. Haemodynamic parameters such as pulse and blood pressure were not significantly altered in tramadol group but there was a slight decrease in patients who received buprenorphine with variations in pulse by 2-6/min and blood pressure by 2-10 mmHg systolic and 2-8 mmHg diastolic, however this was not clinically significant. Respiratory rate remained unchanged in both the groups. Postoperative period seemed to be smoother without the feeling of drowsiness and vomiting in the patients who received epidural tramadol in contrast to the patients who received epidural buprenorphine as some drowsiness and vomiting often persisted. **Conclusion:** Epidural buprenorphine has a slower onset of action compared to epidural tramadol with unpleasant side effects of nausea, vomiting and sedation with no significant changes in the duration, degree and respiratory rate in both the groups.

Key Word: Buprenorphine, epidural, postoperative analgesia, tramadol.

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INTRODUCTION

"For all the happiness mankind can give is not pleasure, but in rest from pain"-John Dryden. Pain is an inevitable component of the postoperative period. It is a sense of damage, hurt, fear, and punishment to the patient (Matisyohu Weisenberg, 1975). Although postoperative pain is self-limiting and will pass away most of the times; its relief is justified from humanitarian grounds and to improve physiological function in postoperative period, since postoperative pain has its own hazards. Breecher developed an idea originally proposed by the psychologist Charles Strong in the 1980s that pain was not merely a sensory phenomenon, but a compound of sensory, cognitive, and affective factors [1]. Patient's pain was perceived as more severe in hospital because of the individual's anxiety and fear over the outcome of the injury or illness[2]. Pain being a subjective phenomenon is perceived only by the sufferer. Post-operative pain is considered a form of acute pain due to surgical trauma with an inflammatory reaction and initiation of an afferent neuronal barrage. It is a combined constellation of several unpleasant sensory, emotional and mental experiences precipitated by the surgical trauma and associated with autonomic, endocrine–metabolic,

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physiological and behavioral responses[3]. Traditionally opioids and NSAIDs have been given by various means to provide an effective postoperative analgesia however all of these have their limitations and drawbacks[4]. Over the years many approaches for postoperative pain relief have been used. Relief of postoperative pain is receiving an increasing amount of attention. Identification of specific opiate receptors in the cord by Pert and Synder (1973) has opened a new vista for the treatment of pain.[5] Bonica (1953) opined segmental epidural analgesia to any other method for managing postoperative pain. He used the method of intermittent injection through an epidural catheter and found advantage of complete relief. Dawkins (1950) recommended continuous epidural analgesia for relief of postoperative pain. Epidural analgesia is a safe technique for postoperative pain relief and equivalent to traditional analgesic methods[6].With epidural analgesia patient can be mobilized early and can resume activities quickly as compared to parenteral opioids[7]. Other benefits of postoperative epidural analgesia are superior analgesia, fewer cardiac ischemic events, shorter recuperation after joint surgery, improved pulmonary function, better graft survival after lower limb vascular procedures, increased bowel motility, associated with an early aggressive mobilization[8]. Tramadol is a weak opioid agonist analgesic with a typical clinical profile. It interacts with opioid receptors mu, alpha and delta[9]. It is a centrally acting opiate analgesic agent with less sedative action. Incidence of respiratory depression is also said to be very low and the quality of analgesia is said to be excellent. Opioid Buprenorphine is a thebaine derivative, semi-synthetic having both agonist as well as antagonist properties. It is highly lipid soluble and has higher affinity for opioid receptor, so the chances of side effects and addiction will be minimal and can safely be used epidurally[10]. Hambrook *et al* (1976) found that Buprenorphine differs from all other clinically useful opioids in having very slow receptor kinetics, so that rate of receptor association and disassociation are likely to be rate limiting for the onset and offset of the effect[11]. Comfort of patient through relief of pain is given first priority – especially in immediate postoperative period. Degree of respiratory depression rather than analgesic property influences or limits the use of any particular analgesic after major surgery.

Epidural analgesia with opiates has gained importance over parenteral because:

1. Adequate analgesia is attained even with low doses.
2. Analgesia for visceral pain without somatic or sympathetic nervous system involvement.
3. No skeletal muscle weakness.
4. No loss of proprioception.
5. No orthostatic hypotension.
6. Superior analgesia for prolonged periods.

The present study is done to:

1. To assess efficacy of epidurally administered Tramadol and Buprenorphine in relieving postoperative pain.
2. To study the degree and duration of postoperative analgesia.
3. To observe side effects and complication of both the drugs.

MATERIAL AND METHOD

This study was carried out in Department of Anaesthesiology, Byramjee Jeejeebhoy Medical College and Sassoon General Hospital, Pune. After ethical committee approval.

No. of cases: Group 1: 30 cases of epidural Tramadol.Group2: 30 cases of epidural Buprenorphine.

Inclusion Criteria: ASA I-II; Posted for lower abdominal surgery, perineal surgery, orthopaedic surgery and Gynaecological surgery, Male – Female: 20 to 60 years.

Exclusion Criteria: absence of any cardiac, respiratory, renal or other pathology that may affect the parameters for clinical evaluation of cardio-respiratory performance for the purpose of the trial, absence of mental illness, patient must not be on psychotropic drugs, analgesic, anti-inflammatory or other drugs likely to influence sensation of pain. All pre-op relevant investigation and pre-anaesthetic assessment was done.

Procedure: Confirmation of suitable cases for study. Explaining procedure to the patient. Taking written consent. Before giving anaesthesia following points will be noted: Pulse –rate, rhythm; blood pressure; respiratory rate. After shifting the patient to operation theatre, vital Parameters were recorded. Intravenous infusion was started. For every patient a combined spinal epidural procedure was performed under all aseptic precautions. Patients were kept in left or right lateral position and an18G tuohys needle was introduced in L_2-L_3 interspinous space. The epidural space was identified using loss of resistance technique and the catheter was threaded in the space. 2ml of 2% xylocaine+adrenaline (1:2,00,000) was given as test dose to rule out intrathecal and intravascular placement of the epidural catheter. Subarachnoid block was performed in L_3-L_4 space using 25G spinal needle with 15mg of inj. Bupivacaine 0.5% heavy. No analgesics were administered during the intra-operative period and patient was shifted to post-operative ward after completion of the surgery. In the postoperative period in the recovery room patients were observed for vital signs and asked about pain. When effect of epidural analgesia was wearing and pain appeared, single dose of

tramadol 1 to 2 mg/kg diluted with 10cc of normal saline or distilled water was injected in the epidural space of 30 patients and single dose buprenorphine 2-3ug/kg diluted with 10ml of normal saline or distilled water injected in the epidural space of remaining 30 patients randomly. No systemic analgesics were administered to the patients until they complained of persistent pain. All patients will be monitored/observed every hourly for 24 Postoperatively.1) Assessment of analgesia both subjectively and by scoring with pain scale (by McGills' classification)-No pain:0, Slight pain:1, Moderate pain:2, Severe pain:3, Excruciating:4.2)Rate of respiration;3)Pulse rate;4)Blood pressure-Systolic and Diastolic, 5)Sedation –arousable, drowsy, asleep;6)Onset of action and duration of action;7)Recording of side effects in the form of nausea, vomiting, urinary retention, itching or any other.

STATISTICAL ANALYSIS

1. Continuous variables are expresses as mean ± S.D. or median (Range).
2. Between-group degree of pain relief is analyzed with X^2 test.
3. Statistical analysis is defined as P <0.5.
4. Significance of onset and duration of analgesia is calculated by Z value.

Table 1: Baseline Data of Pulse And Blood Pressure In Each Group Preoperatively

Parameter	Group I (Tramadol)		Group II (Buprenorphine)	
	Mean	Range	Mean	Range
Pulse/min.	80.03	60-96	81.13	60-94
Bp(mmHg) Systolic	122.3	108-130	121.79	108-136
Diastolic	79.73	68-90	79.4	66-90

Table 2: Baseline Data Of Pulse And Blood Pressure In Each Group Post operatively

Group I (Tramadol)		Group II (Buprenorphine)	
Mean	Range	Mean	Range
80.46	61-96	79.42	60-92.2
121.41	110-130	118.61	131.5-105.58
78.97	69-90	76.53	66-88.08

Table 3: Average preoperative and postoperative respiratory rate

	Group I	Group II
Preoperative (RR/min)	17.9 (range 5-22)	18.73 (range 16-21)
Postoperative(RR/min)	18.4 (range 16-22)	18.59 (range 16-22)

Table 4: Onset of analgesia in group I

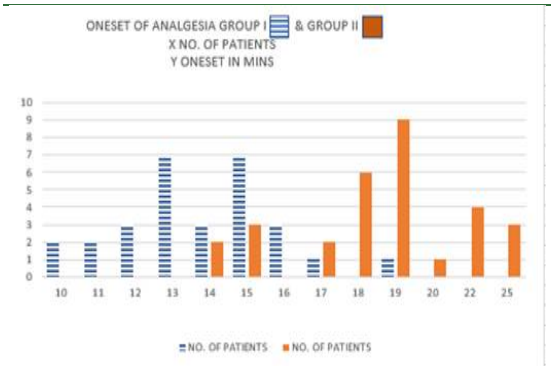
Mean:13.793min S.D. :2.076 min		
Onset in minutes	No. Of patients	Percentage
10	2	6.67
11	2	6.67
12	3	10.0
13	7	23.34
14	3	10.0
15	7	23.34
16	3	10.0
17	1	3.33
18	0	0
19	1	3.33
No analgesia	1	3.33

There was no change in Respiratory rate in both the group.

Table 5: Onset of analgesia in group II

Mean:18.96 min S.D.2.984 min		
Onset in minutes	No. Of patients	Percentage
14	2	6.67
15	3	10.0
17	2	6.67
18	6	20.0
19	9	30.0
20	1	3.33

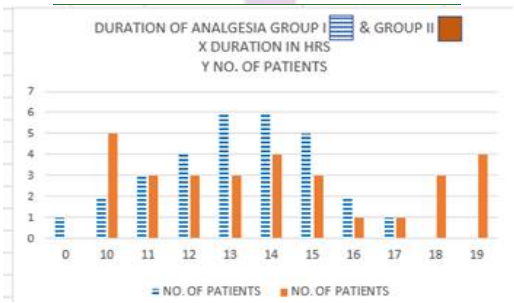
22	4	13.33
25	3	10.0
Total	30	100



From Table 4 and 5, we get Z =7.79 i.e. Greater than 2, so the above finding is significant. (i.e. onset of analgesia is late in group II patients as compared to group I patients).

Table 6: Duration Of Analgesia

Duration in Hr	No. Of patients	
	Group I	Group II
0	1	0
10	2	5
11	3	3
12	4	3
13	6	3
14	6	4
15	5	3
16	2	1
17	1	1
18	0	3
19	0	4
Total	30	30
Mean in Hrs	12.9	14.06
SD in Hrs	3.009	3.140



Calculating 'Z' value from two groups (Table 6) we get Z value=1.462 i.e. <2. So above finding is not statistical significant. We cannot say that duration of analgesia is more in group II.

Table 7: Degree of pain relief X^2=1.342 D.F=5 P<0.05 ,Degree of analgesia is equal in group I and II, difference is not statistically significant

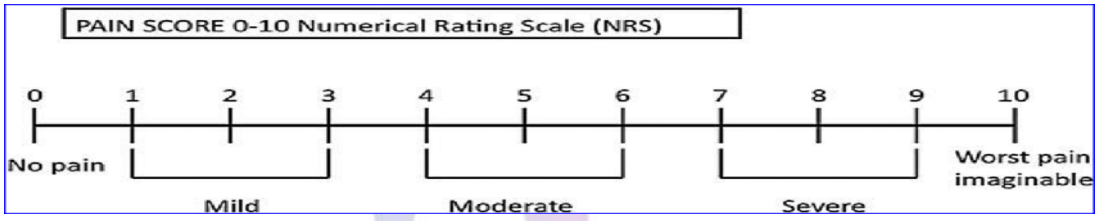
Degree of pain	No. Of patients	
	Group I	Group II
No pain(0)	22	21
Slight (1)	5	7
Moderate (2)	2	2
Severe (3)	1	0
Excruciating(4)	0	0
Total	**30**	**30**

Table 8: Side effects and Complications

Side effects	Group I	Group II
	No.	No.
Nausea	1	2
Vomiting	1	3
Itching	-	-
Headache	-	-
Sedation	3	14
Hypotension	-	-
Urinary retention	-	-
Body temperature	3(mildly febrile)	-

DISCUSSION

Clinical Assessment of Pain: Assessment of pain is difficult because it is a subjective sensation. Clinical pain has a disadvantage that it increases and decreases spontaneously. A number of methods have been devised to measure pain. In past, the effect of narcotic drugs on pain has been measured by interviewing patients before and after the administration of the drug (Beecher H.K., 1951)2. They had been instructed to report pain relief if more than half their pain was relieved. In a further development, the effectiveness of narcotic drugs was evaluated numerically, grading pain in a no, slight, moderate, severe and agonizing categories (Houde R.W., 1953)12. A more sophisticated method has been devised to rate well being (Clarke P.R.F., 1964)13. This technique, known as the linear analogue, involves the use of 10cm line on a piece of white paper and represents the patient's opinion of the degree of pain. It is explained to the patient that one end of the line represent as much pain as he can imagine while the other end represents no pain at all. The subject rates the degree of pain by making a mark on line. Scale values are then obtained by measuring distance from zero to that mark.



This method requires the patient to have normal visual and motor co-ordination and should have a proper memory of pain to make this method of assessing pain reliable. Patients in this study were illiterate and it was difficult for them to mark properly on line. For this reason, in this study, McGill's pain scale is used: No pain-0, Slight pain-1, Moderate pain-2, Severe pain-3, Excruciating-4. Intrathecal and epidural narcotics have been widely used since 1979 to relieve pain and provide postoperative pain relief (Cousins 1984) [14]. However, the incidence of respiratory depression with narcotics has led to the use of substances that have the advantages of opioids but not their drawbacks.

Onset of Analgesia: In a study by W. Lintz *et al* (1986)[15] onset of action after oral administration of 100mg tramadol capsules was 40 min (068±0.175). This late onset of action is due to time taken for absorption of tramadol. In this study, onset of analgesia after epidural administration of tramadol was 13.793 min with standard deviation of 2.076. Onset of analgesia after epidural administration of 2-3 µg/ kg of buprenorphine was 18.96 minutes with standard deviation of 2.984 minutes. This is comparable with the studies of K.H.Simpson and co-workers in 1988[16]. Bullingham in 1980 noted the onset of analgesia of intravenous buprenorphine in 5-15 minutes with peak effect in a variable range of 30 to 60 minutes[17]. Buprenorphine, unlike other opioids, has slow rates of association and dissociation with the opioid receptors. It takes about 30 minutes for the receptor binding to achieve an equilibrium (Dundee, 1988)[18]. This slow rate of association with the opioid receptors explains the late onset of action of buprenorphine (mean 18.96 min., S.D. 2.984 min) as compared to the early onset of action of tramadol (mean 3.793 min, S.D. 2.076 min.).

Duration Of Analgesia: W. Lintz, H. Barth, G.Osteriah and E.Schmidt Bothelt (1986) found that, the intravenous injection of 100mg of tramadol hydrochloride, provided duration of analgesia for 11.2±2 hrs [15]. Fu Y.P. *et al* (1991) in their study of the analgesic effect of epidural tramadol with a dose of 75 mg had a mean duration of

pain relief 12±5.9 hrs[19]. In this study, we have 1-2 mg/kg tramadol epidurally diluted in 10ml normal saline. The mean duration of analgesia in present study was 12.9 hr. with S.D. 3.009 hr. with range of 10 to 17 hrs, which was comparable to the study by Fu YP *et al* (1991)[19]. In the study by Wolff J.(1986)[20] mean duration of action of buprenorphine was 10.33 hrs and that of Morphine was 9.60 hrs. Lanz *et al* (1984)[21] in a double blind study of analgesic effect of epidural buprenorphine with a dose of 0.3 mg had mean duration of action of 12 hours. Damle (1990)[22] in a study of buprenorphine 0.3mg epidural for postoperative pain relief found the duration of action ranging from 4.2 to 15 hrs with mean duration of 10.2 hrs. In this study, we have 2-3 µg/kg buprenorphine epidurally diluted in 10 ml. normal saline. The mean duration of analgesia in this study was 14.06 hrs with S.D. 3.140 hr which was comparable to the studies mentioned above**.** Thus duration of analgesia with epidural tramadol was 12.9 hrs, with S.D. of 3.00 hrs and with epidural buprenorphine was 14.06 hrs, with S.D. of 3.140 hrs.

Degree Of Pain Relief: There was excellent pain relief (score 0) in 22 patients of tramadol group and 21 patients of Buprenorphine group. Slight pain (score 1) in 5 patients in tramadol group and 7 patients in buprenorphine group. Moderate pain (score 2) in 2 patients in tramadol group and 2 patients in Buprenorphine group. No analgesia (severe pain - score 3) in 1 patient of tramadol and '0' patient in Buprenorphine. By calculating $X^2 = 1.342$, D.F. = 5, p is < 0.05**.** Difference is not statistically significant. Degree of analgesia was equal in both groups.

Pulse and Blood Pressure: Vogel *et al* (1978) showed that tramadol has only a negligible effect on the systemic and pulmonary circulation[23]. Prof. R. G. Ofoegbu and Dr. -O. Mbonu showed no change or variation in blood pressure and pulse after i.v. tramadol[24]. In this study also there was no significant change in pulse and blood pressure in tramadol group. In buprenorphine group there was slight decrease in pulse by 2 - 6/min and blood pressure 2 to 10 mm Hg systolic and 2 to 8 mm Hg diastolic which was not clinically significant.

Respiratory Rate: Vogel *et al* (1978) showed that therapeutic dose tramadol do not depress respiration, has no significant effect on respiratory rate, tidal volume, minute volume, arterial Co_2 and ventilator Co_2 response[23]. Anis Baraka (1992), in his study by comparing epidural tramadol and other epidural opiates found that, unlike other opiates, (Morphine, Buprenorphine) epidural tramadol provided good analgesia without respiratory depression[25]. In his study he found that respiratory rate was not affected in both the groups[25]. In this study respiratory rate remained unchanged in both Groups.

Side Effects: In study by Professor V.O. Oviasu (with oral tramadol) side effects were minimal and did not warrant stopping the drug[26]. Nausea was complained of in 14%, drowsiness in 10%, vomiting in 3%.In this study, with epidural tramadol group, one (3.33%) had nausea; one (3.33%) patient had vomiting; only three patients were sedated (drowsy). Three (10%) patients were mildly febrile. With epidural buprenorphine group, two patients (6.66%) had nausea, three patients (10%) had vomiting, fourteen (46.67%) were sedated. In a study by Damle N. (1990) the incidence of nausea was found to be 8%. They had given a dose of 0.3 mg buprenorphine epidurally[22] Postoperative period of those who had epidural tramadol seemed to be smoother without the feeling of drowsiness and vomiting while for those given epidural buprenorphine some drowsiness and vomiting often persisted.

SUMMARY AND CONCLUSIONS

Thus in the present study, we can derive the following conclusions:

1. Onset of analgesia is late in buprenorphine group as compared to tramadol given epidurally. This is because slow association and dissociation of buprenorphine with opioid receptors.
2. Duration of analgesia is same in both the groups.
3. Respiratory rate remains same with both the groups.4) Incidence of nausea, vomiting and sedation is high with buprenorphine as compared to tramadol, so postoperative period with epidural tramadol is smoother than epidural buprenorphine.5) Degree of analgesia is same with epidural tramadol and epidural buprenorphine.

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