Optimum Dose of Epidural Tramadol Hydrochloride for Post Operative Analgesia

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ABSTRACT:

Background: *Tramadol hydrochloride is a centrally acting analgesic with a combination of opioid and non-opioid receptor mechanisms and a benign side effect profile. The epidural route appears to be a logical choice because of the direct effect in the transmission and processing of pain. The purpose of this study was to find out the effective dose of epidurally administered tramadol for postoperative analgesia in urological surgical patients.*

Method: *60 healthy patients of American Society of Anesthesiologists(ASA) physical status classification I and II, with age ranging from 20-60 years, scheduled to undergo elective surgeries were equally divided into 3 groups(I,II & III) receiving 1mg/kg, 2mg/kg and 3mg/kg of tramadol hydrochloride epidurally respectively post-operatively in PACU. Time to first request for analgesia and side effects like nausea, vomiting, dizziness and pruritus were also noted.*

Results: *There was a statistically significant difference in the period of postoperative pain relief in Group-I (6.8±2.3 hours), Group-II(14±8 hours) and Group-III(21.4±3.7 hours). There was significant increase in postoperative nausea and vomiting in group III (40%) as compared to group I (10%) and group II (5%).*

Conclusion: *These findings suggest that 2mg/kg body weight of epidural tramadol is an optimum dose for postoperative analgesia without increase in side effects. 3mg/kg dose can also be used with appropriate anti emetics to decrease the incidence of PONV with this dose.*

Keywords: *Analgesia, Epidural, Tramadol, Urological surgeries.*

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INTRODUCTION

Pain is one of the most distressing symptoms and adequate, effective pain control is essential for optimal care of surgical patients[1,2]. Epidural analgesia is achieved by the introduction of local anesthetics or opioids or mixture of the two in the epidural space. Tramadol hydrochloride is an atypical centrally acting opioid with mixed opioid and non-opioid activity[3]. The non-opioid analgesic effect of tramadol hydrochloride reflects the ability of this drug to inhibit norepinephrine and 5-Hydroxytryptamine(5HT) neuronal uptake and facilitate 5HT release in vitro, which are the neurotransmitters in descending pathways and thus enhance analgesia[4].The combination of a local anesthetic and an opioid produces excellent post-operative analgesia[5,6]. Tramadol hydrochloride also has been shown to provide effective, long lasting analgesia[7] after extradural administration and prolongs the duration of action of mepivacaine for brachial plexus block without serious side effects[8]. Epidural tramadol hydrochloride can be used to provide prolonged post-operative analgesia without side effects[9]. We conducted a dose finding study based on body weight to find out an optimum dose of tramadol hydrochloride to be used epidurally in urological surgical patients for postoperative analgesia.

MATERIALS AND METHODS

After obtaining written and informed consent and hospital ethics committee approval, a prospective, double blind, randomized controlled study was conducted on 60 patients of either sex, American Society of Anesthesiologists (ASA) physical status classification I and II in the age group of 20-60 years scheduled for urological procedures. The patients were randomly divided into three groups (Group-I, II & III) of 20 patients each to receive either 1mg/kg, 2mg/kg or 3mg/kg body weight of epidural tramadol hydrochloride respectively. Exclusion criteria were contraindication to regional blockade, obesity, pregnancy, ASA>II and age<20 years or >60 years.

At the preoperative visit, the patients were instructed about the use of 10 point Visual Analogue Scale(VAS) for evaluation of post-operative pain(VAS=0 No pain; VAS=10 Worst pain). Prior to induction of anesthesia, an epidural catheter was placed in L1-L2 or L2-L3 interspace in sitting position by using a 18G Tuohy's needle with loss of resistance technique. The epidural catheter position was rechecked

with a test dose comprising of 3ml of 2% lignocaine with 1:200000 adrenaline (5µg/ml). General anesthesia was adminstered using propofol 2mg/kg intravenously (IV) with morphine sulphate 0.1mg/kg IV and tracheal intubation was facilitated with atracuriumbesylate 0.5mg/kg IV. Anesthesia was maintained with oxygen (33%), nitrous oxide(67%) and isoflurane(0.5-1.5%). Muscle relaxant $1/4^{th}$ of the induction dose was administered as and when required. Ondansetron-hydrochloride(0.1mg/kg IV) was given 15 minutes before the completion of surgery.

After the end of the surgery and reversal of neuromuscular blockade with neostigmine methyl sulphate 50µg/kg IV and glycopyrollate 10µg/kg IV, the patient was shifted to post anesthesia care unit (PACU). In the PACU, as per the randomization, epidural tramadol hydrochloride either 1, 2 or 3 mg/kg body weight was given when the patient would complain of pain and VAS was more than 3. Vital signs were recorded for 30 minutes after the injection and the patients were shifted to the ward. Rescue analgesia if required was given with 10ml of 0.25% preservative free bupivacaine via epidural catheter and the time to first request for analgesia was noted. If analgesia was not achieved with bupivacaine also, this was considered as failure of epidural and same were excluded from study. In these patients, monitoring of heart rate and blood pressure every 15 minutes for 1 hour and then hourly for another 6 hours was done. Dexamethasone 8mg IV was given as a rescue anti emetic.

STATISTICAL ANALYSIS

It was done using MS Excel and SPSS version 12.0 for windows. The primary outcome measure was presented in Mean and Standard deviation(SD) and statistically significant difference evaluated using One Way ANOVA. The primary outcome was pain relief in terms of hours and the secondary outcome was the dose of tramadol hydrochloride required. Statistically significant difference of qualitable variables among the 3 groups was evaluated using Chi square/Fishers exact test. A p-value<0.05 was considered as significant. The power of study was 0.8.

RESULTS

The demographic profile in all the three groups was comparable (Table 1& Figures 1, 2 and 3). Comparison of age and weight between group I and group II, group II and III, group I and III and between the groups was insignificant.

There was no statistically significant difference in the types of surgeries, intra-operative as well as post operativehemodynamics when the three groups were compared. A non-significant difference was observed when post-operative VAS was compared at 0, 30, 60 and 90 minutes between the groups. But it became highly significant at 2 hours between groups I and II and groups I and III, but was non-significant for groups II and III. A significant difference was observed at 3, 4 and 6 hours between groups I and II and groups I and III but was not significant for groups II and III. Comparison between the three groups became significant at 6, 8, 10, 12, 14, 16, 18 and 20 hours and became non-significant at 24 hours (Table-2& Figure 4). A significant difference (p>0.05) was observed in the post-operative analgesic requirements at 6, 10, 12, 14, 20 hours between the three groups. A significant difference was observed in Post Operative Nausea and Vomiting (PONV) between groups II and III and groups I and III (Table 3 & Figure 5). The mean time period for post-operative analgesia was 6 hrs; 14hrs 8 minutes and 21hrs 4minutes in groups I, II, and III respectively which was a statistically significant difference.

Table 1: Demographic profile:

	Group-I (n=20)	**Group-II (n=20**	**Group-III (n=20)**	**p value**
Age(years)	32.6±11.5	37.4±13.2	39.8±9.9	0.145
Sex(male/female)	8/12	12/8	12/8	0.349
Weight(kgs)	58.0±7.4	62.4±7.6	62.9±8.9	0.115

Values expressed as Mean±SD

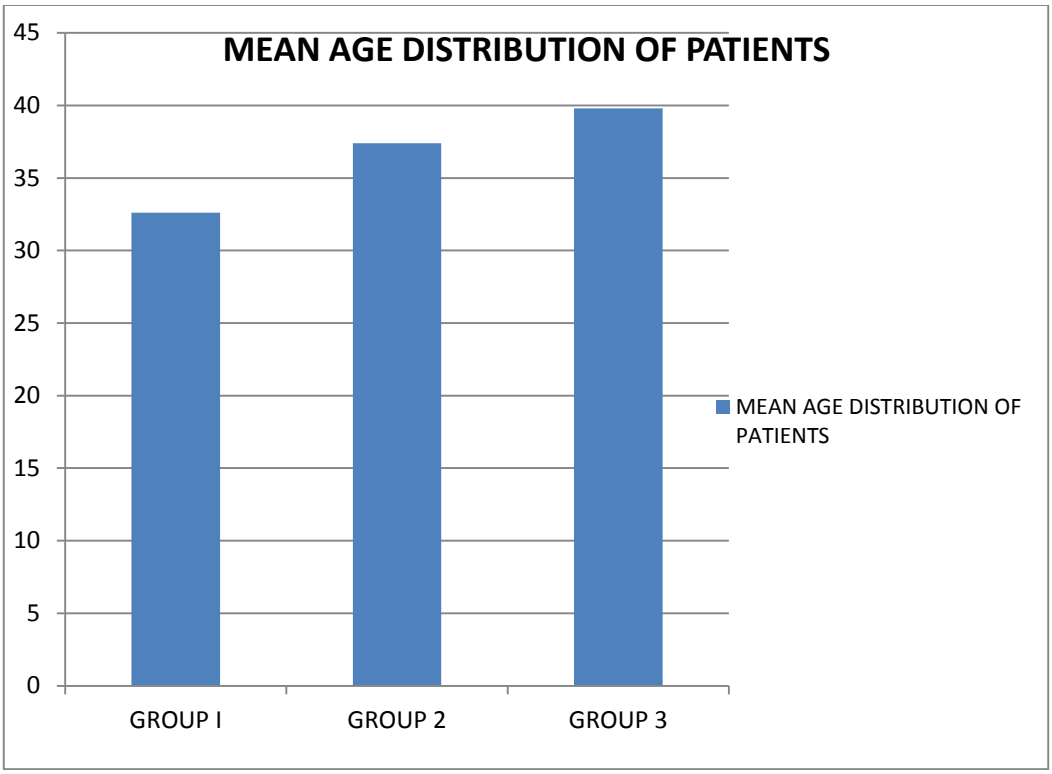

Fig. 1: Mean Age distribution of patients.

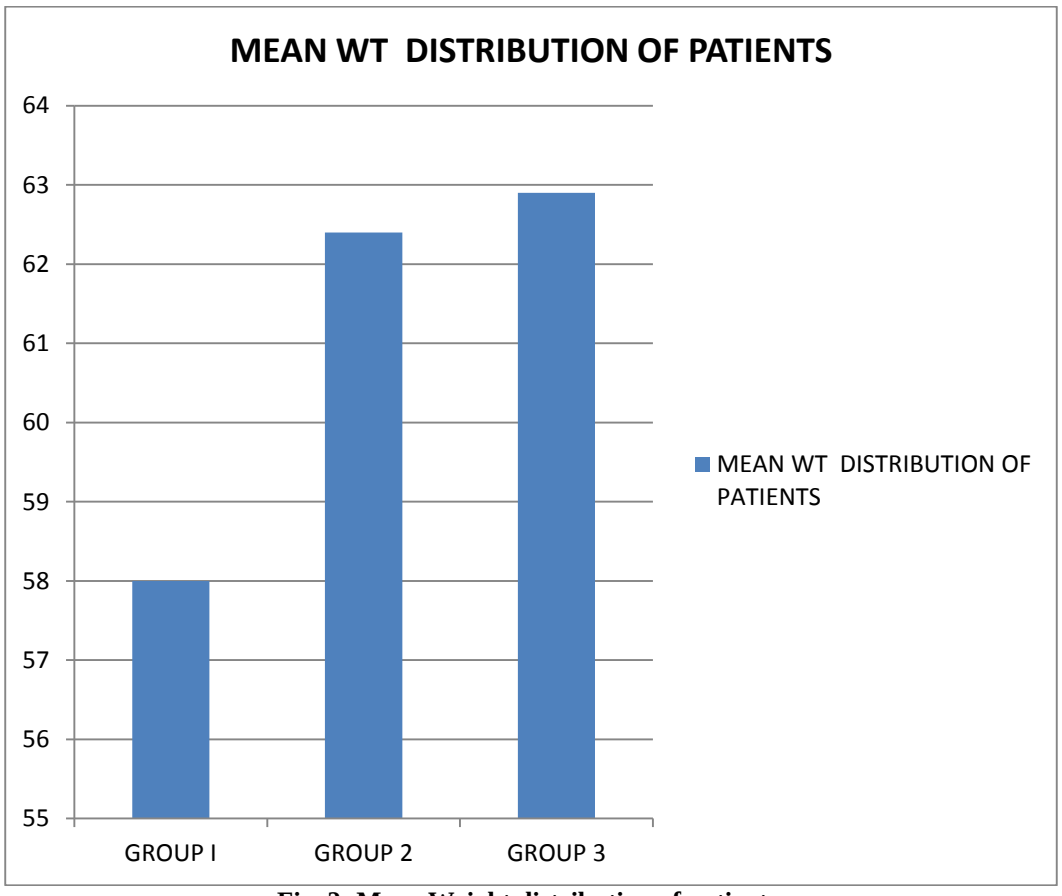

Fig. 2: Mean Weight distribution of patients.

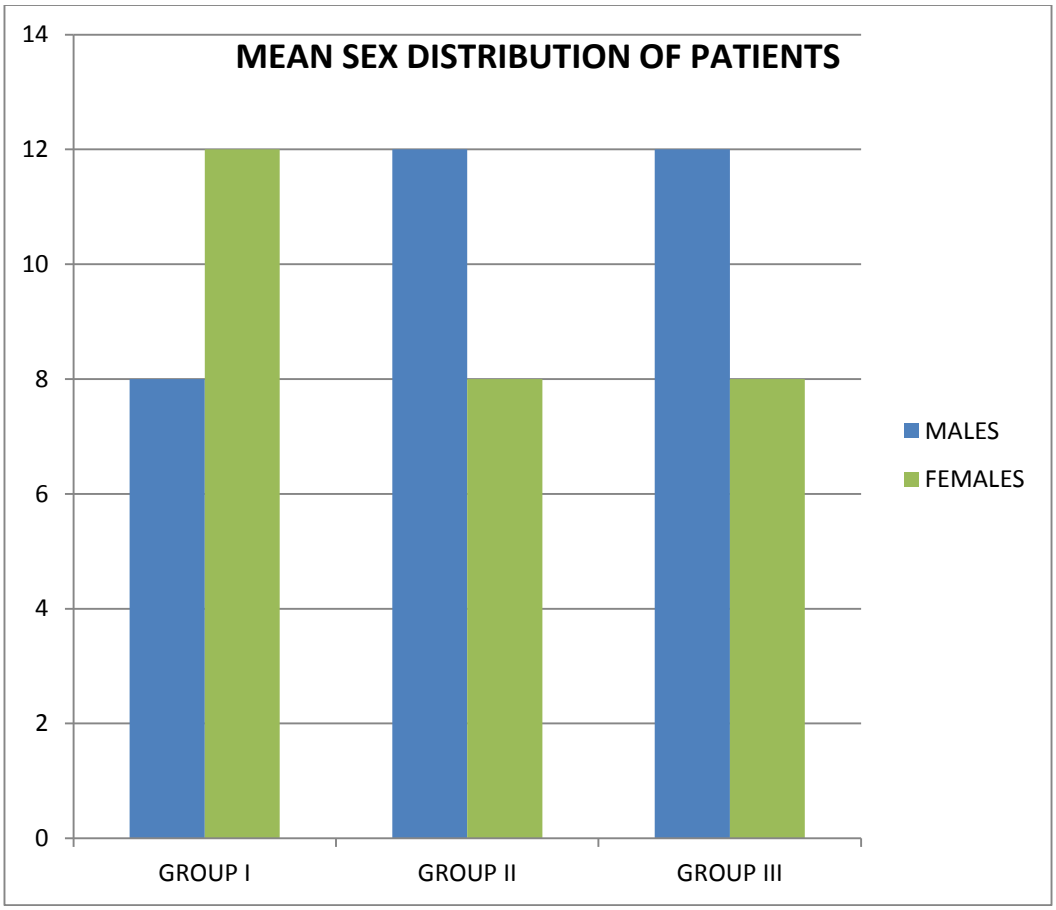

Fig. 3: Mean Sex distribution of patients.

Table 2: Intergroup comparison for post operative VAS in the three study groups:

Visual Analogue Score(VAS) At	Group-I (n=20)	Group-II (n=20)	Group-III (n=20)	P Value
0 hrs	5.7±1.38	5.3±1.41	5.9±0.85	0.307
30 minutes	0.3±1.11	0.6±1.84	0.5±0.94	0.718
60 minutes	0.4±1.08	0.0	0.0	0.159
90 minutes	0.0	0.0	0.0	-
120 minutes	0.0	0.0	0.0	-
3 hours	0.0	0.0	0.0	-
4 hours	0.2±0.68	0.0	0.0	0.375
6 hours	1.3±2.08	0.0	0.1±0.44	0.003
8 hours	2.5±2.11	0.0	0.0	0.000
10 hours	2.5±2.07	0.3±1.17	0.0	0.000
12 hours	3.5±0.70	0.3±1.25	0.2±0.89	0.001
14 hours	0.0	1.0±1.84	0.0	0.023
16 hours	0.0	0.4±0.84	0.0	0.045
18 hours	0.0	4.1±2.92	0.3±1.14	0.000
20hours	0.0	3.3±3.21	0.1±0.47	0.000
24 hours	0.0	6.5±0.70	2.2±3.04	0.067

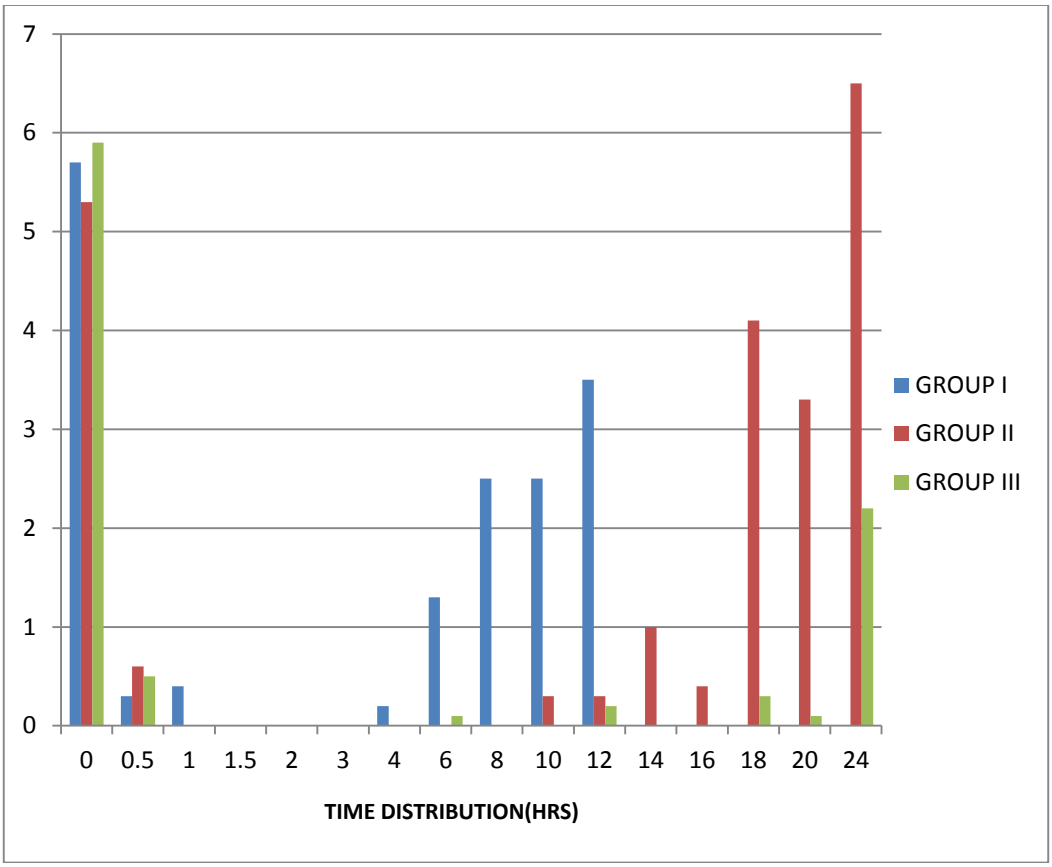

Fig. 4: Intergroup comparison for post operative VAS

Table 3: PONV across the three study groups

Time	Group-I		Group-II		Group-III		p-value
	N	%	n	%	n	%	
0 hour	1	5.6	0	0.0	3	15.0	0.172
30 minutes	2	10.0	0	0.0	3	15.0	0.223
60 minutes	2	10.0	0	0.0	1	5.0	0.387
90 minutes	0	0.0	0	0.0	1	5.0	0.397
120 minutes	0	0.0	0	0.0	1	5.0	0.407
3 hours	0	0.0	0	0.0	2	10.0	0.160
4 hours	0	0.0	0	0.0	1	5.0	0.407
6 hours	0	0.0	0	0.0	0	0.0	1.000
8 hours	0	0.0	0	0.0	0	100.0	1.000
10 hours	0	0.0	0	0.0	2	10.0	0.308
12 hours	0	0.0	0	0.0	1	5.0	0.638
14 hours	0	0.0	0	0.0	3	15.8	0.125
16 hours	0	0.0	0	0.0	0	0.0	1.000
18 hours	0	0.0	0	0.0	0	0.0	1.000
20 hours	0	0.0	1	33.3	0	0.0	1.000
24 hours	0	0.0	0	0.0	0	0.0	1.000

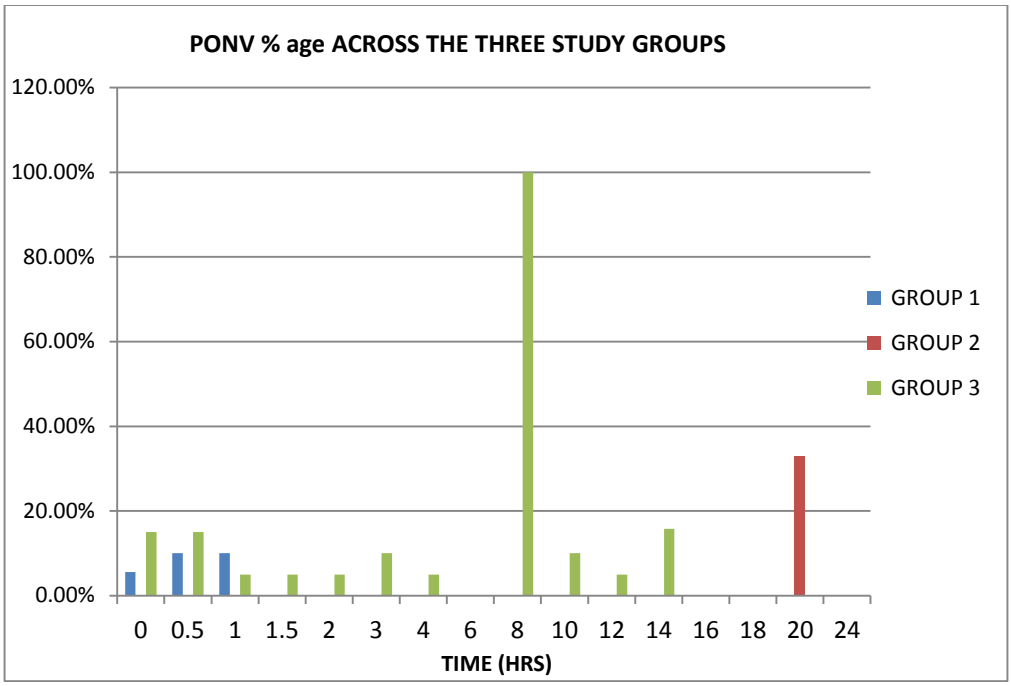

Fig. 5: PONV percentage across the three study groups

DISCUSSION

A number of workers have stressed the superiority of epidural analgesia over other techniques for post-operative pain relief[11]. Despite advances in epidural analgesia for the relief of post-operative pain, the undesirable properties and side effects of commonly used narcotics in epidural space still remains a problem[12].

This dose finding study was undertaken to find out the optimum single dose of Tramadol hydrochloride based on body weight to be administered epidurally to provide post-operative pain relief for maximum time period with minimal side effects for urological surgeries in adults. Our study demonstrated that pain relief in 18/20 patients in Group-I lasted for 6 hours and in the remaining 2, it lasted upto 12 hours. In Group-II, 18/20 patients had pain relief upto 10 hours and only 2 were pain free for 24 hours. In Group III, all patients were pain free upto 24 hours. ANOVA between the groups did not show any statistically significant difference for the first 4 hours, but was highly significant from 4th hour onwards upto 24 hours post injection. The mean time to request analgesia was significant between the groups. It varied from 6±2.3 hours in Group-I to 21.4±3.7 hours in Group-III. Rescue analgesia was required for ten patients in group I, five patients in group II and four patients in group III.

The only side effect was PONV. Within first hour of injection, 2 patients in Group-I and 8 in Group-III vomited. However after the first hour,11 patients had PONV in Group-III as compared to none in Groups I and II.PONV was mild to moderate in nature and was easily controlled with a single dose of dexamethasone 8mg IV. Previous dose finding studies have examined various doses of Tramadol hydrochloride and some have even compared epidural tramadol hydrochloride with epidural morphine sulphate and found tramadol to be very effective[13,14,15]. Some studies have found the efficacy of Tramadol hydrochloride to be comparable to morphine, but reported a huge incidence of respiratory depression with morphine(16,17).

In our study, hemodynamic variables and respiratory rate showed a benign profile and no clinically relevant change was observed in these variables. The incidence of PONV has been quite high especially when opioids are administered in epidural or intrathecal space. An incidence of 20-80% has been reported[15,18,19]. Our study has demonstrated a 40% incidence of PONV in Group-III.

CONCLUSION

Tramadol hydrochloride is an effective analgesic when administered epidurally for post-operative pain relief without serious side effects like hemodynamic instability and respiratory depression. Increasing the dose of tramadol increased the duration of post-operative analgesia, but with increased incidence of PONV. 2mg/kg body weight of tramadol hydrochloride is an optimum dose for post-operative analgesia when given epidurally without significant increase in side effects. However 3mg/kg dose can also be used safely, but with appropriate anti emetics to decrease the high incidence of PONV associated with this dose.

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