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INTRAVENOUS VERSUS EPIDURAL TRAMADOL FOR POST-OPERATIVE ANALGESIA: A COMPARATIVE STUDY

Anaesthesiology

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ABSTRACT

Background: Tramadol, a synthetic opioid, is regarded as having lesser side effects as opposed to traditional opioids. This randomized controlled study compares Tramadol given intravenously and epidurally for post-operative analgesia in lower abdominal and lower limb surgeries under general anaesthesia (GA). **Methods:** Fifty patients were randomly allocated into two groups receiving tramadol intravenously (Gp I) and epidurally (Gp II), at the time of wound closure. Visual Analogue Scale (VAS) score was noted post-operatively and the average duration of analgesia, post-operative respiratory/hemodynamic parameters and side effects were noted. Values obtained were statistically analysed using unpaired student 't' test. **Results:** The average duration of analgesia was 2 hours 40 mins in Gp I as compared to 5 hours 18 mins in Gp II, the difference being statistically significant ($p<0.05$) at 95% confidence intervals. Orthopaedic cases showed maximum peak analgesic effect. (Gp I 45-60 mins, Gp II 65-90 mins). Stable respiratory/hemodynamic parameters prevailed in both groups. Post-operative nausea and vomiting (PONV) was the most common side effect with tramadol (IV > Epidural; 56% vs 36%; $p<0.05$). **Conclusion:** Epidural tramadol is more efficacious as compared to intravenous tramadol. However, a larger sample size is needed for further validation of these findings.

KEYWORDS

Tramadol; Intravenous vs Epidural; Post-operative analgesia

Introduction

Triumph over surgical pain has been a major challenge to the Anaesthesiologists. Although intra-operative pain has been nullified to a large extent, many patients continue to experience considerable discomfort from post-operative pain despite techniques and agents available for its effective treatment.[1] Effective control of post-operative pain is the need of the hour as it decreases morbidity, cuts down the stress response and encourages early recovery. Use of opioids via the IV (intravenous) and epidural route is one of the most effective ways of tackling post-operative pain. The reasons for under treatment include lack of knowledge of the pharmacokinetics of the opioids and the unwarranted fear of respiratory depression and addiction in hospitalised patients.[2] Ever since the discovery of opioid receptors in the spinal cord the use of opioid agents via the epidural route has gained popularity as compared to the traditional intravenous route.[3]

Tramadol, a relatively newer centrally acting synthetic opioid agent, has mixed mu opioid and non opioid activity with lesser side effects effectively making it a central analgesic with low affinity for opioid receptors.[4] This study attempted to compare the efficacy of tramadol given by IV and epidural route for post-operative analgesia. The degree and duration of analgesia, hemodynamic and respiratory parameters and also the adverse effects of tramadol via both the routes were studied.

Methodology

This prospective randomized control study was carried out in a tertiary care teaching hospital spanning over 12 months. A sample size of 50 patients was studied and randomly allocated via a computer into two groups – Group I and Group II (25 patients in each group) receiving IV and epidural tramadol respectively at wound closure following GA. Ethical clearance was taken from the hospital ethical committee.

Inclusion criteria

- Age between 20 yrs to 60 yrs;
- Patients undergoing elective lower abdominal (general surgical, gynaecological and urological), lower limb and orthopaedic surgeries under GA;
- ASA (American Society of Anesthesiologists) physical status I and II

Exclusion criteria

- Paediatric and geriatric cases
- Spinal deformities / prolapsed intervertebral discs
- Emergency cases
- Patient refusal for epidural

The characteristics of patients are as depicted in **Table 1.**

	Group I (IV)	Group II (Epidural)
No. of patients	25	25
Sex Ratio (M:F)	14:11	12:13
Age distribution in years (Avg)	20-50 (35.92)	24-50 (39.04)
Weight in Kgs (Avg)	36-80 (58.36)	38-87 (58.00)

- The selected patients were made familiar with the Visual Analogue Scale (VAS) score a day before the surgery (0 – No Pain, and 10 – Worst Pain Imaginable). All patients received GA with oral endotracheal tube (ETT) intubation, while Gp II patients receiving an epidural catheter prior to induction of GA. IV access was secured and the patient received an epidural catheter in the L2-3 intervertebral space. Standard GA technique was followed in all patients:
- Pre-medication: Injection Glycopyrrolate 0.2 mg IV
- Injection Fentanyl 1 mcg/kg IV
- Induction: Injection Thiopentone 4 mg/kg IV
- Intubation: Injection Vecuronium 0.1 mg/kg IV; Intubated with adult size cuffed endotracheal tube
- Maintenance: Oxygen + Nitrous Oxide + Isoflurane/Sevoflurane
- Injection Vecuronium 1mg IV every 45 mins
- Injection Fentanyl (supplementary doses as required until one hour before surgical wound closure)
- Neuromuscular blockade reversal: Injection Neostigmine 50mcg/kg IV + Injection Glycopyrrolate 10 mcg/Kg IV

Intra-operative monitoring done included continuous electrocar diography (ECG), non-invasive blood pressure (NIBP), pulse oximetry (SpO2) and end tidal carbon dioxide (EtCO2) measurements.

At the time of wound closure, Injection Tramadol 2 mg/Kg was given either IV in Gp I patients or 100 mg diluted in normal saline via the epidural catheter in Gp II patients.

Post operatively VAS score was recorded at half hourly intervals and the study was terminated at VAS score of 6. Both the groups were statistically analysed.

Results

The breakdown of types of surgeries done in both groups is depicted in Table 2 (Figure 1) The values obtained were statistically analysed using unpaired student 't' test on account of small sample size (<30) and unknown population variances assumed unequal.

Table 2			
S No	SURGERY	GROUP I (I.V)	GROUP II (Epidural)
1.	Gynaecology	6	10
2.	Urology	7	3
3.	Orthopaedics	4	6
4.	Gen Surgery	8	6
	TOTAL	25	25

Types of Surgery (Cases in numbers)

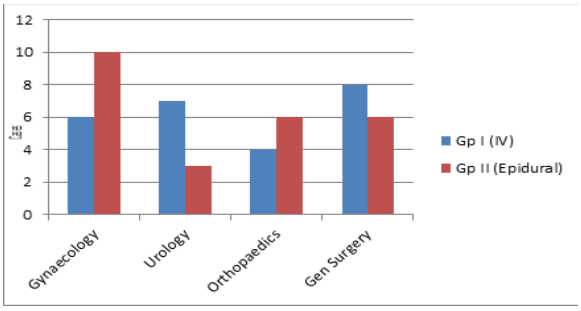


Figure 1

The average duration of analgesia in both groups is depicted in Table 3. The difference between the two groups was found to be statistically significant ($p<0.05$) at 95% confidence intervals.

Table 3

	Range	Mean
Group I (IV Tramadol)	1-4 hours	2 hours 40 minutes (159 .4 mins)
Group II (Epidural Tramadol)	2-10 hours	5 hours 18 minutes (318 mins)

The mean duration of analgesia in patients undergoing different surgeries is depicted in Table 4. This difference between the various surgeries in both the groups was found to be statistically significant ($p<0.05$).

Table 4

SURGERY	GROUP I (Mins)	GROUP II (Mins)	Statistical Analysis (Unpaired student 't' test)
Gynaecology	165 (n=6)	286.66 (n=9)	P<0.05
Urology	167.14 (n=7)	320 (n=3)	P<0.05
Orthopaedics	187.5 (n=4)	375 (n=6)	P<0.05
Gen Surgery	131.25 (n=8)	308.57 (n=7)	P<0.05

The duration of analgesia in different surgeries is further depicted in the bar graph in Figure 2.

Duration of Analgesia in Different Surgeries (in minutes)

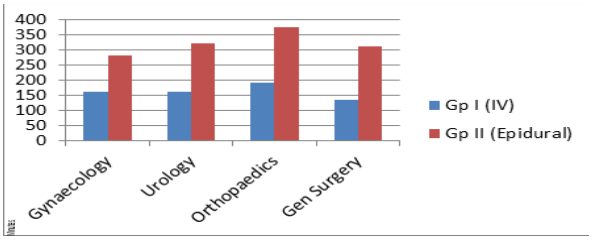


Figure 2

The orthopaedic cases maximally benefitted in both the groups with average peak analgesic effect of 45-60 minutes in Gp I and 65-90 minutes in Gp II.

Patients exhibited stable respiratory and hemodynamic parameters post operatively as depicted in Table 5.

Table 5
Post-op Respiratory & Hemodynamic parameters (average values)

	Group I	Group II	Statistical analysis (Unpaired 't' test)
Oxygen saturation (SpO2 %)	97.5	97.9	p>0.05
Respiratory rate (per min)	16.84	16.49	p>0.05
Heart rate (per min)	86.64	83.58	p>0.05
Mean systolic BP (mmHg)	126.68	125.46	p>0.05

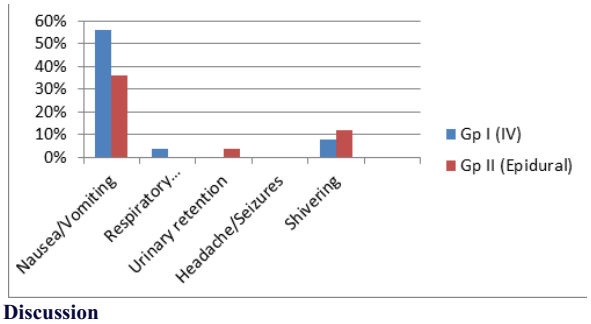
Post-operative nausea and vomiting (PONV) was the most common side effect noted (IV more than Epidural). The side effects and their incidence are depicted in Table 6.

Table 6.

	GROUP I (I.V)	GROUP II (Epidural)
Nausea/Vomiting	14/25 (56%)	9/25 (36%)
Respiratory depression	1/25 (4%)	Nil
Urinary retention	Nil	1/25 (4%)
Headache/Seizures	Nil	Nil
Shivering	2/25 (8%)	3/25 (12%)

The other relevant but statistically insignificant side effect was shivering (Fig 3).

Side Effects (Incidence in percentage) Figure 3



Discussion

In this study, the efficacy of Tramadol for post-operative analgesia was studied comparing the IV and the epidural route of administration following a single dose given at wound closure. Morphine has been considered the 'gold standard' opioid with an average duration of action of 04 hours for a single IV dose and about 18 hours for a single epidural dose. [5] However early and delayed respiratory depression remains a consideration with morphine. Analgesia that follows epidural placement of opioids reflects diffusion of the drug across the dura to gain access to mu opioid rectors on the spinal cord as well as systemic absorption to produce effects similar to those following IV administration.

Hartjen K et al studied the effects of 100 mg tramadol IV bolus at the time of extubation for early post-operative pain prevention. [6] The average interval between extubation and first expression of pain was 106.3 +/-84.2 mins, whereupon a subsequent dose of 50 mg IV tramadol was given as a rescue analgesic. Our study showed the average duration of analgesia in IV tramadol group as 158.4 mins but that was because we had taken a VAS score of 6 (and not just the first expression of pain) as the criteria for subsequent pain relief in the form of rescue analgesic. The average peak effect of analgesia (VAS 3 or below) was found to be 45 minutes in IV tramadol group.

Epidural administration of tramadol at wound closure showed a significantly longer lasting analgesic effect of 5 hours 18 minutes (318 minutes) on an average. In another study Siddik Sayyed S et al compared the post-operative analgesic effect of 100 mg vs 200 mg tramadol given to healthy women via the epidural catheter at skin closure while undergoing caeserian section.[7] The mean time to analgesic administration in patients who received 100 mg tramadol was 4.5+/-3.1 hours while in those who received 200 mg tramadol it was 6.6+/-3.4 hours.

The mean duration of analgesia (Table 4) was found to be greater in the

epidural tramadol group as compared to the IV group across all surgeries: Gynaecological 165 mins (IV) vs 286 mins (Epidural), $p<0.05$; Urological 167 mins vs 320 mins (IV vs Epidural), $p<0.05$; Orthopaedics 187 mins vs 375 mins (IV vs Epidural), $p< 0.05$; and General Surgery 131 mins vs 308 mins (IV vs Epidural), $p<0.05$.

All patients underwent pulse oximetry (SpO2) monitoring post-operatively while the respiratory rate was monitored every half-hourly till termination of study. Both the parameters remained within normal limits throughout the study period in both groups (Table 5). All patients were routinely monitored for heart rate and blood pressure every 30 minutes post-operatively for the duration of the study and there was no significant difference in the mean heart rate and blood pressure between the two groups.

This study revealed that Tramadol was found to provide adequate analgesia for moderate to severe pain. The average duration of analgesia was significantly longer for epidural Tramadol as compared to IV. The incidence of respiratory depression was very mild and transient if at all, and was noted only in one case in the IV group.

PONV was noted to be the most common side effect of Tramadol in this study (Table 6). This was significant in both groups but more so with IV than epidural tramadol (56% patients in the Gp I and 36% in Gp II). In a study by Vicker et al nausea was noted in 6 out of 20 patients (30%) given IV Tramadol.[8] The incidence was lesser in the epidural group but still significantly high (Figure 3). Baraka et al found PONV in 20% of their patients given tramadol epidurally combined with general anaesthesia.[9] However it was not certain if this effect could be ascribed to tramadol. PONV is mostly due to indirect activation of visceral nuclei such as nucleus solitaries or the rostral spread of opioid in cerebrospinal fluid to the vomiting center and chemoreceptor trigger zone.

Tramadol was also found to be associated with reduced shivering in both groups with only 8% of patients in the IV group and 12% experiencing some amount of shivering in the Epidural group (Table 6). An earlier study comparing Tramadol with Pethidine for post-operative shivering via the IV route found shivering to have significantly reduced / ceased in the tramadol group.[10] Tramadol is an inhibitor of the re-uptake of serotonin (5-HT) and norepinephrine in the spinal cord. This facilitates 5-HT release which influences thermoregulatory control. This result of reduced shivering in the post-operative period in both groups in our study compared favourably with other studies.

Conclusion

Epidural Tramadol is more efficacious as compared to IV Tramadol and enjoys certain advantages like longer duration of analgesia, negligible respiratory depression, stable hemodynamic parameters, and a reduced incidence of post-operative shivering. However, there is a need to further evaluate the comparative efficacy of this drug given via the two routes with a larger sample size.

Conflict of Interest

Nil

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