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Comparative evaluation of tramadol via two different routes for post-operative analgesia after inguinal herniorrhaphy

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Abstract

Aims: To compare the duration of analgesia and side effects of tramadol via two different routes i.e intravenous and rectal administration.
Settings and Design: The study design was Prospective, randomized, single blind and hospital based.
Methods and Material: Sixty adult patients of ASA grade I and II posted for inguinal hernia surgery were randomized to receive either rectal suppository of tramadol 100mg (n=30) Group R or I.V. tramadol 50 mg (n=30) Group I. Pain measurement was performed using visual analogue scale (VAS). Rescue analgesia was given when the VAS was >3 in the postoperative period up to 24 hrs. Side effects like nausea, vomiting, were recorded during the same period.
Statistical analysis used: All data was analysed using the Chi square test and Z-test.
Results: Duration of analgesia was prolonged and requirement of rescue analgesic was less with the suppository group. Nausea and vomiting were also lower with the suppository group.
Conclusions: Rectal suppository of tramadol as well as intravenous tramadol are effective for postoperative analgesia after inguinal herniorraphy, but rectal tramadol is better alternative than I.V. tramadol as it has longer duration of pain relief and lesser incidence of nausea and vomiting.

Keywords: Post-operative analgesia, tramadol, suppository, intravenous, inguinal herniorraphy

Introduction

Pain is an extremely complex and distressing subjective feeling. The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience of differing intensity, either caused by actual or potential damage or described in such type of damage“ [2].

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Pain after surgery is inevitable and providing acute pain relief management services in the perioperative period is regarded as one of the main duties of the perioperative team specially anaesthesiologist [1, 2].

Globally the inguinal hernia contribute to 75% of all abdominal wall hernias, and surgery for inguinal hernia repair is one among most common general surgery, worldwide accounting for about 10-15% of all surgical procedures [3].

It is well documented that inadequately relieved pain causes distress to the patient and can skeptically affects physical and physiological function leading to number of complications in post-operative period [4]. Also if not treated correctly it may lead to potential development of chronic pain, which imprint negative psychological effects in patient and also have health economic impact [5].

Modalities of postoperative analgesia are systemic analgesic drugs which includes both opioids and non-opioids, various regional analgesia techniques such as peripheral and neuraxial block [6]. Rectal route is also one among them and it is easier and more patient compatible.

Opioids are well-entrenched and most accepted analgesics in all age groups [7], and Tramadol is a centrally acting opiod with various mode of action. It acts on serotonergic and noradrenergic nociception, whereas its metabolite O-desmethyltramadol acts on the μ-opioid receptor [8]. Its use is established worldwide and also listed in many medical guidelines for management of both acute and chronic pain [9]. Tramadol when used via different routes such as intravenous, intramuscular, rectal or local infiltration, have analgesic efficacy with variable duration and incidence of side effects [6, 8]. Intravenous tramadol is used frequently, however rectal route of tramadol has not been studied much. Keeping above in mind, in present study we decided to compare the duration of analgesia and side effects of tramadol via two different routes i.e. rectal and intravenous, in patients undergoing inguinal herniorraphy.

Subjects and Methods

This study design was randomized, prospective, single blinded and hospital based. After taking the institutional and ethical clearance (SVIC/ON/MEDI/SRP/14220 dated 15/05/14), sixty adult patients (age group of 18-50 yrs) scheduled for inguinal hernia surgery with ASA grade I & II were included in the study. Using block randomization method, patients were randomized to receive either rectal suppository of tramadol 100mg (n=30) group R, or I.V. tramadol 50 mg (n=30) group I.

The exclusion criteria was history of systemic diseases, obesity, known sensitivity to tramadol, contraindication to spinal anesthesia, anorectal complaints if any, ASA grade more than II and patients on monoamine oxidase inhibitors.

Written informed consent was be obtained from all the patients, also preoperatively patients were explained about visual analogue scale (VAS), which is a graded ruler that ranges from 0 -10, showing the no pain and maximum pain score respectively.

Subarachnoid block with injection 0.5% bupivacaine (hyperbaric) 3.2 ml was given at L3-4 interspace using 25 gauge spinal needle. After achieving appropriate level of anaesthesia patients of group R and group I were given tramadol 100 mg rectal suppository and tramadol 50 mg intravenously respectively. This was taken as hour 0. Post operatively time of first onset of pain was noted. Thereafter VAS score was noted at 2, 4, 6, 8, 10, 12, 16, 20 & 24 hours. Rescue analgesia (Inj. Diclofenac sodium 75mg I.V. in 100ml of saline) was given when the VAS score was >3 during postoperative period for up to 24 hrs. Side effects like nausea, vomiting, were also recorded during the same period.

Statistical analysis

The data collected was tabulated. All the continuous variables were presented as mean and standard deviation (SD), while the categorical variables were presented as frequency and percentage. As regard continuous variables; unpaired student-t test was used for between-groups comparison and paired t-test for within group comparison, while for categorical variables we used chi-square test. The $p<0.05$ was considered significant statistically.

Results

The two groups were comparable with reference to sex, age, weight, and duration of surgery (Table 1). The total duration of analgesia till VAS score ≤ 3 was 514±147.3 (360-720) min and 421±80.30 (360-600) min in Group R and Group I respectively (Table 2), and this difference was statistically highly significant ($p < 0.001$). Table 3 shows the number of rescue analgesia doses required and Table 4 shows the time gap of when rescue analgesia was given. The duration of analgesia was increased with Group R, which is inferred by time required for need of first rescue analgesic and also by percentage of patients who required it in both groups. Incidence of side effects like nausea and vomiting were more in group I than in group R, and this difference was also statistically significant (Table 5).

Table 1: Demographic data

Criteria	Group R Mean (range)	Group I Mean (range)	P – value
No. of patients	30	30	
Sex (M/F)	24/6	25/5	
Age (years)	36.3(21-54)	33.9(19-45)	> 0.05 (not significant)
Weight (Kg)	54.7(45-60)	52.1(42-57)	> 0.05 (not significant)
Length of surgery (min)	72.6(60-90)	63(45-90)	> 0.05 (not significant)

Table 2: Duration of analgesia till VAS ≤ 3

Group R Mean±SD (range) (mins)	Group I Mean±SD (range) (mins)	P - value
514±147.3 (360-720)	421±80.30 (360-600)	0.003 (Highly significant)

Table 3: Rescue analgesia

No. of doses needed	No. of patients (%)	
	Group R	Group I
1	17 (56)	30 (100)
2	5(16)	12 (40)

Table 4: Rescue analgesia time

Time	No. of patients (%)	
(hours)	Group R	Group I
4	0	0
6	1 (3)	18 (60)
8	9 (30)	9 (30)
10	5 (16)	3 (10)
12	2 (6.5)	0
18	0	12 (40) second dose
20	5 (16) second dose	0
24	0	0

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Table 5: Side effects

	Group R	Group I	P-value
Nausea	3 (10%)	10 (33%)	0.039 (significant)
Vomiting	1 (3%)	7 (23%)	0.028 (significant)

Discussion

Acute postoperative pain is a multiplex physiological reaction to injury to tissues, visceral distention, or disease. And is manifested as autonomic, behavioural and psychological responses that result in unpleasant, unwanted, patient specific sensory and emotional experience.

Painful incision site hamper adequate breathing, may cause pneumonic consolidation, delays ambulation and limits physical activity which may lead to DVT, slow down wound healing, thus increases the cost of care [4]. As per psychological aspect it lead to fear, demoralization, hospital anxiety, affects sleep, poorly controlled pain can sometime transits into persistent pain, leading to frequent visit to psychologist, general physician or pain physician, may also continue to prolonged use of opioids, drug dependence. All these adds on to the health infrastructure negatively.

Meticulous management of the post-operative pain is vital for good care of the patient. Opioid are routinely used in management of postoperative pain. Tramadol is an atypical opioid being having action on opioid receptor as well as effect on nor epinephrine and serotonin pathways [8]. Its analgesic potency has been claimed to be about one tenth that of morphine [8]. It has lesser risk of producing respiratory depression and low potential for development of tolerance or dependence or abuse, than the other opiods. Thus it gives impression that tramadol may be suitable to treat the postoperative pain. Various formulations of tramadol like oral, rectal and parenteral are available. Use of the same drug by different routes have difference in onset, duration, efficacy and incidence of side effects [10]. Post intravenous and oral administration, the peak concentration are attained rapidly, and this has been associated with nausea and vomiting. This restricts the use of tramadol as a postoperative analgesic, particularly in day care surgery. Rectal administration seems to be an practical alternative in these situations. It is convenient to use and has been established as treatment for postoperative pain in adults [10]. Taking all this into consideration the present study was designed to assess safety and efficacy of tramadol given via two different routes in inguinal herniorraphy patients.

Patients generally are not comfortable being given suppositories when awake. In our study we have introduced tramadol suppository under the effect of spinal anesthesia at the end of surgery, so as to avoid patient's discomfort. A rectal dose of 1.5–2.0 mg/kg is therapeutic [11]. Therefore; we selected a dose of 100 mg in our study for suppository. Tramadol is rapidly distributed after intravenous administration and the onset is fast with a distribution half-life in the initial 6 minutes. And after rectal administration, tramadol was detected in plasma from 5 minute up to 10 hour in dogs [12]. After inserting suppository, absorption of the active ingredient is rapid enough for therapeutic motives and that the extent of absolute bioavailability is higher as after the oral administration of tramadol, this is probably due to reduced first-pass metabolism. Its metabolism quickly transformed the parent drug to high levels metabolites such as N-desmethyl-tramadol (M2) and N, Odidesmethyl-tramadol (M5) [8, 12].

With regard to demographic characteristics i.e. age, sex, weight, and duration of surgery, in our study, both groups were comparable (Table 1). In our study the mean span of analgesia i.e. mean duration of first onset of pain of VAS score of ≤ 3, in rectal tramadol group was prolonged i.e. 514 ± 147.3 minutes, as compared to 421 ± 80.3 minute in intravenous tramadol group (Table 2), this was statistically highly significant (tailed significance value of

p = 0.003). This is in accord with observation made in the study done by Hina N. Gadani *et al*., [12] wherealso the mean duration of analgesia was significantly prolonged with rectal tramadol group than compared to intravenous tramadol, among adult patients undergoing tonsillectomy. Lotfalizade *et al*. [14] studied diclofenac suppository against intravenous tramadol and combination of these two for analgesia in caesarean section and they found mean analgesic duration of 134.7 minutes in the intravenous tramadol group.

We calculated the time of need for rescue analgesia (Table 4), and it was shown that 60% of patients needed first rescue analgesia dose at 6 hrs in Group I, while it were only 3.5% in patients of Group R, which is a significantly lower proportion. In the suppository group, 30% patients needed first rescue analgesia at 8 hrs, 16% needed the same at 10 hrs and another 6.5% needed at 12 hrs. Thus, only 56% of the patients needed rescue analgesia in Group R within 12 hrs of the postoperative period. Other 44% patients in Group R did not require rescue analgesia at all, which was not with Group I patients. In Group I, all 100% patients required rescue analgesia within 10 hrs of the postoperative period. This goes in agreement with what was observed by Hina N. Gadani *et al*. [13] and M Lotfalizade *et al*. [14] in their study. 40% of patients of Group I required rescue analgesia a second time at 18 hrs, while in Group R this was only 16% and that too at 20 hrs (Table 3). Thus the duration of analgesia was more in Group R, which was confirmed by both, the time required for need of first rescue analgesic and percentage of patients who required it in both groups. These observations of our study are also in agreement with the study of Spagnoli *et al.*, [15] who compared the analgesic efficacy between combination of tramadol and paracetamol to paracetamol alone for acute postoperative pain post hand and foot surgeries. They found that the pain score after surgery was significantly lesser in the group which received tramadol and paracetamol combination.

Tramadol is having nausea and vomiting as troublesome side effect. Different authors studied this side effect by using tramadol by different route. In our study, ten patients of Group I had nausea and seven patients had vomiting, while in Group R, only three patients had nausea and one had vomiting [Table 5]. More patients suffered with side effects in Group I as compared to Group R and this difference was also statistically significant ($P < 0.05$). As far as the side effects profile is concerned, various authors have also reported decreased side effects with tramadol suppository than intravenous. Hina N. Gadani et al. [13] also found 15% incidence of postoperative nausea-vomiting (PONV) in intravenous tramadol group as against 5% in rectal suppository group. Joshi V.S. *et al*. [16] studied rectal suppository of tramadol and diclofenac in caesarean section, they reported 3.33% incidence of PONV among rectal tramadol group. Not one patient from both groups complained of local rectal site burning. Our all above mentioned results are comparable with previous studies [16, 17, 18].

Thus rectal suppository of tramadol is a better alternative as postoperative analgesic in inguinal herniorraphy as compared to intravenous tramadol. Rectal route is easy, well accepted, and practical and require no special technique. Although individual variations subsists, there is sufficient absorption of drug after rectal administration [19]. There are few limitations of our study as well. First, we had only 2 study groups and our study lacked a 3rd group of control patients, to compare the effect of placebo with those two groups. Also the number of patients included in our study were less, so further study including large number of patients is also needed.

Cconclusion

Rectal suppository of tramadol, as well as the intravenous form of tramadol, both are effective as postoperative analgesic after inguinal herniorraphy, but rectal tramadol is a better alternative than I.V. tramadol as it provides longer duration of analgesia, which in turn decreases the requirement of rescue analgesia. It also adds to the patient comfort by

decreasing the incidence of nausea and vomiting as compared with intravenous route. Thus rectal route is a safe, effective, easy, and non-invasive means for pain relief.

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