Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(4) (Part - I): 1156-1160
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6419.14

Comparison of the Analgesic Effect of Tramadol Suppository with a Combination of Tramadol and Diclofenac Suppository after Lower Abdominal Surgeries

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Abstract

Background and aim of the study: The rationale behind this study was to reduce the side effects of standard dose of tramadol by reducing the dose of tramadol and to achieve same analgesic effect by combining with diclofenac. So this study compares the analgesic efficacy and side effect profile of rectal tramadol 100 mg with combination of rectal tramadol 50 mg and rectal diclofenac 50 mg in patients undergoing lower abdominal surgeries. *Materials and Methods:* Two hours after the establishment of spinal anaesthesia, patient were administered either tramadol 100 mg rectally in Group T (n=50) or combination of tramadol 50 mg rectally and diclofenac 50 mg rectally in Group TD (n=50). Using 0-10 numeric rating scale (NRS), pain at the surgical site at rest during postoperative period was measured. Any side effects like nausea, vomiting, pruritus, dizziness, headache, drowsiness, gastritis, Sweating etc. for 24 h was noted. *Results:* The mean duration of effective postoperative analgesia was 314.5 ± 7 minutes and 318.9 ± 5 minutes in group T and TD respectively. The difference between the groups with respect to duration of effective postoperative analgesia was not statistically significant. Group T had a statistically higher incidence of nausea and vomiting than group TD. *Conclusion:* The combination of low dose tramadol and diclofenac may be a better alternative to standard dose tramadol as it provides same quality and duration of analgesia with fewer side effects.

Keywords: Tramadol; Diclofenac; Postoperative analgesia; Nausea and vomiting.

How to cite this article:

Mahantesh Mudakanagoudar, Santhosh MCB. Comparison of the Analgesic Effect of Tramadol Suppository with a Combination of Tramadol and Diclofenac Suppository after Lower Abdominal Surgeries. Indian J Anesth Analg. 2019;6(4):1156-1160.

Introduction

Postoperative pain relief is a universal concern because pain relief is a fundamental human right. Unrelieved acute pain results in potentially life-threatening adverse physiological effects, development of chronic pain syndromes and may cause psychological disturbances. Systemically administered analgesics include NSAIDS and opiates which are administered either parenterally or rectally in the postoperative period [1].

Tramadol is a centrally acting opioid analgesic, which acts on μ opioid receptors, and is classified as a phase II analgesic according to the WHO

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Received on 27.03.2019, **Accepted on** 04.05.2019

pain score [2] but its analgesic effect is because of mixed opioid and non-opioid activities [3,4]. Analgesic Action of Tramadol has multiple mechanism like inhibition of the opioid receptor, inhibition of noradrenaline (norepinephrine) and serotonin (5-hydroxytryptamine; 5-HT) reuptake. One of the most frequent side effects of tramadol is nausea and vomiting [5]. Other adverse effects are generally similar to those of opioids, although they are usually less severe, and can include respiratory depression, dysphoria and constipation [5].

Diclofenac is one of the most commonly used Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and is classified as a phase II analgesic according to the WHO pain score. This acts by potent cyclo-oxygenase inhibition, reduction of arachidonic acid release, and enhancement of arachidonic acid uptake. Its common adverse effects are gastric irritation, dyspepsia, peptic ulcer or bleeding, nephrotoxicity, asthma, and anaphylactic reactions [6]. However, after intravenous and oral administration of tramadol, peak concentrations are reached rapidly and this has been associated with higher incidence of nausea and vomiting. This limits the use of tramadol as a postoperative analgesic [7]. Rectal administration of tramadol may be an alternative in this situation as the incidence of nausea and vomiting is relatively less than intravenous tramadol [8]. Rectal administration of tramadol is convenient to use, and is an established route of administration of the drug for postoperative pain in adults [2,9]. But the incidence of nausea and vomiting associated with rectal tramadol (100 mg) is relatively more when compared to rectal diclofenac (100 mg) [10].

The present study has been carried with hypothesis that the reduction of dose of tramadol and diclofenac to half of standalone dose of the both drugs will lead to reduction in incidence of side effects of both the drugs with same analgesic efficacy in patients undergoing lower abdominal surgeries.

Materials and Methods

This was a prospective, randomised, double-blind, parallel-group controlled trial. After Institutional Ethic Committee approval and informed consent, 100 ASA 1 or 2 patients aged between 18-60 years, undergoing elective lower abdominal surgeries under spinal anaesthesia were prospectively included in the study. The exclusion criteria were ASA status more than 2; major co-existing medical illness such as severe asthma, uncontrolled hypertension or diabetes; peptic ulcer disease or gastrointestinal bleeding; already on long-term analgesics and known hypersensitivity to any of the study medications.

After inclusion, patients were randomized by using computerised generated random table numbers and allotment was done using coded sealed opaque envelopes and informed written consent was obtained. Participants were enrolled by one of the authors, and the group assignment was done by another.

All the patients were pre-medicated with oral alprazolam 0.5 mg and oral ranitidine 150 mg on the previous night of surgery. Patients was kept nil orally for at least 8 hours.

On arrival to the operating room, intravenous line was secured with 18G intravenous cannula in all patients and was preloaded with lactated ringer's solution at 15 ml/kg. Patients were connected to all standard monitors such as pulse oximetry, ECG, Non-invasive Blood pressure monitors. Baseline values of parameters like heart rate, blood pressure, and SPO_2 were recorded.

All patients received Inj. Ranitidine 50 mg intravenously. Under aseptic precaution, all patients underwent lumbar puncture in left lateral position at L3-4 inter laminar space using 25G Quincke's spinal needle and received standard spinal anaesthesia with 3.5 ml of bupivacaine (heavy) 0.5% to achieve block level up to T4. Two hours after the establishment of spinal anaesthesia, patient were administered with either tramadol 100 mg rectally in Group T (n=50) or combination of diclofenac 50 mg rectally and tramadol 50 mg rectally in Group TD (n=50).

Vital parameters like heart rate, blood pressure, SPO_2 were monitored during intraoperative and postoperative period.

Using 0-10 numeric rating scale (NRS), pain at the surgical site at rest during postoperative period was measured at intervals of 0, 1, 2, 3, 4, 8, 12, 16, 20 and 24 h. Time 0 begins when study drug was administered. Effective pain control was defined as NRS score ≤ 3. The duration for which NRS score was ≤3 after insertion of suppository was considered as duration of effective postoperative analgesia. When NRS score was more than 3, supplementary rescue analgesic intravenous morphine was administered initially 0.1 mg/kg. If pain relief was not adequate, patients were administered with subsequent doses of intravenous morphine 0.02mg/kg to maximum dose of 0.2 mg/kg.

Any side effects like nausea, vomiting, pruritus, dizziness, drowsiness, gastritis were noted for

24 h. Side effects were treated with intravenous Ondansetron 4 mg (Nausea and Vomiting), intravenous promethazine 25 mg (pruritus), and intravenous pantoprazole 40 mg (Gastritis). Patients who had dizziness and drowsiness were monitored till above side effects subside.

Severity of nausea and vomiting was assessed using 0-10 numeric rating scale (NRS) where scale "0" (labelled "no nausea") and "10" (labelled "unbearable vomiting"), patients with score of 1-3, 4-7, 8-10 were considered as equivalent adjectival scale mild, moderate and severe respectively.

Statistical analysis

As our pilot study was with no previous information being available regarding expected means or standard deviations, a pre-study power calculation was not possible. The number of participants was based on a feasible convenience sample and was therefore arbitrarily decided. The study was analysed with null hypothesis that the postoperative analgesia in both the groups will be adequate. The primary outcome of the study was to compare the analgesic efficacy between the two groups. The secondary outcome of the study was to compare the side effect profile between the groups in patients undergoing lower abdominal surgeries. Pearson's chi-squared test was used to determine the normality of distribution of data. Statistical testing of ordinal data (age and sex of the patient, weight and height of the patients, Type and duration of surgery) was done using fisher's exact test. The remaining variables were analysed for statistical significance using two tailed unpaired 't' test. The results are presented as mean ± standard deviation (SD), number (n) of cases. A p value of < 0.05 was considered statistically significant.

Results

The two groups were more or less homogenous with regard to age and sex distribution, weight and height of patients, type and duration of surgery. There was no significant difference between the two groups with regard to cardiorespiratory parameter in the intraoperative and postoperative period. The mean duration of effective postoperative analgesia was 314.5 ± 7 minutes and 318.9 ± 5 minutes in group T and TD respectively. The difference between the groups with respect to duration of effective postoperative analgesia was not statistically significant. The incidence of nausea was comparatively high in group T (n= 15) than in group TD (n=3). The incidence of vomiting was comparatively high in group T (n=9) than in group TD (n=0). So the difference in incidence of nausea and vomiting was statistically significant between group T and group TD. There was no statistically significant difference between the two groups regarding the incidence of other side-effects.

Table 1: Demographic profile of patients, duration of surgery

Variables	Group T (n= 50) (Mean ± SD)	Group TD (n= 50) (Mean ± SD)	'p' value
Age (years)	48.4 ± 2.45	50.1 ± 3.04	0.238
Sex (Male:Female)	9:51	10:50	0.342
Height (cm)	155.3 ± 3.05	156.6 ± 2.48	0.432
Weight (Kg)	53.7 ± 3.25	55.6 ± 3.65	0.602
Type of Surgery			
• Vaginal Hysterectomy	51	50	
• Inguinal Hernioplasty	9	10	0.456
Duration of Surgery (minutes)	95 ± 82	92 ± 10	0.125

Table 2: Number of patients with NRS < 3 after insertion of suppository

Time (after insertion of suppository) (minutes)	60	120	180	240	270	300	315	330	345
Group T (n)	50	50	50	50	50	50	49	10	0
Group TD (n)	50	50	50	50	50	50	50	15	0
'p' value	0.999	0.999	0.999	0.999	0.999	0.999	0.876	0.234	

Table 3: Total rescue analgesic consumption (Intravenous morphine in mg) in 24 hours (Mean ± SD)

Group T	Group TD	'p' value
9.54 ± 0.34	9.13 ± 0.43	0.675

Table 4: Postoperative characteristics

Characteristics	Group T	Group TD	p value
Duration of effective postoperative analgesia (Minutes) (Mean ± SD)	314.5±7	318.9±5	0.435
Side-effect Profile			
• Nausea and Vomiting (n)	15	3	0.0013
Mild (NRS 1-3)	2	2	
Moderate (NRS 4-7)	6	1	
Severe (NRS 8-10)	7	0	
• Drowsiness (n)	1	0	0.436
• Gastritis (n)	0	1	0.437
• Dizziness (n)	1	0	0.442
• Headache (n)	2	0	0.586
• Sweating (n)	1	0	0.441

Discussion

Postoperative pain relief is one of the most important aspects of postoperative care of the surgical patients. Postoperative pain is associated with grave physiological and psychological trauma, resulting in altered cardiorespiratory parameters, restless and delirium. Most of the times, pain relief is inadequate in anticipation of side-effects associated with the analgesics. The lower abdominal surgeries like vaginal hysterectomy, inguinal hernioplasty etc. are associated with moderately severe postoperative pain which can be treated effectively with tramadol (Phase 2 analgesic in WHO ladder). But administration of tramadol either intravenously or rectally in postoperative period is associated with side-effects such as nausea or vomiting, headache, sedation, delirium, sweating. Among these, nausea and vomiting are minor but most common and troublesome side-effect associated with tramadol which makes its less suitable for use as a postoperative analgesic [11]. Various routes of tramadol administration have been tried to reduce the incidence and severity of postoperative nausea and vomiting but with limited success.

Our study shows that low dose combination of tramadol and diclofenac will provide similar quality and duration of analgesia as the standard dose of tramadol alone with significantly less incidence of nausea and vomiting when compared to the standard dose of tramadol alone.

The review of literatures in Medline to best our ability did not show any similar studies to compare our study results.

In our study, both groups were demographical comparable. Patients in group T had NRS score less than 3 for 314.5 ± 7 h whereas patients in group TD had NRS score less than 3 for 318.9 ± 5 h. So the analgesic efficacies of both groups were comparable with regards to duration and quality of analgesia. So pain relief provided by combination of tramadol 50 mg and diclofenac 50 mg was similar to the tramadol 100 mg alone.

The incidence and severity of nausea and vomiting was clinically and statistically high in group T patients when compared to group TD. Incidence of headache was also high in group T than group TD. Incidence and severity of other side effects were comparable between two study groups. This significant difference between the two groups with regards to incidence of nausea and vomiting is explained by the fact that it is the peak concentration of tramadol achieved which determines the incidence and severity of the nausea and vomiting [7,12].

We also observed that the incidence of gastritis which is a common side effect associated with standard dose diclofenacas observed by various studies [13,14,15] was also significantly less in our low dose tramadol and diclofenac combination group.

The limitation of our study is that patients who were undergoing vaginal hysterectomy and inguinal hernioplasty were included. So the results cannot be generalized to other gynaecologic and general lower abdominal surgeries.

Conclusion

The combination of low dose tramadol and diclofenac may be a better alternative to standard dose tramadol as it provides same quality and duration of analgesia with fewer side effect.

Source(s) of support: Nil

Presentation at a meeting: Nil

Conflicting Interest: Nil

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