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RESEARCH ARTICLE

COMPARE THE ANALGESIC EFFICACY OF INTRAVENOUS VERSUS WOUND INSTILLATION OF TRAMADOL FOR POSTOPERATIVE ANALGESIA

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ABSTRACT

Background and Aim: Effective postoperative analgesia improves early mobilization, patient's satisfaction and reduces psychological stress. Now a days wound instillation of local anaesthetic is commonly used method to provide post-operative analgesia. We design this study to compare the post-operative analgesic effect of tramadol when administered intravenously or in wound instillation with bupivacaine.

Materials and Methods: In this study, 100 patients posted for elective abdominal surgeries under general anaesthesia were randomly divided into two groups (n=50) and were given the following drugs after surgery as per group allocation: Group A patients received 2mg/kg tramadol intravenously plus wound instillation with 15 ml 0.5% bupivacaine and Group B received 2mg/kg tramadol with 15 ml 0.5% bupivacaine in wound instillation. Rescue analgesia was provided by intravenous morphine 0.05mg/kg. Verbal Numerical Rating Scale (VNRS) on movement was assessed at 0, 1, 3, 6, 8, 12 and 24 h following surgery. Patients were also observed for post-operative 24 hrs rescue analgesic requirement, patients satisfaction score and any adverse effects.

Results: VNRS on movement was significantly reduced at 1 and 3 h after surgery in Group B as compared to Group A (P=0.001). Analgesic efficacy was similar in both the groups at all time intervals. The satisfaction scores at 12 and 24 h post-operatively were superior in group B as compared to group A (P <0.05). Patients receiving IV tramadol had more vomiting and sedation.

Conclusions: Analgesic efficacy of wound instillation with tramadol was comparable to intravenous tramadol after lower abdominal surgeries along with better satisfactory scores and lessor side effects.

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INTRODUCTION

Providing adequate postoperative analgesia is one of the fundamental responsibilities of Anaesthesiologists. Insufficient postoperative pain therapy leads to coronary ischeamia, myocardial infarction, poor wound healing and psychological stress. (Vadivelu *et al*., 2010) Improvement in the field of postoperative analgesia is still in progress. The intensity of acute post-operative pain is a important predictor of chronic post-operative pain. Now a days multimodal analgesia including peripheral nerve blocks, intravenous catheters, wound infiltration or instillations of local anaesthetics are used for post-operative analgesia. But every technique has some side effects and limitations. Wound instillation with local anaesthetics is safe and cost-effective method to provide postoperative analgesia. (Jonnavithula *et al*., 2015) Tramadol is a racemic compound made up of two isomers that have opioid and non-opioid activities. It is structurally related codeine, which is methyl morphine. (Jou *et al*., 2003) Tramadol has both systemic analgesic and local anaesthetic effects. (Altunkaya *et al*., 2004) The primary objective of the present study was to determine the analgesic efficacy of tramadol in wound instillation with bupivacaine and to compare it with intravenous tramadol in patients undergoing lower abdominal surgeries for postoperative analgesic requirement and side effects.

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MATERIALS AND METHODS

After obtaining the permission of appropriate authority of the institute and written informed consent, 100 patients were enrolled in the study. The study was designed as a prospective, randomized and double-blinded comparative study.

Inclusion criteria

- Patients aged between 35-60 years
- ASA‑I and ASA‑II physical status

- Scheduled for elective lower abdominal surgery with midline incision (surgical and gynecological) under general anesthesia

Exclusion criteria

- ASA Grades III and IV patients
- Obese patients (BMI >30kg/m2)
- Patients on chronic analgesic medication, opioids or substance abuse
- Patient with significant cardiovascular, respiratory, renal, hepatic, neurological or psychiatric disease

During preanaesthetic checkup, all patients were explained about the procedure and Verbal Numerical Rating Scale (VNRS). Tablet ranitidine 150 mg & alprazolam 0.25 mg were given orally 2h before surgery. Randomization to two equally distributed groups of 50 patients each was done by computer generated random numbers and blinding was done from opaque sealed envelopes. The Anaesthesiologist who prepared the study drugs did not aware of group allocation and data collection. On arrival at the operation-theatre, patients were continuously monitored by electrocardiogram, pulse oximetry, noninvasive blood pressure and end tidal carbon dioxide using multipara monitor. An 18G intravenous cannula was secured. After proper pre-oxygenation for 3minutes, general anesthesia was induced with intravenous propofol (2 mg/kg) and fentanyl (2µg/kg). Intubation of trachea was facilitated by i.v. vecuronium bromide 0.1 mg/kg and maintained with 50% nitrous oxide, 50% oxygen and isoflurane 1%. Muscle relaxation was maintained with i.v. vecuronium bromide 0.08 mg/kg. Intraoperative analgesia was provided by bolus of 1µg/kg of IV fentanyl. At the end of the surgery a multipore suction catheter (Romovac) was placed between peritoneal and muscular layer and other end of the catheter led out through separate wound. Patients were given the following drugs as per group allocation.

Group A patients received intravenous (I.V.) tramadol 2mg/kg in 20 ml normal saline infusion over 10 min and wound instillation with 15 ml of 0.5% bupivacaine at the end of surgery.

Group B patients received I.V. 20 ml normal saline infusion over 10 min and wound instillation with 2mg/kg tramadol with 15 ml of 0.5% bupivacaine at the end of surgery. For wound instillation 15 ml solution was given through catheter and after that catheter was clamped for 10 minutes.

All the patients received fluid in the form of normal saline as per standardized calculations. Patients were extubated after reversal of neuromuscular blockade with intravenous 0.05 mg/kg neostigmine and 0.01 mg/kg glycopyrolate, and the patients were shifted to post anesthesia care unit (PACU) for further monitoring. In PACU, pain scoring was assessed by using four-point VNRS on movement (Holdgate *et al*., 2003) (0=none, 1-3=mild, 4-7=moderate, 7-10=severe pain) at 0h(baseline), 1h, 3h, 6hr, 8h, 12h and 24h postoperatively by an Anaesthesiologist who was blinded to the study group. Rescue analgesia was provided by intravenous morphine 0.05mg/kg, if the VNRS on movement was >3 during the study period. After 12 hrs of surgery, bolus of 15 ml of study drugs was repeated through drain as per group allocation. Total morphine consumption during first 24 hrs after surgery was recorded. Side effects such as nausea, vomiting, sedation, respiratory depression, hypotension and bradycardia were recorded. Nausea and vomiting were recorded using categorical score (0=none, 1=slight, 2=moderate, 3=severe/request treatment). When moderate or severe nausea or vomiting was present, we administered 0.1 mg/kg of IV ondansetron. Sedation was monitored using the following scale (1=alert, 2= occasionally drowsy, 3=frequently drowsy, 4=sleepy, easy to arouse, 5=somnolent, difficult to arouse). Patient's satisfaction with technique was also assessed at 12 and 24 hrs after surgery on five point scale (very satisfied, satisfied, neutral, dissatisfied, and very dissatisfied).

Statistical Analysis

Data were expressed as mean values ± SD. The patient characteristics (nonparametric data) was analyzed using the "Chi-square tests" and the inter group comparison of the parametric data was done using the Student's *t*-test. Wilcoxon Mann Whitney test was applied for analysis of VNRS, 24-h rescue analgesic requirement and patient's satisfaction score. Considering a difference of 30% regarding the 24-h rescue analgesic requirement significant and taking an α value of 0.05 with power of the study (1- β) to be 80%, the number of patients was calculated to be 44 in each group. The inclusion of 50 patients in each group was done for better validation of results. $P < 0.05$ was considered as statistically significant.

RESULTS

Hundred patients were randomized into the two groups (n=50), and all the patients completed the study. There were no differences between the groups regarding demographics and duration of surgery. (Table 1) Intra-operative heamodynamic parameters were comparable among the groups. Patients in group B exhibited lower VNRS on movement as compared to group A at 1h and 3h postoperatively (P=0.001) (Table 2). On intragroup comparison, in group B, VNRS on movement at 3h was statistically significant with baseline (0 h) (P=0.01).

Table 1. Patient characteristics

Demographics	Group A (Tramadol intravenous) (n=50)	Group B (Tramadol wound instillation) (n=50)	P value
Age (years)	52.63±5.13	53.47±6.11	0.423
Gender (M:F)	20:30	24:26	NA
Weight (Kg)	61.05±8.86	62.13±7.70	0.871
ASA grade (I:II)	26: 24	28: 22	NA
Duration of surgery(hours)	1.9±0.9	2.0±0.5	0.472

Data expressed as mean±SD and n, SD = Standard deviation, n=Number of patients,
ASA= American Society of Anaesthesiologist

The 24 h requirement of morphine was reduced in group B as compared to group A, but it was not statistically significant. The incidence of postoperative nausea and vomiting were high in the group A as compared to group B. Ten patients had nausea and vomiting in group A while only two patients in group B. The incidence of sedation was also high in the

Table 2. VNRS on movement post-operatively

Time	Group A (Tramadol intravenous) (n=50)	Group B (Tramadol wound instillation) (n=50)	P value
0 hr	1.21±0.85	1.83±0.74	0.06
1 hr	1.30±0.59	1.88±0.36	0.001*
3 hr	1.34±1.40	1.86±1.31	0.001*
6 hr	2.68±1.01	3.78±1.36	0.38
8 hr	1.38±0.36	1.84±0.66	0.92
12 hr	2.76±0.93	3.66±0.63	0.08
24 hr	1.78±0.99	1.33±0.36	0.81

Data expressed as mean±SD, SD = Standard deviation, P <0.05 considered statistically significant. VNRS=Verbal Numerical Rating Scale

Table 3. Postoperative side effects

Side effects	Group A (Tramadol intravenous) (n=50)	Group B (Tramadol wound instillation) (n=50)
Nausea/ Vomiting	10 (20%)	2 (4%)
Sedation	5 (10%)	0
Respiratory depression	0	0
Hypotension	0	0
Bradycardia	0	0
Skin rash	0	0

Data expressed as number and % of patients

Table 4. Postoperative patients satisfaction

Time of assessment	Group A (Tramadol intravenous) (n=50)	Group B (Tramadol wound instillation) (n=50)	P value
12 hr	1.63±33	1.98±61	0.01
24 hr	1.16±63	1.69±0.73	0.03

Data expressed as mean±SD and n, SD = Standard deviation. Statistically significant at P <0.05

group A. (Table 3) The satisfaction scores at 12h and 24h postoperatively were better in group B as compared to group A (P=0.01, 0.03 respectively) (Table 4). There was no technical failure, wound infection and impaired wound healing in any patients.

DISCUSSION

The wound instillation of local anaesthetics to provide analgesia is well established technique in various surgeries like laproscopic cholecystectomy, abdominal hysterectomy and cosmetic breast surgery. (Boddy *et al*., 2006; Zohar *et al*., 2001; Kazmier *et al*., 2008) Wound instillation with local anaesthetics agent is simple, safe and inexpensive method to provide postoperative analgesia. Various adjuvants were used in this technique such as morphine, buprenorphine and ketamine. (Shadangi *et al*., 2012; Mehta *et al*., 2011; Zohar *et al*., 2002) In the present study, analgesic efficacy of tramadol in wound instillation was comparable with intravenous tramadol up to first 24 hrs postoperatively with superior satisfaction score and less side effects in patients undergoing lower abdominal surgeries. VNRS was reduced in early postoperative period at 1hr and 3hr in group B. However, at other time intervals no statistically significant difference in VNRS was found between the study groups. Demiraran (2006) *et al*. demonstrated lower pain scores for first 8 hrs in tramadol group compared to bupivacaine group after herniotomy of paediatric patients. They compared by using 2mg/kg tramadol and 0.2 ml/kg of 0.25% bupivacaine subcutaneously. Malik *et al*. (2011) had found that local wound infiltration with tramadol in hernia repair provide prolonged postoperative analgesia when compared to bupivacaine (onset of postoperative pain 11.60 ± 3.49 hours vs 8.20 ± 2.94 hours for tramadol and bupivacaine respectively). In present study, there was no significant difference in 24 h postoperative morphine requirement between the study groups. This finding was in concurrence with another study. (Immer *et al*., 2003) Though, the mechanism of the topical tramadol remains unclear. It has been suggested that tramadol had a local anaesthatic effects similar to that of prilocaine and bupivacaine after intradermal and subcutaneous administration. (Atunkaya *et al*., 2003) There are various theories, (Mert *et al*., 2002) tramadol may act on voltage dependant sodium channels, leading to axonal blockage or the presence of large ca+ concentration in the external medium increases tramadol's activity. Inspite of local anaesthetic effects, tramadol extends its antinocciceptive effects by activation of both opioids and nonopiods (descending monoaminergic system) systems. Nonopiods component is mediated through α2-agonistic and serotonergic activities by inhibiting the reuptake of norepinephrine and 5-hydroxytryptamine.

Nausea, vomiting and sedation are common adverse effects of parentral administration of tramadol. Khajavi *et al*. (2009) found that subcutaneous wound infiltration of tramadol reduces postoperative opiods consumption and incidences of nausea and vomiting compared with i.v. tramadol. In another study, subcutaneous tramadol infiltration resulted in effective analgesia and anti-inflammatory effects with minimal sedation. (Gercek *et al*., 2004) Similarly, in our study, incidences of nausea and vomiting and sedation were higher in patients who received i. v. tramadol but not in wound instillation. Many studies (Gadani and Chaudhary, 2010; Nossaman *et al*., 2010) found higher incidences of nausea and vomiting in patients who received i. v. tramadol compared with other routes of tramadol administration. The satisfaction score at 12hr and 24 hr postoperatively were better in wound instillation group as compared to I. V. group. It could be due to reduce incidences of nausea and vomiting in wound instillation groups so further trials are required regarding this finding. One of the limitations to our study was that we did not include placebo group. Secondly, we could not follow the patients after 24 hrs postoperatively. Thirdly, we did not estimate the serum concentration of tramadol which could be more reliable to choose mode of drug administration. We suggest adding of these parameters during future studies. We concluded that

wound instillation of tramadol with bupivacaine could be used as an alternate mode of postoperative analgesia after abdominal surgeries with better satisfaction score and lessor side effects compared to I. V. tramadol.

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