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Original Article

Post-operative Analgesia: Side Effects Of Tramadol Infusion Alone And With Combination A Comparative Study

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ABSTRACT

Background: Pain management is the key to a successful surgery. Various classes of analgesics are used in the post-operative period.Tramadol can be used intravenously for moderate and severe post-operative pain. The intention of this study is to compare the incidence of common side effects occurring with different combinations of post-operative tramadol infusion. **Methodology:** At General Surgery Unit-III, Civil Hospital and Dow University of Health Sciences, Karachi. 200 patients who under went laparoscopic or open elective surgery were categorized into four groups according to the type of analgesia received. Group A received tramadol and metoclopramide while group B received tramadol with diclofenac. Group C received tramadol, metoclopramide and paracetamol whilegroup D received Nalbuphine with Diclofenac. Pain score was recorded on visual analogue scale of 1 to 10 at 12 hours post-surgery. Common side effects of tramadol including nausea, vomiting and dizziness were recorded. **Statistical Analysis:** Data analysis was carried out using SPSS version 22.0. Chi-square test was used to make comparisons and p-values <0.05 were considered significant. **Results:** Final analysis was carried out on 191 patients. The mean pain score was 2.64 with SD ± 1.64. It was found that 62.8% (n=120) of patients had no side effects after surgery. Overall, patients who had post-operative side effects of nausea, vomiting and dizziness were 19.9% (n=38), 5.2% (n=10) and 14.1% (n=27), respectively. **Conclusions:** Tramadol may be used as infusion without metoclopramide with no increase in post-operative nausea and vomiting.

KEYWORDS: Tramadol; Paracetamol; Diclofenac; Nalbuphine; Postoperative pain; VAS score.

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INTRODUCTION

Pain management is the key to a successful surgery. Postoperative pain management begins in the preoperative period and is tailored to the individual and the surgical procedure involved. Most surgical patients receive inadequate pain relief, which can increase the risk for prolonged postoperative pain, mood disorders, and physical impairment.[1] These complications affect hospital functioning, which leads to decreased patient satisfaction, a worse reputation for the hospital, prolonged hospitalizations, higher incidence of re-surgeries and re-admissions, and higher costs for care and treatment, as well as higher numbers of claims and compensations [2, 3].

Post-operative pain is most severe in the immediate 24 hours and use of good analgesia is important for the comfort and speedy discharge of patient. During the post-operative period, occurrence of serious side effects of drugs may also delay discharge of patients. Post-operative nausea vomiting (PONV) termed as the little big problem of surgery and the incidence of which is quoted to be around 30% and as high as 80% in high risk patients. Some risk factors for PONV include female gender, post-operative opioid use, and history of motion sickness, non-smoking status and post puberty patients.[4,5]

Opioids such as tramadol and nalbuphine are kept as a third line of analgesia after surgery due to reported complications but are the most effective among the management options. However, studies suggest that opioids remain the popular choice for surgical pain management in most patients.[6, 7] Opioids are not entirely devoid of undesirable effects like postoperative nausea and vomiting, respiratory depression, sedation and constipation.

Tramadol, one of the weak agonist opioid receptors, is a synthetic analogue of codeine that acts centrally. It has been successfully used for moder-ate and severe pain. The increased analgesic action results from the dual action of inhibi-tion of noradrenaline and serotonin reuptake in neurons. Tramadol's capacity to induce respiratory depression is minimal, and therefore, it enables very good pain control and active rehabilitation after orthopedic and abdominal surgeries, labor analgesia, pain relief in children, short-term and day case surgeries and after trauma.[8,9,10,11] However its side effect of causing nausea and vomiting reported to be up to 20% in the literature is a deterrent for its use for many physicians.

Tramadol has been administered through many routes including enteral, intramuscular, intravenous, epidural and even as local infiltrate in wounds[12] but enteral and intravenous routes remain the most commonly employed. Intravenous administration can be as IV bolus or as slow infusion with the latter strategy reported to cause lower incidence of nausea vomiting with the same analgesic efficacy. Use of an anti-emetic agent along with tramadol administration has the theoretical effect of reducing nausea vomiting but the studies performed have controversial results.[13-17] Also use of some anti emetics like serotonin antagonist e.g. ondansetron has been shown to increase tramadol requirements for analgesia involved in some studies due to common chemical pathways.[18, 19]

Metoclopramide is a centrally acting dopamine receptor antagonist in the chemoreceptor trigger zone. It also has muscarinic activity which is responsible for its gastro-prokinetic activity.

The present prospective comparative study was done to assess the common side effects with slow intravenous infusion of tramadol alone and in combination with other commonly used analgesics such as diclofenac sodium, paracetamol while using an anti-emetic in some combinations

MATERIAL AND METHODS

Patient selection and recording: All patients who underwent either laparoscopic or open elective surgery at Civil Hospital Karachi, were chosen by convenient sampling after obtaining consent from patient to participate in the study. Patient's pain score was recorded on visual analogue scale of 1 to 10 at 12 hours post operatively. Common side effect of tramadol including nausea, vomiting and dizziness were also recorded.

Inclusion criteria

Patients undergoing elective surgery either laparoscopic or open were chosen by convenient sampling to participate in the study.

Exclusion criteria

Patients whose liver function tests were abnormal (Serum bilirubin >2 mg%), recent myocardial infarction history (<6 months), a known case of allergy to tramadol, diclofenac, nalbuphine, paracetamol or metoclopramide, recent cerebrovascular accident within 6 months, angina pectoris, congestive heart failure (left ventricular ejection fraction <30%), severe pulmonary diseases, pregnancy or lactation, patients with a history of seizures, serum creatinine >2 mg% or coagulopathy were excluded. Patients who underwent procedures under spinal anesthesia, having epidural analgesia or requiring post-operative ventilator care were also excluded.

Drug administration:

Almost all patients underwent same anesthesia protocol. Patients were started analgesics within one hour of surgery. Tramadol where administered was given as 200 mg tramadol diluted in 500 ml N/S and infused over 8-12 hours. The maximum total dose for tramadol was 400 mg/day. Metoclopramide in group A and C was added as 10 mg metoclopramide in the diluted tramadol. Paracetamol was given as 1 gram IV over 15 to 30 minutes 8 hourly. The maximum total dose for paracetamol was 4 g/day. Diclofenac was given as 75 mg IG with maximum dose being 150 mg/day. Nalbuphine was given as 5 mg IV slow diluted in 10 ml with repeat doses as required 3-6 hourly.

Patients were categorized into four groups according to type of analgesia received.

Group A received tramadol infusion and metoclopramide.

Group B received tramadol infusion with diclofenac.

Group C received Tramadol infusion & metoclopramide

TABLE 1
Background characteristics of the patients (n = 193)

Characteristics	n	%
Gender		
Male	57	29.5
Female	136	70.5
Type of Surgery		
Laparoscopic	107	55.4
Laparotomy / Open	86	44.6
Group of Analgesia		
Tramadol & metoclopramide	46	23.8
Tramadol with diclofenac	50	25.9
Tramadol & metoclopramide with paracetamol	50	25.9
Nalbuphine with Diclofenac	47	24.4
Post-Operative Conditions		
Post-Operative Nausea		
Yes	39	20.2
No	154	79.8
Post-Operative Vomiting		
Yes	10	5.2
No	183	94.8
Post-Operative Dizziness		
Yes	27	14
No	166	86
Pain on Scale	2.64[a]	1.64[b]

[a]Mean, [b]Standard deviation

TABLE 2
Frequency of Post-operative side effects by group of Analgesia (n=193)

Group of Analgesia	Total	Nausea	Vomiting	Dizziness
		n (%)	n (%)	n (%)
Tramadol & metoclopramide	46	10 (21.7)	4 (8.7)	6 (13)
Tramadol with diclofenac	50	11 (22)	2 (4)	2 (4)
Tramadol & metoclopramide with paracetamol	50	13 (26)	4 (8)	9 (18)
Nalbuphine with Diclofenac	47	5 (10.6)	0	10 (21.3)
	193	39 (20.2)	10 (5.2)	27 (14)

with paracetamol.
Group D received Nalbuphine with Diclofenac.

Statistical Analysis

The data analysis was carried out using Statistical Package for Social Sciences (SPSS) version 22. Percentages and frequencies were reported for categorical variables and means and standard deviations were reported for continuous variables. Chi-square test was used to assess the relationship between groups of analgesia and post-operative side effects.

RESULTS

A total of 200 patients were involved in this study. After excluding missing values, final analysis was carried out on 193 patients. Among all the individuals, 29.5% (n=57) were males and 70.5% (n=136) were females. Mean age was 38 years± 12 years. Most patients underwent laparoscopic procedure i.e. 55.4% (n=107). Almost equal proportions of the patients received different groups of analgesia. The mean pain score was 2.64 with SD ±1.64 (Table 1).

Overall 67.3% (n=130) of patients had no side effects after surgery whereas 32.6% (n=63) of patients had one or more than one. Overall, patients who had post-operative side effects of nausea, vomiting and dizziness were 20.2% (n=39), 5.2% (n=10) and 14% (n=27), respectively. It was found that side effect was not significantly associated with analgesia group$(\chi^2 = 6.62, df = 3, p - value = 0.085)$. (See Table 2)

Overall no significant difference was observed in incidence of nausea, vomiting and dizziness between the groups containing metoclopramide and those not containing metoclopramide. It was also observed that side effects of vomiting and dizziness occurred more in female patients.(Table 3)

DISCUSSION

Tramadol, a centrally acting synthetic opioid like analgesic seems to act by modifying the transmission of pain impulses via inhibition of noradrenaline and serotonin reuptake. The efficacy of tramadol for the management of moderate to severe postoperative pain has been demonstrated. The relative lack of respiratory depression, major organ toxicity or abuse potential affords credence to the drug. [11] Tramadol may prove particularly useful in patients with poor cardiopulmonary function, including the elderly, the obese, smokers, in patients with impaired hepatic or renal function, and in patients in whom NSAIDs are not tolerated.

Administration of tramadol through various routes including epidural and local wound infiltration has been studied and mode of administration in IV route has also been a subject under study. Ijichi *et al.* compared intravenous versus epidural tramadol infusion for post-operative analgesia and found that intravenous tramadol infusion provides effective and safe postoperative analgesia.[20]Rüd *et al.* observed that continuous infusion of the opioid tramadol produce better analgesia than repetitive administration of boluses.[21]

Several studies have been done to know the efficacy and safety profile of tramadol and results have been

TABLE 3
Frequency of Post-operative side effects by gender (n=193)

	Total	Nausea	Vomiting	Dizziness
		n (%)	n (%)	n (%)
Male		11 (19.3)	1 (1.7)	3 (5)
Female		28 (20.5)	9 (6)	24 (17.6)
	193	39 (20.2)	10 (5.2)	27 (14)

mixed. Friedrichsdorf *et al.* perceived that as part of multimodal analgesia, scheduled plus as-needed tramadol may be considered for children in the postoperative setting due to its analgesic properties, low potential for side effects, and good safety profile.[22]Shahid *et al.* found IV paracetamol and tramadol tends to offer adequate postoperative analgesia and IV paracetamol is a safer alternative to tramadol with less post-operative nausea and vomiting in the postoperative period.[23]Bugada *et al.* compared effect of ketorolac and tramadol after herniotomy. They found that ketorolac or tramadol are equally effective on acute pain and persistent post-surgical pain after inguinal hernia repair.[24]

With PONV reported to be around 25 to 30% [4,5,17,19,25], and tramadol being considered as an incremental factor for PONV, our study does not demonstrate any increase in the incidence of PONV when tramadol is given as infusion form. Further studies are needed to confirm this effect comparing PONV in tramadol bolus versus tramadol infusion.

CONCLUSION

Tramadol maybe used as infusion without metoclopramide without causing an increase in -PONV.

REFERENCES

1. Roger Chou, Debra B. Gordon, Oscar A. de Leon-Casasola et al. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. February 2016, Volume 17, Issue 2, Pages 131–157. doi: 10.1016/j.jpain.2015.12.008.
2. Oderda G: Challenges in the management of acute postsurgical pain. Pharmacotherapy 2012; 32 (9 Suppl): 6S–11S. doi: 10.1002/j.1875-9114.2012.01177.x.
3. Allegri M, Grossi P: Management of postoperative pain: how accurate and successful is our acute pain management? Minerva Anestesiol 2012; 78: 1: 1-3. https://www.ncbi.nlm.nih.gov/pubmed/21750488
4. Kovac AL. Prevention and Treatment of Postoperative Nausea and Vomiting. Drugs 2000; 59:213–243. https://www.ncbi.nlm.nih.gov/pubmed/10730546.
5. Gan TJ. Risk Factors for Postoperative Nausea and Vomiting. Anest Analg 2006; 102:1884–98. doi: 10.1213/01.ANE.0000219597.16143.4D
6. Lavand'homme, P. 'The progression from acute to chronic pain'. In Current Opinion in Anaesthesiology, 2011; Vol. 24, 545-550.doi: 10.1097/ACO.0b013e32834a4f74
7. Mathiesen O, Thomsen BA, Kitter B, Dahl JB, Kehlet H: Need for improved treatment of postoperative pain. Dan Med J 2012; 59: A4401. https://www.ncbi.nlm.nih.gov/pubmed/22459715
8. Kela M, Umbarkar S, Sarkar M, Garasia M. Comparative study of efficacy of IV paracetamol vs IV tramadol for postoperative pain relief after cardiac surgery. Bombay Hosp J. 2011; 53: 582–6. Doi: 10.4103/0259-1162.158005
9. Grond S, Sablotzki A: Clinical pharmacology of tramadol. ClinPharma-cokinet 2004; 43: 879"923. https://www.ncbi.nlm.nih.gov/pubmed/15509185.
10. Rawal N, Macquaire V, Catalá E, Berti M et al.: Tramadol/paracetamol combination tablet for postoperative pain following ambulatory hand surgery: a double-blind, double-dummy, randomized, parallel-group trial. J Pain Res 2011; 4. Doi: 10.2147/JPR.S16760
11. Scott LJ, Perry CM. Tramadol: A review of its use in perioperative pain. Drugs. 2000; 60:139–76. https://www.ncbi.nlm.nih.gov/pubmed/10929933.
12. Vahabi S, Heidari M, Ahmadinejad M, Akhlaghi J, Birjandi M. Comparison of local anesthetic effects of tramadol and lidocaine used subcutaneously in minor surgeries with local anesthesia. Middle East J Anaesthesiol. 2011 Feb; 21(1):9-14. https://www.ncbi.nlm.nih.gov/pubmed/21991727.
13. Kainz C, Joura E, Obwegeser R, Plockinger B, Gruber W. Efficacy and tolerance of tramadol with or without antiemetic compared to pethidine in obstetric analgesia. Zeitschrift fur Geburtshilfe und Perinatologie. 1992; 196:78–82. doi: 10.1002/14651858.CD007396.pub2.
14. De Witte, Jan L.; Schoenmaekers, Bart; Sessler, Daniel I.; Deloof, Thierry. The Analgesic Efficacy of Tramadol is Impaired by Concurrent Administration of Ondansetron.

Anesthesia & Analgesia: May 2001 - Volume 92 - Issue 5 - p 1319–1321.doi: 10.1097/00000539-200105000-00045

15. Rauers NI, Stüber F, Lee EH, Musshoff F, Fimmers R, Barann M, Stamer UM. Antagonistic effects of ondansetron and tramadol? A randomized placebo and active drug controlled study:J Pain. 2010 Dec;11(12):1274-81.doi: 10.1016/j.jpain.2010.03.003
16. Vale C, Oliveira F, Assunção J, Fontes-Ribeiro C, Pereira F. Co-administration of ondansetron decreases the analgesic efficacy of tramadol in humans. Pharmacology. 2011;88(3-4):182-7. doi: 10.1159/000330740. Epub 2011 Sep 27
17. Dehrshwitz M. Antiemetic drugs. In: Hite PF, editors. Ambulatory Anesthesia and Surgery. London: WB Saunders, 1997, 445–56. https://pdfs.semanticscholar.org/0323/576e106c49e74d9c49de077b55e1bfcfb33d.pdf.
18. Pang WW, Wu HS, Lin CH, Chang DP, Huang MH. Metoclopramide decreases emesis but increases sedation in tramadol patient-controlled analgesia. Can J Anaesth. 2002 Dec; 49(10):1029-33. doi: 10.1007/BF03017896
19. Ting PH. Post-operative Nausea and Vomiting (PONV): An Overview. [cited 2009 April 30]. Available from: http://www.anesthesiologyinfo.com/articles/04252004.php
20. Ijichi K, Nijima K, Iwagaki T, Irie J, Uratsuji Y. A randomized double-blind comparison of epidural versus intravenous tramadol infusion for postoperative analgesia. Masui. 2005 Jun;54(6):615-21.https://www.ncbi.nlm.nih.gov/pubmed/15966377.
21. Rüd U, Fischer MV, Mewes R, Paravicini D. Postoperative analgesia with tramadol. Continuous infusion versus repetitive bolus administration. Anesthetist. 1994 May;43(5):316-21.https://www.ncbi.nlm.nih.gov/pubmed/8042760.
22. Friedrichsdorf SJ, Postier AC, Foster LP, Lander TA, Tibesar RJ, Lu Y, Sidman JD. Tramadol versus codeine/acetaminophen after pediatric tonsillectomy: A prospective, double-blinded, randomized controlled trial. J Opioid Manag. 2015 Jul-Aug;11(4):283-94.doi: 10.5055/jom.2015.0277
23. Mohammed Shahid, B. P. Manjula, and B. V. Sunil; A comparative study of intravenous paracetamol and intravenous tramadol for postoperative analgesia in laparotomies. Anesth Essays Res. 2015 Sep-Dec; 9(3): 314–319. Doi: 10.4103/0259-1162.158005
24. Bugada D, Lavand'homme P, Ambrosoli AL, Klersy C, Braschi A, Fanelli G *et al.* Effect of Post-operative analgesia on acute and persistent postherniotomy pain: a randomized study. J Clin Anesth. 2015 Dec; 27 (8): 658-64.doi: 10.1016/j.jclinane.2015.06.008
25. Kazemi-Kjellberg F, Henzi I, Tramér MR. Treatment of Established Postoperative Nausea and Vomiting: A Quantitative Systematic Review. BMC Anesthesiology 2001;1:2 [cited 2009 April 30]. Available from: http://www.biomedcentral.com/1471–2253/1/2.

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