Original Research Article

Indian Journal of Anesthesia and Analgesia
March – April 2020; 7(2): 629–635
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.7220.28

Efficacy of Tramadol and Butorphanol As Postoperative Rescue Analgesia: A Comparative Study

Soumya Samal[1], Sulochana Dash[2], Nupur Moda[3], Subhasis Das[4]

[1,2]Professor, [3]Assistant Professor, [4]Senior Resident, Department of Anaesthesiology, Institute of Medical Sciences and SUM Hospital, Kalinganagar, Bhubaneswar, Odisha 751003, India.

Abstract

Aim: To compare the efficacy of butorphanol and tramadol in mitigating postoperative pain as rescue analgesia while observing its effect on hemodynamic stability. *Setting and Design:* This prospective, double-blinded randomized controlled study was conducted at the postoperative recovery area. *Materials and Methods:* Hundred patients of 18–60 years of age, American Society of Anesthesiologists physical status Class I and II of both sex who underwent elective laparoscopic cholecystectomy, were enrolled in this study after approval from the Institutional Ethics Committee. Patients were randomly allocated into two groups (50 patients each); Group B received injection butorphanol 1 mg and Group T received injection tramadol 100 mg intravenously in the postoperative recovery room when patient complains of pain and Visual Analog Scale (VAS) more than 4. Parameters assessed were pain intensity by Visual analog score at 10, 20, 30, 40 and 60 minutes, relief of pain is described as VAS less than 4 after 30 minutes, sedation score after 30 minutes and side-effects. *Statistical Analysis Used:* Student's *t*-test and Chi-square test were used for statistical analysis. *Results:* Pain intensity was also significantly low with butorphanol than tramadol upto 40 minutes. Relief of pain is 100% with injection butorphanol. More patients were found to be alert in tramadol group as compared with butorphanol. *Conclusions:* Intravenous butorphanol (1 mg) provides superior pain relief than intravenous tramadol (100 mg) when used as rescue analgesia for postoperative pain with lesser incidence of nausea and vomiting.

Keywords: Postoperative, Rescue analgesia, Tramadol, Butorphanol.

How to cite this article:
Soumya Samal, Sulochana Dash, Nupur Moda, et al. Efficacy of Tramadol and Butorphanol As Postoperative Rescue Analgesia: A Comparative Study. Indian J Anesth Analg. 2020;7(2):629–635.

Introduction

The international association for the study of pain (IASP) has defined pain in 1979 as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". One of the most common symptoms for which a patient seeks medical advice is pain. Relief of pain is by far the most frequent indication of surgical intervention. But the surgeon in his mission often induces pain more severe than the original complaint.

Postoperative pain forms acute categories of nonmalignant pain. Though pain may be protective, defensive or diagnostic, it produces or precipitates many psychological and systemic

Corresponding Author: **Sulochana Dash,** Professor, Department of Anaesthesiology, Institute of Medical Sciences and SUM Hospital, Kalinganagar, Bhubaneswar, Odisha 751003, India.

E-mail: samalsoumya11@gmail.com

Received on 09.12.2019, **Accepted on** 28.01.2020

side effects. Management of postoperative pain is done in two phases: one of which, is the preventive aspect (preemptive analgesia) and the other is therapeutic aspect (rescue analgesia). Postoperative pain relief can be achieved by several methods, including the use of systemic opioids and regional anesthesia with intrathecal or epidural opioids or local anesthesia. Opioids are very effective as postoperative analgesics, influencing emotional aspects of pain as well as reducing the actual pain threshold.[1] The analgesic effects of opioids arise from their ability to inhibit directly the ascending transmission of nociceptive information from the spinal cord dorsal horn and to activate pain control circuits that descend from the midbrain, through the Rostral Ventromedial Medulla (RVM) to the spinal cord dorsal horn. Pain in the perioperative setting or thereafter plays a significant role in delaying an otherwise successful recovery.[2]

Tramadol is a synthetic 4-phenyl-piperidine analog of codeine with a dual mechanism of action. Tramadol stimulates the μ-receptor and to a lesser extent the δ and κ-opioid receptors. It also activates spinal inhibition of pain by decreasing the reuptake of norepinephrine and serotonin as well as presynaptic stimulation of 5-hydroxytryptamine release.[3] Tramadol is also α_7 nicotinic acetylcholine receptor antagonist.[4] Tramadol is one fifth to one tenth as potent as morphine.[4] Tramadol is metabolized by hepatic P450 enzyme systems to the major metabolite O-desmethyltramadol, which also exerts modest stereoselective analgesic effects.[5] The primary O-demethylated metabolite of tramadol is two to four times as potent as the parent drug and may account for part of the analgesic effect.

Butorphanol is an agonist at κ-receptors. Its activity at μ-receptors is either antagonistic or partially agonistic.[6] Butorphanol has minimal affinity for σ receptors, so the incidence of dysphoria is low. The elimination half-time of butorphanol is 2.5 to 3.5 hours.[7] The analgesic activity of butorphanol is dose related and is five to eight times as potent as morphine.[8]

Thus, this study was conducted to compare the efficacy of butorphanol and tramadol in mitigating postoperative pain as rescue analgesia while observing its effect on hemodynamic stability and the presence of adverse drug reactions.

Materials and Methods

After obtaining approval from institutional ethical committee and informed written consent from all the patients, this prospective randomized, double blinded experimental study was conducted on 100 patients undergoing elective laparoscopic cholecystectomy under general anesthesia.

Inclusion criteria: were patients of age 18–60 years, ASA I or II and both sex posted for laparoscopic cholecystectomy under general anesthesia.

Exclusion criteria: were ASA III and IV, uncooperative patient, patient not giving consent, history of drug abuse, patients with coagulation disorders, pregnancy and lactation.

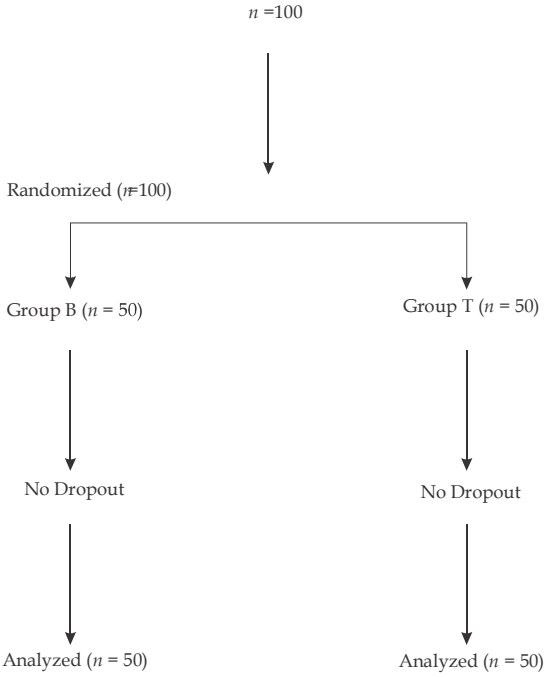

Fig. 1: Consort flow diagram of participants through each stage of randomized trial

Materials

Drugs

Drugs used in study are as follows:

(a) Injection of tramadol hydrochloride (100 mg);

(b) Injection of butorphanol tartarate (1 mg);

(c) All emergency drugs were kept ready at recovery room for safety in case of any adverse reaction occurs.

Visual Analog Scale (VAS)

Intensity of pain in postoperative period was assessed by Visual analog scale in which a score of "0" as "no pain" and a score of "10" as worst pain.

Patients with VAS of 4 or more were given rescue analgesia.

Methodology

During preoperative visit, patient's detailed history, general physical examination and clinical examination was carried out. Basic investigations like complete blood count, random blood sugar, blood urea, serum creatinine, Electrocardiogram and chest *X*-ray were carried out. The patients were explained about the anesthesia technique & research study and informed written consent was taken. They were taught how to assess intensity by using visual analog scale postoperatively. Patients were randomly allocated into two groups (50 patients each) by computer generated randomization into Group B receiving injection butorphanol 1 mg and Group T receiving injection 100 mg intravenously as rescue analgesia. Patients and the anesthetic technician who prepared the drug for study were blinded. Drugs were prepared in identical 2 ml syringes and administered according to the randomization list.

Patients were prescribed tablet lorazepam 1 mg on the night before surgery and advised nil per orally for 8 hours. On the day of surgery, intravenous cannulation (IV) was done with an 18 guage cannula. In the operation theater, baseline heart rate, blood pressure, oxygen saturation, electrocardiograph were recorded. All patients were premedicated with injection midazolam (0.05 mg. kg^{-1}) and glycopyrrolate (0.2 mg) IV. Anesthesia technique was standardized for all the cases. Injection fentanyl 2 mcg. kg^{-1} was used as analgesia. They were induced with injection propofol 2 mg. kg^{-1} IV. Intubation was facilitated by using injection vecuronium 0.1 mg. kg^{-1} IV. Anesthesia was maintained with nitrous oxide (66%) and isoflurane (1–2%) in oxygen. End tidal carbon dioxide was maintained between 35 and 40 mm Hg. Hemodynamic response to laparoscopy was attenuated by additional doses of injection fentanyl. Intraoperative muscle relaxation was maintained with intermittent doses of injection vecuronium. Reversal of neuromuscular blockade was performed with injection neostigmine 0.05 mg. kg^{-1} IV and glycopyrrolate 0.1 mg. kg^{-1} IV.

In the recovery room when patients complaint of pain and VAS score 4 or more, Group T received injection tramadol hydrochloride 100 mg intravenously and Group B received injection butorphanol tartarate 1mg intravenously as rescue analgesia.

Following clinical parameters were assessed:

I. Pain intensity by Visual analog score at 10, 20, 30, 40 and 60 minutes.

II. Relief of pain is described as VAS less than 4 after 30 minutes.

III. Sedation score after 30 minutes.

0. Alert;
1. Drowsy but arousable by verbal command;
2. Drowsy but not arousable by verbal command;
3. Arousable by deep pain;
4. Unarousable;

IV. Side-effects like Nausea and vomiting, respiratory depression (Respiratory rate < 10), bradycardia, hypotension and any allergic reaction

V. Heart rate, Systolic blood pressure, Diastolic blood pressure, SpO_2 and Respiratory rate before administration of rescue analgesia and 30 minutes after its administration.

If, patients still complains of pain after 30 minutes or VAS > 4, Injection diclofenac 75 mg in 100 ml normal saline was infused over 20 minutes. Hypotension was said to be significant if, MAP was less by 30% of prerescue analgesia value & was treated with intravenous fluids & vasopressor drugs. Simultaneously 100% oxygen was administered through face mask. Bradycardia was considered when PR was below 50 beats per minute and treated with injection atropine sulphate IV 6 mg increments. Nausea and vomiting–in these cases hypotension was first ruled out & then injection ondanstren 4 mg was given.

Sample size

Keeping power of study at 90%, confidence interval of 95%, to detect a 20 % difference in VAS score, the sample size of 27 was required in each group; however 50 patients were included in each group.

Statistical analysis

Data were expressed as mean, standard deviation & percentage. Parametric data were analyzed by unpaired student *t*-test. Nonparametric data were analyzed by Chi-square test. Analysis was performed using statistical software Statistical Product for Social Sciences (SPSS version 20.0 for Windows, Chicago, SPSS Inc.). Results were considered to be statistically significant if when p - value was < 0.05.

Results

All hundred patients were successfully enrolled in the study without anydropouts. The butorphanol and tramadol group were comparable with respect to age, sex, height, weight, ASA grading I:II, has shown in Table 1. Visual Analog Scale (VAS) score was assessed every 10 minutes interval after the intravenous dose of either butorphanol (1 mg) or tramadol (100 mg) as rescue analgesia, Table 2.

VAS score was significantly high in tramadol group as compared to butorphanol group after 10 minutes ($p < 0.05$) of injection. Pain intensity was also significantly low in Group B at 20, 30, 40 minutes. But VAS score was not statistically significant between the groups at 60 minutes. ($p = 0.4314$) Relief of pain is described as VAS score less than 4 after 30 minutes of administering rescue analgesia.

The Table 3 shows, 100% pain relief in patient's receiving injection butorphanol than injection tramadol (100% *vs* 31 %). More patients were found to be alert in tramadol group (48%) as compared with butorphanol (14%) as in Table 4. 58% patients in Group B were drowsy but arousable by verbal commands. None of the patients in the study showed sedation score 4. Sedation score was significantly high in patients receiving butorphanol ($p < 0.05$), Table 4.

The Table 5 shows, 38% of patients in tramadol group had nausea and vomiting as compared with 4% in butorphanol which is highly significant statistically < 0.001. None of the patients in the study had respiratory depression, bradycardia or hypotension.

Table 6 shows, pulse rate was significantly low in patients receiving butorphanol as compared to tramadol ($p < 0.05$) after 30 minutes of rescue analgesia. It shows patients comfort. No significant change in systolic and diastolic blood pressure, oxygen saturation and mean respiratory rate was seen between the Group B and Group T before and 30 minutes after rescue Analgesia, (Tables 7–9).

Table 1: Demographic profile

Characteristics	Group B ($n = 50$)	Group T ($n = 50$)	p - value
Age (Yrs)	43.2 ± 11.3	39.14 ± 11.8	0.082
Sex (Male : Female)	16:34	13:37	0.509
Height (Meters)	1.6 ± 0.074	1.6 ± 0.072	0.655
Weight (kilogram)	61.6 ± 8.6	61.7 ± 7.7	0.932
ASA I: II	32 : 18	34 : 16	

ASA = American Society of Anesthesiology, Data are expressed as mean ± standard deviation. *P* - value < 0.05 denotes statistical significance.

Table 2: Visual analog scale score

Time duration after rescue analgesia	Group B ($n = 50$)	Group T ($n = 50$)	p - value
At 10 minutes	1.9 ± 0.27	3.8 ± 1.3	0.0001
At 20 minutes	1.8 ± 0.38	3.74 ± 1.17	0.0001
At 30 minutes	1.6 ± 0.47	2.9 ± 0.4	0.0001
At 40 minutes	2.2 ± 0.46	2.4 ± 0.45	0.03
At 60 minutes	2.7 ± 0.69	2.8 ± 0.57	0.4314

Data are expressed as mean ± standard deviation . *P* - value < 0.05 denotes statistical significance.

Table 3: Relief of pain

Relief of pain	Group B ($n = 50$)	Group T ($n = 50$)	p - value
Yes	50 (100%)	31 (62%)	0.0009
No	0	19 (38%)	
Total	50	50	

Data are expressed as patients number or percentage.

Table 4: Sedation score

Score	0 (%)	1 (%)	2 (%)	3 (%)	4 (%)	Total
Group B	7 (14)	29 (58)	10 (20)	4 (8)	0	50
Group T	24 (48)	20 (40)	6 (12)	0	0	50

0: Alert, 1: Drowsy but arousable by verbal commands,
2: Drowsy but not arousable by verbal commands,
3: Arousable by deep pain,
4: Not arousable.

Table 5: Side-effects

Side-effects	Group B (n = 50)	Group T (n = 50)	p - value
Nausea & Vomiting	2 (4%)	19 (38%)	0.0003
Respiratory depression	0	0	
Bradycardia	0	0	
Hypotension	0	0	

Data are expressed as patients number and percentage.

Table 6: Pulse rate

Pulse rate	Group B (n = 50)	Group T (n = 50)	p - value
Before rescue analgesia	98.5 ± 4.9	97.8 ± 4.7	0.482
30 minutes after rescue analgesia	81.02 ± 4.7	89.9 ± 3.9	0.000

Data are expressed as mean ± standard deviation. p - value < 0.05 denotes statistical significance.

Table 7: Blood pressure

Blood pressure		Group B (n = 50)	Group T (n = 50)	p - value
Systolic	Before rescue analgesia	126.76 ± 15.3	123.32 ± 13.82	0.24
	30 Minutes after rescue analgesia	117.52 ± 11.92	117.48 ± 12.56	0.98
Diastolic	Before rescue analgesia	75.16 ± 7.06	73.96 7 ± .25	0.40
	30 Minutes after rescue analgesia	70.14 ± 5.2	71.04 ± 6.05	0.42

Data are expressed as mean ± standard deviation . p - value < 0.05 denotes statistical significance. Blood pressure in mm of Hg.

Table 8: Pulse oximetry (SpO_2)

SpO_2	Group B (n = 50)	Group T (n = 50)	p - value
Before rescue analgesia	98 ± 0.008	98 ± 0.008	1.00
30 Minutes after rescue analgesia	98 ± 0.07	98 ± 0.06	1.00

Data are expressed as mean ± standard deviation. p - value < 0.05 denotes statistical significance. SpO_2 in percentage.

Table 9: Respiratory rate

Respiratory rate (per minute)	Group B (n = 50)	Group T (n = 50)	p - value
Before rescue analgesia	13.5 ± 0.735	13.4 ± 0.808	0.51
30 Minutes after rescue analgesia	13.4 ± 0.782	13.32 ± 0.843	0.62

Data are expressed as mean ± standard deviation. p - value < 0.05 denotes statistical significance.

Discussion

Postoperative pain may result in psychological, physiological, neuroendocrine, respiratory and cardiovascular problems ultimately increasing the risk of postoperative morbidity and mortality Effective control of postoperative pain remains one of the most important & pressing issues in the field of anesthesia. Opioids are being widely used either alone or in combination with NSAIDS for postoperative analgesia.

Thus, the present study "efficacy of tramadol and butorphanol as postoperative rescue analgesia - A comparative study"was taken up with 100 patients of 18–60 years. The main aim of postoperative pain relief is to provide subjective comfort, in addition to inhibiting nociceptive impulse caused by trauma and to blunt autonomic as well as somatic reflexes to pain. Subsequently, this might enhance restoration of function by allowing the patient to breath, cough and to be easily ambulant.

Butorphanol is used to treat moderate to severe pain. It is an agonist at κ-receptor, but it is a weak antagonist at the μ-receptor. Several clinical studies with the injectable form of butorphanol have shown effectiveness in relieving moderate-to-severe postoperative pain.[9]

Tramadol, a weak opioid which acts on μ-receptor has been most commonly used for management of postoperative pain.[10] Tramadol has been chosen as a reference substance, as its effects are well-documented. Since, the study used identical protocols, the results obtained were comparable, combine analysis of trial was valid.

In our study, comparing the mean differences in VAS scores in two groups, it was clear that there was a greater reduction in VAS score of butorphanol group compared to tramadol group 10 minutes after injection ($p < 0.05$). But there was no difference in pain intensity 60 minutes after the injection of study drugs ($p = 0.43$). Sung et al.[1] conducted a retrospective study to compare butorphanol with morphine for use in a balanced anesthesia technique with nitrous oxide, oxygen, and neuromuscular relaxants. Neru et al.[11] have compared butorphanol and tramadol for analgesic efficacy and safety. The onset of analgesia is rapid with butorphanol as studied by Andrews.[12] The results of Galloway et al.[13] and Del Pizzo[14] were comparable with our results.

In our study, we found that relief of pain is described as VAS score less than 4 thirty minutes after injection of study drugs, was better with butorphanol as compared to tramadol ($p < 0.001$). In a comparative Study of analgesic efficacy of tramadol and butorphanol in mandibular third molar surgery four patients reported no pain and also had not taken any rescue medications in butorphanol group compared to tramadol group.[15]

From a double-blind, randomized trial conducted on postoperative patients, it appears that butorphanol tartrate provided substantial relief from moderate to severe postsurgical pain.[16,17]

Patients who received the lowest dose of butorphanol (1 mg) experienced their peak response at about 30 minutes, and the remaining treatment groups obtained maximum relief at about 60 minutes after medication.[18]

Sedation was high with butorphanol but the patients were arousable as compared to tramadol group where most of the patients were alert. None of the cases had sedation score of 4.

A side from drowsiness, the incidence of side-effects with butorphanol was negligible in a study conducted by Dobkin et al.[19] Authors have found less sedation after tramadol administration compared with equianalgesic doses of morphine.[20]

Incidence of nausea and vomiting was high with tramadol (38%) than butorphanol (4%) which is found to be highly significant ($p < 0.001$) Butorphanol does not increase the incidence of postoperative nausea and vomiting as observed by Onake and Yamamoto.[21] Nausea and vomiting were more frequent with tramadol 28% and 18% *versus* 81% and 51% than with pethidine in a study Ahluwalia et al.[22] Ofoegbu[23] found that with IM tramadol the incidence of nausea and vomiting was 19%. No other side-effects like bradycardia, hypotension, respiratory depression or allergic reaction was seen.

There was a reduction in pulse rate overall but reduction was more seen in Group B (from 98.5 to 81.02) than Group T (from 98.2 to 85.5) after giving rescue analgesia. The difference in mean pulse rate was found to be statistically significant in both groups implying decrease of pain intensity after 30 minutes was more with butorphanol.

No significant difference was seen between the groups with respect to systolic and diastolic blood pressure, oxygen saturation and respiratory rate. Patients in butorphanol group were hemodynamically more stable throughout the postoperative period which is consistent with previous report by gupta et al.[24]

Conclusion

Our study concluded that intravenous butorphanol (1 mg) provides superior pain relief than intravenous tramadol (100 mg) when used as rescue analgesia for postoperative pain with lesser incidence of nausea and vomiting. Though sedation is more with butorphanol but patients are arousable.

Source of Support: NIL

References

1. Thakore Bhoomika, Jacqueline D'Mello Jacqueline, Saksena Shalini, et al. Comparison of fentanyl and butorphanol for postoperative pain relief with intravenous patient controlled analgesia. Acute Pain 2009;11:93–99
2. Shahid M, Manjula BP, Sunil BV. A comparative study of intravenous paracetamol and intravenous tramadol for postoperative analgesia in laparotomies. Anesth Essays Res 2015;9:314–19.
3. Scott LJ, Perry CM. Tramadol: A review of its use in perioperative pain. Drugs 2000 July;60(1):139–76.
4. Minami K, Ogata J, Uezono Y. What is the main mechanism of tramadol? Naunyn Schmiedebergs Arch. Pharmacol 2015 Oct; (10): 999–1007.
5. Baraka A, Jabbour S, Ghabash M, et al. Can J Anesth 1993 Apr;40(4):308–313.
6. Miller's anesthesia 8th edition, opioid analgesics, p. 904.
7. Rosow CE. Butorphanol in perspective. Acute Care 1988; 12 Suppl 1:2–7.
8. Ameer B, Salter FJ. Drug therapy reviews: Evaluation of butorphanol tartrate. Am J Hosp Pharm 1979 Dec;36(12):1683–691.
9. Bowdle TA, Greichen SL, Bjurstrom RL, et al. Butorphanol improves CO_2 responses and ventilation after fentanyl anesthesia. AnesthAnalg 1987 Jun;66(6):517–22.
10. Putland AJ, McCluskey A. The analgesic efficacy of tramadol *versus* ketorolac in daycase laparoscopic sterilization. Anesthesia 1999 Apr;54(4):382–85.
11. Neru G, Anand S, Gulati S, et al. Comparison of tramadol and butorphanol for analgesic efficacy and safety. JK Sci 2008;10:132–34.
12. Andrews IC. Butorphanol and pentazocine. A double blind intramuscular comparison in patients with moderate to severe postoperative pain. Curr Ther Res 1977;22:647.
13. Galloway FM, Hrdlicka J, Losada M, et al. Comparison of analgesia by intravenous butorphanol and meperidine in patients with postoperative pain. Can Anesth Soc J 1977;24:90–102.
14. Del Pizzo A. A double blind study of effects of butorphanol compared with morphine in balanced anesthesia. Can Anesth Soc J 1978;25:392–97.
15. Hassan SS, Ahmed A, Rai M, et al. Analgesic efficacy of tramadol and butorphanol in mandibular third molar surgery: A comparative study. J Contemp Dent Pract 2012;13(3):364–70.
16. Sung YF, Weinstein MS, Ghani GA. Balanced anesthesia; A comparison of butorphanol and morphine. South Med J 1984;77:180–82.
17. Popio K, Kenneth A. Hemodynamic and respiratory effects of morphine and butorphanol. Clin Pharmacol Ther 1978;23(3):281–87.
18. Nagashima H, Karamanian A. Respiratory and circulatory effects of intravenous butorphanol and morphine. Clin Pharmacol Ther 1976;19:738–45.
19. Dobkin AB, Eamkaow S, Zak S et al. Butorphanol: A double-blind evaluation in postoperative patients with moderate or severe pain. Can Anesth Soc J 1974;21:600–610.
20. Lehmann KA, Jung C, Hoeckel W. Tramadol and pethidine zur postoperative schmerztherapie eine randomisierte dopple blind studie under den bedingunum der in intraverosen on demand analgesia. Schmerzther Pain Douler 1995;6:88-100.
21. Onake M, Yamamoto H. Comparison of analgesics used during balanced anesthesia on the incidence of PONV. Masui 2004;53:161–66.
22. Ahluwalia P, Rehman F, Ahluwalia A. comparison of butorphanol tartrate and tramadol hydrochloride for postoperative pain relief following abdominal surgery: A prospective, randomized, double-blind study. Int J Sci Stud 2015;3(9):120–24.
23. Ofoegbu RO. Report on a clinical trial with tramadol in the prevention of postoperative pain. Curr Ther Res 1984;36:436–44.
24. Gupta N, Anand S, Gulati S, et al. Comparison of tramadol and butorphanol for analgesic efficacy and safety. JK Science 2008;10(3):124–26.