

# Comparison of intravenous ketorolac and tramadol as Adjuvants in control of post-operative pain in patients undergoing laparoscopic surgeries under general Anesthesia in a tertiary care hospital

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## Abstract

**Aim and Objectives:** To assess and compare the analgesic effects of adjuvants like intravenous Ketorolac and Tramadol in laparoscopic surgeries on post-operative pain and their side effects.

**Methodology:** In this quasi experimental study, after approval from ethical committee and written informed consent taken from 90 patients of ASA physical status I, II of either sex scheduled to undergo elective laparoscopic surgeries under general anaesthesia were enrolled. Patients were randomly divided into one of the two groups of 45 patients each, patient received either Ketorolac (Group K) or Tramadol (Group T) 30 minutes before extubation. The degree of post-operative pain was assessed using VAS at 0, 2, 4 hours post operatively upto 24 hours and the need of rescue analgesic and the side effects of both drugs.

**Results:** The pain score at 0 hours were more than 4 in both the groups. Statistical analysis showed a significant difference between the 2 groups in the second and fourth hour. Thereafter, the difference in pain scores in both Ketorolac group and Tramadol group were not significant.

**Conclusion:** We conclude that both Ketorolac and Tramadol offer equal post-operative analgesia while Ketorolac had lesser side effects when compared to Tramadol.

**Keyword:** Ketorolac, tramadol, laparoscopic surgeries, post-operative pain

## Background

Laparoscopic surgery is very popular due to the small incision, less bleeding, short hospital stay and less pain compared to open surgical procedures for the same disease. Hence patients prefer laparoscopic procedures over open procedures. However in first 24 hours laparoscopic procedures can cause severe pain due to stretching of abdominal muscles, retention of gases under the diaphragm and pain at the port site<sup>[1]</sup>. Uncontrolled post-operative pain delays resumption of normal pulmonary function, restriction of mobility, nausea and vomiting, increase in systemic vascular resistance, cardiac functions and myocardial oxygen consumption through increase in catecholamine, induced by stress response<sup>[4]</sup>.

Balanced analgesia can be obtained by combining opioids with non-opioids<sup>[2]</sup>. Injection Fentanyl is a powerful analgesic drug when used at a dose of 2 mcg/kg but to control pain, it is required in higher doses which results in side effects like nausea, vomiting, chest wall rigidity, drowsiness and desaturation<sup>[3, 17]</sup>. So adjuvants are needed to control the pain in first 24 hours following laparoscopic procedures.

Hence the present study is undertaken to know which adjuvant, Ketorolac or Tramadol is better along with fentanyl to control post-operative pain in patients undergoing laparoscopic surgeries<sup>[6-7, 18-19]</sup>.

### Method

In this quasi experimental study, after ethical committee approval and informed consent, 90 patients belonging to "American Society of Anaesthesiology" (ASA) grade I, II aged between 18 to 65 years, scheduled for elective laparoscopic surgeries December 2017 to May 2019 in our hospital were selected. Thorough preanaesthetic evaluation and routine investigations were carried out before taking up the patient for surgery. An informed and written consent was taken from the patients enrolled for the study and patients were explained regarding Visual Analogue Scale. The patients were divided into two groups of 45 patients each, Group K-45, Group P-45, using closed envelope method.

### Premedication

Tab Ranitidine 150 mg at night before surgery and at the morning of the surgery. Tab Alprazolam 0.5 mg at night before surgery were given to all participants.

After shifting to the operating room, routine monitoring was done for the following parameters like heart rate (HR), Blood pressure (BP), Electrocardiogram (ECG), Oxygen-hemoglobin saturation (SPO<sub>2</sub>).

A peripheral cannula was secured. Intravenous infusion of Ringer lactate was started. Intravenous Midazolam 1 mg and intravenous Fentanyl 1.0 mcg/kg was given. After preoxygenation with 100% oxygen for 3 minutes, patient was induced with intravenous Propofol 2 mg/kg and endotracheal intubation was facilitated by Vecuronium 0.1 mg/kg.

Anesthesia was maintained with Isoflurane (1 MAC) and nitrous oxide in oxygen (70%:30%). Thirty minutes before the end of surgery, intravenous infusion of 30 mg Ketorolac or 50 mg Tramadol in 100 ml saline was given as infusion over a period of 20 minutes.

Residual neuromuscular paralysis was antagonized with Neostigmine 0.05 mg/kg and Glycopyrrolate 0.01 mg/kg. Patient was shifted to post anesthesia care unit.

Assessment of pain was started from the time of extubation till the point of need of rescue analgesia (Study period). On arrival to the post-operative unit (time 0), patient's vitals-heart rate, blood pressure and oxygen saturation was recorded.

Postoperative pain was assessed by a blinded observer at time 0, 2, 4 hours post-operative till 24 hours using VAS score<sup>[16]</sup>. Rescue analgesia with bolus doses of intravenous Fentanyl (25 mcg) at VAS score more than or equal to 4 was given. Pain Assessment was done by a 10 cm visual analogue scale (VAS) 0, no pain; 10, worst imaginable pain. Patient was reassessed for pain and for any side effects like nausea, vomiting, and gastric irritation, respiratory depression.

### Statistical Analysis

Sample size was calculated using the formula, Total sample n=90.

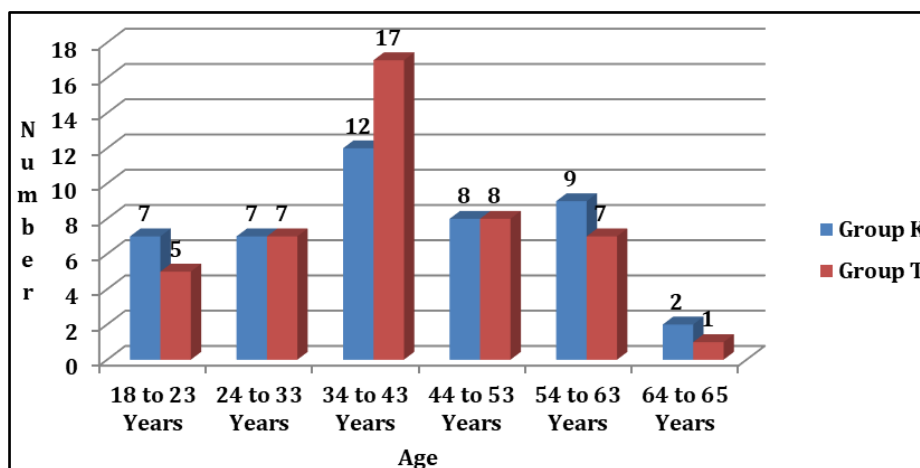
$$n = \frac{2 \sigma^2 (Z_{\alpha/2} + Z_{\beta})^2}{d^2}$$

$\alpha=0.05$ , power  $(1-\beta) = 0.8$ , SD ( $\sigma$ ) - 11.9

Data were analyzed using SPSS version 20.0. Results were analysed using Chi square test and Independent t-test.

**Table 1:** Age distribution

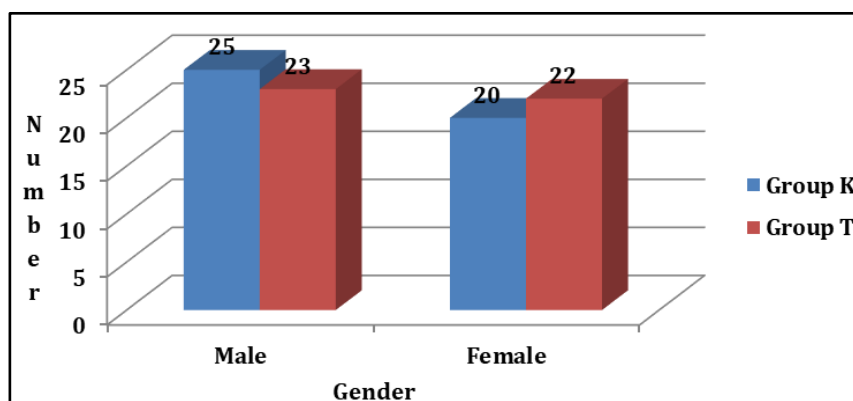
| Age            | Group K  | Group T  |
|----------------|----------|----------|
| 18 to 23 Years | 07(15.6) | 05(11.1) |
| 24 to 33 Years | 07(15.6) | 07(15.6) |
| 34 to 43 Years | 12(26.7) | 17(37.8) |
| 44 to 53 Years | 08(17.8) | 08(17.8) |
| 54 to 63 Years | 09(20.0) | 07(15.6) |
| 64 to 65 Years | 02(4.4)  | 01(2.2)  |
| Total          | 45(100)  | 45(100)  |



**Fig 1:** Age distribution of study participants

**Table 2:** Gender Distribution

| Gender | Group K  | Group T  |
|--------|----------|----------|
| Male   | 25(55.6) | 23(51.1) |
| Female | 20(44.4) | 22(48.9) |
| Total  | 45(100)  | 45(100)  |



**Fig 2:** Gender distribution of study participants

**Table 3:** Distribution of Procedures

| Procedure       | Group K  | Group T  |
|-----------------|----------|----------|
| Cholecystectomy | 29(64.4) | 30(66.6) |
| Appendicectomy  | 11(24.5) | 07(15.6) |
| Diagnostic      | 02(4.4)  | 01(2.2)  |
| Hernioplasty    | 03(6.7)  | 07(15.6) |
| Total           | 45(100)  | 45(100)  |

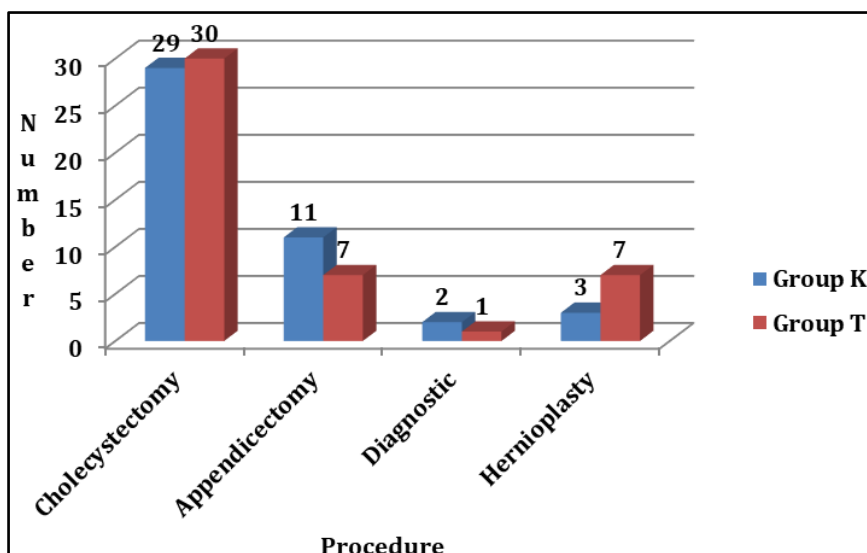


Fig 3: Distribution of procedures among study participants

Laparoscopic appendicectomy was done in 18 patients.  
 Laparoscopic cholecystectomy in 59 patients.  
 Diagnostic laparoscopy in 3 patients.  
 Laparoscopic hernioplasty in 10 patients.

Table 4: Comparison of Pain scores between the groups

| VAS    | Group K   | Group T   | P Value |
|--------|-----------|-----------|---------|
| 0 HRS  | 4.20±1.34 | 4.31±1.15 | 0.674   |
| 2 HRS  | 2.91±0.95 | 3.49±1.06 | 0.008*  |
| 4 HRS  | 2.84±0.82 | 3.38±1.21 | 0.017*  |
| 8 HRS  | 2.47±0.73 | 2.73±0.72 | 0.084   |
| 12 HRS | 2.11±0.75 | 2.07±0.65 | 0.764   |
| 24 HRS | 1.64±0.74 | 1.73±0.62 | 0.539   |

\*indicates significant difference between the groups

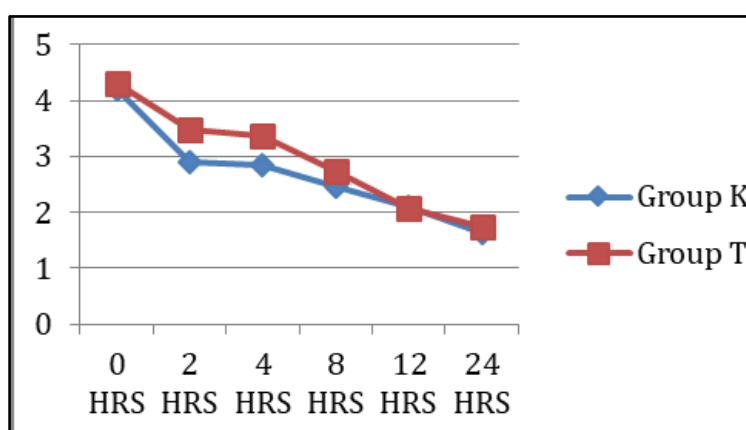


Fig 4: Vas Score of different time

Pain scores in immediate post-operative period were initially more in both the groups (>4), but there was statistical difference in 2nd and 4th hour (p value<0.05), later till 24 hours there was no statistical difference.

Table 5: Rescue Analgesic Requirement in both groups

| Rescue Analgesia | Group K  | Group T  | P Value |
|------------------|----------|----------|---------|
| 0                | 14(31.1) | 10(22.2) | 0.598   |
| 1                | 25(55.6) | 27(60.0) |         |

|       |          |          |  |
|-------|----------|----------|--|
| 2     | 06(13.3) | 08(17.8) |  |
| Total | 45(100)  | 45(100)  |  |

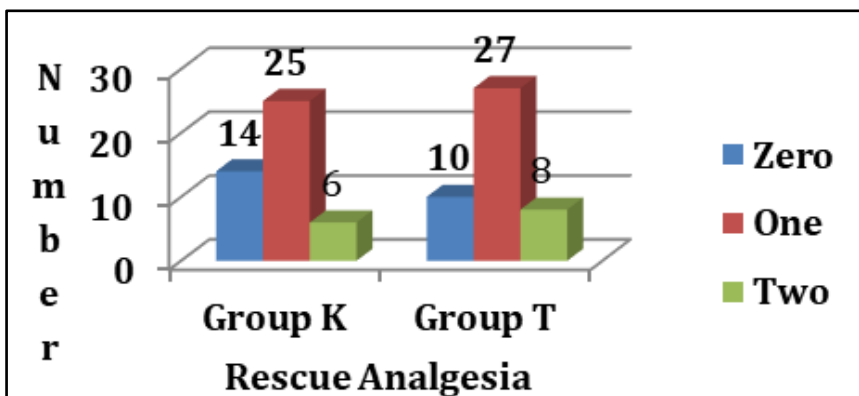


Fig 5: Rescue Analgesia in two groups

Most of the patients (52 out of 90) required rescue analgesia only once in 24 hours and about 24 patients did not require any rescue analgesia in 24 hours. A small proportion of patients (14) required two rescue analgesics in 24 hours

The above indicates that both adjuvants were equally effective in controlling post-operative pain and there was no statistical difference among two groups ( $p > 0.05$ ).

Table 6: Number of rescue analgesics needed among various procedures

| Procedure       | Rescue Analgesia |          |           | Total     |
|-----------------|------------------|----------|-----------|-----------|
|                 | 0                | 1        | 2         |           |
| Appendicectomy  | 6(25.0)          | 11(21.2) | 1(7.1)    | 18(20.0)  |
| Cholecystectomy | 18(75.0)         | 31(59.6) | 10(71.4)  | 59(65.6)  |
| Diagnostic      | 0(0)             | 2(3.8)   | 1(7.1)    | 03(3.3)   |
| Hernioplasty    | 0(0)             | 8(15.4)  | 2(14.3)   | 10(11.1)  |
| Total           | 24(100.0)        | 52(100)  | 14(100.0) | 90(100.0) |

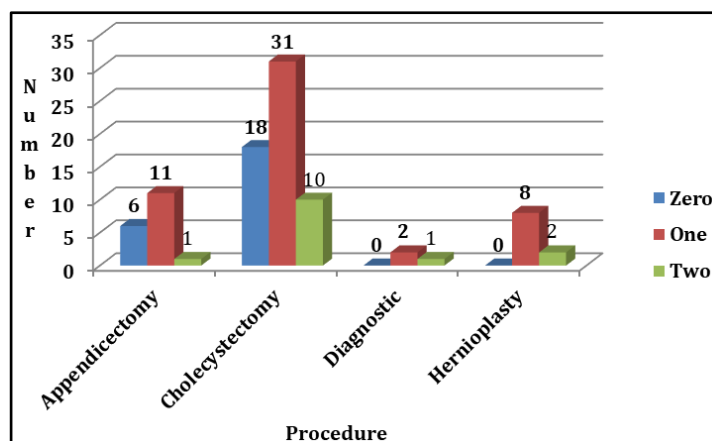


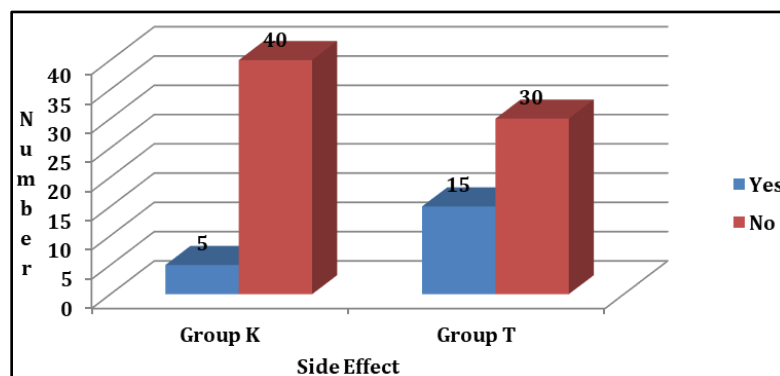
Fig 6: Procedure and Rescue Analgesia

Among 18 patients who underwent laparoscopic appendicectomy, 6 patients did not require any rescue analgesics, while 11 patients required once and only 1 patient required two times over 24 hours. Among 59 patients who underwent laparoscopic cholecystectomy, 18 patients did not require any rescue analgesics, while 31 patients required once and only 10 patients required two times over 24 hours.

**Table 7:** Side effects seen among participants in both groups

| Side Effect | Group K  | Group T  | P Value |
|-------------|----------|----------|---------|
| Yes         | 05(11.1) | 15(33.3) | 0.011*  |
| No          | 40(88.9) | 30(66.7) |         |
| Total       | 45(100)  | 45(100)  |         |

\*indicates significant difference between the groups

**Fig 7:** Side Effects in two groups

The above table shows increase in side effects with opioid group like Tramadol (n=15) when compared to NSAID group like Ketorolac (n=5), the p value was 0.011, which was statistically significant ( $p < 0.05$ ).

## Discussion

The study was undertaken to assess the efficacy of Ketorolac and Tramadol as a post-operative analgesics in laparoscopic surgeries. The pain score and requirement of rescue analgesia and side effects for both the groups were compared. Patients admitted in Yenepoya Medical College Hospital, who underwent laparoscopic procedures between December 2017 and May 2019 were included in the study. Patients were randomized by closed envelope method and divided into two groups. Either 30 mg of intravenous Ketorolac or 50 mg of Tramadol in 100 ml normal saline was administered based on randomization.

All patients were assessed for post-operative Pain score and need for rescue analgesia were observed at 0, 2, 4, 8, 12 and 24 hours and side effects of both drugs were studied.

## Demographic data

The demographic data of both the groups were compared with respect to age and gender which was not statistically significant. Laparoscopic appendectomy was done in 18 patients, laparoscopic cholecystectomy in 59 patients, diagnostic laparoscopy in 3 patients and laparoscopic Hernioplasty in 10 patients.

## Vas score and rescue analgesia

It was observed that the visual analogue score for both groups were almost similar ( $>4$ ) at 0 hour postoperatively. The mean pain score was 2.70 in Ketorolac group and 2.95 in Tramadol group, which was statistically insignificant.

The difference in pain scores between the two groups was statistically significant only at second and fourth hour postoperatively as p value was 0.008 and 0.017 ( $< 0.05$ ) respectively. Thereafter till 24 hours, the pain scores in both Ketorolac group and Tramadol group were not statistically significant.

In a recent study conducted by Bhawana Rastogi *et al.*, (2016) where they had compared preemptive use of intravenous Ketorolac and Paracetamol in patients undergoing laparoscopic cholecystectomy, concluded that preemptive use of single-dose of IV ketorolac

can provide effective analgesia in postoperative period with reduced consumption of rescue analgesic<sup>[15]</sup>.

In a study conducted by Manjunath *et al.*, (2012) in which they had compared Ketorolac and Tramadol for post-operative pain relief concluded that both the drugs were equally effective in controlling postoperative pain and had negligible side effects which were not statistically significant<sup>[6]</sup>.

In a similar study conducted by Amir Farshchi *et al.*, (2010) in which they had compared efficacy of Tramadol versus NSAID (Piroxicam) in controlling post-operative pain concluded that NSAIDs like Piroxicam that are devoid of adverse side effect of opioids and were equally effective to Tramadol in controlling pain, so can be appropriate for reducing the use of opioids like Tramadol in management of pain<sup>[11]</sup>.

In another study conducted by Mishra *et al.*, (2012) in which they had compared Ketorolac and Tramadol for post-operative pain control post dental extraction concluded that postoperative administration of Tramadol is equally effective as traditional NSAID's in relieving pain<sup>[14]</sup>.

These studies were in accordance with our study in reducing pain score in post-operative period with use of adjuvants like intravenous Ketorolac and Tramadol. After the initial hours there was no statistical significance in both the groups in our study. Our study also shows increase in side effects with opioid group like Tramadol (n=15) when compared to NSAID group like Ketorolac (n=5), the p value was 0.011, which was statistically significant (p < 0.05) which were in accordance with the above studies

### Rescue analgesia

Majority of the patients required rescue analgesia (Injection Fentanyl 25 micrograms given if VAS >4) only once in 24 hours (group K-55.5%, group T-60.0%). A small percentage of patients required rescue analgesia twice (group K-13.3%, group T-17.7%). While in group K -31.1% and group T- 22.2% did not require any rescue analgesia over 24 hours.

The requirement for rescue analgesia did not show any statistical significance among both groups. We evaluated the pain score and rescue analgesia requirement in various laparoscopic procedures. There was no statistically significant difference in pain score and need for rescue analgesia among patients undergoing laparoscopic cholecystectomy, laparoscopic appendectomy, laparoscopic Hernioplasty and diagnostic laparoscopy.

One of the limitations of our study was inability to blind the Anaesthesiologist, while giving the adjuvants among the allotted group of patients.

### Conclusions

1. The pain score in immediate post-operative period '0' hour were high (>4) in both the groups. However there was statistically significant difference in the pain scores between Ketorolac and Tramadol group in the '2'nd and '4'th hour post operatively (p < 0.05). There after the difference in pain score in between the two groups were not statistically significant till 24 hours.
2. Majority of the patients (about 52 of 90 patients) required rescue analgesia only once in the 24 hour period most of them being in the immediate post-operative period. About (24 of 90 patients) did not require any rescue analgesic over 24 hour period. A small percentage (14 of 90 patients) only required rescue analgesia twice, all the above indicates both drugs were sufficient enough to control post-operative pain over a period of 24 hours post operatively.
3. The pre-operative and post-operative haemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and percentage saturation of oxygen were not statistically significant.
4. The side effects seen were more in the Tramadol group (n=15) of 45 patients compared to Ketorolac group (n=5) of 45 patients respectively and it was also statistically significant where p value was 0.011.

Therefore, we conclude that both adjuvants when used post operatively along with intraoperative Fentanyl given at the time of induction, were equally effective in providing post-operative analgesia after laparoscopic surgeries over a period of 24 hours and Ketorolac being an NSAID can be used as an alternative to opioid like Tramadol which has lesser side effects than Tramadol.

## References

- 1 Joris JE, Thiry P, Paris J, Weerts M, Lamy. Pain after Laparoscopic Cholecystectomy: Characteristics and Effect of Intraperitoneal Bupivacaine, *Anesthesia & Analgesia*. 1995;81(2):379-384.
- 2 Heo BH, Park JH, Choi JI, Kim WM, Lee HG, Cho SY, *et al.*, A Comparative Efficacy of Propacetamol and Ketorolac in Postoperative Patient Controlled Analgesia. *The Korean journal of pain*. 2015;28(3):203-9.
- 3 Pavlin DJ, Chen C, Penaloza DA. Pain as a factor complicating recovery and discharge after ambulatory surgery. *Anesth Analg*. 2003;97:1627-32.
- 4 Rawal N, Allvin R, Amilon A. Postoperative analgesia at home after ambulatory hand surgery: a controlled comparison of tramadol, metamizol and paracetamol. *Anesth Analg*. 2001;92:347-51
- 5 Miller RD, Fleisher LA, Roger AJ, Savarese JJ, Wiener-Kronish JP, Young WL. *Anesthesia*, Eight edition, 2015.
- 6 Shankariah M, Mishra M, Kamath RA. Tramadol versus ketorolac in the treatment of postoperative pain following maxillofacial surgery. *Journal of maxillofacial and oral surgery*. 2012;11(3):264-70.
- 7 Gopalraju P, Lalitha RM, Prasad K, Ranganath K. Comparative study of intravenous Tramadol versus Ketorolac for preventing postoperative pain after third molar surgery-A prospective randomized study. *Journal of Cranio-Maxillofacial Surgery*. 2014;42(5):629-33
- 8 Manne VS, Gondi SR. Comparative study of the effect of intravenous paracetamol and tramadol in relieving of postoperative pain after general anesthesia in nephrectomy patients. *Anesth Essays Res*. 2017;11:117-20.
- 9 Sunil B, Shahid M, Manjula B. A comparative study of intravenous paracetamol and intravenous tramadol for postoperative analgesia in laparotomies. *Anesth Essays and Res*. 2015;9(3):314-319.
- 10 Russo A, Marana E, Scarano AM, Bevilacqua F, Di Staiso E. Efficacy of scheduled time ketorolac administration compared to continuous infusion for post-operative pain after abdominal surgery: 14AP5- 3. *European Journal of Anaesthesiology (EJA)*. 2012;29:202.
- 11 Farshchi A, Ghiasi G. Comparison the analgesic effects of single dose administration of tramadol or piroxicam on postoperative pain after cesarean delivery. *Acta Medica Iranica*. 2010;48(3):148.
- 12 Isik B, Arslan M, Ozsoylar O, Akçabay M. Effects of preoperative lornoxicam versus tramadol on postoperative pain and adverse effects in adult tonsillectomy patients. *Agri*. 2009;21(3):113-20.
- 13 Putland A, McCluskey A. The analgesic efficacy of tramadol versus ketorolac in day-case laparoscopic sterilisation. *Anaesthesia*. 1999;54(4):382-385.
- 14 Mishra H, Khan FA. A double-blind, placebo-controlled randomized comparison of pre and postoperative administration of ketorolac and tramadol for dental extraction pain. *Journal of Anaesthesiology, clinical pharmacology*. 2012 Apr;28(2):221.
- 15 Rastogi B, Singh VP, Gupta K, Jain M, Singh M, Singh I. Postoperative analgesia after laparoscopic cholecystectomy by preemptive use of intravenous paracetamol or ketorolac: A comparative study. *Indian Journal of Pain*. 2016 Jan 1;30(1):29.
- 16 McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. *Psychol Med*. 1988;18:1007-19.
- 17 Howard BG, Akil H. Opioid Analgesics. In: Brunton LL, Lazo JS, Parker KL, editors. *Goodman and Gilman's: The Pharmacological Basis of Therapeutics*. 11th ed. New York:



Mc Graw Hill. 2006, 547-90p.

- 18 Macario A, Lipman A. Ketorolac in the era of cyclooxygenase-2 selective Nonsteroidal anti-inflammatory drugs: a systematic review of its efficacy, side effects and regulatory issues. *Pain Med.* 2001;2:336-351
- 19 BeakleyBD, KayeAM, KayeAD. Tramadol, pharmacology, side effects, and serotonin syndrome: a review. *Pain Physician.* 2015;18:395-400.