

## To Compare the Pre-emptive Analgesic Effect of I.V. Ketorolac Versus I.V. Tramadol in Pediatric Inguinal Herniotomy and Penile Surgeries

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### Abstract

Pre-emptive analgesia aims at preventing central nervous system from reaching the hyper excitable state known as central sensitization, in which it responds excessively to afferent inputs. The effective pain management pre-operatively can reduce the post-operative pain and analgesic requirement in pediatric age group. Inguinal hernia repair and penile surgeries are one of the most common and painful ambulatory surgeries with 40–50% patients reporting moderate to severe pain within 24 hours. Hence it is the prime concern of anesthesiologist for post-operative pain relief. Our study was conducted in 60 patients of ASA Grade I/II aged between 2–8 years, who were randomly divided into two Groups, Group K and Group T. We used intravenous ketorolac 1 mg/kg body weight and tramadol 1 mg/kg body weight as pre-emptive analgesics and compared intra-operative parameters like mean heart rate, mean arterial pressure, post-operative pain with FLACC score (face, legs, activity, cry, consolability) and time for first rescue analgesia. The study results showed that both the groups were comparable in various demographic data. In our study, intra-operative mean heart rate and mean arterial pressure were significantly higher in case of ketorolac as compared to tramadol. Our results showed that FLACC score is significantly higher and time for first rescue analgesia is significantly earlier in ketorolac group compared with tramadol group. The mean time for first rescue in Group T and Group K was  $5.50 \pm 0.68$  (hours) and  $2.33 \pm 0.76$  (hours) respectively.

**Keywords:** Pre-emptive analgesia; FLACC score; Rescue analgesia; Tramadol, Ketorolac.

### How to cite this article:

Harish Kumar, Pooja Bhosle. To Compare the Pre-emptive Analgesic Effect of I.V. Ketorolac Versus I.V. Tramadol in Pediatric Inguinal Herniotomy and Penile Surgeries. Indian J Anesth Analg. 2019;6(6 Part -I):1944-1948.

### Introduction

Pre-emptive analgesia is defined as an anti-nociceptive treatment that prevents the establishment of altered central processing of afferent input from the sites of injury. By administering an analgesic before the painful stimulus [referred to as pre-emptive analgesia], the development of pain hypersensitization may be reduced or abolished, thus resulting in less post-stimulus pain.

About 75% of children who undergo abdominal

surgery experience moderate to severe pain and do not receive adequate pain management. The administration of adequate analgesics may minimize and prevent complications, reduce morbidity and mortality rates.

Ketorolac tromethamine is a non-steroidal anti-inflammatory drug (NSAID) that has analgesic efficacy is similar to commonly used opioids, and recently has found wide acceptance in treatment of post-operative pain in variety of surgical procedures. It acts on central and peripheral sites in the body and inhibits (cyclo-oxygenase) cox-1

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**Received on** 16.08.2019, **Accepted on** 23.10.2019

and cox-2 enzymes. It is primarily metabolized through hepatic conjugation with glucuronic acid and excreted through urine.<sup>1</sup>

Tramadol is a synthetic analogue of codeine and causes activation of both the opioid and non-opioid pain inhibition systems. The effect of non-opioid component of tramadol is mediated through the inhibition of reuptake of serotonin and nor-epinephrine and by displacing the stored serotonin from the nerve endings. Its opioid component has an affinity for  $\mu$  receptors. Tramadol causes minimal respiratory depression and few gastrointestinal effects and has less potential for opiate like physical dependence or abuse.<sup>2</sup> Thus, we conducted randomized comparative study of pre-emptive analgesic effect of tramadol and ketorolac in pediatric age group.

**Aim**

To compare analgesic effect of I.V. Ketorolac vs I.V. Tramadol in pediatric age group.

**Objectives**

1. Intra-operative monitoring of heart rate, MAP, SpO<sub>2</sub>, EtCO<sub>2</sub>;
2. To access pain in post-operative anesthesia care unit (PACU) with FLACC score;
3. To access sedation in PACU with Ramsay sedation score;
4. Transfer patient from PACU to ward with Modified Alderate score;
5. To access time for first rescue analgesia.

**Materials and Methods**

After ethical committee approval, the study was conducted at the attached tertiary care teaching hospital from September 2016 till January 2018. The study was Prospective Randomized Comparative study. A written informed consent was taken from each parent, in the language he or she understands.

Our study included 60 patients belonging to ASA I/II. They were randomly divided by chit method into 2 Groups of 30 each. Namely Group K and Group T. Group K received INJ. Ketorolac 1 mg/kg and Group T received INJ. Tramadol 1 mg/kg. patients within age of 2 year to 8 years, ASA I/II grades, undergoing elective inguinal herniotomy or penile surgeries of duration 45–60 minutes were included in the surgery.

Patients with known hypersensitivity to

drug, coagulation abnormalities, deranged renal function tests, seizure disorder were excluded from the study. Intra-operatively, protocol was followed as follows Patients were taken in operation theatre and monitors were attached. Pre-induction with inj. midazolam 0.05 mg/kg (I.V.), inj. Ondansetron 2 mg (I.V.) (In children more than 3 years of age). Immediately patient was given inj. tramadol 1 mg/kg intravenously or ketorolac 1 mg/kg intravenously as pre-emptive analgesia in each group.

Pre-oxygenation for 3 minutes with 100% O<sub>2</sub>. Induction with Inj. Thiopentone sodium 5 mg/kg (I.V.). Intubation under the effect of inj. Succinylcholine 2 mg/kg after confirming mask ventilation. Patient was maintained on Sevoflurane with nitrous oxide 50% and oxygen 50%, inj. Vecuronium as muscle relaxant and controlled ventilation was maintained.

Intra-operative monitoring of heart rate, MAP, SpO<sub>2</sub>, EtCO<sub>2</sub> was done as per proforma. At the end patient was reversed with inj. Neostigmine 0.04 mg/kg + inj. glycopyrrolate 0.01 mg/kg and extubated after adequate muscle tone was achieved. Pain was assessed in post-operative care unit with FLACC score for every 15 minutes till the discharge from PACU. Sedation was assessed using Ramsay sedation score. Patient was shifted from PACU to ward once modified Alderate score is above 9 Time for first rescue analgesia was noted.

All the patients were observed for outward effects of both the drugs post-operatively. The entire data is statistically analyzed using Statistical Package for Social Sciences (SPSS ver 21.0, IBM Corporation, USA) for MS Windows. The inter-group comparison of categorical variables is done using Chi-square test.

**Results**

**Table 1:** Demographic Data

Group Code	Description	No of cases	% of cases
Group K	Ketorolac	30	50.0
Group T	Tramadol	30	50.0

**Table 2:** Demographic Data

	Group K (n = 30)		Group T (n = 30)		p-value
	Mean	SD	Mean	SD	
Age (years)	4.37	4.85	4.40	2.03	0.947 <sup>NS</sup>
Weight in kg	16.23	2.75	16.33	3.97	0.921 <sup>NS</sup>

Shown as in **Tables 1 and 2** values are mean and SD, *P*-value by independent sample *t*-test. *p*-value < 0.05 is considered to be statistically significant. NS-Statistically significant. Demographic data were comparable in both the groups, shows in **Table 3**.

**Table 3:** Comparison of Mean Heart Rate in Study Groups

Heart Rate (Per Min)	Group K (n = 30)		Group T (n = 30)		<i>p</i> -value
	Mean	SD	Mean	SD	
0-min	108.5	7.1	114.3	6.4	0.001***
10-min	121.5	6.5	117.5	5.9	0.015*
20-min	125.6	6.2	118.5	5.6	0.001***
30-min	128.6	6.5	120.4	6.1	0.001***
45-min	128.2	7.1	114.4	6.4	0.001***
60-min	122.7	8.3	118.0	6.0	0.016*

Values are mean and SD, *p*-values by independent sample *t*-test. *p*-value < 0.05 is considered to be statistically significant. \**p*-value < 0.05, \*\**p*-value < 0.01, \*\*\**p*-value < 0.001.

The distribution of mean heart rate at 10-min, 20-min, 30-min, 45-min and 60-min is significantly higher in Group K compared to mean heart rate in Group T (*p*-value < 0.05 for all) during intra-operative period, shows in (**Table 4**).

**Table 4:** Comparison of Mean Arterial Pressure (MAP) in study groups

MAP (mmHg)	Group K (n = 30)		Group T (n = 30)		<i>p</i> -value
	Mean	SD	Mean	SD	
0-min	82.4	3.6	80.8	3.2	0.062 <sup>NS</sup>
10-min	86.7	2.5	81.4	1.9	0.001***
20-min	86.9	2.4	82.7	1.9	0.001***
30-min	87.9	1.9	82.3	2.1	0.001***
45-min	87.9	2.0	82.5	1.4	0.001***
60-min	85.2	1.5	82.5	1.4	0.001***

Values are mean and SD, *p*-values by independent sample *t*-test. *p*-value < 0.05 is considered to be statistically significant. \*\*\**p*-value < 0.001, NS-Statistically non-significant.

The distribution of mean arterial pressure at 10-min, 20-min, 30-min, 45-min and 60-min is significantly higher in Group K compared to mean arterial pressure in Group T (*p*-value < 0.05 for all) during intraoperative period, shows in **Table 5**.

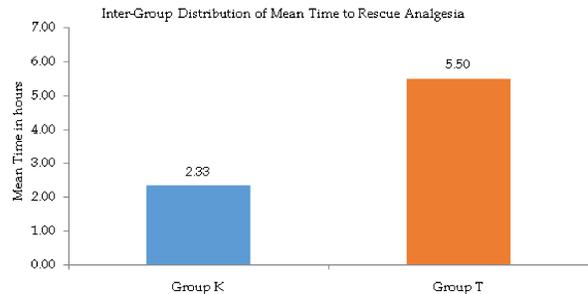
**Table 5:** Comparison of mean FLACC Score in study groups

FLACC Score	Group K (n = 30)		Group T (n = 30)		<i>p</i> -value
	Mean	SD	Mean	SD	
15-min	3.47	0.51	2.33	0.48	0.001***
30-min	4.00	0.79	2.20	0.41	0.001***

45-min	4.70	0.75	2.27	0.64	0.001***
60-min	6.07	0.83	3.30	0.91	0.001***

Values are mean and SD, *p*-values by independent sample *t*-test. *p*-value < 0.05 is considered to be statistically significant. \*\*\**p*-value < 0.001.

The distribution of mean FLACC score at 15-min, 30-min, 45-min and 60-min is significantly higher in Group K compared to mean FLACC Score in Group T (*P*-value < 0.001 for all) and it is statistically highly significant, displays in (**Fig. 1**).



**Fig. 1:** Comparison of mean time to rescue analgesia in study groups

The distribution of mean time to rescue analgesia is significantly higher in Group T compared to mean time to rescue analgesia in Group K (*p*-value < 0.001).

**Discussion**

Post-operative pain relief in pediatric age group is a topic of very much concern as it causes agony to parents and care givers. Inguinal hernia repair and penile surgeries are one of the most common and painful ambulatory surgeries, with 40-50% patients reporting moderate to severe pain, hence it is the prime concern of anesthesiologist for post-operative pain relief.

In present study, intra-operative mean heart rate and mean arterial pressure was significantly higher in case of ketorolac as compared to tramadol, which is comparable to Ozkose *Z et al.* they evaluated pre-emptive efficacy and safety of low dose tramadol in children undergoing tonsillectomy and observed that intra-operative mean arterial pressure and heart rate were higher in patients receiving placebo when compared with patients receiving tramadol. they concluded that Tramadol in lower doses (0.5-1 mg/kg) is an efficient pre-emptive analgesia during operation as well as early post-operative period,<sup>3</sup> but the comparison was with placebo hence it is study of only tramadol as pre-emptive analgesic. The mean time for first rescue

in Group T and Group K was  $5.50 \pm 0.68$  hours and  $2.33 \pm 0.76$  hours respectively.

Study conducted in adult patients by Putland and McCluskey compared the pre-emptive analgesic effect of tramadol versus ketorolac in day care laparoscopic sterilization and concluded that pre-emptive administration of tramadol at induction of anesthesia significantly reduced pain following day-care laparoscopic sterilization compared with patients who received ketorolac.<sup>5</sup> Guldenturan MD *et al.* compared the pre-emptive analgesia with tramadol and paracetamol in pediatric adeno-tonsillectomy they stated that low dose tramadol given at induction, provided efficient pre-emptive analgesia for the intra-and immediate post-operative periods and tramadol had few side effects like nausea, vomiting and prolongation of the sedation but in our study no nausea, vomiting or prolonged sedation was observed with either of the drugs.<sup>6</sup>

Cheryl B Aporado *et al.* studied the analgesic effect of tramadol as a pre-emptive analgesic in pediatric appendectomy patients they reported that low doses of tramadol given pre-emptively provided good intra-operative analgesia and less post-operative pain during first 1 to 2 hours.<sup>7</sup> but we had longer analgesic effect.

Muhammad falhm *et al.* assessed the pre-emptive analgesic effect of tramadol in inguinal hernioplasty. They observed pain relief with visual analog scale for a period of six hours and concluded that administration of tramadol before the start of the surgical procedures can produce effective post-operative analgesia in the context of inguinal hernioplasty surgery.<sup>8</sup>

There are few studies which are contradictory to our study like Ashwin V Shah *et al.* Evaluated the pre-emptive analgesic effect of intramuscular ketorolac versus tramadol following third molar surgery. They observed ketorolac has better analgesia post-operatively than tramadol, which is completely opposite to our observation.<sup>9</sup> Similarly Md Rafiqul Hasankhan *et al.* studied the pre-emptive use of diclofenac, ketorolac and tramadol for post-operative pain in laparoscopic cholecystectomy and reported that post-operative pain can be managed by pre-emptive use of diclofenac, ketorolac and tramadol for the 1<sup>st</sup> 24 hours with little or no supplementation of low dose intravenous pethidine. The analgesic efficacy of ketorolac and tramadol is similar and better than diclofenac.<sup>10</sup> Post-operative Ramsay sedation score and Modified Aldrete score were comparable in both the study groups as observed in our

present study.

None of the patients in either group of study had any significant side-effects intra-operatively or post-operatively like nausea, vomiting, excessive bleeding at the sight of surgery or over sedation. Similar studies have been proved in various studies mentioned.

In ketorolac group 6 of our patients required intra-operative rescue analgesia which was supplemented with inj. fentanyl in the dose of 1 mcg per kg body weight, while in tramadol group no rescue analgesia was required.

Thus in our study, it was observed that pre-emptive intravenous tramadol 1 mg/kg provides better intra-operative and post-operative analgesia when compared with intravenous ketorolac 1 mg/kg with no incidence of significant side effects in either group.

## Summary

The study was conducted on 60 patients posted for elective inguinal herniotomy or penile surgeries after pre-operative evaluation and necessary investigations. All the patients were randomly divided into two Groups, Group K received inj. Ketorolac 1 mg/kg while the other Group T received intravenous Tramadol 1 mg/kg pre-emptively. All patients were observed for intra-operative mean arterial pressure, heart rate and end tidal carbondioxide, post-operative pain was measured by using FLACC score and time for first rescue analgesia was assessed. The pre-emptive analgesic efficacy of intravenous tramadol is better than intravenous ketorolac providing both good analgesia during operation as well as early post-operative period in pediatric age group of 2-8 years undergoing elective inguinal herniotomy or penile surgeries.

There were no significant adverse effects observed in any of the patients in either group.

## Conclusion

- Pre-emptive tramadol provided longer duration of post-operative analgesia as compared to ketorolac;
- It also provides better intra-operative analgesia than ketorolac and smooth and quiet recovery in pediatric patients;
- There were reduction in requirement of

systemic analgesics post-operatively;

- There were no major adverse effects in both tramadol and ketorolac study group;

Thus, pre-emptive tramadol in a dose of 1 mg/kg body weight has significant intra-operative and post-operative analgesia without any significant adverse effects.

### Limitations

There were no limitations in our study.

### Abbreviations

MAP- Mean Arterial Pressure;

PACU- Post Anesthetic Care Unit;

FLACC - Face, Legs, Activity, Cry, Consolability.

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