

Efficacy of Oral Toradol (Ketorolac) Compared to Oral Tramadol as a Preemptive Analgesic in Impacted Third Molar Surgery

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ABSTRACT

Objective: To compare ketorolac with Tramadol as a preemptive analgesic in impacted third molar surgery in terms of mean pain score, mean time of first analgesic and mean total analgesic consumption postoperatively.

Study Design: Experimental study.

Place and Duration of the Study: Department of Oral and Maxillofacial Surgery, Islamic International Dental Hospital, (IIDH) Riphah International University, Islamabad, from March 2018 to March 2020.

Methodology: Ninety-four patients, aged 18-45 years with impacted third molars were divided into two groups. Preoperatively oral tramadol 50 mg was given in group A and oral ketorolac 10 mg was given in group B. Pain score was measured 3 hours postoperatively, using the visual analogue scale (VAS), the time was noted for first analgesic consumption in hours and total consumption of analgesics.

Results: The mean postoperative pain was measured for both groups. Pain was significantly less in Group B. The mean pain score was 4.02 ± 1.20 in group A and 3.42 ± 1.08 in group B measured at 3 hours postoperatively ($p=0.02$). The mean time interval for 1st postoperative analgesic was 2.90 ± 1.24 hours in group A and 3.61 ± 1.02 in group B ($p=0.007$). The mean total analgesic consumption was 3.75 ± 1.27 grams in Group A and 2.27 ± 1.74 grams min Group B ($p=0.006$).

Conclusion: Preemptive Ketorolac has a more prolonged analgesic effect as compared to tramadol.

Key Words: Preemptive analgesia, Tramadol, Ketorolac, Pain score, Third molar surgery.

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INTRODUCTION

Pain, swelling, and trismus have been reported postoperatively either as direct or immediate consequences of third molar extraction. Associated pain with surgical removal of mandibular third molar under conventional local anaesthesia ranges between moderate to severe during the first 24 hours, and most intense between 6 and 8 hours.¹

Preemptive analgesia is the administration of anaesthetic before surgery in an attempt to abort postoperative pain and disability. It is an antinociceptive treatment that prevents the establishment of altered processing of afferent input, which results in amplification of postoperative pain.

Commonly two medicines are used as preemptive analgesics for third molar surgery. Tramadol being the centrally acting analgesic has combined effects as an opioid agonist and a serotonin and adrenaline reuptake inhibitor. Ketorolac tromethamine is a member of the pyrrolo-pyrrole group which inhibits prostaglandin synthesis by competitive blocking of the enzyme cyclooxygenase (COX).^{2,3}

For effective pain relief after mandibular third molar surgery, three categories of analgesics are conventionally used including local anaesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids or their combination.⁴ Several studies have also compared the efficiency of these two agents as a preemptive analgesic. Furthermore, NSAIDs (Ketorolac) have a superior analgesic effect and safety profile as compared to a single dose of Tramadol.⁵ Ketorolac is better than tramadol for managing pain prior to oral surgery.^{6,7} Mandibular third molar surgery causes swelling, trismus, and moderate pain; post-surgery pain control improves recovery and oral function.⁸ Swelling and trismus are common sequelae which may persist for several days.⁹ Mandibular third molars develop horizontally, shifting to mesioangular, and then becoming vertical as the jaw grows. If not rotated, they may erupt in the oral cavity.¹⁰ It is suggested that insufficient

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retromandibular space in mandible leads to impaction of 3rd molar.^{11,12}

Dento-alveolar pain is mostly of inflammatory origin and several researches have presented that NSAIDs are the best analgesics for this type of pain.¹³ This leads to the use of a high number of analgesics postoperatively.

Bauer found ibuprofen 800mg insufficient for preemptive analgesia, while ibuprofen 800mg + dexamethasone 8mg was more effective.¹⁴ Some authors found a significant difference in risk assessment for inferior alveolar nerve canal injury using OPG compared to CBCT imaging, with CBCT imaging contributing to more comprehensive surgical planning and minimising injury risk.¹⁵⁻¹⁷

Surgical removal (Invention of surgical drills for conservative tooth removal) of the third molar leads to severe pain postoperatively with the resultant consumption of a large quantity of analgesics.^{16,18} The routes used for the administration of analgesics for pain relief for third molar surgery were submucosal and intramuscular in the previously performed studies. Using oral routes may enhance patients' compliance towards preemptive analgesia. The purpose of this study was to assess the effectiveness of two groups of preemptive analgesics in controlling pain in impacted third molar surgery by oral route.

METHODOLOGY

This experimental study was conducted at the Oral and Maxillofacial Surgery Department, Islamic International Dental Hospital, (IIDH) Riphah International University, Islamabad, from March 2018 to March 2020.

Adult patients undergoing impacted third molar surgery were included. Those with hypersensitivity to the study agents were excluded. The sample size was calculated by WHO calculator with a hypothesis test for two populations as two-sided test, power of test was 80% and level of significance was 5%. A thorough clinical examination was carried out for each patient with examination also included an evaluation of potential complications associated with the study agents. A total of 94 patients were equally divided in two groups. Each group was given Tramadol (50mg) and Ketorolac (10 mg), respectively half an hour preoperatively orally for surgical third molar extraction.

All data were entered and analysed using Statistical Package for Social Sciences (SPSS version 20). Qualitative variables such as pain and gender were measured as frequency and percentage. Mean and standard deviation values were calculated for quantitative variables such as age, time of first rescue analgesic and total analgesic consumption. Pain score was measured 3 hours postoperatively in both groups by using a visual analogue scale, ranging from 0-10. Zero (0) represents absence of pain and 10 represents severe pain. Chi-square test was applied to compare the severity of pain between two

groups and independent sample t-test was applied to compare the time for the first analgesic and mean total analgesic consumption effects modifiers such as age, gender, class II and class B were controlled by stratification. Poststratification independent t-test was applied for the quantitative variables and chi-square test was applied for the qualitative variable. The p-value of less than 0.05 was considered as significant.

RESULTS

Out of a total of 94 patients, 41 (43%) were males and 53 (57%) were females. In the tramadol group, 23 out of 47 patients were males and 24 were females. In the ketorolac group, 18 were males and 29 were females. The mean age of both groups is demonstrated in Table I. There was no statistically significant difference between the mean age of both groups.

Group A was assigned to the patients in which oral tramadol 50 mg was given preoperatively and group B was assigned to patients in whom ketorolac 10mg was given preoperatively. Their effects were seen on the pain score of patients 3 hours postsurgery and time interval for initial rescue analgesic was noted postoperatively.

The mean pain score 3 hours postoperatively was 4.02 ± 1.20 and 3.42 ± 1.08 for group A and B, respectively ($p=0.02$) as shown in Table I. The time interval for 1st rescue analgesic postoperatively was 2.90 ± 1.24 and 3.6 ± 1.02 hours for group A and B, respectively and ($p = 0.007$). For group A the mean total analgesic postoperatively was 3.75 ± 1.27 , for group B it was 2.27 ± 1.74 ($p = 0.006$).

Effect modifiers such as gender and age were stratified and compared in both groups for pain score and time interval of the first rescue analgesic. The mean pain score at 3 hours postoperatively for males was 3.89 ± 1.19 and 3.40 ± 1.15 , respectively in each group ($p = 0.17$). The mean pain score for females was 4.14 ± 1.23 and 3.47 ± 0.99 in each group, respectively with a ($p = 0.09$). Age was stratified into 18-30 years and 31-45 years. Patients between 18-30 years of age in group A had 3.88 ± 1.2 mean pain score of and in group B had 3.23 ± 1.03 ($p = 0.04$). The mean pain score for the age range 31-45 years was 4.27 ± 1.22 for group A and 3.79 ± 1.12 for group B ($p = 0.28$) as shown in Table II.

Both effect modifiers (gender and age) were compared for time interval of 1st rescue analgesic postoperatively in both groups. For males, the mean time interval was 3.16 ± 1.58 in group A and 3.66 ± 1.01 in group B ($p = 0.21$). For females, the mean time, interval was 2.67 ± 0.79 in group A and in group B was 3.53 ± 1.08 ($p = 0.009$). Patients between 18-30 years had mean time intervals of 2.90 ± 1.18 minutes in group A and 3.69 ± 0.93 in group B ($p = 0.01$). Patients with age range of 31-45 years had mean time interval of 2.90 ± 1.39 minutes in group A and 3.46 ± 1.20 minutes in group B ($p = 0.25$).

Table I: Mean age for groups A and B, mean pain at 3 hours postoperatively, mean time interval for 1st rescue analgesic (hours) and mean total consumption of analgesics (gm).

	Group	N	Mean	Std. Deviation	p-value
Age (years)	Total patients	94	30.87	4.40	0.97
	Group A	47	29.98	4.00	
Pain score at 3 hours postoperatively	Group B	47	29.00	4.52	0.02
	Group A	47	4.02	1.20	
Time interval for 1 st rescue analgesic (hours)	Group B	47	3.42	1.08	0.007
	Group A	47	2.90	1.24	
Mean total analgesic consumption	Group B	47	3.61	1.02	0.006
	Group A	47	3.75	1.27	
	Group B	47	2.27	1.74	

Table II: Stratification of pain score at 3 hours postoperatively and time interval for 1st rescue analgesic with respect to gender and age.

Gender	Groups	Pain score at 3 hours postoperatively Mean ± SD	p-value	Time interval of 1 st rescue analgesic (hr) Mean ± SD	p-value
Male	A	3.89± 1.19	0.17	3.16± 1.58	0.21
	B	3.40± 1.15		3.66± 1.01	
Female	A	4.14± 1.23	0.09	2.67± 0.79	0.009
	B	3.47± 0.99		3.53± 1.08	
18-30 years of age	GA	3.88± 1.2	0.04	2.90 ± 1.18	0.01
	GB	3.23± 1.03		3.69± 0.93	
31-35 years of age	GA	4.27± 1.22	0.28	2.90± 1.39	0.25
	GB	3.79± 1.12		3.46± 1.20	

DISCUSSION

Preventive techniques that tend to block transmission of the painful nerve impulses before, during, and after surgery are emerging in practice rather than merely treating the pain after surgical third molar extraction. The development of pain hypersensitization may be decreased or eliminated by administering analgesics prior to the painful stimulation, resulting in less postoperative discomfort.¹⁹ Surgical removal of the third molar leads to severe postoperative pain and inflammation. The peak pain after the third molar surgery is experienced within 24 hours.²⁰

When NSAIDs are administered preoperatively, they provide improved and extended pain relief by blocking the release of prostaglandins and leukotrienes ultimately leading to the blockage of peripheral and central sensitization. It will also reduce the number of analgesics postoperatively which in turn leads to better patient compliance.⁵

In this study, the authors compared the preemptive effect of oral ketorolac and tramadol was compared in patients undergoing surgical removal of impacted third molars. Ketorolac provided better preemptive analgesia in reducing pain intensity and prolonged pain control postoperatively. The mean time interval for the first rescue analgesic postoperatively was measured between both groups, and also showed significantly longer pain control with ketorolac.

In this study, 94 patients were included which were divided into two groups. The mean age of the patients was 28.98 ± 4.00 years in the tramadol group and 29.00 ± 4.42 years in ketorolac group, there was no statistical difference between

either the mean age in both groups or in the outcome when stratified.

Similarly, the mean pain score at 3 hours and time intervals for 1st rescue analgesic was measured between subgroups within each group which was not significant for age stratification. The mean total analgesic consumption was measured postoperatively between groups which were also not significant.

Gender distribution was not equal in both groups in this study but further stratification in males and females in each group showed no statistical difference in the time interval for first rescue analgesics post-operatively.

Several studies have also compared the efficacy of these two analgesics as a preemptive analgesic.^{1,3,8,14,21,22} Mario et al. demonstrated that ketorolac 10mg group (73.3%) was more effective in providing preemptive analgesia as compared to Tramadol 50 mg group (26.6%).¹ He demonstrated that the time of taking the first rescue analgesic after the surgical procedure for the ketorolac group is more with mean SD (4.8 ± 1.5) (3.4 - 9.5) than the Tramadol group with mean SD (3.1 ± 5.25) (3-24) p-value 0.215. He also demonstrated that the total analgesic consumption for the ketorolac group was less than the Tramadol group.¹

Review and meta-analysis of randomised clinical trials found no evidence supporting ketorolac as superior to tramadol for postoperative pain reduction after impacted third molar extraction.²¹ Cochrane review shows ibuprofen superior to paracetamol for postoperative pain management.²² Aimuamwosa et al. found transdermal diclofenac sodium as a viable

alternative to oral diclofenac for pain relief in patients unable to take the medication orally, especially in third molar surgery.²³ Submucosal Tramadol and local anaesthesia provide effective, prolonged analgesia for impacted third molar extraction surgery.²⁴ Another study conducted by Tai *et al.* also supports the results of this study that ketoprofen provides better analgesia. They matched ketoprofen 200 mg and diclofenac 100 mg in several doses for 4 days after the third molar extraction. Paracetamol 500 mg was administered as the rescue painkiller. Study showed ketoprofen offers better pain control with p-value of 0.086.⁸

Limitations of this study are due to sampling errors (probability sampling method) is used to select sample and that population does not reflect the general population.

CONCLUSION

Preemptive analgesics work best in aforementioned cases and thus reduce post-operative pain by not only blocking the release of prostaglandins but also neurons responsible for peripheral and central sensitization of pain. Oral ketorolac (10mg) offered superior analgesic effects than oral tramadol (50mg) in reducing pain intensity and pain control for a longer duration.

DISCLOSURE:

This article is derived from a dissertation written in partial fulfilment of FCPS requirements.

ETHICAL APPROVAL:

The study was conducted after obtaining ethical approval from the Ethics Committee of Islamic International Dental Hospital (Ref. IIDC/IRC/2017/09/001) prior to the initiation of the research work.

PATIENTS' CONSENT:

Informed consent was obtained from patients to publish the data concerning this case.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

UR: Planning, critical review, material analysis, conception of study, study conduction interpretation, manuscript writing, conception of the work, acquisition, analysis, and interpretation of data for the work. Drafting the work and revising it critically for important intellectual content. Final approval of the version to be published. Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

MF: Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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