

Comparative Evaluation of Analgesic Efficacy of Oral Ketorolac and Tramadol after Impacted Mandibular Third Molar Surgery: A Short Clinical Study with Literature Review

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Abstract

Aim & objectives: The aim of this study was to evaluate the analgesic efficacy of oral ketorolac versus tramadol after a mandibular third molar surgery. **Material and Methods:** Total of 100 healthy patients under the age group of 20-60 years requiring surgical extraction of an impacted mandibular third molar were divided randomly into 2 groups of 50 each Group A (Ketorolac) & Group B (Tramadol) and received 10 mg of ketorolac thrice and 50 mg Tramadol twice a day respectively. Pain intensity was recorded after 30 minutes; 1st hrs, 4th hrs, 6th hrs, 12th hrs & 24 hrs after surgical procedure using the visual analog scale. **Results:** Mean age was 31± 8.1 years in Group A and 33 ± 10.4 in Group B. Group A included 34 males (68%), 16 females (32%) whereas Group B included 30 males (60%), 20 females (40%). Average weight of patients in Group A was 58.8 kg and in Group B was 61.4 kg. 75% Study includes Mesioangular (75%), 15% Horizontal (15%) and 10% Distoangular (10%) type of impacted teeth. Mean difficulty index for group A was 7.4 and for group B was 7.8 (Pederson Scale). Mean duration of surgery in Group A was 45 ± 6 minutes and in Group B was 48 ± 8 minutes. Acute pain relief was observed in Ketorolac group with in half hour (min VAS was 2.68) but for shorter duration of 4-5 hrs. However depth (min VAS score 1.65) and duration of analgesia (8-10 hrs) was more in tramadol group. Complications like nausea/vomiting (8%) and drowsiness/sedation (6%) was observed more in tramadol group whereas upper gastric pain/acidity (8%) was more in Ketorolac group. **Conclusion:** Oralketorolac is a good analgesic drug (NSAID) for acute pain of inflammatory etiology like surgical extraction of impacted teeth.

Keywords: Non-steroidal anti-inflammatory drugs (NSAIDs); Ketorolac; Tramadol; Visual analogue scale (VAS); Impacted teeth

Introduction

Impacted third molar extraction involves both soft and bone tissue trauma and may result in an acute inflammation with intense discomfort as well as pain. Pain is a subjective symptom and can be influenced by various factors like age, sex, anxiety, pain threshold and surgical difficulty etc. pain experienced after impacted third molar surgery under local anesthesia has been shown to be of short duration and reaches its maximum intensity in early post-operative period which requires analgesics for relief. Post-operative pain can cause distress to the patient and affect the patient's quality of life after surgery. So various research studies have been done for better pain control following impacted third molar surgery and different types of medications have been proposed.^[1]

Pain management after third molar surgery is more crucial and should be treated before the development of significant intensity of pain. Longer the pain remain uncontrolled more sensitive the patient may become to painful stimuli. Pain following third

molar surgery reaches to severe intensity or peak with in first 5-8 hrs after the surgery.^[2] Many clinicians have attempted to reduce the post-operative pain by using anti-inflammatory drugs. The anti-inflammatory drugs broadly categorized into steroidal (Narcotic analgesics) and non-steroidal (NSAIDs). Narcotic analgesics, which act directly on central nervous system opiate receptors, but can cause drug dependence, respiratory depression, constipation, nausea, vomiting and sedation. Non-steroidal anti-inflammatory drugs (NSAIDs), which act by prostaglandin synthesis to achieve analgesic and anti-inflammatory actions, but associated with poor gastrointestinal and renal tolerance and risk of interference with coagulation

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system. The best postoperative medication is one that provides long analgesic cover, easy administrable, should be safe and cost economical.^[3]

Tramadol is a synthetic opioid of the benzenoid class used to treat moderate to severe pain both acute and chronic. Its effectiveness is equivalent to that of morphine and analgesics effects last for approximately 6 hrs. It act by two different mechanisms. First, it works by binding to the μ -opioid receptor. Secondly, it acts as a serotonin–norepinephrine reuptake inhibitor (SNRI).^[4,5] Ketorolac is first-generation non-steroidal anti-inflammatory drug (NSAID) of family heterocyclic acetic acid derivatives, used for short-term management of moderate to severe pain and usually not prescribed for longer than five days. Ketorolac is a non-selective COX inhibitor. Its mode of actions is by inhibiting the bodily synthesis of prostaglandins by competitive blocking of the enzyme cyclooxygenase (COX). Its onset of action is approx. 30 minutes reaches its peak effects in 45-60 minutes and having half-life of 4-6 hours.^[6]

The use of tramadol has not reported very widely after extraction of the impacted third molar. However Ketorolac has been used successfully to replace opioid in mild-to-moderate postsurgical painlike surgical extraction of impacted teeth. The main aim of our study was to compare the efficacy of two different analgesics, Tramadol and Ketorolac after impacted mandibular third molar surgery

Materials and Methods

Total of 100 patients requiring surgical extraction of an impacted mandibular third molar, under local anesthesia were selected. Inclusion criteria were the patient of age group between 20–60 years having mandibular impacted teeth indicated for surgical extraction that were willing to participate in the study. Exclusion criteria includes medically compromised patients, pregnancy, patient on steroid therapy, metabolic disorder patients, those who had taken any type of analgesic in the past 48 hrs, patients allergic to the drugs and patients who are not willing to participate in the study.

All the patients who were included in the study were informed about the treatment procedure and possible complications were also explained to them. Informed consent was taken from them. Detailed history was recorded in a standardized format. All the patients were examined clinically and radiographically. Pre-operative opg radiograph was recorded to assess the type of impaction (mesioangular, distoangular, horizontal and vertical). The patients were randomly divided into two groups (Group K & Group T) of 50 each. Group K patients were given ketorolac 10 mg [Ketorolac DT, Dr. Reddy's lab], and Group T patients were given Tramadol 50 mg postoperatively. Pain intensity was recorded after 30 minutes, 1st hr., 4th hrs, 6th hrs, 12th hrs and 24 hrs using the visual analog scale.

Comparison of pain intensity was also done on 1st, 2nd and 3rd postoperative days. Pain was recorded on VAS (visual analogue scale) [0-no pain, 2-mild pain, 4- tolerable, 6-distressful pain, 8-severe pain and 10-totally disabling pain]. The patient's vital

signs including heart rate, respiratory rate and blood pressure were recorded at every time point after the assessment of pain intensity.

Surgical Procedure

All the patients included in the study were operated under local anesthesia by same operator using standard inferior alveolar nerve block technique of involved side. Ward's Incision was given using 15 no blade, mucoperiosteal flap was then reflected by Molt's periosteal elevator, protecting the lingual nerve. Guttering of the bone was done on buccal and distal portion with surgical round bur (#6) and sectioning of the third molar was done if required as per the standard methodology of extraction of impacted teeth. After the surgery, the socket was inspected, irrigated with betadine and normal saline and the flap was primarily closed with 3-0 silk suture. Post extractions instructions were explained to the patients. Patients were asked to take medicine 1 hour after the surgery in both groups. The patients were recalled on the 7th day postoperatively for suture removal.

Results

A total of 100 patients were enrolled in the study to compare the analgesic efficacy of Ketorolac versus Tramadol were equally divided into Group A (Ketorol) and Group B (Tramadol). Mean age was 31 ± 8.1 years in Group A and 33 ± 10.4 in Group B. Group A included 34 males (68%), 16 females (32%) whereas Group B included 30 males (60%), 20 females (40%)

Average weight of patients in Group A was 58.8 kg and in Group B was 61.4 kg. Among all patients, 75% had mesioangular, 15% horizontal and 10% distoangular type of impacted teeth. Degree of difficulty index was calculated with Pederson difficulty index. Similar impacted teeth with same difficulty indexed teeth were compared in two groups. Mean difficulty index for group A was 7.4 and for group B was 7.8 (Pederson Scale)

Duration of surgery is important factors responsible for post-operative inflammation and pain. Mean duration of surgery in Group A was 45 ± 6 minutes and in Group B was 48 ± 8 minutes. The data for this study were collected at different time points; analysis for the longitudinal study was done. Patient's demographic and surgical data didn't not show any statistically significant differences [Figure 1].

The study shows that the mean time taken for surgery in Group A (Ketorol) and Group B (Tramadol) under local anaesthesia is relatively same. Similar result was obtained while comparing difficulty level of extraction with similar age groups. There was no significant difference in the level of difficulty of extraction and time taken for same in case we either administer ketrol and tramadol in similar age groups [Table 1].

In our study (Group A) we observed that the analgesic effect of ketorolac started with in half hour and reached it maximum analgesic effect about 1 hrs and continued upto 4-5 hrs. Minimum average pain intensity given by patient was 2.68 (Visual analog scale) at first hour and maximum was 6.20 at 8

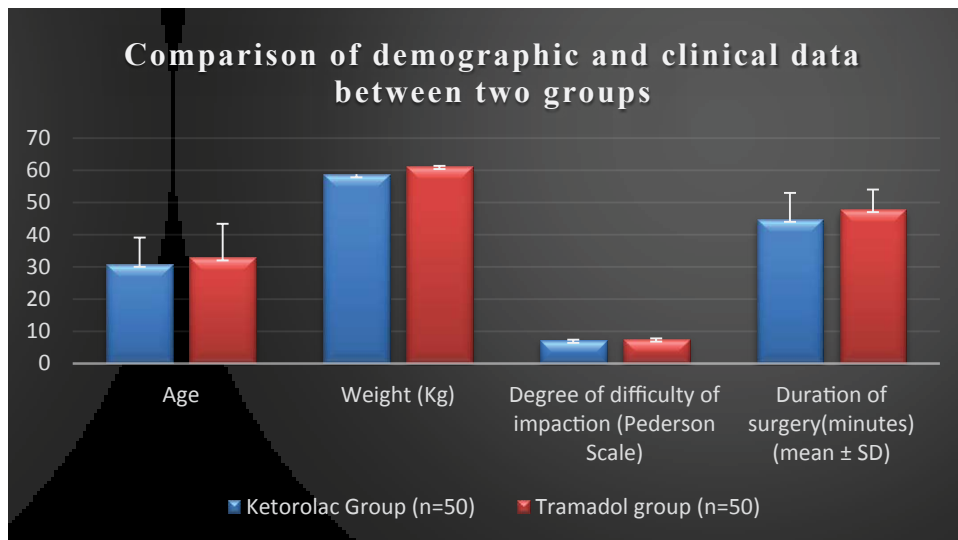


Figure 1: Comparison of demographic and clinical data between two groups.

Table 1: Categorical analysis comparing different age groups, extraction difficulty and time taken for surgery.

Age group	Group A (Ketorolac)			Group B (Tramadol).		
	No. of subjects	Extraction difficulty (Pederson Scale)	Time taken for surgery (minutes)	No. of subjects	Extraction difficulty (Pederson Scale)	Time taken for surgery (minutes)
20-25	6	6.8	42	8	7.6	42
25-30	10	7.2	44	15	7.8	45
30-35	12	7.4	45	10	8.0	50
35-40	8	7.8	50	7	7.6	48
40-45	6	8.0	51	5	8.4	55
45-50	4	7.2	42	2	7.6	46
50-55	3	7.4	45	1	7.8	52
55-60	1	7.8	48	2	8.0	48
Total	50	7.4	45	50	7.8	48

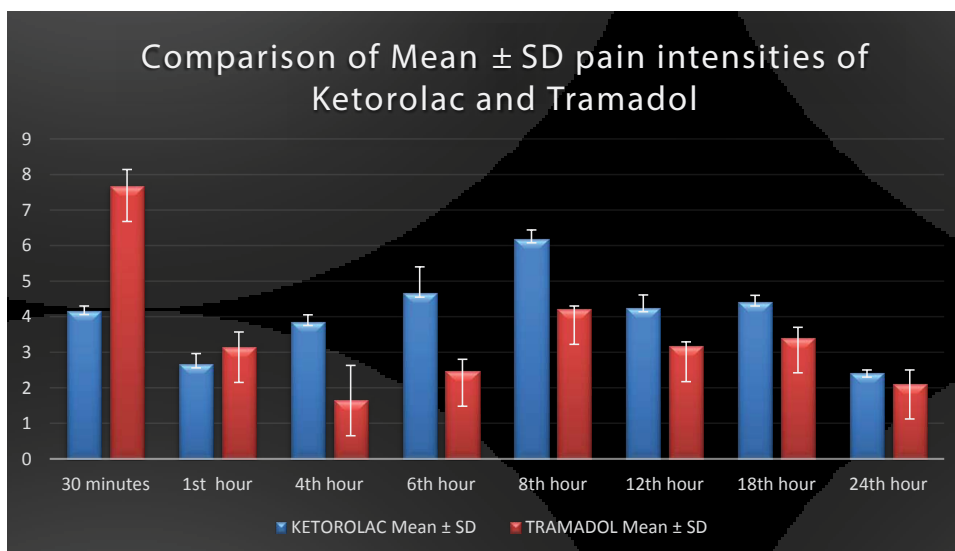


Figure 2: Distribution of pain intensity score (VAS) between two groups at different time intervals post-operatively.

hrs postoperatively. In group B, analgesic effect of Tramadol observed at the end of first hour and reached its maximum analgesic effect within three hours and continued upto for 8-10 hours. The patients scored a minimum pain intensity of 1.65 at 4thhrs and maximum of 7.68 at half hrs on visual analog scale.

Acute pain relief was observed in ketorolac group with in half hour however duration of analgesia was more in tramadol group. However duration of analgesia was more in tramadol group as

compared to ketorolac group. At the end of 24 hrs patient scored 2.42 and 2.12 on Visual analog scale. The result of analysis shows statistically significant results difference between the groups ($P > 0.05$) [Figure 2].

Pain intensity decreases from first post-operative days to third day. Maximum pain felt by patients was 3 in ketorolac group and 4 in tramadol group on first post-operativeday. Inwardly there

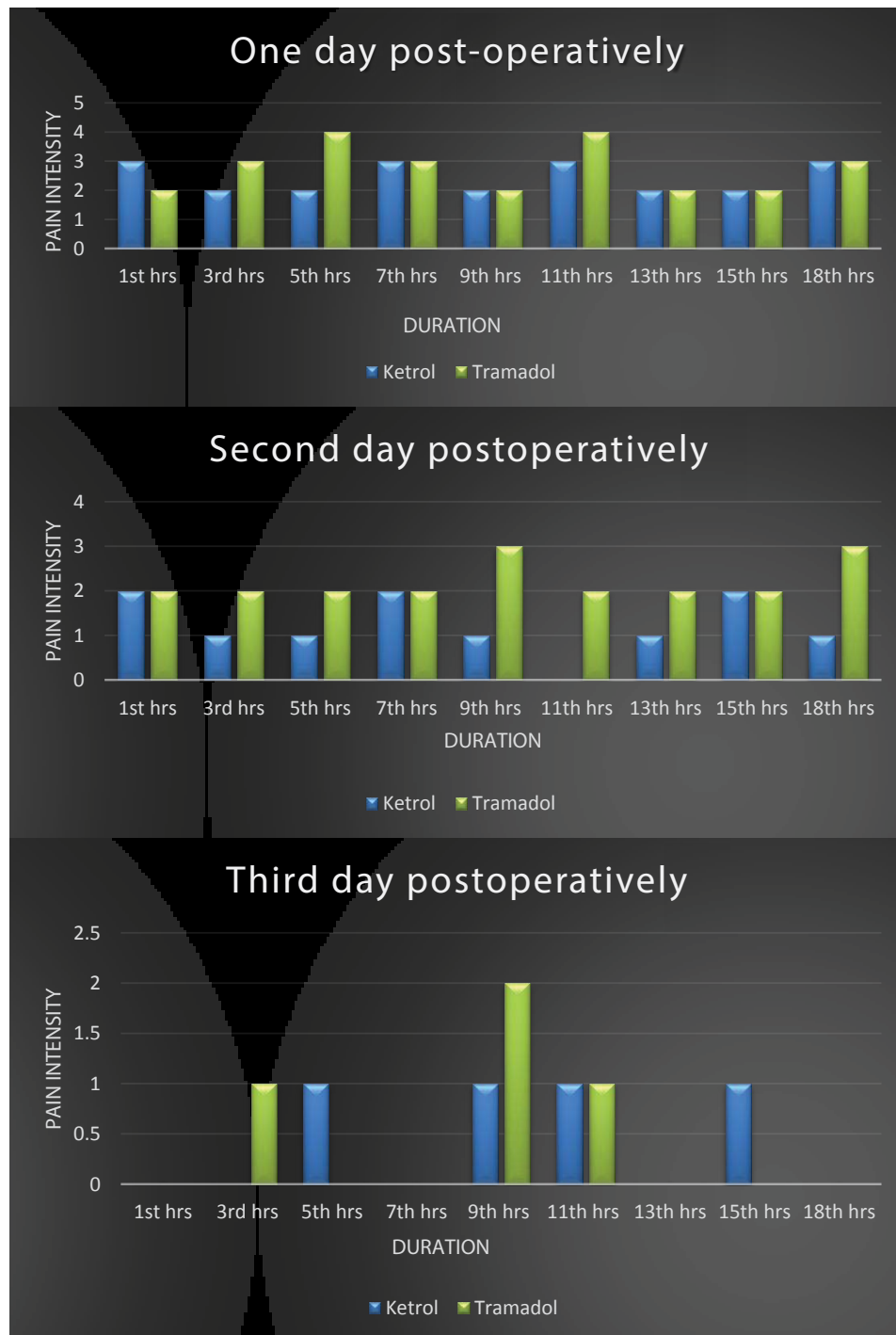


Figure 3: Distribution of pain intensity score in 1st, 2nd and 3rd post-operative days.

was no statistically significant results was observed between two groups in next postoperative days [Figure 3].

The common adverse effects observed in ketorolac group are gastric acidity and epigastric pain which was seen in 8% of patients. 4 % of patients observed nausea and vomiting. There were appearances of oral ulceration in 6% of patients in post-operative periods. One patient present with bleeding at surgical site. In 2% of patients sweating and constipation occurred. In tramadol group 8% of cases complaints of nausea and vomiting. 2% patients observed gastric pain and sweating. About 6% of patients in this group observed lethargicity, drowsiness and sedation. Overall complications rates in ketorolac group and tramadol group shows no significant result. The intensity of

Table 2: Comparison of side effects between two groups.

Adverse Side effects	Ketorolac group N (%)	Tramadol group N (%)
Oral ulcers	3 (6%)	0
Nausea and vomiting	2 (4%)	4 (8%)
Gastric pain and acidity	4 (8%)	1 (2%)
Bleeding	1 (2%)	0
Drowsiness and sedation	0	3 (6%)
Sweating	1(2%)	1(2%)
Diarrhea/ Constipation	1(2%)	0

adverse effects here increased as dose increased [Table 2]. Vital signs (blood pressure, pulse rate, respiratory rate and

temperature) were recorded regularly in both the groups during the initial 24 hours. The vital signs were however within normal limits in both the groups.

Discussion

It is said that “the pain of mind is worse than the pain in body” and its management would require alleviating both the mental and physical pain, making the patient comfortable. Post-operative pain is considered a form of acute pain due to surgical trauma.^[7]

Ketorolac induces early analgesic effect with half hour and show its maximum effect after that. Its analgesic effect lasts for about 4-5 hrs. Tramadol induces delayed analgesia around 1 hour and reached its maximum effect in 3-4 hours. Its analgesic effect lasts longer duration for about 8-10 hrs. Similar results are observed by Shaik Kim K et al. and Mario et al. respectively. Both the medication provides good analgesic effect.^[8,9] Gopalraju et al. observed intravenous ketorolac 30 mg provides better pain control postoperatively as compared to 50 mg of tramadol after third molar surgery.^[10] In the double-blind, randomized, clinical trial Mishra et al. 2012 proved that 100 mg of tramadol is equally effective as 20 mg of ketorolac in the relief of postoperative pain.^[11] Shah et al. 2013 in their study concluded that intramuscular 30 mg ketorolac gives better pain management, if given prior to oral surgical procedure than intravenous 50 mg tramadol.^[12] Ong et al. 2004 showed ketorolac had better pain scores and total post-operative analgesic consumption than tramadol.^[13]

Ketorolac should be avoided in patient with kidney and coagulation disorders as it interfere in renal and platelet functions. In our study only 1 patient (2%) presented with post-operative surgical site bleeding in ketorolac group. No bleeding episodes were observed in tramadol group. Post-operative nausea, vomiting and sedation are most common side effects of tramadol. Our study shows 8% patients complaints about nausea/vomiting and 6% for drowsiness and sedation. Similar results were observed by Collins et al.^[14] and Zackova M et al.^[15]. Gastric pain with acidity was observed in 8% cases in ketorolac group. This is due to fact that ketorolac Inhibit the prostaglandin synthesis which reduce the protective mechanism of prostaglandins on the gastric mucosa leading to dyspepsia and upper gastric pain. Only 2% cases presented with acidity in tramadol group.

Effective and safe analgesia is one of the main challenges in health care industry. Tramadol is a relatively new opioid drug with better analgesic property and without the risk of tolerance and physical dependence. It is known to be a one of the safest postoperative analgesic medicine used for chronic pain management. However systematic review and meta-analysis showed that a single dose of tramadol has a lower analgesic efficacy and safety than NSAIDs in oral surgery.^[16] Ketorolac is a commonly used NSAID for the short term management of acute postoperative pain in dentistry. Main focus of the study was to compare the analgesic efficacy on pain intensity after impacted teeth surgery and the adverse effects of the commonly used analgesics, tramadol and ketorolac. For maximum analgesic

effect Ketorolac DT manufacturer [Dr. Reddy's lab] promotes two dose of 10 mg ketorolac immediately or stat basis followed by two next doses of 10 mg 12 hourly to a maximum of 40 mg/day. The better analgesic efficacy of ketorolac in comparison to tramadol is attributed to the pathogenesis of dental pain, which is largely inflammatory and is different from general surgical pain. The evidence-based medicine has also shown that dental pain is better treated with NSAIDs than opioids.

Conclusion

The best postoperative regimen is one that offers broad analgesic coverage, easy to administer, is safe and economical. From the observation of our study we can conclude that early pain relief is mandatory for dental pain especially of impacted third molar surgical extraction to avoid patient discomfort and morbidity. Oral ketorolac induces early analgesic effect with half hour and provides maximum analgesic effect upto 4 hrs but next dose is needed after that. Tramadol induce delayed analgesic effect at 1 hour but its analgesic effect lasts for about 6-8 hrs. After surgical extraction of third molar, for post-operative acute pain, ketorolac DT is a good analgesic drug given for shorter duration to provide relief and prevent referred pain keeping risk versus benefit ratio in consideration. Further more advanced research is required with larger sample size for conclusive results.

Conflict of Interest

The authors disclose that they have no conflicts of interest.

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