



## "INTRAMUSCULAR ADMINISTRATION OF KETOROLAC VERSUS TRAMADOL POST OPERATIVELY IN MINOR ORAL SURGERY"

### Surgery

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### ABSTRACT

**BACKGROUND & OBJECTIVES:** Surgical removal of impacted mandibular third molars is a procedure frequently carried out on an out-patient basis and analgesia is necessarily a balance between achieving adequate pain relief while causing minimum side effects. Pain is a common complaint often occurring with inflammatory processes after a tooth extraction. Postoperative pain following surgical removal of a mandibular third molar is validated, well documented and highly sensitive model to assess therapeutic relief of moderate to severe pain. The ultimate goal of oral health care providers is not only to restore function, but also to relieve pain. Analgesics are commonly prescribed to alleviate pain induced by the inflammation. Patients with post - operative pain are currently treated with various drugs in two main categories:

- i) Non - steroidal anti - inflammatory drugs (NSAIDS)
- ii) Narcotic analgesics.

Ketorolac is a potent NSAID that avoids the problems associated with narcotic analgesics [potential for addiction, drug tolerance and respiratory depression while still achieving a narcotic like efficacy. Tramadol is a synthetic analogue of codeine and causes minimal respiratory depression, few gastrointestinal effects and has less potential for opioid like dependence. The objective of this study was to compare the analgesic efficacy of post - operative intramuscular ketorolac versus tramadol in preventing post-operative pain after mandibular third molar surgery.

**PATIENTS & METHOD:** Forty patients under the age group of 16 - 40 yrs with asymptomatic impacted mandibular third molars were randomly assigned into one of the two groups (20 in each group), and underwent third molar surgery under local anesthesia. Group I received IM ketorolac 30mg and Group II received tramadol 50 mg post - operatively. The difference in post - operative pain was assessed by five primary end points : pain intensity measured every hourly by a 10 cm visual analogue scale for 12 hours, onset of analgesia, duration of action, total no of analgesics consumed, and patient's global assessment.

**RESULT:** Throughout the 12 hours investigation period, patients reported significantly lower pain intensity scores, longer duration of action, lesser post - operative analgesics consumption and better global assessment in ketorolac when compared to tramadol group. Patients in the ketorolac group significantly performed better than the tramadol group in terms of all parameters except onset of analgesia. All the drug related complications were mild and did not require any intervention.

**CONCLUSION:** The results of the present study shows that post-operative intramuscular ketorolac 30 mg is more effective than tramadol 50 mg for post-operative pain following third molar surgery.

### KEYWORDS

Ketorolac ; Tramadol ; Pain ; Third molar surgery

### INTRODUCTION

Surgical extraction of impacted mandibular third molars is a procedure frequently carried out for pericoronitis, infection, pain, cyst or a tumor and to facilitate orthodontic treatment on an out patient or day-care basis. Post-operative pain following the same is frequently severe, and is often validated and well documented since it is considered to be a highly sensitive model to assess the efficacy of analgesic agents in terms of achieving an adequate pain relief while causing minimum side effects. Pain following third molar surgery may be controlled by the use of L.A, opioids or NSAIDS. In spite of the availability of the various pain relieving agents, an inadequate pain relief remains a routine problem in ambulatory oral surgery.

Although the mechanism of action of all the NSAIDS is same i.e. inhibition of prostaglandin synthesis, the efficacy may vary from one drug to another. Ketorolac tromethamine; a member of pyrrolopyrrole group is believed to be equivalent to meperidine in terms of analgesic potency. It has an analgesic, anti-inflammatory and antipyretic activity and has been shown to be significantly effective for post-operative dental pain while having no effect on opioid receptors and possesses no sedative or anxiolytic properties. Its primary action appears to be the inhibition of COX enzyme that metabolizes arachidonic acid to endoperoxide intermediates and prostaglandins

that promote pain. Ketorolac tromethamine is available for IV, IM and oral administration. Addition of the tromethamine salts enhances stability and facilitates better bioavailability.

Tramadol hydrochloride with is a synthetic analogue of codeine, has been proved clinically effective in treating moderately severe pain while bearing a low addiction potential and causing minimal respiratory depression. Its therapeutic usage includes post surgical pain, obstetric pain, and pain of coronary origin. It has multiple mode of action that is, centrally it binds to the receptor (O-demethyl tramadol an active metabolite has a greater affinity for  $\mu$  receptors) and also causes inhibitory of neuronal uptake of nor-epinephrine and serotonin at the synapses in the descending inhibitory pain pathways, as well as having a, local anesthetic action.

In the present study the analgesic efficacy of intramuscular ketorolac has been compared against tramadol following minor oral surgery.

### Aims and objectives of the study

To compare the post-operative analgesic efficacy of IM ketorolac versus tramadol following minor oral surgical procedures.

To compare the analgesic efficacy of ketorolac versus tramadol in terms of

- Onset of analgesia.
- Duration of analgesia.
- Sum of pain intensity differences calculated from the hourly scores for 12 hrs post-operatively.
- Associated adverse effects.

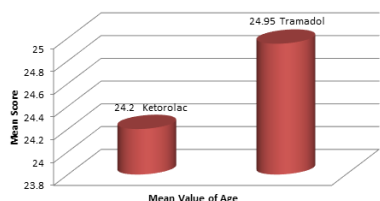
## PATIENTS & METHOD

Forty patients under the age group of 16 - 40 yrs with asymptomatic impacted mandibular third molars were randomly assigned into one of the two groups (20 in each group), and underwent third molar surgery under local anesthesia. Group I received IM ketorolac 30mg and Group II received tramadol 50 mg post - operatively. The difference in post - operative pain was assessed by five primary end points : pain intensity measured every hourly by a 10 cm visual analogue scale for 12 hours, onset of analgesia, duration of action, total no of analgesics consumed, and patient's global assessment.

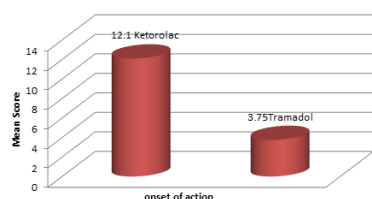
## RESULTS

Throughout the 12 hours investigation period, patients reported significantly lower pain intensity scores, longer duration of action, lesser post - operative analgesics consumption and better global assessment in ketorolac when compared to tramadol group. Patients in the ketorolac group significantly performed better than the tramadol group in terms of all parameters except onset of analgesia. All the drug related complications were mild and did not require any intervention.

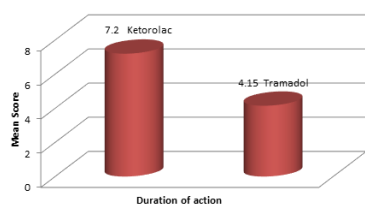
**Graph 1 : Comparision of mean value of age between study groups**



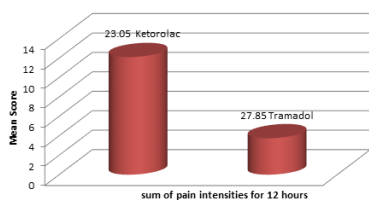
**Graph 1A: Onset of action between study groups**



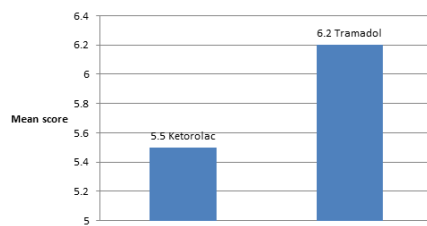
**Graph 2: Duration of action between study groups**



**Graph 3: Sum of pain intensities for 12 hours between study groups**



**Graph 4 : Total no. of analgesics consumed during 5 post operative days between study groups**



## DISCUSSION

The international association for the study of pain (IASP), defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or terms of such damage".

Post-operative pain has both physiological and psychological components and an unpleasant experience of poorly manage pain related to surgical procedures, especially third molar surgeries can lead the patients to either avoid or postpone the treatment as well as difficult in compliances with the prescribed regimens . Even though efficient pain control has permitted surgery to progress enormously ,post-operative pain still tends to be significantly under estimated thus harming the patient and impeding a successful recovery . a demonstration of the negative effects of insufficient administration of analgesia in cases of acute diseases on CVS, pulmonary and emotional system have aroused an interest and have highlighted the clinical importance of adequate post-operative pain management . The search for an appropriate agent to satisfactorily treat post-operative pain has led to the availability of a variety of analgesics.

There is an increase in need for clinical models that accurately reflect the efficacy of various analgesics commonly used. Third molar surgery is the model commonly used to test the efficacy of analgesics since the procedure induces pain that generally is consistent in severity allowing for a good discrimination between weak and strong analgesics .

Of late ketorolac has been introduced as a parenteral NSAID for the control of post-operative pain and analgesic potency has been shown to be comparable with morphine. Comparative studies have also shown that ketorolac suppositories are more efficacious than diclofenac .

In spite of being an opioid , tramadol can routinely be used because of lack of abuse, drug tolerance and respiratory depression. With an analgesic efficacy equivalent to pentazocaine, tramadol is believed to have a multimodal action . Comparative studies of analgesic efficacy between ketorolac and tramadol are relatively rare.

This study compared the post-operative analgesic efficacy of IM ketorolac with tramadol for the post-operative pain management following third molar surgery under local anesthesia . Patients in both the group did not differ in their demographic characteristics. Any significant difference between both the study groups in terms of pain is thus attributable to the drug effect.

A single dose of pre-operative IV tramadol was ketorolac in terms of analgesic potency after third molar surgery was and K.S. ong et al noted that the analgesic duration was longer with ketorolac than tramadol, with the overall fewer rescue analgesic consumption . In the present study post-operative intramuscular ketorolac performed better than tramadol with respect duration of analgesia. Patients when treated with tramadol reported of pain relief 3.75 mins after the injection while the same noted as 12 mins after ketorolac treatment. The faster onset of action of tramadol could be possibly attributed to its central mode of action .

Lanzetta A et al in his study , those who are undergoing orthopaedic procedures noted that pain intensity score in tramadol group was 84+/- 1.5 mm while a reduction of 41.7% was noted after 1 hours , 52.5% after 2 hours , 58.9% after 4 hours and 53.5% after 6 hours with ketorolac, the mean initial was comparable at 83.7+/- 1.4 mm and at the intervals as above, reductions of 33.9%, 42.1%, 49.8% and 43.4% were seen. Tramadol gave the same level of pain relief as did ketorolac, but it did so sooner.

Post-operative pain was assessed after third molar surgery for a 12 hour investigation period by K.S. Ong et al and patients in the ketorolac group experience significantly less pain throughout the investigation period, then when they received tramadol.

In our clinical study intramuscular ketorolac showed a greater pain relief with lesser pain intensity scores. Ketorolac proved to be a better drug for postoperative pain management following third molar surgery; due to its peripheral mechanisms of action.

The total number of analgesic consumption was higher in tramadol group as compared to the diclofenac as observed by Aysegül Mine Tuzumer et al for pain relief after bimaxillary osteotomy procedures.

Vittorio Colletti et al conducted a clinical trial to compare the postoperative analgesic effect and therapeutic tolerability of tramadol administered by IM injection when compared with that of ketorolac. During the 3 days of the trial, the number of ampoules on the day of surgery, decreasing to  $0.4 \pm 0.1$  ampoules on day 1 and  $0.1 \pm 0.1$  ampoules on day 2 postoperatively. For ketorolac, the mean number of ampoules was  $1.5 \pm 0.1$  on the day of surgery, decreasing to  $0.6 \pm 0.1$  on day 1 and  $0.1 \pm 0.1$  on day 2.

The total postoperative analgesic consumption for preventing postoperative pain after molar surgery, for the ketorolac group was significantly less than the tramadol group noted by K.S. Ong et al.

In the present study that total number of analgesic consumption was found to be lesser in the ketorolac group compared to tramadol group. Because group I has better analgesic efficacy than group II for third molar surgical pain, may be that has pathogenesis of dental pain relief, where tramadol does not affect prostaglandin synthesis and it does not have anti-inflammatory effects.

The study evaluated the efficacy of pre-emptive ketorolac in a cross over design in patients undergoing bilateral mandibular third molar surgery by K.S. Ong et al. whereas patients' overall assessment of the postoperative pain indicate that more patients in the ketorolac treated sides (46.7%) scored that analgesic intervention as excellent in relation to minimum pain after the surgery compared with the post-treated sides.

K.S. Ong et al conducted a study comparing pre-operative IV tramadol versus ketorolac for preventing post-operative after third molar surgery, where the patients' overall assessment of the surgery in relation to pain shows that more patients in the ketorolac group (43.3%) scored the surgery as excellent in relation to minimum pain after the surgery as compared with tramadol group.

In the present study the patients' overall assessment of the surgery in relation to pain shown that group I has scored 3 patients as excellent, 7 patients as very good, 5 patients as good and 5 patients as fair and group II has scored, 4 patients as very good.

8 patients as good and 8 patients as fair respectively to minimum pain after the surgery.

Nausea and vomiting are the major adverse effects of tramadol when used for the post-operative analgesia. In our study one patient complained nausea and patient complained vomiting. Respiratory depression and sweating are also the known adverse events associated with parenteral tramadol. Vickers et al found that there was a rapid drop in the respiratory rate following IV administration of tramadol, but it was noted only during the first five minutes post injection while it was sustained in case of morphine administration. He concluded that tramadol has much less effect on the respiratory system with a higher therapeutic ratio. In contrast to our results Vittorio et al in their study rated tramadol as a better drug when compared to ketorolac when used for post-operative pain management following nasal surgeries.

Shah et al conducted a study to compare the analgesic efficacy of tramadol hydrochloride with diclofenac sodium in dentoalveolar surgery. The purpose of this study was to find safe and effective analgesic efficacy alternative to nonsteroidal anti-inflammatory drugs (NSAIDs) for patients undergoing dentoalveolar surgery who could not tolerate NSAIDs. The analgesic efficacy of the two drugs was equal but tramadol did better than diclofenac. Tramadol can be used for post-operative analgesia after dento-alveolar surgery especially in

situation where NSAIDs are contraindicated.

In our study ketorolac rate better than tramadol because of the nature of pain following third molar surgeries. The pathogenesis of dental pain and the general surgical pain are different. Dental pain being largely inflammatory, is better managed with NSAIDs than with opioids. Most common adverse effects of parenteral ketorolac are pain and skin reactions at the site of injection, but in our study only 3 patients reported of severe pain at the site of injection but none of them had local skin reactions. In conclusion the result of our study suggests that post-operative IM ketorolac is better than tramadol for post-operative pain management following mandibular third molar surgeries.

## CONCLUSION

NSAIDs are routinely prescribed for the management of postoperative pain, supplemented by the use of opioids for moderate to severe pain. The analgesic potency of each drug varies and a number of clinical trials have been carried out to compare the same. Third molar surgeries were performed in 40 patients who are divided into two equal groups and the postoperative analgesic efficacy of injection ketorolac 30mg IM (group 1) was compared against injection tramadol 50mg IM (group 2) in terms of onset of action, duration of action, sum of pain intensity scores for 12 hours post-operatively, total number of analgesic consumption during 5 postoperative days and global assessment. All the outcomes of the above mentioned parameters were subjected to a statistical analysis and a  $P < 0.05$  was considered as significant.  $P < 0.01$  as highly significant.

Though the onset of analgesia was found to be a significant quicker with tramadol. Ketorolac favoured over tramadol as a better pain relieving agent when evaluated with respect to duration of analgesia, total postoperative analgesic consumption, pain intensity scores and patients' self evaluation using global assessment scale. Adverse reaction attributable to the study drugs were clinically mild and did not require any intervention.

Though tramadol is an opioid, ketorolac performed better in terms of pain relief following third molar surgery. The possible reason could be the nature of dental pain being largely inflammatory, is better managed with the use of an NSAID than an opioid, with a limited sample size, we conclude that ketorolac could be given a priority over tramadol for the management of postoperative pain following surgical removal of impacted mandibular third molars.

However to substantiate the result, further research trials are needed with a larger sample size and a considerable duration of follow up.

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