Prevention of Post Operative Pain by Minimizing the use of Analgesic Consumption and Evaluation of Efficacy of Two Different Group of Intra Venous Pre-Emptive Analgesia in Lower Third Molar Surgery –A Study

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ABSTRACT

Background: This study compared intravenous ketorolac and tramadol for post-operative discomfort prevention following mandibular 3rd molar extractions. Preemptive analgesia may reduce postoperative analgesic need by preventing pain.

Materials & methods: Forty patients who required surgical extraction of mandibular third molars were divided randomly into two groups. Group- I [Tramadol Group (n=20)] & Group-II [Ketorolac Group (n=20)] patients were given preemptive analgesia i.v. preoperatively. The parameters under evaluation were hourly postoperative pain intensity measurement for 12 postoperative hours, mean time after which rescue analgesic (acetaminophen) was taken within first 12 postoperative hours, total analgesic (acetaminophen) consumption over 5 day recovery period, and patient's assessment of the surgical procedure.

Results: The study's findings indicated that there existed no statistically significant disparity between each of the groups. A significant proportion of those in the ketorolac group said that the surgery was comparatively more favourable and less painful, as evidenced by their higher scores and reduced consumption of post-operative analgesics.

Conclusion: There is no statistically significant difference in the two groups except global assessment. Clinically, we found that, ketorolac has a slightly better preemptive analgesia profile as the patients in ketorolac group experienced less pain, required rescue analgesic late, required less analgesics postoperatively and rated overall the procedure as relatively better.

Keywords: Ketorolac; Preemptive Analgesia; Tramadol; Third Molar Surgery; Transalveolar Extraction.

INTRODUCTION

When third molars become impacted, transalveolar extraction is frequently necessary and is regarded as one of the most prevalent oral surgical procedures. [1] The most impacted teeth are third molar (98%) afterwards the permanent maxillary canine (1.3%) and mandibular premolar (0.11%). [2,3] Impacted mandibular 3rd molars could require extraction due to caries, infection, pain, pathologies, 2nd molar root resorption, etc. However, post-operative pain management is crucial for patients. [4,5]

Moderate to severe pain is experienced following transalveolar extraction of the 3rd mandibular molar. Postoperatively, the intensity of the pain escalates, reaching its maximum within a time frame of 6 to 8 hours under the use of conventional local anaesthetics. Preventing post-operative pain is preferable than treating it since it is predictable. [6]

First-author Crile introduced preemptive analgesia, the study found that inhibiting pain pathways before surgery reduces post-operative morbidity. By inhibiting the sensitization of periphery and central pain routes preemptive analgesia reduces the postoperative amplification of pain impulses. Pre-emptive analgesia was based on the idea that using analgesics before unpleasant stimuli might be better than afterward. The benefits of pre-operative analgesic management would outlast the drug's pharmacological lifespan. [7]

Pharmacological medications were utilised to treat postoperative pain, a novel approach in this context is the proactive administration of the medication. Thus, prospective comparative research examined tramadol and ketorolac's preemptive pain relief following transalveolar extraction of mandibular 3rd molar.

MATERIAL AND METHODS

This research was conducted in Oral & Maxillofacial Surgery from June 2017 to March 2018, focusing on patients requiring transalveolar extraction of their lower wisdom teeth. The 40 adults requiring these extractions, ranging in age from 18 to 45, were divided equitably into two groups of 20. One group was administered 50 mg Tramadol pre-extraction intravenously, whereas the other cohort was given 30 mg Ketorolac.

Adults between the ages of 18 and 45 who met the following inclusion criteria: Pederson difficulty index level 3 to 7 lower

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wisdom teeth, and good health (ASA I or II status). The exclusion criteria comprised pregnancy or lactation, ASA III, IV, or V classifications, pre-extraction swelling, pain, or trismus, active infection at the site around surgery and tramadol, ketorolac, paracetamol, or amoxicillin allergies.

MATERIAL AND METODS

All patients were assessed medically for extraction procedure. Patients were explained regarding the surgical procedure, potential risks and benefits of the procedure and possibilities of postoperative complications. Patients enrolled in the study have signed the consent in written format. Approval for the study was taken from the ethical review committee.

IV Ketorolac & IV Tramadol was injected intravenously in respective group of patients by a nursing staff. Antibiotic prophylaxis was given to all the patients preoperatively. 1 tablet of amoxicillin (500 mg) was given 1 hour prior to procedure. In all the patients transalveolar extractions were performed by the same surgeon under similar clinical conditions to rule out any bias. Strict sterilization protocol was followed with proper barrier techniques. All the patients used chlorhexidine mouthwash (0.2%) for mouth rinsing, just before administration of local anesthesia. Transalveolar mandibular 3rd molar extractions were performed under local anaesthesia with 2% Xylocaine and 1:200000 Adrenaline. The Ward's incision was used on all patients. Incision was made using B.P. blade 15. Simple interrupted 3-0 black silk suture closed the surgical incision. All patients received postoperative antibiotics. One 500-mg amoxicillin tablet was given three times a day for five days.

Patients were evaluated postoperatively for the following parameters:

1. Estimation of Postoperative Pain Intensity (Within 12 Hours Postoperatively)- Postoperative pain intensity was evaluated by "Numerical Pain Intensity Scale" (NPIS). In this method, the patients were instructed to mark the intensity of their pain by pointing on a 0-10 point scale. The two extreme values of the NPIS are value 0 indicating no pain and value 10 indicating worst possible pain. Patients were instructed to keep on recording their pain intensity on NPIS every hourly for 12 hours after the surgery.

2. Postoperative Use of Analgesics in the First 12 Hours & Calculation of Mean Time to Remedication- All the patients were allowed to take analgesic medication postoperatively depending on the pain intensity and their tolerance capacity. The rescue analgesic used in the study was Tablet Paracetamol 500 mg. The time lag between completion of surgical procedure and the first use of rescue analgesic was recorded in all the patients. The mean value was calculated and was considered for statistical evaluation. After the subject has consumed a rescue analgesic, the patient was excluded from the Numerical Pain Intensity Scale (NPIS) measurement (hourly assessment for 12 hours) and their last NPIS reading was extrapolated and used for remaining time points.

3. Postoperative Use of Analgesics After 12 Hours & Calculation of Total Amount of Analgesic Consumption During 5 Day Recovery Period- Postoperatively, analgesic were not prescribed for regular use. Patients were told to use analgesics only when necessary based on pain level and tolerance. Study analgesic were Tablet Paracetamol 500 mg, patients were given directions to record their analgesic medication for 5 days upon recovery.

4. Patients were asked about the surgical procedure. For total assessment, patients must grade the procedure based on their pain perception. Patients were assessed using 5-point scales. Lower scores indicate poor surgical performance and patient suffering.

Patient's Assessment Score

Score	Interpretation
0	Poor
1	Fair
2	Good
3	Very Good
4	Excellent

RESULTS

Pederson difficulty index (PDI) was used as an indicator of anticipated difficulty during surgery. Out of 40 impaction surgeries 42% were rated minimally difficult impactions (PDI score 3-4) and 58% were rated as moderately difficult impactions (PDI score 5-7) (Table- 2).

Postoperatively, the pain intensity was calculated based on numerical pain intensity scale (NPIS). Mean NPIS was

Age Group (Years)	Ketorolac Group	Tramadol Group	Total
≤20 Years	3	4	7
21-30 Years	10	10	20
31-40 Years	5	4	9
≥ 41 Years	2	2	4
Chi-square value = 0.254, p-value =0.968#, Chi-square test, #Non-significant difference			

Table-1: Distribution of Patients- According to Age

Pederson Difficulty Index	Ketorolac Group	Tramadol Group	Total
3-4	9	8	17
5-7	11	12	23
Chi-square value = 0.102, p-value = 0.749#, Chi-square test, #Non-significant difference			

Table-2: Distribution of Patients- According to Pederson Difficulty Index

Numerical Pain Intensity Score (NPIS)	Ketorolac Group	Tramadol Group	Total
≤ 3	4	2	6
>3- 6	16	18	34
>6- 9	0	0	0
>9-10	0	0	0
Chi-square value = 0.784, p-value = 0.376#, Chi-square test, # Non-significant difference			

Table-3: Distribution of Patients- According to Numerical Pain Intensity Score (NPIS)

calculated for every individual over 12 hour period and was used for calculation of mean NPIS for the group. The distribution of patients based on NPIS revealed that, the two groups were comparable to each other [Graph- 7, 8 & Table- 4, 5]. There is no statistically significant difference between two groups in relation to NPIS (Table- 3, 4). The mean NPIS of ketorolac group was 3.724 and that of tramadol group was 3.985. No statistically significant difference was observed.

The mean time to rescue analgesic intake was calculated for the experimental groups. It was 539 minutes for ketorolac group and 494 minutes for tramadol group. The difference was found to be statistically insignificant (Table- 5). Mean analgesic requirement over a period of 5 recovery days was calculated for each individual and for whole group. The mean analgesic requirement per patient during recovery period was 6.8 tablets for ketorolac group and 7.6 tablets for tramadol group. The difference was found to be statistically insignificant (Table- 6). Overall assessment of the surgical procedure was based on patient's assessment score. Mean patient's assessment score was 3.0 for ketorolac group and 2.3 for tramadol group. The difference was found to be statistically significant (Table- 7).

Numerical Pain Intensity Score (NPIS)	Ketorolac Group	Tramadol Group	Total
>3- 4.5	13	14	27
>4.5- 6.0	3	4	7
Chi-square value = 0.062, p-value = 0.803#, Chi-square test # Non-significant difference			

Table-4: Distribution of Patients- According to Numerical Pain Intensity Score (NPIS) Ranging Between > 3 to 6 (Moderate Pain)

Study Group	Mean Numerical Pain Intensity Score (NPIS)	Mean Difference	t-test value	p value
Ketorolac Group	3.724±1.04	-0.26	-0.892	0.378#
Tramadol Group	3.985±0.80			
Unpaired t-test, # Non-significant difference				

Table- 5- Mean Numerical Pain Intensity Score (NPIS) in Study Groups

DISCUSSION

Inflammation is an inevitable tissue response and essential part of tissue healing following any surgical trauma. Once initiated it may sometimes far exceed the essential physiological limits and can lead to excessive swelling, pain and trismus. [8] Pain following third molar surgery usually reaches a moderate to severe intensity within first 5 hours of the surgery. [9,10] However, few studies showed that, the range of peak pain intensity varies between 6-8 hours postoperatively when the conventional local anesthetics are used. [11]

Ketorolac is one of the commonly employed NSAIDs for short term pain relief. The mechanism of action is based on inhibition of COX enzymes responsible for production of various allgogenic chemical mediators of inflammation. The analgesic effect of ketorolac usually last for about 6 hours [12]

Tramadol is a synthetic derivative of codeine. Its analgesic action is mediated centrally by action on opioid receptors. Its primary mechanism of action is by inhibition of nor-epinephrine reuptake and serotonin at synapses in descending pain pathways. Tramadol is safer, more effective, and more acceptable than other opioids. [13]

Preventing post-operative pain is preferable than treating it since it is predictable. [6] Crile was among the first to propose preemptive analgesia. The study showed that inhibiting pain pathways before surgery can reduce post-operative morbidity. Preemptive analgesia precludes peripheral & central pain pathway sensitization, lessening postoperative pain impulses. [14] Preemptive analgesia had the basic premise that using analgesics before noxious stimuli (i.e., prior nociception) would make it more successful than

Study Group	Mean Time (Minutes)	Mean difference	t-test value	p-value
Ketorolac Group	539±98.03	45.00	1.611	0.116#
Tramadol Group	494±77.49			
Unpaired t-test, # Non-significant difference				

Table-6: Mean Time to Take Rescue Analgesic

Study Group	Mean Analgesic Requirement (Tablets)	Mean difference	t-test value	p-value
Ketorolac Group	6.8±1.64	-0.80	-1.744	0.089
Tramadol Group	7.6±1.23			
Unpaired t-test, * Significant difference				

Table-7: Mean Analgesic Requirement per Patient during Recovery Period of 5 days

Study Group	Mean Patient Assessment Score	Mean Difference	t-test Value	p-value
Ketorolac Group	3.00±1.38	0.70	1.820	0.047*
Tramadol Group	2.30±1.03			
Unpaired t-test, * Significant difference				

Table-8: Mean Patient Assessment Score for Surgical Procedure

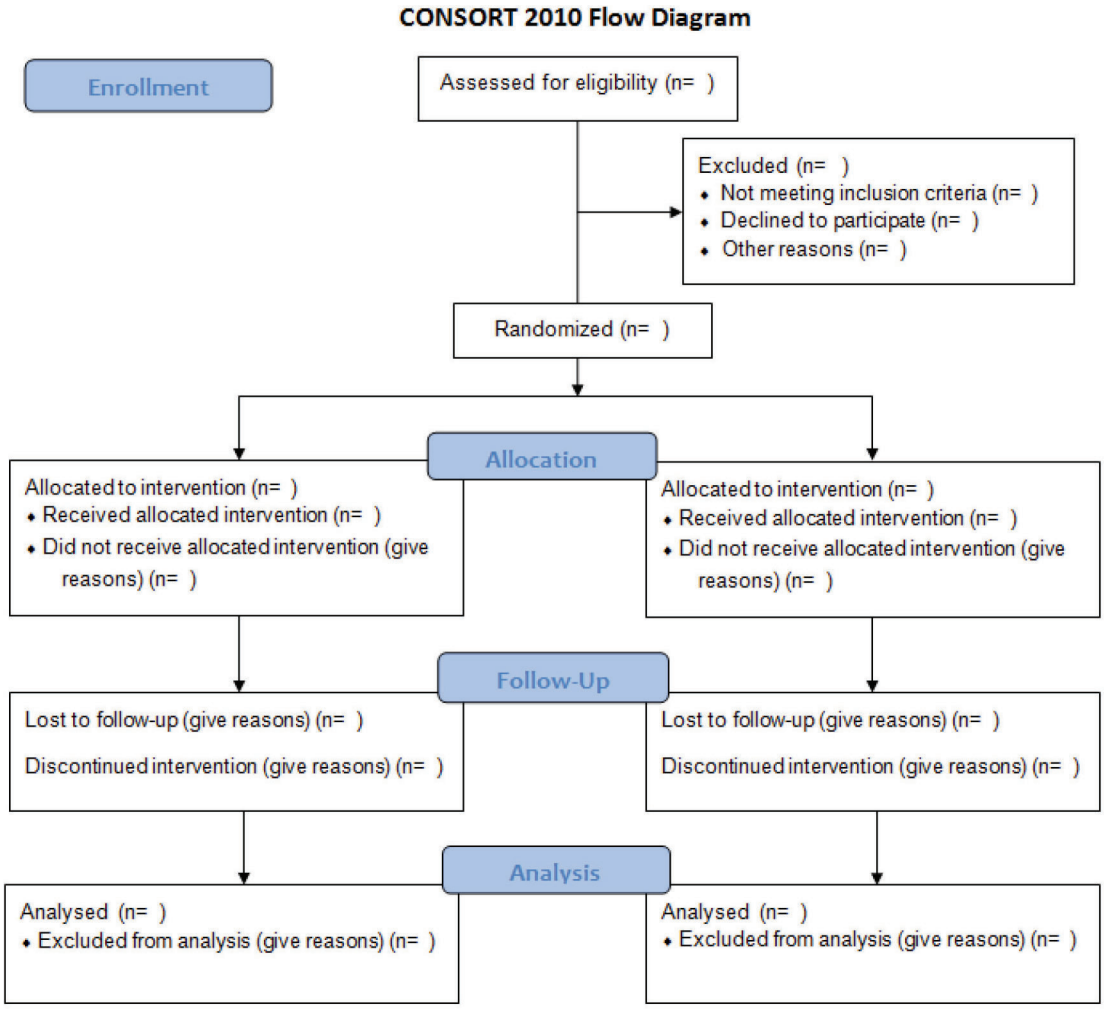

Figure-1: The CONSORT Flow Diagram.

afterward. The health advantages of pre-operative analgesic management would outlast the drug's pharmacological lifespan. [7]

The results of various preemptive analgesia studies related to third molar surgery pain were variable and the review of literature is inconclusive regarding the efficacy of preemptive analgesia in prevention of third molar surgery pain. Therefore this study was conducted to evaluate the preemptive efficacy of tramadol and ketorolac in eliminating pain after transalveolar extraction of mandibular 3rd molar and how it reduces the post-operative consumption of analgesics, thereby minimizing the side effects of analgesics in patients. Pain varies considerably from person to person. A patient who reacts mildly to a noxious stimulus is considered to have a higher pain threshold and is called hypo-reactive. On the other hand a hyper-reactive patient with lower pain threshold may react aggressively to the stimulus of same intensity. Various factors can alter the pain threshold of the patient and can modulate the pain reaction and therefore, the suffering aspect of the pain. These factors are emotional state of the individual, fear and apprehension, fatigue, age, sex, racial characteristics. [15]

In the present study, Pederson's difficulty index was used to predict the anticipated difficulty that may be encountered during surgical procedure. The two groups in the present study were comparable and no statistically significant difference presented in relation to PDI.

In our study the surgical procedure was undertaken under local anesthesia immediately after the i.v. administration of preemptive analgesic drugs. Therefore, it was practically not possible to evaluate the onset on analgesia. The studies in which time of onset of first and second pain peaks were evaluated used the same drug preoperatively as well postoperatively. NSAIDS are not a better agent for control of postoperative swelling and trismus. Corticosteroids are better drugs in such regards. The present study concentrated on preemptive analgesia, not additional 3rd molar surgery symptoms.

The parameters evaluated in our study was postoperative pain intensity with in a time frame, need for rescue analgesic in a specified first few hours postoperatively, mean time after which the rescue analgesic was taken during the specified first few hours postoperatively, total analgesic consumption during recovery period and patient's assessment of the surgical procedure (Global Assessment). The same clinical parameters were evaluated by various authors in the past preemptive analgesia studies as well. [16, 17, 18, 19]

The mean value was calculated for the groups and was

considered for statistical evaluation. If the patient took rescue analgesic during the first 12 hours of the evaluation, the time of intake was noted and the patient was excluded from the Numerical Pain Intensity Scale (NPIS) measurement (hourly assessment for 12 hours). Their last NPIS reading was extrapolated and used for the remaining time points. The Ong KS et al. investigation used a similar criterion. [16]

Mean postoperative pain intensity during first 12 postoperative hours was calculated for the individual as well as for the whole group. The similar method of calculation of mean pain intensity was also employed in the study conducted by other authors. [16, 17] Our study found that ketorolac reduced postoperative pain compared to tramadol. This result is consistent with the research undertaken by Goplaraju P et al. [19] and Ong KS et al. [16].

The time after which the rescue analgesic was taken (during first 12 hour postoperative hours) was noted and the mean time was calculated for the group as a whole. The mean time of rescue analgesic intake in the ketorolac group was 8.99 hrs, and for tramadol group it was 8.23 hours. Ong KS and associates [16] found slightly higher values. The mean rescue analgesic dosage among the ketorolac group remained 9.5 hours while in the tramadol group 7.6 hours. The mean rescue analgesic time following preoperative ketorolac administration was 8.9 hours in another investigation. [17].

Our investigation found that ketorolac & tramadol groups had rescue analgesic intakes over 8 hours. This proved both of the medications prevented postsurgical pain, which peaked at 6-8 hours, this matched Ong KS and colleagues study [17]. This supported another study by Ong KS et al.16 & Gopalraju P et al. [19] regarding ketorolac but not tramadol. Research by Gopalraju P et al. [19] and Ong KS et al. [16] demonstrated that the postoperative analgesia for the ketorolac group exceeded 8 hours, while that for the tramadol group it lasted less than 8 hours. However, all studies concur that ketorolac patients needed rescue analgesics late in their initial twelve-hour period postoperatively.

We calculated 5-day analgesic usage in our study. Pain following mandibular 3rd molar surgery often intensifies in the initial days and fades over time. Although it may last longer than 5 days, the computation up to 5 days is safe. The research we conducted found that ketorolac & tramadol groups used 6.8 and 7.6 tablets respectively, over 5 days of recovery. In contrast, Ong KS and colleagues [16] found that ketorolac & tramadol groups used 4.4 and 6.6 tablets, respectively, throughout a 5-day recovery period. However, Gopalraju P et al. [19] found that ketorolac group consumed 6.8 tablets of total analgesics, while tramadol group consumed 10.2 tablets. Previous research found that ketorolac patients needed less analgesics.

The global-assessment was used to determine if the surgical process was painless or uncomfortable. Ketorolac patients had higher global evaluation ratings than tramadol patients, and the operation was painless and well tolerated.

CONCLUSIONS

Both drugs exhibited comparable efficacy as preventative analgesics in this study, with no significance observed in the majority of parameters, with the exception of global assessment. In clinical settings, ketorolac exhibited a preemptive analgesic profile that was marginally superior. The patients assigned to ketorolac group observed reduced pain levels, delayed reliance on rescue analgesics, decreased utilisation of postoperative analgesics throughout the 5-day recuperation period, and overall higher ratings for the procedure.

Disclosure Statement

The authors report no conflicts of interest related to this study.

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