

Comparison of Post-Operative Pain Intensity in Patients Undergoing Impacted Third Molar Surgery with Pre-Operative and Post-Operative Intravenous Ketorolac

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ABSTRACT

OBJECTIVE: To compare post-operative pain intensity in patients undergoing impacted third molar surgery with pre-operative versus post-operative administration of intravenous ketorolac.

STUDY DESIGN: A Qualitative Comparative Analysis.

SETTING: Department of Oral and Maxillofacial Surgery, Punjab Dental Hospital/ de'Montmorency College of Dentistry, Lahore, between 3rd Jan 2017 to 18th Sep 2017.

METHODOLOGY: In a total of 150 patients undergoing third molar surgeries, intravenous administration of ketorolac was done. The patients were divided into two groups. One group received ketorolac pre-operatively while the other received the same immediate post-operatively. Patients were asked to record the pain intensity on a 100mm Visual Analogue Scale after twelve hours of surgery. Anchor points were 0: no pain and 100: worst possible pain.

RESULTS: The mean pain intensity score on VAS for pre-treated group was 45.14 ± 7.94 mm and that of the post-treated group was 52.93 ± 7.61 mm. The mean pain intensity for both groups was compared using student's T test for independent variables. Assuming equal variances of the two groups, after comparing the means of pain intensity for the two groups, the result generated had "p" value of 0.000.

CONCLUSION: The pre-operative pre-emptive administration of intravenous ketorolac provides superior pain control post-operatively as compared to the same drug given post-operatively only.

KEYWORDS: Third Molar Surgery, Post-Operative Pain, Pre-Emptive Analgesia, Ketorolac, NSAIDs.

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INTRODUCTION

Third molar surgeries result in significant trauma and inflammation leading to considerable post-operative pain,

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management of which has been a topic of clinical interest¹. One concept receiving much interest is pre-emptive analgesia defined as the administration of analgesic medication pre-emptively before the surgery in order to minimize pain in the post-operative period. Different agents like opioids, non-steroidal anti-inflammatory agents, and local anesthetic infiltrations have been tested for their efficacy in the control of post-operative dental pain^{2,3}. Intravenous ketorolac, an NSAID, is known to have such pre-emptive analgesic effect⁴.

The exact definition of pre-emptive analgesia is an evaluation of post-operative pain experienced when a medication is given before the surgery as compared to administration of the same medication after the surgery⁵. The main concept is to administer analgesic agent before the CNS reaches a "hyper-excitability" state to noxious stimuli, also called central sensitization⁶. This technique improves patient comfort and reduces the post-operative consumption of analgesics⁷. In this study, the pre-emptive analgesic effect of ketorolac has been assessed in third molar surgeries. Important aspect of this comparative study is that the same drug is given through the same route and in same dosage, the only variable being the "time of administration", i.e. pre-operatively and post-operatively.

In the pursuit of improved quality of life during the immediate

post-operative period in terms of pain reduction, there is need to conduct clinical trials. In literature we could not find any such study conducted in Pakistan. The rationale of this study is to assess the efficacy of intravenous ketorolac as a preemptive analgesic agent in order to reduce the post-operative pain. We hypothesized that Post-operative pain intensity is less in group in which analgesic (intravenous ketorolac) was administered pre operatively as compared to post-treated group, in patients undergoing impacted third molar surgery. The objective of this study was to compare post-operative pain intensity in patients undergoing impacted third molar surgery with pre-operative versus post-operative administration of intravenous ketorolac.

METHODOLOGY

This Qualitative Comparative Analysis was conducted at Department of Oral & Maxillofacial Surgery, Punjab Dental Hospital/ de'Montmorency College of Dentistry, Lahore. A sample size of 150 cases was taken through Purposive Sampling Technique. They were divided into two groups, having 75 cases in each group. The sample size was calculated with 95% confidence level, 80% power of test and taking magnitude of post-operative pain intensity i.e. 19.9 ± 10.2 mm in pre-treated group and 25.3 ± 12.6 mm in post-treated group in patients undergoing impacted third molar surgery⁸.

Patients from both genders, undergoing impacted third molar surgeries, were included in this study. The age group was 16 years and above. Impacted third molars were assessed on standard radiographs. Those patients were included who had no history of pain in the week before surgery, as this could alter the patients perception of pain and act as a confounding factor. Similarly, patients who had taken any anti-inflammatory medication within the week before surgery or who had any history of NSAID allergy were excluded from this study.

Patients were divided into two groups, A and B, using random numbers table. Group A received 30mg intravenous ketorolac (Toradol[®] in the form of 30 mg injectable ampoule) pre-operatively. 1ml of the study drug was diluted with 1ml saline to make a 2ml injection. Group B received the same medication (i.e. 30mg intravenous ketorolac, 1ml of the study drug diluted with 1ml saline to make a 2ml injection) immediately post-operatively. The surgical removal of the impacted third molar was then completed with a standardized technique under local anesthesia.

Both groups were prescribed anti-inflammatory drugs 100 mg flurbiprofen, one tablet as required to be taken only after initial 12 hours of post-operative period, and those who took it before twelve hours of the post-operative period were excluded from the study.

The patients were asked to record the pain intensity on a 100 mm Visual Analogue Scale after twelve hours of surgery. Anchor points were 0: no pain and 100: worst possible pain. All the patients themselves observed and subjectively recorded their pain intensity as a single reading on the VAS after 12 hours of surgery. One of the responsible adult attendants of each patient was also guided about the VAS and objectives of the study to aid in pain score recording. Also patients were

requested to record one pain score reading as a trial only, immediately after the completion of procedure and before discharge from the surgery. Since the patients were under the effect of anesthesia, pain scoring remained minimum and this confirmed their understanding of the VAS. Since these readings were only used to train the patients, they were not included in the data collection and analysis. All 171 patients demonstrated adequate understanding of VAS.

Data Analysis: All data was entered and analyzed by using Statistical Package for Social Sciences (SPSS version 10.0, inc. Chicago, IL, USA).

RESULTS

Total 171 patients fulfilling the inclusion criteria were included in the study. 21 patients were disqualified due to usage of post-operative analgesics within 12 hours of post-operative period. Data of remaining 150 patients was used to generate the results; this matched the pre-determined sample size of 150. Total number of females included in the sample were 83 (55.3% of total sample size) and the total number of males was 67 (44.7% of total sample size) the mean age of the patients was 32.71 ± 12.07 years. The minimum age recorded was 17 years and the maximum age was 79 years. The mean age of pre-treated group was 32.48 ± 12.61 years and that of the post-treated group was 32.93 ± 11.59 years. Mean age of females in the sample was 30.47 ± 8.58 years and mean age of males in the sample was 35.48 ± 14.95 years.

The score for post-operative pain intensity of both pre-treated and post-treated group was recorded and their means were compared. The mean pain intensity score on VAS for pre-treated group was 45.14 ± 7.94 mm and that of the post-treated group was 52.933 ± 7.61 mm. The minimum pain score of the pre-treated group was 30.00 mm as compared with 49.00 mm of post-treated group. The maximum pain score of pre-treated and post-treated group was 68.50 mm and 67.50 mm respectively (Fig-1). The mean pain intensity of both groups was compared by using Student's t- test for independent samples.

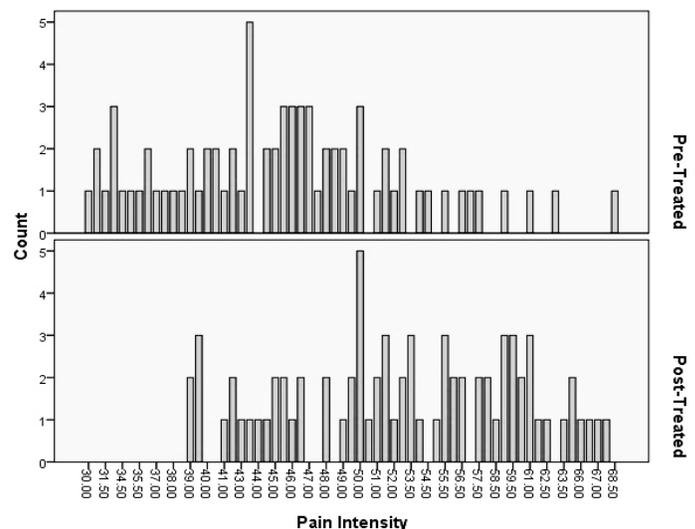


Fig-1: Comparison of Pain Intensity in Pre-Treated and Post Treated Group

DISCUSSION

This study advocates and supports the concept of “Pre-emptive Analgesia”. This idea which was first introduced by Woolf in 1983, indicates that an analgesic intervention if started before the noxious (i.e. surgical) stimulus arises, results in blocking nociception either completely or more effectively. Pre-op administration of analgesics has been known to delay the onset and reduce the peak intensity of pain in the post-op period⁹. The contemporary literature suggests a reduction in post-operative pain intensity in cases where the analgesic agent is administered pre-operatively¹⁰. Gopalraju et al have reported a decrease in post-op pain intensity and a decreased consumption of post-op rescue analgesics¹¹. Ketorolac has been found significantly effective in reducing the post-surgical pain as well as decreasing the number of analgesics consumed post-operatively¹². There is a discussion that COX-2 specific inhibitors contribute to a higher risk of thrombo-embolic events has been ongoing since they were brought into the market; however, the data were conflicting and no conclusion was drawn before the APPROV study¹³. The long acting local anesthetic, Bupivacaine has also been used for post-surgical pain control but it has associated side effects like difficulty in speech and local anesthesia associated systemic toxicity^{14,15}. Considering these facts, ketorolac is a logically better option, especially when given as a single pre-operative dose. The proposal was that the effect of pre-emptive analgesia was to prevent or reduce the development of any “memory” of pain stimulus in the nervous system, and that there is lesser subsequent analgesic requirement as a result of this reduction or prevention of the pain ‘memory’. Whenever there is surgical insult to a tissue, there is a peripheral response involving the arachidonic acid metabolites, leukotrienes and bradykinin leading to a state of local hyperalgesia. On repeated stimulation, it leads to escalation of the degree of excitability of the pain receptors in CNS leading to the “wind up” phenomenon.

Regarding pain sensitivity in both genders, several studies have demonstrated a higher pain sensitivity in women than in men¹⁶. In our study we included patients from both genders, and they were distributed randomly among the pre-treated and post-treated group hence eliminating any bias due to difference in pain perception among both the genders.

Valid and reliable assessment of pain is essential for both clinical trials and effective pain management. The subjective nature of pain makes objective measurement impossible. The well-known visual analogue scale (VAS) and numeric rating scale (NRS) for assessment of pain intensity agree well and are equally sensitive in assessing acute pain after surgery, and they are both superior to a four-point verbal categorical rating scale (VRS). A study using simultaneous recordings of pain intensity on VAS, NRS, and VRS scales in a large number of patients demonstrated the superiority of the VAS and NRS over VRS. A computerized simulation study, randomly sampling 10000 times, repeatedly from simultaneous observations of VAS, NRS, and VRS, documented that the power to detect a difference in pain intensity was higher with the NRS and the VAS data

compared with the VRS data¹⁷. Our study also used this reliable and well established pain scale, i.e. VAS, to assess the post-operative pain intensity.

In all previous studies the patients were asked to record pain intensity at different time intervals, i.e. at 2, 4, 6, 8, 12 and 24 hours post-operatively. The patients obviously experienced less pain in the initial hours of post-operative period as the third molar surgical pain is thought to reach its peak level around 6-8 hours after the surgery. Similarly the pain intensity after 24 hours was less as sufficient time had passed post operatively. In contrast, we recorded a single reading of pain after 12 hours. The patients actually mentioned the total amount or intensity of pain they experienced during the whole 12 hours period. Therefore, it was always expected to be a relatively large reading on the visual analogue scale. On a careful review of the pain scores submitted by the patients, it was observed that both groups had a relative homogeneity in terms of rating the pain they had experienced as in both groups 90% of data regarding pain scoring was within two standard deviations. To make our pain assessment more reliable, we instructed one of the attendants to help the patient in recording their pain score. Furthermore they were asked to give an initial reading just to assess their understanding. The previous studies relied on the patient for this purpose.

As the patients recorded a single reading after a period of 12 hours, this score, therefore, reflected the total outcome of the procedure in initial 12 hours in terms of quality of life. This overall assessment of the patient can also be regarded as the ‘Global Assessment’ which was analyzed as an independent outcome variable in the study carried by Ong et al⁹.

The study regarding pre-emptive efficacy of ketorolac by Ong et al⁸ probably had the best sample selection in terms of control groups. It is well appreciated that factors like gender, age, race, pain tolerance and anxiety levels can alter the levels of perceived pain. Ong et al managed and controlled these confounding inter-patient variables excellently by choosing patients with bilaterally impacted third molars. One side was pre-treated with ketorolac and post-treated with a placebo, whereas, the other side was pre-treated with a placebo and post-treated with ketorolac, at a later appointment. This was a double blind study and restricted randomization was used to decide which side would be pre-treated or post-treated with ketorolac. By using this within-subject cross over design, the patients were able to act as their own control, thereby increasing the power and sensitivity of the study. In our study, however, it was not feasible to select the subjects with bilateral impacted third molars considering the large sample size, i.e. 75 patients in each group as compared to 15 in the study done by Ong et al. On the other hand, the patients who required bilateral impacted third molar surgeries were excluded from the sample to control the patient bias, since we did not use a placebo. Also, each group in our study was the control for the other group.

To make it more sensitive and reliable the study was conducted on out-patient basis. Forbes et al¹⁸ demonstrated that out-patient studies are more sensitive than those conducted among the in-patients.

CONCLUSION

The pre-operative pre-emptive administration of intravenous ketorolac provides superior pain control post-operatively as compared to the same drug given post-operatively only.

CONTRIBUTION OF AUTHORS

Mirza AI: Conceived idea, Designed research methodology, Literature review, Manuscript final reading, Manuscript approval

Ali Farooq: Intervention, Data collection

Ali S: Performing Impacted Third Molar Surgeries.

Azeem M: Literature Search, Data Collection, Data Interpretation, Statistical Analysis, Manuscript Writing.

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REFERENCES

- Kunkel M, Morbach T, Klies W, Wagner W. Third molar complications requiring hospitalization. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006; 102:300-306.
- Tighe KE, Gillan G, Korczak PKJ, Crossley AWA. An assessment of morphine requirement after wisdom teeth extraction under general anaesthesia. *Anaesthesia* 1995; 50:816-18.
- Turner GA, Anson N, Williamson R. A comparison of intramuscular ketorolac with indomethacin suppositories in the treatment of pain after oral surgery. *Anaesth Intens Care* 1996; 26:665-68.
- Mony D, Kulkarni D, Shetty L. Comparative evaluation of preemptive analgesic effect of injected intramuscular diclofenac and ketorolac after third molar surgery-a randomized controlled trial. *J Clin Diag Res.* 2016; 10(6):102.
- Savage MG, Henry MA. Preoperative non-steroidal anti-inflammatory agents: Review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; 98:146-52.
- Shah AV, Kumar KA, Rai KK, Kumar BR. Comparative evaluation of pre-emptive analgesic efficacy of intramuscular ketorolac versus tramadol following third molar surgery. *J Oral Maxillofac Surg* 2013; 12(2):197-202.
- Baygin O, Tuzuner T, Isik B, Kusgoz A, Tanriver M. Comparison of pre-emptive ibuprofen, paracetamol, and placebo administration in reducing post-operative pain in primary tooth extraction. *Int J Paed Dent* 2011; 21(4):306-13.
- Ong KS, Seymour RA, Chen FG, Ho VCL. Preoperative ketorolac has a preemptive effect for postoperative third molar surgical pain. *Int J Oral Maxillofac Surg* 2004; 33: 771-76.
- Kim K, Brar P, Jakubowski J, Kaltman S, Lopez E. The use of corticosteroids and nonsteroidal anti-in medication for the management of pain and inflammation after third molar surgery: a review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009; 107(5):630-40.
- Vadivelu N, Mitra S, Schermer E, Kodumudi V, Kaye AD, Urman RD. Preventive analgesia for postoperative pain control: a broader concept. *Local Region Anesth* 2014; 7:17.
- Gopalraju P, Lalitha RM, Prasad K, Ranganath K. Comparative study of intravenous Tramadol versus Ketorolac for preventing postoperative pain after third molar surgery—A prospective randomized study. *J Cranio-maxillo-fac Surg* 2014;42(5):629-33.
- Ong KS, Tan JML. Preoperative intravenous tramadol versus ketorolac for preventing post-operative pain after third molar surgery. *Int J Oral Maxillofac Surg* 2004; 33:274-78.
- Fitzgerald GA. Coxibs and cardiovascular disease. *N Engl J Med* 2004; 351:1709-11.
- Wilson IH, Richmond MN, Strike PW. Regional analgesia with bupivacaine in dental analgesia. *Br J Anaesth* 1986; 58:401-405.
- Wolfe JW, Butterworth JF. Local anesthetic systemic toxicity: update on mechanisms and treatment. *Curr Opin Anesth* 2011;24(5):561-66.
- Paller CJ, Campbell CM, Edwards RR, Dobs AS. Sex-based differences in pain perception and treatment. *Pain Medicine.* 2009 1;10(2):289-99.
- Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EKB, et al. Assessment of pain. *Br J Anaesth* 2008;101(1):17-24.
- Desjardins TJ, Grossman EH, Kuss ME, Talwalker S. The injectable cyclooxygenase-2-specific inhibitor parecoxib sodium has analgesic efficacy when administered preoperatively. *Anesth Analg* 2001; 93:721-27.