 DOI: 10.18231/2395-6194.2017.0003

A single blind, randomized prospective controlled clinical trial to study the effect of ibuprofen as a pre-emptive analgesic agent in impacted third molar post extraction pain

Hemanth Kumar HR[1,*], RM Lalitha[2], Kavitha Prasad[3], Ranganath K[4]

[1]Assistant Professor, Dept. of Dentistry, Karwar Institute of Medical Sciences, Karwar, [2,3,4]Professor, Dept. of Oral & Maxillofacial Surgery, The Faculty of Dental Sciences, MSRUAS, Bengaluru

***Corresponding Author:**
Email: dr_hemanth82@yahoo.com, kr7514915@gmail.com

Abstract

Background: Surgical removal of impacted third molar involves manipulation of both hard and soft tissues,(1) and is associated with postoperative complications like pain, swelling and trismus. Analgesics are routinely given after surgical removal of third molar for three to five days.(2) Aim of the study was to know whether analgesics given preoperatively will reduce the post-operative pain and the amount of analgesic requirement.

Materials and Methods: This study was conducted in Department of Oral Maxillofacial Surgery of Mathikere Sampangi Ramaiah Dental College and Hospital Bangalore, India**.** 30 Patients requiring surgical extraction of impacted mandibular third molar were enrolled in the study. Patients were divided into group 1 (pre-emptive group) and group 2 (postoperative group) comprising of fifteen patients each. To group1 oral Ibuprofen-400mg tablet was administered 1 hour prior to the procedure and for group 2 oral Ibuprofen-400 mg tablets was administered 1 hour after the procedure. The first effective dosing time was obtained and the time taken for the first onset of postoperative pain and the influence of these analgesic administration times on post-operative pain, and clinical recovery was evaluated.

Results: Pre-emptive use of Ibuprofen 400mg was effective in reducing postoperative pain, discomfort and number of analgesics required and also delayed the usual early in setting of post-operative pain.

Conclusion: Pre-emptive Ibuprofen tablets of 400mg dosage can be used to reduce the severity of the post-operative squeal of the impacted mandibular third molar surgery**.**

Keywords: Pre-emptive analgesia, Ibuprofen, Impacted third molar, Post extraction.

Introduction

Surgical removal of impacted mandibular third molar is a most common minor oral surgical procedure which usually represents reproducible surgical trauma that causes moderate to severe pain and needs an effective analgesia for the patients for at least a 24-hour period.(3) The inhibition of prostaglandin production by Non Steroidal Anti-inflammatory Drugs (NSAIDs) decreases the synthesis of inflammatory mediators such as Bradykinin, Substance P, Serotonin, and Histamine.(4) Studies have proved that pre-operative use of an analgesic agent can be more beneficial.(5)

The concept of preemptive analgesia based on clinical observations has been used as an evaluation model for surgical pain, this model has been shown to have a sufficiently high sensitivity to enable it to distinguish between different analgesic agents. The associated tissue injury with surgical procedures activates peripheral nociceptors and also has a significant effect on the central nervous system leading to the development of primary and secondary hyperalgesia.The key chemicals involved in the sensitization of peripheral nociceptors are proststaglandins.The usual definition and critical analysis of the concept of preemptive analgesia is based upon the evaluation of the postoperative pain experience when a medication is administered before injury as compared to the administration of the same medication after injury.(6) The theoretical concept behind pre-emptive analgesia is simple, logical and its goal is straight forward.(7) It prevents central sensitization of peripheral receptors which usually occurs as a result of surgical trauma which amplifies postoperative pain.(8)

In order to assess efficacy of Ibuprofen as a pre-emptive analgesic agent, we have undertaken this single blind, randomized prospective controlled clinical trial to study the effect of Ibuprofen as a preemptive analgesic agent in impacted third molar post extraction pain and to determine whether pre-treatment with Ibuprofen could delay the onset and decrease the severity of postoperative pain.

Materials and Methods

Study design: This study was a randomized, single blind, prospective study conducted in the Department of Oral and Maxillofacial Surgery, Mathikere Sampangi Ramaiah Dental College Hospital (MSRDC & H), Bangalore. The protocol for the study was approved by the ethics committee of the institution and informed consent was obtained from the participating patients. 30 patients reporting to the Department of Oral and Maxillofacial Surgery, MSRDC & H, Bangalore, requiring surgical removal of impacted mandibular third molar was recruited in the study.

Inclusion criteria

1. Patients requiring prophylactic removal of third molars.
2. Patients with no history of infection, pain or other problems 1 week before the surgery.
3. Patients who have not taken analgesics in the past 2 weeks for any purpose.

Exclusion criteria

1. Patients with history of hypersensitivity to NSAID's(Non Steroidal Anti-Inflammatory Drugs)
2. Pregnant patients and patients with peptic ulcers.
3. Medically compromised patients.
4. Patients not willing for follow up and patients not reporting after 1 week.

Patient selection: Thirty patients of the either gender with age group ranging from 18 – 40 years who visited the Oral Surgery Department, for extraction of the impacted mandibular third molars either due to orthodontic, prophylactic or any other purpose and who were in good health and able to follow the post-operative instruction were included in the study. Allocation of the treatment was done by sealed envelope technique. On the day of surgery an independent investigator opened the envelope and allocated the patients to the particular group. Patients were divided into Group1 (pre-emptive group) and Group2 (postoperative group) consisting of 15 patients in each group. Group 1 patients were administered with 400mg of Ibuprofen (oral) 1 hour prior to the procedure and group 2 patients were administered Ibuprofen 400mg (oral) 1 hour after the procedure. Same surgeon performed the surgery in both group and was blinded. Patients were asked to take same drug when moderate to severe pain arise after surgery. Recording forms were given to patients and were explained how to enter the details. Of the two administrations times, the first effective dosing time was obtained as the time taken for the first onset of postoperative pain (central sensitization). Once it has taken place, the difference in pain intensity and time taken for the onset of pain in postoperative group was compared with the pre-operative administration group .Filled forms were collected at the time of suture removal.

Preoperative recording of data: Type of impaction, duration of the surgery (Time from the incision till the placement of the last suture), amount of local anesthesia used, and facial measure were recorded. Pain was assessed subjectively and accordingly marked by the patient on the VAS of 100mm which was collected at the time of suture removal(0= No pain, 100=severe pain). Evaluation of the facial swelling was performed using a horizontal and vertical guide with a flexible ruler on the 2nd and 7th post-operative day. The horizontal measure corresponds to the distance between the labial cant and the ear lobe. The vertical measure corresponds to the distance between external canthus of the eye and the angle of the mandible. The arithmetic mean of the two measures determined the facial measure. Operation was performed using a standardized surgical technique, with elevation of a buccal mucoperiosteal flap, distobuccal bone guttering and removal of the tooth .The treatment was performed under 2% Xylocaine which was used as an anesthetic agent comprising lignocaine hydrochloride with 1:200,000 epinephrine. All patients had inferior dental block and long buccal block nerve block.

Medications: Identical medications were used in the study in both groups Tab Ibuprofen 400mg (CIPLA LTD. Dabhel, Daman) and Capsule Amoxicillin 500 mg three times daily for five days (ALKEM LABS. HP, India).

Post–operative follow up

1. Facial measurements on second post-operative day.
2. Visual Analogue Scale (VAS) values.
3. Time for re-medication of analgesic (Mean time for rededications the time from the end of the surgery until the intake of analgesic medication became necessary for the patient).
4. Total number of analgesic tablets consumed by patient during recovery period (5 days) was recorded.
5. Global assessment (Patients were asked to provide an overall evaluation of the efficacy of analgesic with regard to pain on a five point categorical scale, at the end of the trial).
6. Facial measurements on the seventh post-operative day.

Statistical Methods: Independent t–test has been used to find the significance of time taken for the onset of postoperative pain, pain intensity, number of analgesics consumed and overall assessment among the two groups. Statistical software, SPSS 16 (Chicago), has been used for the analysis of the data and Microsoft office have been used to generate graphs, tables. Results were said to be statistically significant if the value was <0.05.

Results

The age group in the present study ranged between 18-40 years and in the group1 the mean age was 23.86 years and in group 2 mean age was 26.8 years as represented in Table 1. Gender distribution of the study groups involved 66.6 % of males and 33.3% of females in Group1 and in Group 2, 60% were males and 40% were females. In both the groups' percentage of males were more than females [Table 1]. The mean time taken to perform the surgery was 37.33 minutes in Group 1 and in the Group 2, the mean time taken to perform the surgery was 39.07 minutes. The difference was not statistically significant (p-value <0.6) [Table 2]. In Group 1 the average time taken for onset of post-operative pain was 217.5 minutes as compared with Group 2 in which the time taken for first onset of post-operative pain was 152 minutes (Fig. 1), with a significant delay of 65.5 minutes in Group 1. VAS scores were recorded for pain intensity the results

obtained from the VAS scores between the 2 groups for pain intensity was statistically significant (P< 0.05). Group 2 had 21.7 mm more pain score as compared to Group 1 (Fig. 2). The mean number of analgesic consumption in Group 1 was 5.27, and in Group 2 it was 8.47 (Fig. 3).

Table 1: Baseline characteristics of the 2 compared groups

Characteristics	**Pre-emptive group**		**Post-operative group**	
Age (in years)	***N***	**%**	***n***	**%**
<20	2	13.3	3	20
21-25	9	60	8	53.3
26-30	3	22	1	6.6
>30	1	6.6	3	20
Total	15		15	
Gender	***N***	**%**	***n***	**%**
Male	10	66.66	9	60
Female	5	33.33	6	40
Total	15		15	
Type of impaction	***N***	**%**	***n***	**%**
Mesioangular	10	66.6	8	53.3
Vertical	2	13.3	3	20
Horizontal	3	20	3	20
Distoangular	0	0	1	6.6
Total	15		15	
Note – Mesioangular impaction was most common type of impaction with a male predominance in the both the groups and more number subjects were in a age group ranging between 21-25 years of age.				

Table 2: Operative and patient variables for each treatment groups

Variables	**Group1 *(n=15)* Mean ± *SD***	**Group 2 *(n=15)* Mean ± *SD***	***p-value***
Duration of surgery	37.33 ± 11.24	39.07 ± 10.31	0.6
Time taken for first onset of post-operative pain (in minutes)	217 ±11.8 *	152 ± 7.2	0.0002
Pain Level (VAS scores in mm)	32.92 ± 8.18 *	54 .68 ± 7.10	0.0003
Total number of analgesic consumed by each group	5.27 ± 1.38 *	8.47 ± 1.5	0.0003
Global assessment scores	2.87±0.7*	2.07±0.7	0.08
*Significant difference between pretreated and post treated sides *(P< 0.05)*			

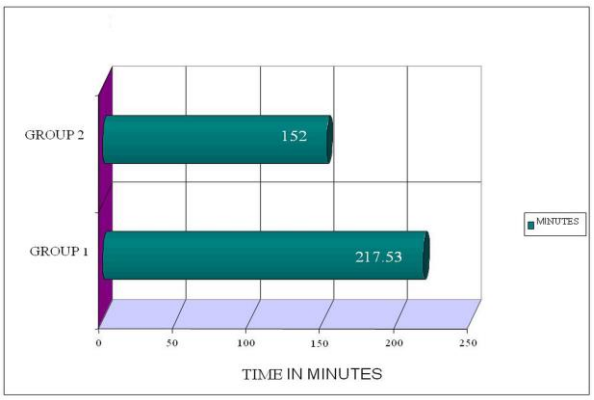

Fig. 1: Time taken for first onset of post-operative pain

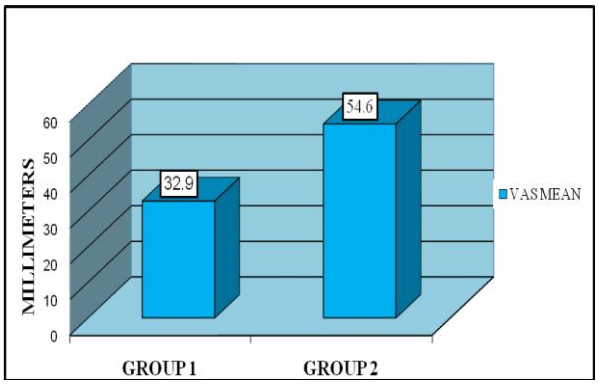

Fig. 2: Mean VAS scores among the study groups

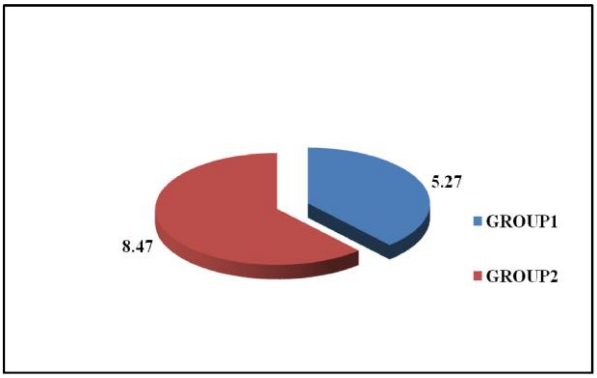

Fig. 3: Mean number of analgesic's consumed by each group during recovery period

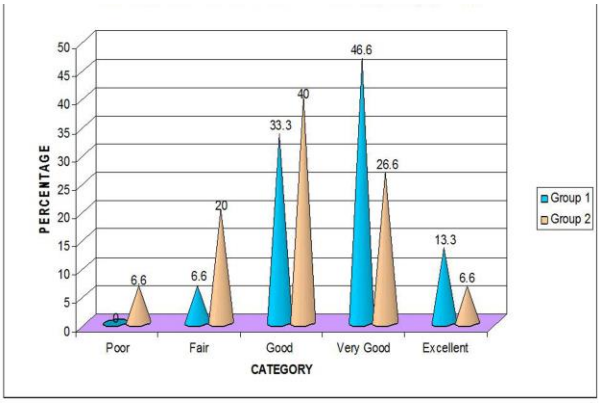

Fig. 4: Distribution of overall assessment (Patient comfort) scores on a 5 point numerical scale

Discussion

Treatment of postsurgical pain is more than a psychological issue of improving patient comfort.[9] The waiting policy to report severe pain by the patient before the prescription of an analgesic produces unnecessary discomfort and also reduces the efficacy of any subsequent treatment. NSAIDs provide excellent analgesia for mild to moderate pain. They are particularly useful in the initial management of pain that has an inflammatory component and Ibuprofen is the best studied drug in third molar surgery.[10,11]

NSAIDs have a longer onset of action as compared to opioids as they have peripheral mechanisms of action, which makes them to be administered long before the surgical incisions to permit concentration of the drug at the surgical site before the incision,[12] in our study oral Ibuprofen 400mg was administered 1 hour before the procedure.

In the present study the mean times taken for the first onset of post-operative pain was 217.5 minutes in pre-emptive group and 152 minutes in post-operative group (Fig. 1). The mean difference of 65.5 minutes delay for onset of post-operative pain was noted in preoperative group as compared to post-operative group which were statistically highly significant [Table 2], which denoted better pain control in pre-emptive group and was consistent with other studies. In a pre-emptive comparative study most of the reports demonstrated the pre-emptive analgesic effect and in some studies pre-emptive treatments resulted in delayed onset of postoperative pain.[13] Hill concluded that Ibuprofen given preoperatively delayed the onset of pain with a mean time of 1.5 – 2 hours.[14]

The majority of patient's age group in this study ranged between 21-25 years in both the groups [Table 1], and it is an advantage that these patients are usually young and healthy and are not associated with any other concomitant pain conditions,[1] which correlates with another study where the most frequent age group of patients with an impacted molar tooth was 21-30 years.[14,15,16]

Regarding gender distribution of the study groups involved 10 (66.6 %) were males and 5 (33.3%) were females in group1 and in control group 2, 9 (60%) were males and 6 (40%) were females [Table 1]. In both the groups' percentage of males were more than females.

In this study the values for the mean time taken to perform the surgery was 37.33 minutes in Group 1 and in the Group 2, the mean time taken to perform the surgery was 39.07 minutes. The difference was not statistically significant (p-value <0.6) [Table 2].[16]

The duration of surgery influences the tissue reaction factors during the immediate postoperative period following impacted third molar surgery, the longer the duration of tissue injury the more the amount of mediators released and therefore could be a reflection of the severity of pain, swelling and trismus similar findings were found in the present study [Table 2].

The type of impaction gives a prediction of the difficulty of extraction and hence the severity of postoperative tissue reactions. In this study the commonest type of impaction, was Mesioangular impaction 66.6% (10 impactions) in Group 1 and 53.3% (8 impactions) recorded in this study is similar to the reports from earlier studies.[17,18] The lower third molar begins its development in a horizontal angulation and as the normal growth and development of the jaw proceeds the angulation changes from horizontal to mesioangular then to vertical. Failure of this rotation from the mesioangular to the vertical direction is the most common cause of a tooth becomes impacted.[19] Distoangular and horizontal type of impaction have been shown to be associated with higher degree of pain, swelling and trismus when compared with vertical and mesioangular type of impactions.[20] They concluded that this observation could be a reflection of surgical aggressiveness that is associated with this type of impaction,[21] [Table 1].

Pain was assessed by using a visual analogue scale (VAS), as it takes less time to describe to the patient and is easily understood. The results showed highly significant difference between the pre-emptive and post-operative group, with a mean difference 21.7 mm on VAS with a high statistical difference suggesting

lesser pain intensity in the pre-emptive analgesia group[22] **[**Table 2]**.**

Number of analgesic requirement was 3.2 tablets less in the pre-emptive group (Group 1) as compared with the postoperative (Group 2)[23] (Fig. 3).

Overall assessment values in Group 1, was towards the higher range denoting the less post-surgical discomfort to the patients in pre-emptive group[24] (Fig. 4)**.**

Conclusion

The preoperative use of tablet Ibuprofen 400mg offers an added advantage to the patients, who undergo routine third molar extraction in terms of delay in the onset of post-operative pain and also increasing the pain threshold as compared with the same dose of analgesics given postoperatively. There was also a remarkable reduction in number of analgesic requirement postoperatively. The overall postoperative discomfort experienced by the patients during recovery period was also minimal. Routine use of the preemptive analgesia with simple NSAIDS like ibuprofen is definitely a recommended protocol in day to day practice of oral surgery.

Reference

1. Choudhury R, Kukreja P, Kumar K, Bhatnagar A, Anand KR, Chhabra V Pedicle flap design - A newer technique in mandibular third molar surgery for reduction of post-operative complications. J Dent Specialities, 2015;3(1):76-80.
2. Shah R, Mahajan A, Shah N, Dadhania AP. Preemptive analgesia in third molar impaction surgery. *National Journal of Maxillofacial Surgery*. 2012;3(2):144-147.
3. Ørholt SE, Aagaard E, Svensson P, Sindet-Pedersen S. Evaluation of trismus, bite force and pressure algometry after third molar surgery: a placebo-controlled study. Journal of Oral and Maxillofacial Surgery. 1998;56:420-427.
4. Taylor BK, Brennan TJ. Preemptive analgesia: moving beyond conventional strategies and confusing terminology. J Pain 200;1:77–84.
5. Joshi A, Parara E, Macfarlane TV. A double-blind randomised controlled clinical trial of the effect of preoperative ibuprofen, diclofenac, paracetamol with codeine and placebo tablets for relief of postoperative pain after removal of impacted third molars. Br J Oral Maxillofac Surg. 2004 Aug;42(4):299-306.
6. Michael GS, Michael AH. Preoperative nonsteroidal anti-inflammatory agents: Review of the literature. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2004 Aug;98(2),146–152.
7. Grape S, Tramèr MR. Do we need preemptive analgesia for the treatment of postoperative pain? Best Pract Res Clin Anaesthesiol. 2007 Mar;21(1):51-63.
8. Jung YS, Kim MK, Um YJ, Park HS, Lee EW, Kang JW. The effects on postoperative oral surgery pain by varying NSAID administration times: comparison on effect of preemptive analgesia.Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005 Nov;100(5):559-63.
9. Goodwin, Susan A. A review of preemptive analgesia. J Post Anesth Nurs, 1998 Apr;13(2):109-14.
10. Becker DE, Phero JC. Drug Therapy in Dental Practice: Nonopioid and Opioid Analgesics. *Anesthesia Progress*. 2005;52(4):140-149.
11. Becker DE. Pain Management: Part 1: Managing Acute and Postoperative Dental Pain. *Anesthesia Progress*. 2010;57(2):67-79.
12. Dionne RA, Cooper SA. Evaluation of preoperative ibuprofen for postoperative pain after removal of third molars. Oral Surg Oral Med Oral Pathol. 1978 Jun;45(6):851-6.
13. 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 Diagn Res. 2016 Jun;10(6):ZC102-6.
14. Unwerawattana W. Common symptoms and type of impacted molar tooth in King Chulalongkorn Memorial Hospital J Med Assoc Thai. 2006 Sep;89 Suppl 3:S134-9.
15. Paul C, Rahman QB, Alam S, Kundu GC, Uzzaman H. Effect of age on immediate postoperative tissue reaction following surgical extraction of impacted mandibular third molar. Bangabandhu Sheikh Mujib Medical University Journal,7(2),120-128.
16. Kulkarni H, Kulkarni G, Iqbal E, Biradar J. Khaji S.Variables of Clinical Significance Predictive of Difficulty of Third Molar Surgery: An Institutional Analysis of 200 Consecutive Procedures. J Dent Allied Sci 2015;4(1):8-12.
17. Quek SL, Tay CK, Tay KH, Toh SL, Lim KC. Pattern of third molar impaction in a Singapore Chinese population: a retrospective radiographic survey. Int J Oral Maxillofac Surg. 2003 Oct;32(5):548-52.
18. Saheeb, B.D.O. and Obuekwe, O.N. (2001) An audit of mandibular third molar. Nigerian Journal of Surgical Research, 3, 66-74.
19. Peterson LJ, Ellis E, Hupp JR, Tucker MR: Contemporary Oral and Maxillofacial sugery. Mosby, St Louis; 2 1993, 225-260.
20. Gbotolorun OM, Arotiba GT, Ladeinde AL. Assessment of factors associated with surgical difficulty in impacted mandibular third molar extraction. J Oral Maxillofac Surg. 2007 Oct;65(10):1977-83.
21. Bello SA, Adeyemo WL, Bamgbose BO, Obi EV, Adeyinka AA. Effect of age, impaction types and operative time on inflammatory tissue reactions following lower third molar surgery. Head Face Med. 2011 Apr 28;7:8.
22. Shah R, Mahajan A, Shah N, Dadhania AP. Preemptive analgesia in third molar impaction surgery. Natl J Maxillofac Surg. 2012 Jul;3(2):144-7.
23. Woolf CJ, Chong MS. Preemptive analgesia--treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg. 1993 Aug;77(2):362-79.
24. Ong KS, Seymour RA, Yeo JF, Ho KH, Lirk P. The efficacy of preoperative versus postoperative rofecoxib for preventing acute postoperative dental pain: a prospective randomized crossover study using bilateral symmetrical oral surgery. Clin J Pain. 2005 Nov-Dec;21(6):536-42.