



## A Randomised Controlled Trial of effect of Antibiotics, Corticosteroids and NSAIDs on post-operative morbidity following impacted third molar extractions

Brig Anil Dhingra<sup>1</sup>, Ashish Chakranarayan<sup>2</sup> and Priya Jeyaraj<sup>3\*</sup>

<sup>1</sup>Command Military Dental Centre (Northern Command), India

<sup>2</sup>Classified Specialist (Oral and Maxillofacial Surgery), Dental Centre, INHS Kalyani, Vishakhapatnam, Andhra Pradesh, India

<sup>3</sup>Classified Specialist (Oral and Maxillofacial Surgery), Officer in Charge Trauma and Rehabilitation, Command Military Dental Centre (Northern Command), Jammu and Kashmir, India

\*Corresponding Author: Priya Jeyaraj, Classified Specialist (Oral and Maxillofacial Surgery), Officer in Charge Trauma and Rehabilitation, Command Military Dental Centre (Northern Command), Jammu and Kashmir, India.

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### Abstract

Third molar surgery is a common surgical procedure. Prescription of Analgesics-Antipyretics and the use of Antibiotic prophylaxis in third molar surgery is the debate of the day and its use is controversial. In this study, the potential value of prophylactic/postoperative antibiotics and corticosteroids to reduce morbidity following surgical extractions of impacted third molars, has been explored and examined. This research is relevant in that it will set guidelines for Analgesics-Antipyretics, Steroid and Antibiotic prophylaxis in third molar surgery.

**Keywords:** Prophylactic; Corticosteroids; Antibiotic Prophylaxis; Analgesics-Antipyretics; Third Molars

### Introduction

Third molar surgery is a common surgical procedure. Prescription of Analgesics-Antipyretics and the use of Antibiotic prophylaxis in third molar surgery is the debate of the day and its use is controversial. The motivation for the study comes from the number of patients who go through third molar surgery every year. This research is relevant in that it will set guidelines for Analgesics-Antipyretics, Steroid and Antibiotic prophylaxis in third molar surgery.

Surgical removal of the impacted mandibular third molars is one of the most commonly performed dentoalveolar surgeries by Oral and Maxillofacial Surgeons and Dental Surgeons around the globe. The procedure has been colloquially cited it to be a humbling experience very often proving to be technically challenging even in the best of hands. Routinely carried out under local anesthesia the limited accessibility and visualization of the posterior part of the oral cavity makes the procedure technique sensitive [1]. It is known to be associated with clinically significant post-operative morbidity including swelling, pain, trismus, fever, infection etc. An impacted mandibular molar tooth can clinically present with a range of problems extending from simple food impaction to severe pain and trismus. Despite the potential, not all impacted teeth present with clinically significant issues. However when indicated e.g. pericoronitis, periodontal pathology, caries control and prevention, orthodontic considerations, periapical pathological, prevention of fractures, pre-prosthetic concerns, orthognathic considerations, unexplained pain/pressure symptoms, the impacted mandibular molar has to be extracted [2]. The surgical removal of mandibular third molar involves reflection of mucoperiosteal flaps for access, removal of overlying bone, sectioning the tooth (odontectomy), delivery of the tooth, debridement of the socket and closure of the soft tissue flap.

This leads to a surgical insult resulting in post-operative inflammatory response ranging from pain and swelling to acute trismus and fever etc [3]. In some cases other less frequent complications e.g. infection, mandibular fracture, nerve damage etc have also been reported [4,5]. In order to alleviate the anxiety, to lessen the morbidity and to positively influence the patient's experience, one of the primary concerns is minimizing postoperative morbidity consequent to the unavoidable surgical insult. To achieve this objective various drugs which are in vogue are NSAIDS, antibiotics, enzymes, sedatives, opioids and corticosteroids. This study aims to establish the efficacy of three different group of the pharmacological agents used in isolation and in combination in the management of post-operative morbidity following surgical removal of the mandibular third molar.

### Aim

To evaluate the potential value of prophylactic/postoperative antibiotics and corticosteroids to reduce morbidity following surgical extractions of impacted third molars.

### Objectives

- To evaluate the frequency of post-operative complications in third molar surgery.
- To compare the rate of post-operative complications between the three groups.
- To recommend specific guidelines for prophylaxis of third molar surgery.

### Material and Methods

The authors designed a prospective cohort study from 1<sup>st</sup> September 15 to 30<sup>th</sup> April 2017. The study population consisted of 94

randomly selected, healthy, consecutive patients referred for mandibular third molar extractions.

### Patient Selection

#### Inclusion criteria

The selection criteria include clinically and radiologically impacted mandibular third molar cases presenting with a complaint of food impaction, caries, recurrent pericoronitis, cheek biting, pain and or restriction in mandibular movements. However, medically compromised patients were excluded (Table 1).

#### Exclusion criteria

1. Patients with active pericoronitis or infection.
2. Patients with blood dyscrasias or using anticoagulants.
3. Patients with rheumatic heart disease.
4. Patients with associated third molar pathology.

Thorough preoperative assessment including clinical examination, routine hematological investigation and orthopantomogram were carried out in all patients in the preparation for surgery under local anesthesia. Surgery was carried out under local anaesthesia using a standard operative technique for all patients.

Prior to the trial, each patient was informed about the study, its aim, implications and possible complications. Signed informed consent was obtained. The patients were examined clinically and those with infections or on antibiotics were excluded. The angulations and depth of the third molars were recorded from the orthopantomograph using the Pell and Gregory. The Pell and Gregory system classifies the relative depth of impaction on the basis of its vertical relationship to the second molar and the ramus.

#### Ethical Considerations

- This proposal was approved by the Research and Ethics Committee of the institution.
- Participation in this study was on voluntary basis.
- Patients were adequately informed about the objective of the trial.
- Written informed consent was obtained from every patient.
- Patients with any other dental problems were referred to the appropriate departments.
- Participants had the right to withdraw from the study at any stage and this would not prejudice them in regard to future treatments.
- The rights of patients were protected at all times.

#### Preoperative Care

At least 1 week before surgery, all patients underwent professional oral prophylaxis and scaling/ tooth cleaning to decrease the bacterial load.

#### Intraoperative Care

Following part preparation using strict aseptic protocol, inferior alveolar and long buccal nerve block was given using 2ml of 2% lignocaine containing 1:80,000 adrenaline. Ward's incision was given from distal of second molar posteriorly, mucoperiosteal flap elevated to expose the impacted third molar tooth using a Ward's

periosteal elevator. Austin's cheek retractor was then used to retractor the mucoperiosteal flap and overlying bone was removed using a stainless steel straight fissure bur on a micromotor at 25000 rpm using copious normal saline irrigation in a disposable 10cc hypodermic syringe. A bony gutter was created on the buccal and distal aspect of the third molar tooth. Odontectomy was done where indicated i.e. in cases of severe mesioangular, distoangular and horizontally impacted teeth. The tooth was then elevated and delivered using a straight elevator. Extraction socket was then copiously irrigated with normal saline and finally with 5% w/v povidone iodine solution. Hemostasis verified and incision closed by three interrupted sutures using 3-0 silk.

#### Postoperative Care

The patient was instructed to bite on a gauze pack placed on the operated site for half an hour. Soft and cold diet was recommended for the first post-operative day with ice pack application on the posterior cheek @ 20/min per hour three to four times a day. Standard post extraction instructions were given to the patients. The patients were randomly divided into three groups.

- **Group I** patients were prescribed Ibuprofen 400 Mg + Paracetamol 325 mg tid for 5 days.
- **Group II** were prescribed Ibuprofen 400 mg + Paracetamol 325 mg and Amoxicillin 500 mg tid for 5 days.
- **Group III** was prescribed Ibuprofen 400 mg + Paracetamol 325 mg tid, Amoxicillin 500mg tid for 5 days along with Inj Hydrocortisone 100 mg iv stat.

The patients were reviewed clinically on the 2<sup>nd</sup>, 4<sup>th</sup> and 6<sup>th</sup> post-operative day. Interincisal mouth opening and buccal swelling between the angle of the mouth and lower border of ear lobule were measured using scale and flexible scale respectively (Figure 1, 2). To measure the buccal swelling a line was marked between the angle of mouth and lower border of ear lobule. Another line was marked from the outer canthus of the eye to the angle of mandible. The distance between the angle of mouth and intersection of the lines mentioned above was used to measure the post-operative swelling (Figure 3). Sutures were removed on the 6<sup>th</sup> post-operative day.

#### Criteria for Evaluation

##### Swelling



Figure 1



Figure 2

**Pain**

Visual analogue scale was used to assess the pain (Figure 3). Postoperative pain was evaluated on a 10-cm horizontal visual analog scale (VAS), with degree of pain intensity ranging from “no pain” to “unbearable pain.” On this form, each patient reported pain intensity immediately after surgery, 6 hours after surgery, and during the following 6 days, in the morning (7 to 9 AM) and evening (8 to 9 PM).

To allow a continuous assessment of pain, visual analogue scale uses a 10 cm line labeled at ‘0’ with ‘no pain’ and ‘10’ with ‘worst’. The line is marked at a point corresponding to the assessment of the pain. The distance of the mark from zero is measured. In this study, pain severity was recorded on a Visual Analogue Scale (VAS). Pain was recorded three times a day for two weeks. Patients were instructed to rate and record pain intensity on the VAS.

**Variables Score**

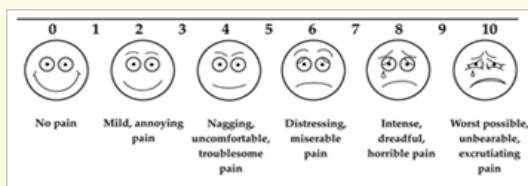


Figure 3

Pain	Variables Score
None	0
Mild	1
Moderate	2
Severe	3
Could not be worse	4

**Trismus (in mm)**

Maximum mouth opening ability was measured in millimeters between the upper and lower right central incisors using Vernier-calibrated sliding caliper preoperatively, and on every visit.

**Temperature (> 38°C)**

Temperature was recorded pre-operatively and on every visit. Temperature > 38°C was considered a fever.

Temperature (> 38°C)	Variables Score
No	0
Yes (> 38° C)	1

**Pus collection and/or discharge**

Clinical signs of pus collection were recorded on every visit.

Clinical collection of pus	Variables Score
None	0
Yes	1

**Null hypothesis**

There will be no difference in post-operative complications (pain, trismus, swelling, infection) in patients with or without antibiotic and corticosteroid administration in third molar surgery.

**Results**

A total of 150 patients i.e. randomly divided into three groups of 50 patients in each group, aged 18 to 61 years were included in the study with peak age incidence being between 20 to 30 years. Most patients (48.6%) presented with a complaint of recurrent pericoronitis. The clinical signs and symptoms observed are shown in table 1. All cases were operated by a single operator with the same support staff and the same instruments in the same operatory. The average operating time ranged from 12 to 14 minutes irrespective of the type and severity of impaction. Postoperatively, cases were reviewed clinically by comparing preoperative and postoperative inter incisal mouth opening (Figure 4-7) and cheek swelling (Figure 8-10). Other parameters observed were wound dehiscence, infection and neurological deficit.

S. No	Clinical feature	Percentage of patients
	Pericoronitis	48.6 % (73)
	Caries	35.5% (53)
	Periapical pathology	14.6% (22)
	Pain	1.3% (2)

Table 1: Clinical features.

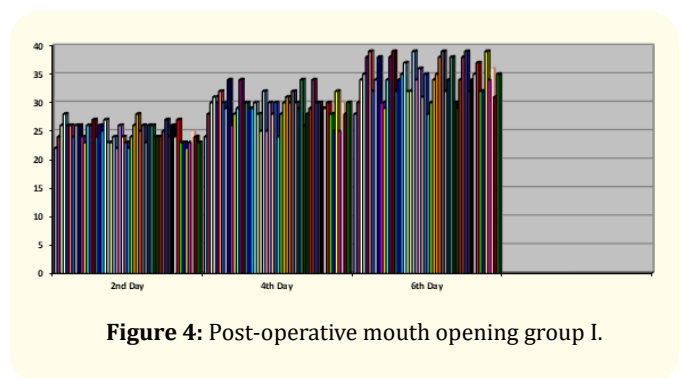


Figure 4: Post-operative mouth opening group I.

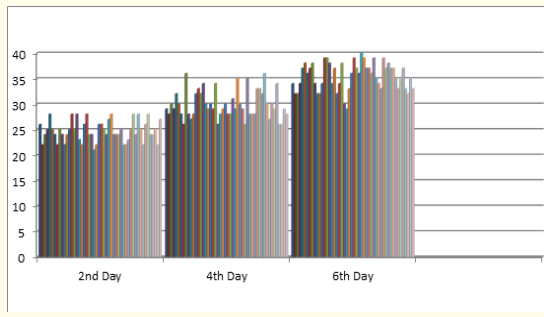


Figure 5: Postoperative mouth opening group II.

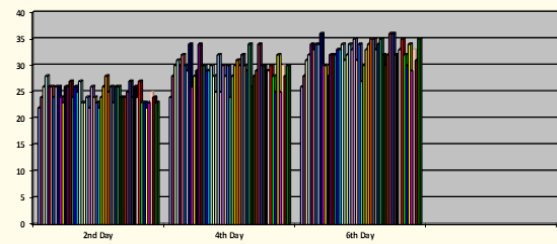


Figure 6: Post-operative mouth opening group III.

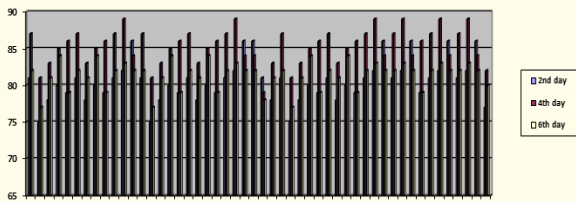


Figure 7: Post-operative swelling group I.

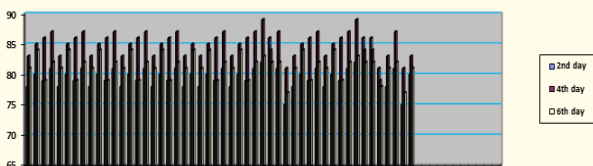


Figure 8: Post-operative swelling group II.

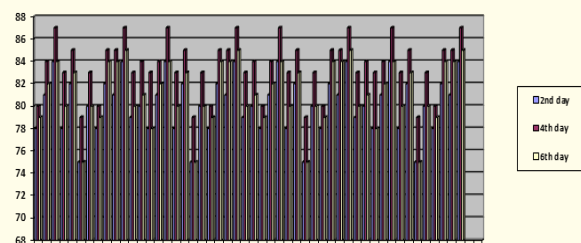


Figure 9: Post-operative swelling group III.

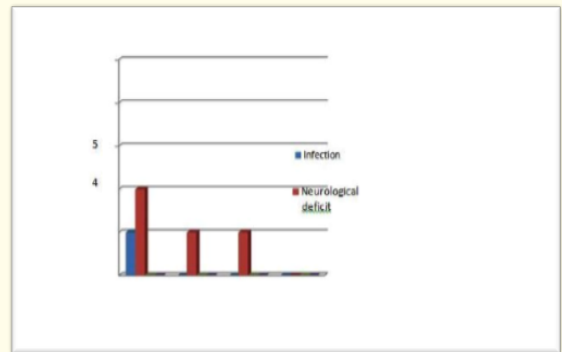


Figure 10: Comparison of complication rates between the three groups

Two patients in group I presented with a complaint of severe pain and pus discharge with fever on the 3<sup>rd</sup> and 4<sup>th</sup> post-operative day. They were prescribed capsule Amoxicillin 500 mg tid for five days following which the infection subsided. Two patients in group I and one patient in group II and III each presented with transient paresthesia of the lower lip which resolved in three to four weeks.

### Discussion

The primary post-operative objective of any surgical procedure is quick recovery with minimum morbidity. The surgical removal of an impacted mandibular molar results in a normal physiologic responses i.e. mild bleeding, swelling, trismus, and pain. The tolerance and acceptability of post-operative morbidity is subjective and hence warrants measures to curtail such events to the best of our abilities, without going overboard. It's an open secret that contemporary medical practice to a certain extent is driven by the pharmaceutical industry and one cannot deny the fact there seems to be a pressure of sorts to prescribe [6]. Also, there is a plethora of information available on the internet, the interpretation of which is very subjective. This sometimes instills unrealistic expectations in the patients thus indirectly burdening the clinician to cater to such requirements [7]. Various methods have been used to minimize the post-operative morbidity secondary to the surgical insult. Compliance to standard post-operative instructions like soft and cold food, avoid spitting, avoid smoking and liquor, warm saline rinses from the second post-operative day remains a common denominator. However drugs in different combinations remain the mainstay in the management of post-operative morbidity.

Pain after third molar surgery usually begins when the effect of anesthesia subsides. It reaches its peak at 6 to 12 hours post-operatively. Effective manage pain management is regarded as an essential skill of the prudent surgeon. Preoperative and post-operative systemic analgesics reduce pain by inhibition of central and peripheral pain receptors. Prophylactic analgesic therapy is intended to inhibit the effects of the surgery on the surrounding tissue. The first drug to consider for pain is paracetamol (acetaminophen). It is indicated for the management of mild to moderate pain. Its favorable risk/benefit balance makes it a popular choice for acute postoperative dental pain.

In our study, the group I patients were managed exclusively with a combination of Ibuprofen and Paracetamol (Combiflam). Ibuprofen has a dose-dependent duration of action of approximately 4 to 6 hours, which is longer than suggested by its short half-life. Ibuprofen is a non-selective COX inhibitor i.e. it inhibits two isoforms of cyclooxygenase, COX-1 and COX-2 [8]. While paracetamol has analgesic and antipyretic properties comparable to those of aspirin, it does not have a significant anti-inflammatory action due to its susceptibility to the high level of peroxides present in areas of inflammation. However, Paracetamol is also known to inhibit another isoform i.e. COX-3 in the CNS [9]. Also, Paracetamol modulates the endogenous cannabinoid system through a metabolite AM404, which inhibits the uptake of the endogenous cannabinoid/vanilloid anandamide by neurons. Anandamide uptake would result in the activation of the main pain receptor (nociceptor) of the body i.e. the TRPV1 thus augmenting the analgesic effect [10]. Except for one patient who developed infection, group I patients showed no difference in the post-operative events as compared to group II thus negating the role of antibiotics in the management of postoperative sequel to surgical extraction of mandibular third molar. However as compared to group III the swelling and trismus was marginally more in group I on the 2<sup>nd</sup> and 4<sup>th</sup> day (Figure 1, 3-6). Corticosteroids have been used to reduce swelling, trismus, and pain in the post-operative management of surgical removal of mandibular third molar [11,12], however, method of usage is extremely variable and evidence based protocols have still not been defined. In our study group III was given Inj Hydrocortisone, however the advantage was marginal and clinically not significant as compared to the other groups (Figure 1,3,4,6).

Based on the findings of this study it appears that the extent of postoperative morbidity may have a greater contribution from the amount of surgical insult irrespective of the pharmacological agent used to curtail it. It is a known fact that the duration of surgery is a good indicator of the surgical insult [14]. In our study the comparable results may be due to the fact that all cases were managed under identical circumstances and the average duration for most cases fell in the narrow range of 12 to 14 min. Although studies have shown some benefit from giving antibiotics after removal of mandibular third molars, it is unclear if the benefit is significant enough to warrant routine use as a protocol [15-17]. In our study Amoxicillin was used in the management of group II cases. Except for one case in group I which presented with pus discharge the remainder cases in group II showed no significant advantage as compared to group I. Thus implying that in the absence of preoperative infection the role of postoperative antibiotics is inconsequential.

Complications invariably occur following the surgical removal of third molars. Attention to the basic principles of surgery, including proper preparation of the patient, a sepsis, hemostasis, use of controlled force, thorough debridement, and meticulous management of both bone and soft tissues can reduce the number and severity of complications.

The results of this study showed that the prophylactic antibiotics do not have statistically significant effects on post-operative infections. Therefore, there is no justification for using antibiotics routinely for third molar surgery. However, we need a safe and effective analgesic and anti-inflammatory combination after third molar surgery to prevent post-operative pain.

The findings in this study were based on periodical clinical examinations. As anticipated, there was a good correlation between the patients' own assessments of pain on a VAS with the difficulty of impacted third molar. Most patients, who reported swelling, also had impaired mouth opening (Trismus). The methods we used to evaluate pain, swelling, trismus and infection are described in the literature. Inter-examiner variability was excluded by using only one research assistant. All assessments were done in the same clinical environment. Post-operative infection of bone and soft tissues is a common complication that can be reduced with good surgical techniques. Some bacterial contamination of a surgical site is inevitable, either from the patient's own bacterial flora or from the environment. Antibiotics are commonly administered prophylactically for major and minor surgical procedures. In many cases, antibiotics are prescribed only after the procedure. No intra-operative antibiotic cover is thus achieved which is in conflict with the basic principles of prophylaxis.

## Conclusion

In this study, the analgesic and anti-inflammatory effects of the combination of Ibuprofen and Paracetamol was found to be clinically effective in management of post-operative morbidity following surgical extraction of mandibular third molars. The presence of preoperative infection may warrant the use of oral antibiotics. The administration of corticosteroids may be reserved for patients with a low tolerance to perceived postoperative discomfort and in cases of increased surgical insult which is directly proportional to the duration of the procedure. However their use as routine pre and or postoperative medication may be investigated with reference to two factors (a) anticipated duration of procedure as an indicator for the use of corticosteroids (b) perceived tolerance to post-operative morbidity. A good surgical technique, adherence to a strict aseptic protocol, good patient compliance and merit based use of drugs appear to be more important than the number of pharmacological agents routinely and empirically used to reduce the post-operative morbidity.

## Compliance with Ethical Standards

### Disclosure of potential Conflicts of Interest

The author of this article has not received any research grant, remuneration, or speaker honorarium from any company or committee whatsoever, and neither owns any stock in any company. The author declares that she does not have any conflict of interest.

### Research Involving Human Participants and/or Animals

All procedures performed on the patients (human participants) involved were in accordance with the ethical standards of the institution and/or national research committee, as well as with the 1964 Helsinki declaration and its later amendments and comparable ethical standards.

### Ethical Approval

This article does not contain any new studies with human participants or animals performed by the author.

### Informed Consent

Informed consent was obtained from all the individual participants in this study.

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