TO COMPARE THE EFFICACY AND SIDE EFFECTS OF DICLOFENAC SODIUM, IBUPROFEN AND NIMESULIDE DURING POST OPERATIVE PERIOD OF SURGICAL REMOVAL OF IMPACTED LOWER THIRD MOLAR TOOTH

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ABSTRACT: BACKGROUND: The surgical removal of impacted third molars is one of the most frequently performed procedures in oral surgery with complications such as postoperative pain, swelling and trismus. Ideal analgesic to be administered after the surgical removal of impacted third molar should alleviate pain and associated symptoms, facilitate healing, and cause no undesirable side effect and for which we usually administer nonsteroidal anti-inflammatory drugs (NSAIDs). In this study comparison of efficacy of nimesulide,diclofenac sodium and ibuprofen to control postoperative sequelae in surgical removal of impacted mandibular third molars has been undertaken.

AIM: To compare drug efficacy in terms of edema, pain and trismus and to compare the side effects of the drugs and to suggest a better pharmaceutical agent that resumes to normalcy at earliest.

METHODS AND MATERIAL: Total of 30 patients reporting to the Department Of Oral And Maxillofacial Surgery, KLE Institute of Dental Sciences was included in the study. Pre and post-operative pain, trismus, swelling and adverse effect of drugs were recorded.

STATISTICAL ANALYSIS USED: p value and t value test (Test of significance of value) were used to compare the results.

RESULT: Nimesulide proved to be the analgesic and anti-inflammatory drug of choice for short term therapy as it demonstrates minimal side effects and early rate of recovery from postoperative sequelae of pain, trismus and swelling after surgical removal of mandibular 3rdmolar. But long term use should be considered and more studies should be carried out regarding long term therapy of Nimesulide in terms of safety and efficacy.

KEYWORDS: Ibuprofen, Diclofenac Sodium, Nimesulide, Anti-inflammatory and Analgesic, Dental Pain.

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INTRODUCTION: The surgical removal of impacted third molars is one of the most frequently performed procedures in oral surgery and postoperative complications such as post-operative pain, swelling and trismus may occur.(1)

The phase after removal of third molar is frequently characterized by pain, trismus and inflammation.(2) It can cause significant suffering, anxiety, fear, anger and depression. Therefore, attention is being focused on aggressive prevention and treatment of pain postoperatively to reduce complications. An ideal drug administered after the surgical removal of impacted third molar should alleviate pain and associated symptoms, facilitate healing, and cause no undesirable side effects.(3)

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Impacted third molar removal with associated cellular and tissue destruction products bring about the release and production of several biochemical mediators involved in the process of pain; in particular, histamine, bradykinin and prostaglandins, and to oppress this cycle inflammatory inhibitors are commonly used now a days.

One of the most significant advances in Maxillofacial Surgery in the last decade has been in the field of pharmacological management in patients with acute postoperative pain and the most prevalent practice being administration of: nonsteroidal anti-inflammatory drugs (NSAIDs).(4) Removal of impacted third molar results in varying amount of postoperative inflammation and because of its unique anatomical position patient experiences more trismus, pain and swelling as compared to surgery in any other part of oral cavity.(5)

Thus efforts are being made to prescribe a drug with better analgesia, anti-inflammatory effect, and minimum adverse effects. In this study, comparison of efficacy of Nimesulide, Diclofenac Sodium and Ibuprofen to control post-operative sequelae in terms of pain, trismus, edema in impacted mandibular third molar surgery and the side effects of the drugs has been taken into consideration.

MATERIALS AND METHOD: A clinical, randomized study which included 30 patients, who reported to the Department of Oral and Maxillofacial Surgery at Kle's Dental college and Research Institute, Belgaum with bilateral mandibular impacted third molars, was done.

The study was approved by the Ethics Committee. Inclusion criteria were patients with bilaterally impacted mandibular third molars assigned randomly. Exclusion criteria were any systemic diseases like blood disorders, uncontrolled diabetes mellitus. Patients with any symptoms of infection were given antibiotics course till it was under control. The study protocol was explained to all patients in detail and written informed consent was obtained.

Patients were randomly allocated into three groups for removal of impacted mandibular third molar unilaterally twice with a time gap of more than 15 days.

Dosage of the drugs was as follows:

- Tablet Nimesulide 100mg/bid (5 days)
- Tablet Diclofenac sodium 50mg/bid (5 days)
- Tablet Ibuprofen 400mg/tid (5 days)

Surgical Procedure: Surgery of impacted third molars (Fig. 1) was carried out under local anesthesia (2% lignocaine hydrochloride with 1:80,000 adrenaline). The patients were painted and draped in usual manner. Standard ward incision was made and flap was reflected. Tooth was removed with buccal and distal guttering using Stainless steel burs No. 8 and sometimes a notch was made near the cemento-enamel junction for elevation under constant irrigation with saline (Fig. 2). Wound was gently irrigated with saline, flap was repositioned and sutured with 3-0 black braided silk (Fig. 3) and pressure pack was given. Regular Postoperative instructions were given to the patients.

Measurement of Pain.[6]: Pain chart was explained to the patients. Peri and postoperative pain was assessed using Visual Analogue Scale (VAS) on 1st, 2nd, 3rd and 7th post-operative day.

Measurement of Trismus (mm): Preoperative interincisal distance was measured with vernier caliper and taken as control for postoperative measurements on 1st,2nd,3rdand 7thdays. Incisal edges of maxillary and mandibular central teeth were used as reference point at the most available maximum mouth opening.

Measurement of swelling[7]: The facial swelling was measured quantitatively using modified single sliding bar face bow,in cubic centimeters by cuboid element method preoperatively and postoperatively on 1st,2nd,3rd and 7thday.

RESULTS: A total of 30 patients (21male and 9 female) who had bilateral impacted third molars were included in the study. The average surgery time was 23.5 minutes. No adverse effects or complications related to surgery were recorded in any treatment group with no alteration in mandibular nerve conductivity assessed with Quantitative sensory testing namely:

1. Mechanoreception (touch pressure,positional sense)
2. Thermoreception (hot,cold)
3. Nociception (pain).

Pain Assessment: Pain was measured on 1st,2nd,3rd and 7th postoperative day by visual analogue scale. It was filled by patient every 6 hours on mentioned days. Mean readings were taken of each day to describe pain as nil, mild, moderate and severe.

- **In group 1:** patients prescribed with Nimesulide none of them presented with severe pain compared to patients prescribed with ibuprofen, where 40% of them presented with severe pain on 1st post-operative day itself. Patients prescribed with nimesulide showed steady recovery with 80% of them having no pain on 3rd post-operative day. Whereas about 60% of patients prescribed with ibuprofen presented with mild pain and remaining 40% presented with moderate pain on 3rd postoperative day.
- Patients taking nimesulide showed no pain on 7th post-operative day compared to 40% of patients prescribed with ibuprofen who had mild pain, thereby nimesulide showed better efficacy compared to ibuprofen in pain control.
- **In group 2:** patients prescribed with diclofenac sodium none had severe pain compared to 40% of patients prescribed with ibuprofen had severe pain on 1st post-operative day.
- Patients prescribed with diclofenac sodium showed steady recovery with 40% of them having no pain on 3rd postoperative day, whereas patients prescribed with ibuprofen in them 80% presented with mild pain and remaining 20% with moderate pain on 3rd post-operative day.

80% of patients prescribed with diclofenac sodium showed no pain on 7th postoperative day compared to 60% of patients prescribed with ibuprofen who had no pain, thereby diclofenac sodium showed better efficacy compared to ibuprofen in pain control.

In group 3 patients who were prescribed with nimesulide none of them presented with severe pain compared to patients prescribed with diclofenac sodium where 10% of them presented with severe pain on 1stpost-operative day.

Patients prescribed with nimesulide they showed better pain control compared to patients prescribed with diclofenac sodium even on 2ndpost-operative day. Patients prescribed with nimesulide showed marked difference with 80% having no pain on 3rd post-operative day compared to patients prescribed with diclofenac sodium where 80% of these patients presented with mild pain and 10% with moderate pain on 3rd postoperative day.

Patients prescribed with Nimesulide showed no pain on 7thpost-operative day compared to patients prescribed with diclofenac sodium who still had 30% of patients with mild pain, thereby nimesulide showed better efficacy compared to diclofenac sodium in pain control, which is also statistically significant.

ADVERSE EFFECTS: The adverse effects associated with all three drugs were also recorded.

In the patients prescribed with Nimesulide, 20% of them had some or the other side effects like three patients reported gastric irritation and one patient had urticarial type reaction. In the patients prescribed with Diclofenac Sodium, 35% of them had side effects of which eight patients reported gastric irritation. In the patients prescribed with ibuprofen, more than 50 % of them had some or the other side effects like eight patients reported gastric irritation and two complained of nausea and vomiting.

DISCUSSION: Impacted mandibular third molar is one of the most common conditions which often necessitate its surgical removal for various reasons like pericoronitis, pericoronal abscess, cyst, orthodontic treatment, involvement in fracture line and various tumors. Literature shows that most common complications observed after surgical extraction of mandibular 3rd molars are pain, trismus and swelling.[8,9,10,11]

To overcome these complications is a major challenge and is in surgeon's perpetual interest for far long. Various measures have been tried clinically including use of antibiotics, surgical drain and bandage neither of which was found to be successful. NSAIDs have proved themselves to be strong analgesic and anti-inflammatory agents for long time.

They showed better results after minor oral surgical procedures as compared to other measures which were found to be less effective giving rise to more complications and with vast side effects.[12,13,14] Taken into account the above mentioned facts, this study was conducted to ascertain for the best possible drug with minimal side effects and maximum effectiveness over control of pain, swelling and trismus.

The study included 30 patients who satisfied the criteria for selection in which efficacy of different NSAIDs compared in the study,were investigated in management of pain, swelling and trismus following 3rd molar surgery.

It was observed that the patients prescribed with Nimesulide experienced minimal pain as compared to those on diclofenac sodium and ibuprofen. Diclofenac sodium had better analgesic efficacy than ibuprofen.

The results showed Nimesulide as having superior efficacy in controlling pain with steady improvement rates which was also evident statistically. Restriction in mouth opening post-operatively as minimal with Nimesulide, whereas patients prescribed with Diclofenac sodium showed more restricted mouth opening with slower rate of improvement but it showed better results compared to Ibuprofen. Patients prescribed with nimesulide showed less swelling compared to diclofenac sodium, whereas patients prescribed with Ibuprofen suffered maximum swelling.

The adverse effects associated with nimesulide therapy were minimum compared to ibuprofen which showed maximum adverse effects during the course of the study.

In view of the mentioned facts, nimesulide proved to be a better analgesic with equivalent anti-inflammatory potential for short term therapy and with additional value of minimal side effects and early rate of recovery from post-operative sequel of pain, trismus and swelling after surgical removal of mandibular 3rd molars.

But long term use should be considered and more studies should be carried out regarding long-term therapy of nimesulide in terms of safety and efficacy index.

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Groups	Left impacted mandibular Third molar	Right impacted mandibular Third molar
Group 1	Ibuprofen	Nimesulide
Group 2	Diclofenac sodium	Ibuprofen
Group 3	Nimesulide	Diclofenac sodium

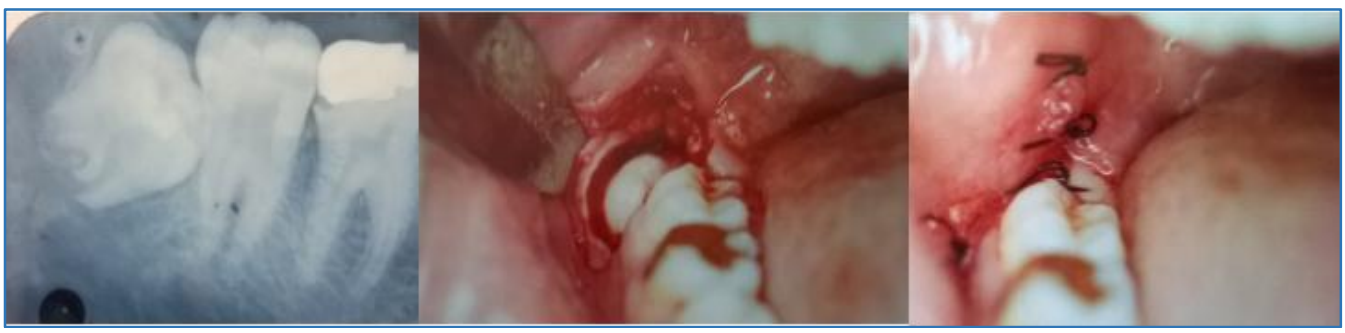

Fig. 1 ***Fig. 2*** ***Fig. 3***

The age distribution of 30 patients was as follows.

Age (Years)	Male	Female
15-19	1	2
20-24	9	3
25-30	7	-
31- above	4	4

Mouth opening ability assessment (Trismus): Swelling was measured by face bow method for all 3 groups preoperatively and on 1st, 2nd, 3rd and 7th day postoperatively (Table 1).

Table 1

Mouth opening ability (Trismus) assessment

GROUP 1 (NIMESULIDE & IBUPROFEN)

Post op days	t value	p value	Inference
1st	1.4985	0.05	Not significant
2nd	2.4431	.05	Significant
3rd	3.8959	.01	very significant
4th	6.0940	.001	highly significant

GROUP 2 (DICLOFENAC SODIUM & IBUPROFEN)

Post op days	t value	p value	Inference
1st	0.9382	0.05	Not significant
2nd	2.5012	0.05	Significant
3rd	4.0833	0.001	very significant
4th	2.7035	0.01	Significant

GROUP 3 (DICLOFENAC SODIUM & NIMESULIDE)

Post op days	t value	p value	Inference
1st	1.8873	0.05	Not significant
2nd	2.0909	0.05	Not significant
3rd	2.8335	0.05	Significant
4th	4.4272	0.001	Highly significant

Pre-operative reading for each patient was taken as standard (Fig.4,5).

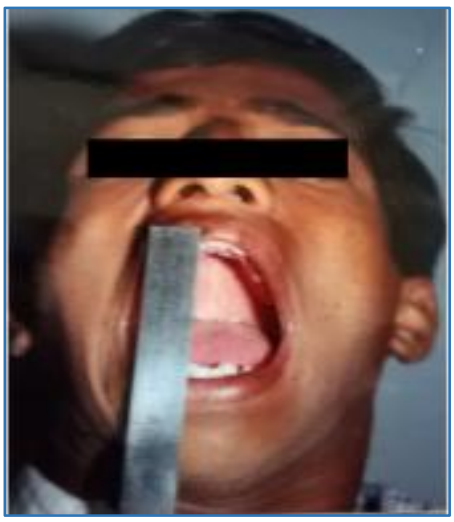

Fig. 4

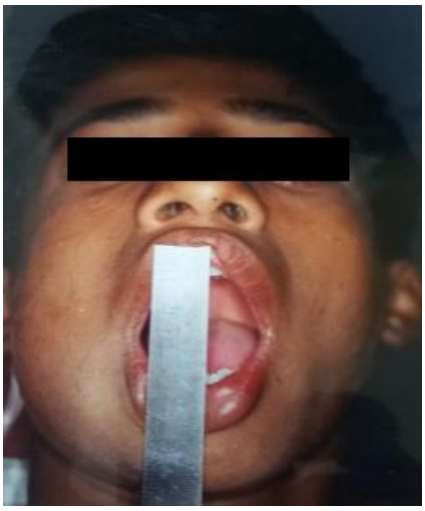

Fig. 5

- In group 1 interincisal distance measured for both the drugs were not statistically significant at the end of 1st post-operative day but later it showed statistically significant values for nimesulide.
- Similarly in group 2 interincisal distance measured for both the drugs were not statistically significant at the end of 1st post-operative day but later it showed statistically significant values for Diclofenac sodium.
- In group 3 the interincisal distance measured for both the drugs were not statistically significant at the end of 1st and 2nd post-operative day but later it showed statistically significant values for nimesulide.

Post-operative swelling assessment: Swelling was measured by face bow method for all 3 groups pre-operatively and on 1st, 2nd, 3rd and 7th day post operatively (Table 2).

Table 2

GROUP 1 (NIMESULIDE & IBUPROFEN)

Post op days	t value	p value	Inference
1st	13.0015	0.001	highly significant
2nd	14.6605	0.001	highly significant
3rd	17.8247	0.001	highly significant

GROUP 2 (IBUPROFEN & DICLOFENAC SODIUM)

Post op days	t value	p value	Inference
1st	6.6217	0.001	highly significant
2nd	8.0333	0.001	highly significant
3rd	11.0611	0.001	highly significant

GROUP 3 (NIMESULIDE & DICLOFENAC SODIUM)

Post op days	t value	p value	Inference
1st	6.8228	0.001	highly significant
2nd	10.7647	0.001	highly significant
3rd	7.2701	0.001	highly significant

Preoperative reading for each patient was taken as standard (Fig. 6, 7)

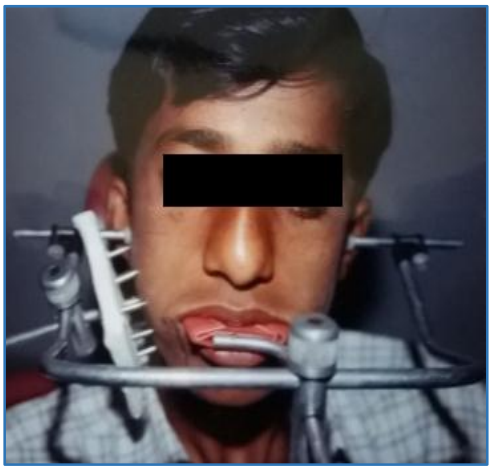

Fig. 6

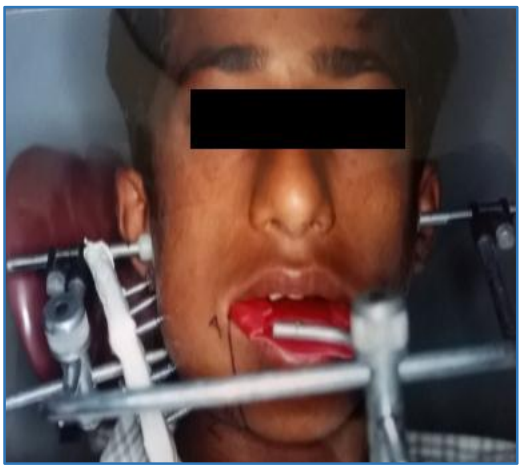

Fig. 7