J. Maxillofac. Oral Surg. (Apr-June 2011) 10(2):118–122
DOI 10.1007/s12663-011-0198-9

COMPARATIVE STUDY

Randomized Double Blind Comparative Study on the Efficacy of Ibuprofen and Aceclofenac in Controlling Post-Operative Sequelae after Third Molar Surgery

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Received: 28 September 2010 / Accepted: 3 March 2011 / Published online: 22 April 2011

Abstract
Objective To compare the efficacy of Ibuprofen and Aceclofenac in controlling pain, swelling and trismus following removal of impacted mandibular third molar teeth. To assess the patient's acceptability of these drugs.
Methods The present double blind study was conducted on 60 adult patients for the surgical removal of impacted mandibular third molars. Drugs administered were Ibuprofen and Aceclofenac. Both the drugs were packed separately and coded with equal in number. After removal of impacted mandibular third molars, following parameters were studied: (1) Analgesic activity, (2) Maximum mouth opening, (3) Swelling.
Results The scores were recorded preoperatively and on 1st, 3rd, 5th and 7th postoperative day.
Conclusion Ibuprofen has a marginal edge over Aceclofenac. Both the drugs were well accepted by the patients with no reported adverse effects.

Keywords Ibuprofen · Aceclofenac · Third molar

Introduction

Third molar removal represents a major part of oral and maxillofacial surgical practice. It is essential that anaesthesia be obtained during removal, but effective postoperative analgesia is equally important for good patient care. Surgical removal of third molar produces local oedema, inflammation and pain [1].

Natural metabolites of arachidonic acid i.e. prostaglandins and leukotrienes play a major role in the inflammatory process by causing vascular dilatation, increasing capillary permeability, hyperalgesia and promoting migration of leukocytes and macrophages to the site of inflammation. Non steroidal anti-inflammatory drugs inhibit cyclooxygenase thus reducing production of prostaglandins thereby controlling pain, trismus and swelling [2].

Aceclofenac is a member of the phenyl-acetic acid class of NSAIDs. Studies have shown that it possesses analgesic and anti-inflammatory properties similar to those obtained with Diclofenac and Indomethacin. In clinical studies it has been shown to treat dental pain and post episiotomy pain effectively. By contrast, the efficacy of ibuprofen, a propionic acid derivative in postoperative dental pain is well established. Although Ibuprofen and Aceclofenac are both NSAIDs, they do not have different chemical structures. Both inhibit the cyclooxygenase enzyme system and hence reduce the biosynthesis of prostaglandins. In addition Ibuprofen inhibits the migration and other functions of leucocytes, whilst Aceclofenac reduces intracellular concentrations of free arachidonate in leukocytes. The additional pharmacological properties of both these NSAIDs could well have an impact on the postoperative outcome after third molar surgery [3].

Pharmacology

Ibuprofen and Aceclofenac are both NSAIDs. Both inhibit cyclooxygenase enzyme system and hence reduce the biosynthesis of prostaglandins.

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Mechanism of Action of NSAIDs

Prostaglandins, prostacyclin (PGI_2) and thromboxane A_2 (TXA_2) are produced from arachidonic acid by the enzymes cyclooxygenase which exists in a constitutive (COX-1) and an inducible (COX-2) isoforms. COX-1—'house keeping' functions and present in most of the cells of the body. COX-2—normally not present, but induced by certain serum factors, cytokines and other signal molecules at the site of inflammation.

Ibuprofen

Ibuprofen was the first member of propionic acid derivatives class and it was introduced in 1969. It is supplied as tablets containing 200, 400, and 600 mg and also 100 mg/5 ml suspension.

Mechanism of Action

Inhibitor of cycloxygenase in the process of prostaglandin synthesis.

Pharmacokinetics and Metabolism

Rapidly absorbed after oral administration. Peak plasma concentration—after 15–30 min. Its plasma half life—2 h. It is 99% bound to plasma protein. It is excreted 90% through urine.

Indications

Osteoarthritis, Rheumatoid arthritis, musculoskeletal disorders, soft tissue injuries, pelvic inflammation, cervical spondylitis, dysmenorrhoea, and tooth extraction.

Adverse Effects

GI side effects experienced by 10–15% of patients. Epigastric pain, nausea, heart burn, sensation of fullness in GI tract. Rarely—thrombocytopenia, skin rashes, headache, dizziness and blurred vision.

Aceclofenac

Aceclofenac is an orally administered phenyl acetic acid derivatives with effects on a variety of inflammatory mediators.

Mechanism of Action

Inhibitor of cyclooxygenase (with selectively COX2 being evident).

Pharmacokinetics and Metabolism

Rapidly absorbed after oral administration. Peak plasma concentration—1–3 h. Plasma half life—4 h. Highly protein bound. 80% excreted in urine and 20% in faeces.

Indications

Pain, inflammation or degenerative arthropathies. Osteoarthritis, Rheumatoid arthritis. Ankylosing spondylitis. Post trauma or post operative inflammation.

Adverse Effects

GI side effects experienced by 2–5% of patients—Dyspepsia, abdominal pain, nausea, diarrhoea, flatulence, gastritis, constipation, vomiting.

Rarely—dizziness (1%), vertigo (0.3%), tremor. History of hypersensitivity [4, 5].

Materials and Methods

The present study was conducted at department of Oral & Maxillofacial Surgery, Modern Dental College & Research Centre, Indore. Approval for this study was obtained from ethical committee. A written informed consent was taken in patient's own mother tongue. The study group comprised of sixty subjects. Age group of 18–40 years. Conducted as a double blind, comparative randomized study.

Inclusion Criteria

Mesioangular totally or partially impacted asymptomatic mandibular third molar.

Patient not having pericoronitis or periapical abscess at the time of removal. All cases were operated on by a single operator.

Exclusion Criteria

History of allergy to local anaesthetic agents were excluded.

Patients with serious renal, hepatic, respiratory, cardiac, endocrine or metabolic impairment, persistent mental confusion, active gastrointestinal symptoms, pregnant or lactating, asthmatic, drug or alcohol misuse or those who

required antibiotic or corticosteroid prophylaxis were excluded from the study.

Procedure

The subjects were explained about the surgical procedure and the nature of the study and after the subject's approval for the procedure, prior to treatment, pertinent data was recorded as per the proforma regarding the name, age, sex, address, date and medical history. This was followed by a clinical, radiological and hematological examination.

The subjects underwent the surgical removal of similarly impacted (mesioangular) mandibular third molar by the same operator. Drugs administered for the study were Ibuprofen (Brufen) and Aceclofenac manufactured by Nicholas Piramal Limited. Both the drugs were packed separately in coded jars. Distribution of drugs and follow up measurements were done by a third person, not by principal investigator. Decoding of samples was done only after completion of study for evaluation of results.

Patients were randomly subdivided into two groups of 30 each—Group I for Drug A and Group II for Drug B.

Following parameters was then studied:

Trismus

Maximum mouth opening was recorded preoperatively between the incisal edges of upper and lower central incisors by using vernier calliper. Patients were reexamined and mouth opening was recorded on first, third and seventh postoperative days [6].

Swelling

Preoperatively, the swelling was measured by taking a horizontal distance from the corner of the mouth to the lobe of the ear and a vertical distance between outer canthus of the eye and angle of lower jaw using silk suture following the natural convexity of the patient's face. The procedure was repeated on first, third and seventh postoperative days [6].

Pain

The patients were asked to rate the pain intensity on 5 point visual analogue scale as—0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain, 4 = very severe.

Assessment of degree of pain relief on 5 point VAS

0 = complete, 1 = good, 2 = moderate, 3 = some, 4 = no relief

To compare the onset of action of each drug, the patients were examined for analgesic activity on first 24 h.

Observations and Results

Master charts were prepared to facilitate analysis of data recorded. After analysis it was sorted into various tables and graphs based upon the parameters of this study.

In the present study, efficacy of Ibuprofen 400 mg was compared with Aceclofenac 100 mg in 60 subjects between age group of 18–40 years. After completion of study, on decoding of samples it was found that Drug A was Aceclofenac 100 mg and Drug B was Ibuprofen 400 mg.

The results were statistically analysed to get a probability (P value) using "Student's t test."

Table 1, bar chart 1—shows mean, standard deviation, range and significance of pain intensity. Non significant differences were observed for pain intensity between Drug A and Drug B with a 't' value of 1.29 and probability of 0.201. Highly significant differences were observed for pain relief between Drug A and Drug B with a 't' value of 3.07 and probability of 0.003.

Table 2, bar chart 2—shows the mean, standard deviation, range and significance of swelling as can be seen the mean scores for facial measurements for both the drugs on preoperative and various postoperative days which shows that the mean scores are less for Drug A but the difference is not significant ($P > 0.5$).

Table 1 't' Test values of pain intensity, drug effectiveness and pain relief

Parameters	Mean Drug A	Mean Drug B	t value	Probability	Significance
Pain intensity (VAS)	2.2	2.0	1.29	0.201	NS*
Drug effective in (min)	30.5	25.8	3.06	0.003	HS**
Pain relief (VAS)	1.3	0.6	3.07	0.003	HS

* Non-significant

** Highly significant

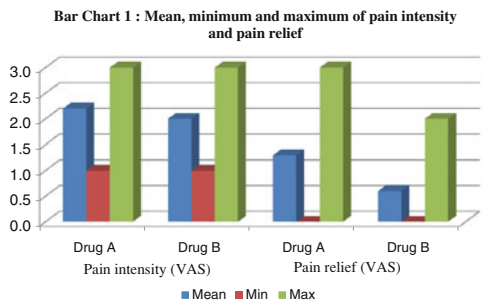

Table 2 '*t*' Test values of facial swelling (mm)

Parameters	Mean Drug A	Mean Drug B	*t* value	Probability	Significance
Pre op	109	111	1.64	0.106	NS
1st day	113	114	0.63	0.529	NS
3rd day	114	117	2.06	0.043	Significant
7th day	113	113	0.16	0.869	NS

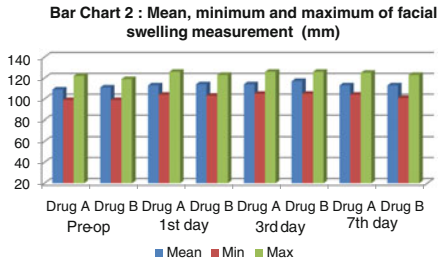

Table 3 '*t*' Test values of measurement of trismus (mm)

Parameters	Mean Drug A	Mean Drug B	*t* value	Probability	Significance
Pre op	37.6	37.3	0.30	0.762	NS
1st day	33.7	34.6	0.99	0.324	NS
3rd day	31.0	30.4	0.75	0.457	NS
7th day	35.9	36.1	0.25	0.800	NS

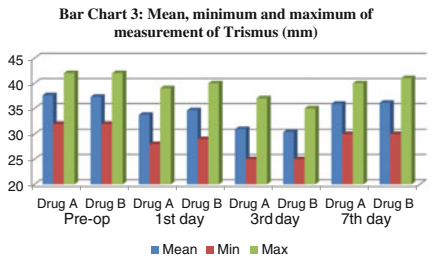

Table 3, bar chart 3—shows the mean, standard deviation, range and significance of trismus. As can be seen the mean interincisal opening for both drugs on preoperative and various postoperative days and their respective '*t*' values which shows no significant difference between the two drugs ($P > 0.05$).

Discussion

Removal of an impacted lower third molar invariably causes some degree of pain, swelling and trismus. Indeed, the immediate post operative sequelae of pain, swelling and trismus provide a useful clinical model for evaluating the efficacy of analgesics and anti-inflammatory drugs [2, 7]. Pain is often of short duration and is usually accompanied by buccal swelling and trismus [3].

There is evidence to state that postsurgical dental pain levels are at their greatest 4–6 h postoperatively. Various doses of Ibuprofen has been used to study dose response relationship after third molar surgery out of which Ibuprofen 400 mg provided maximum relief and the longest duration of analgesic effect. This was the reason for using ibuprofen 400 mg in the present study. Similarly Aceclofenac was prescribed at a dose of 100 mg as recommended for management of dental pain [2].

In the present study, the efficacy of ibuprofen 400 mg was compared with Aceclofenac 100 mg and visual analogue scale was used to measure the intensity of pain at various stages in the post operative period. In various studies done by Jatin Kalra et al. [2], Seymour et al. [3], Habib S et al. [8], Vogel et al. [9] and Mc Quay et al. [10] found that Ibuprofen is an effective analgesic in the control of postoperative dental pain and the results of this study support that finding. Patients treated with ibuprofen 400 mg experience less pain and better pain relief than those treated with aceclofenac. Aceclofenac, which specifically inhibits COX-2, provided consistent efficacy in a standard analgesic model of post dental surgery pain.

Statistical results of present study show significant to highly significant difference for drug effectiveness and pain relief between ibuprofen and Aceclofenac ($P < 0.05$) which indicates ibuprofen has a marginal edge over Aceclofenac.

Post-operative swelling or edema is the result of inflammatory exudate. It is due to combined action of the inflammatory mediators that induce vasodilatation and mediators that are responsible for increase in vascular permeability. It is also a possibility that post-operative swelling might contribute to the post-operative pain because of increased tension in the tissues [2].

For the accurate measurement of post-operative swelling, an objective, reliable, but simple method is required. In the literature, various methods for this have been advocated [11–13]. In the present study, the technique advocated by Amin and Laskin [2] to measure extraoral swelling was used. As can be deduced from the equation described in material and method, facial measurement reflects changes in both horizontal and vertical measurements. Also, lesser scores for percentage reduction mean that there is less post-operative swelling [2].

A prophylactic course of antibiotic was given to all the patients to avoid any possibility of infection that otherwise might lead to exaggerated post-operative swelling.

Statistical results of present study show no significant difference between ibuprofen and Aceclofenac ($P < 0.05$) which indicates that anti-inflammatory activity of ibuprofen and Aceclofenac are almost same.

Archer defined trismus as an inflammation of the muscles of mastication with edema preventing flexibility. In a clinical setup, the best way to measure is by determining the patient's ability to open the mouth. This in turn is determined by measuring the distance between the incisal edges of upper and lower central incisors on pre-operative and various post-operative days [2]. The method is simple, reliable and reproducible. The similar method has been employed in other studies [1, 2, 7, 14–20].

In the present study, after comparing the scores on various post-operative days, it was found that there was no statistical difference between the two groups in post operative mouth opening.

Almost in all the available studies, only the analgesic efficacy of Aceclofenac and ibuprofen is compared. But in our study, efficacy of Aceclofenac in controlling postoperative edema and reduction in mouth opening has also been compared. Both of these factors are essential for patient's overall recovery and therefore play a major role in selection of anti-inflammatory agents.

Conclusion

This study was an attempt to evaluate and compare the efficacy of Ibuprofen and Aceclofenac in controlling postoperative sequelae after third molar surgery. The present study was randomized, double blind conducted on 60 subjects to compare the pain intensity, drug effectiveness, drug relief for the first 24 h, swelling and trismus at immediate post operative, 1st, 3rd and 7th day for both the drugs. The study was carried out by a single experienced operator to standardize the findings. Pain relief was more profound with patients dosed with ibuprofen as compared to Aceclofenac. One patient had to be given rescue medication when he did not get pain relief.

The results of the present study indicate that Ibuprofen was more effective and its onset of action was earlier and the analgesic action lasted for longer time as compared to Aceclofenac in a third molar surgery model. Although statistically there was not much difference noted between Ibuprofen and Aceclofenac on the effect of trismus and anti-inflammatory action.

Both the drugs are easily available, it is found that Ibuprofen is more economical and cost effective as compared to Aceclofenac. Both drugs were well accepted by the patients with no reported adverse effects.

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