

Premedication with Diclofenac and Other Drugs To Prevent Postoperative Pain after Lower Third Molar Removal: A Systematic Review

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Abstract

Background and Objective: The demand for third molar extraction among adult patients is increasing in our society. Currently adult patients seeking the wisdom removal for either orthodontic treatment or functional improvement or both. The drawback of going through third molar extraction among adults is the duration of pain after the extraction that could take up to 10 days. However, the main issue is the nature of pain after like this procedure. Premedication by Diclofenac is conservative step that is aimed to reduce the duration of pain and postoperative complications. The aim of current review is to collect all updated and available studies including imperative information concerning the efficacy and high tolerability of Diclofenac in the preoperative reduction of pain following third molar extraction.

Material and Methods: Two automated databases (Google Scholar and PubMed using English-language literature) were used for this systematic review, using specific keywords together with inclusion and exclusion standards. All included studies in this review from 1987 to 2019 were RCT, Cohort, and Control group (placebo or any other drug). Also, VAS was our Pain assessment tool. Data about relief postoperative pain were extracted and analyzed.

Results: Search detected sixteen studies that achieved the present inclusion and exclusion criteria. These studies illustrated different aspects of Diclofenac, including: Intervention, Control, Pain assessment, Associated Postoperative medication, Side effects, and updating studies in Diclofenac as premedication.

Conclusion: It is possible to effectively make a minimum postoperative pain by a preoperative per oral or systemic single-dose regimen of diclofenac.

Keywords: Premedication; Diclofenac; Third Molar; Postoperative Pain

Introduction

Third molar (wisdom) removal is one of the common surgical procedures performed as a day-case procedure in the oral surgery clinics [1]. Removal of third molars generally causes postoperative pain, difficulty in opening the mouth and facial swelling which are the most common side effects that affect the patient's quality of life in the early days following operation; particularly pain which is considered incapacitating to patient daily activity [2]. Whether, it's indicated for extraction or not, dealing with pain following the surgery in of prime importance [3]. Many disadvantages of third molar if not erupted properly include: pericoronitis, caries, infection, cystic lesions particularly (Dentigerous cyst) and resorption of the adjacent tooth [3]. However, Postoperative pain following surgical removal of impacted

mandibular third molar is decreased by using analgesics (pain killers) and long-acting local anesthetics [4]. Synthesis of prostaglandins, which are important mediators in pain pathway and the administration of nonsteroidal anti-inflammatory drugs preoperatively [5]. Pain prevention is achieved when the peak plasma level of analgesic coincides with maximum pain sensation “5 - 12 hrs” when postoperative pain is at its maximum [5]. One of the common and popular drugs used in reduction of pain following 3rd molar removal are non-steroidal anti-inflammatory drugs (NSAIDs) [6]. One of the famous remedies of the former family is the Diclofenac Sodium [7]. It is well-known by its long term analgesic effect [8].

The aim of current study is to initiate the treatment at an earlier stage than in the past prior to starting the extraction procedure, because it has been shown that postoperative pain can be avoided almost totally through analgesic premedication [9]. There are several studies that were conducted to discuss different drugs to use as postoperative pain. However, few studies have investigated Diclofenac as preoperative medication. Consequently, this reviews aim was to collect all updated and available studies including imperative information concerning the efficacy and high tolerability of Diclofenac in the preoperative reduction of pain following third molar extraction.

Materials and Methods

The following question was asked: “Does Preoperative Administration of Diclofenac reduces Postoperative Pain Following removal of Lower Third Molar?”. Related articles were found and studied. The search strategy was based on PICO question presented in table 1.

Item	Inclusion Criteria
Population	Adult patient, third molar indicated for extraction
Intervention	Diclofenac
Control	Placebo or any other drug
Outcome	Post-operative pain

Table 1: PICO terms.

Criteria for considering studies for this review

The sum up of the inclusion and exclusion criteria for articles is found in table 2. Studies were Randomized Clinical Trials (RCT), Cohort, and Control group “placebo or any other drug”. Also, visual analog scale (VAS) was our Pain assessment tool that was considered in this search.

Inclusion	Exclusion
Adult Healthy patient, third molar indicated for extraction	-
Pain assessment tool VAS (visual analog scale)	-
RCT Cohort studies Control group (placebo or any other drug)	Case series Literature review Letters to editors
English language	Animal study, <i>In-vivo</i>

Table 2: The standards for inclusion and exclusion of the studies.

Search strategy

A web search was done through PubMed and Google Scholar from January 1983 to May 2019, were searched using MeSH terms based on the PICO question in table 1. The MeSH words were: “Diclofenac”, “Third molar”, “postoperative pain”, “Extraction” or “Removal”, “Preoperative”, and “administration”. The reason for exclusion for each study was recorded. Table of evidence was formulated in table 3. Full articles were obtained for most of the titles and abstracts that met the inclusion criteria. From each included article, Study design, population, interventions and controls, and findings were extracted. A summary of this review search strategy was summarized in figure 1.

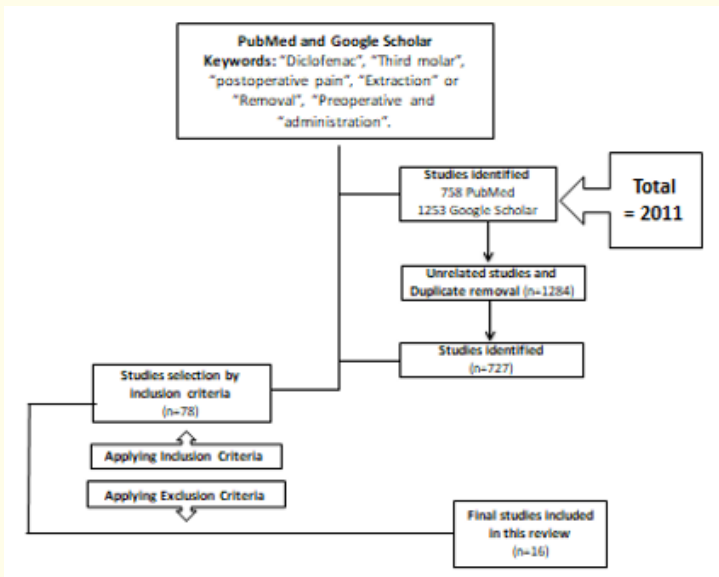


Figure 1: Flow chart of the electronic search strategy used in this systematic review.

Results

The search detected sixteen studies that achieved the present inclusion and exclusion criteria.

The studies included in this review were randomized controlled trial studies “RCT” [3,5,7-20]. The review included sixteen studies with a total sample of 1281 subjects. In all of the studies, the diclofenac medication was used with systemically healthy persons and the third molar was indicated for extraction. These studies illustrated different aspects of Diclofenac, including: Intervention, Control, Pain assessment, Associated Postoperative medication, and Side effects. All included studies were summarized in table 4.

Authors	Intervention	Control	Pain assessment	Associated postoperative medication	Side effects	Outcomes
Wuolijoki E., et al. [7]	75 mg per 3 ml IM.	Placebo injection + placebo tablets Also, placebo injection + diclofenac 50 mg	VAS	Penicillin 660 mg or erythromycin 500 mg Veralgin 5 P. O	Common side effects of NSAIDS	The preoperative administration of diclofenac relieved pain most effectively Veralgin used least in the preoperative diclofenac group
Hyrkas T., et al. [5]	Rapid release diclofenac 50 mg, retarded-release 100-mg tablet PO.	Diclofenac 50mg p.o + placebo Placebo tablet + placebo injection	VAS	Lidocaine (20mg/mL) plus epinephrine (12.5 pg/ mL). once daily orally for 1 week, Dolorin tablets.	Nausea, Vomiting, Headache, Drowsiness, Dizziness	During the first 4 hours, pain was most effectively relieved by Diclofenac. In comparing placebo with Diclofenac, the number of rescue drugs given preoperatively were smaller in Diclofenac group than placebo.

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Hyrkas T., <i>et al.</i> [10]	Single dose of 75 mg Sodium diclofenac IV.	Saline (diluted diclofenac with saline to 100 ml)	VAS	Penicillin 660mg or erythromycin 400mg q8h for 1 week Dolorin as needed	Nausea	Diclofenac given preoperatively by IV route gave greater pain relief than placebo for the 1 st 3 hours.
Hyrkas T., <i>et al.</i> [11]	150-mg diclofenac 20 min before surgery. long acting bupivacaine	150-mg diclofenac 20 min before surgery. short acting lidocaine	VAS	660 mg phenoxymethyl penicillin or 400 mg erythromycin acistrate analgesia Aminopyrine 300 mg, 30mg codeine phosphate, 50 mg phenobarbital, and 100 mg caffeine.	Nausea	Pain after surgery is best reduced by use of a long-acting local anesthetic and preoperative administration of a NSAID.
Bakshi R., <i>et al.</i> [8]	Diclofenac 50 mg.	Ibuprofen 400 mg and placebo.	VAS		Gastrointestinal	Diclofenac quick onset is clinically important.
Zacharias M., <i>et al.</i> [12]	100 mg Diclofenac (60 to 90 minutes) prior to surgery.	Placebo or methadone 10 mg. 60 to 90 min prior to surgery	VAS	20 mg Tenoxicam + 1g Paracetamol + 30 mg codeine	Nausea, abdominal discomfort, vomiting, sleepiness, and tiredness	Continued use of analgesic drugs during the postoperative period is perhaps more useful than preoperative
Lin TC., <i>et al.</i> [13]	50 mg diclofenac PO	Prednisolone (10 mg) + Diclofenac (50 mg) Or placebo	VAS	Analgesics	-	Better analgesic and anti-inflammatory effect were shown with Diclofenac and Prednisolone.
Joshi A., <i>et al.</i> [14]	Ibuprofen 600 mg or diclofenac 100 mg or paracetamol 1 g + codeine 60 mg PO.	(50 mg) Vitamin C	VAS	GA (Propofol, fentanyl)	Nausea, vomiting, dizziness	There was no significant difference in VAS reading between the 4 groups. however, diclofenac had a higher median (32 min) for the 1 st request of postoperative analgesics
López-Carriches C., <i>et al.</i> [15]	Diclofenac	Methylprednisolone	Semi-quantitative and VAS.	Amoxicilin 750 mg and Magnesium metimizol 575 mg.	Nausea, vomiting, headache, gastrointestinal pain, infection and cicatrization.	Patients treated with corticoids feel less pain.

Presser Lima PV, <i>et al.</i> [3]	2 tab (100 mg) aceclofenac PO 1h pre-operative	2 tab (100 mg) aceclofenac PO postoperative	VAS	Acetaminophen	-	Aceclofenac more efficient when taken preoperative
Oncul AMT, <i>et al.</i> [16]	Diclofenac 75mg IM	8mg lornoxicam IV - 1g paracetamol IV	VAS -VPS (Verbal pain scale)	875 mg Amoxicillin hydrate PO and 125 mg Augmentin twice a day for 5 days	Nausea, vomiting, dizziness	IM diclofenac, IV paracetamol or Lornoxicam reduced the postoperative pain intensity.
Pandit MK, <i>et al.</i> [9]	Diclofenac 75mg IV	Tramadol 50mg IV	VAS	(paracetamol 500 mg)	-	preoperative IV diclofenac more effective than tramadol
Shadab Mohammad, <i>et al.</i> [17]	40 mg sublingual piroxicam	150 mg oral Diclofenac	VAS	Amoxicillin 500 mg	Gastrointestinal disturbances	Better efficacy for piroxicam group.
Solis MO, <i>et al.</i> [18]	100 mg of Diclofenac PO	Meloxicam (15 mg).	VAS	Oral Acetaminophen Sub-lingual ketorolac	-	Both reduced post op pain however 15mg meloxicam had less postoperative pain scores than 100mg diclofenac.
Kaplan V, <i>et al.</i> [19]	Diclofenac sodium 100 mg tablet PO.	Flurbiprofen 200mg + Tenoxicam 20mg.	VAS	CHX Acetaminophen	-	Chlorhexidine gluconate 4%. As a rescue analgesic, (paracetamol)
Zupelari-Goncalves P, <i>et al.</i> [20]	Diclofenac 50 mg	Codeine 50 mg	VAS	Paracetamol (acetaminophen)	-	Better pain management of oral Diclofenac with Codeine.

Table 4: Summary all included studies in this review.

Discussion

Diclofenac Sodium is a non-steroidal anti-inflammatory drug that is well-known with its analgesic effect in the minimizing of postoperative pain following 3rd molar extraction [20,21]. The review presents a comprehensive compilation of evidence taken from sixteen articles which included original studies. The sample size was up to 1281 subjects seeking lower third molar removal by surgical extraction. All included studies confirmed best way to prevent the postoperative pain by using of Diclofenac as premedication for lower third molar extraction.

Systematic review conducted to summarize, locate, appraise and synthesis all high quality research evidence scientific experimental studies relevant to scientific research question. The question of this review is “Does Preoperative Administration of Diclofenac reduces Postoperative Pain Following Surgical removal of Lower Third Molar?”. This review use an electronic search only and the result limited to articles that can found a full article. Consequently, the results of all relevant studies were not included in our systematic review. Furthermore, the current review included 16 studies conducted to relieve the pain that is resulted following wisdom tooth extraction with the ethical aim that it is not possible to leave the patient with such amount of pain without giving appropriate analgesic effect that fulfill all the necessary medical requirements [5,10,11]. The review discussed the role of Diclofenac as preoperative medication. Most of investigations in this review showing the diclofenac have significant anti-inflammatory and analgesic activities in preventing postoperative pain after third molar extraction [9]. When administered preoperatively, diclofenac gave better pain reduction than its postoperative administration. Indicating that, early inhibition of the inflammation resulting from operative trauma provides the best pain relief [9].

The new era in pain management and patient comfort necessitated the creation of such type of remedy that cure, minimize and inhibit as much side effects as possible following such type of treatment following third molar extraction. The most effective route of diclofenac is when administered intravenously [7]. Side effects following intravenous administration including irritation at the site of needle injection should also be expected in mind [5,10,11]. The intravenous administration is actually the simplest way to make sure that optimum plasma levels at the time of surgical intervention [5,7,10,11]. The preoperative administration of NSAIDs in general regresses the synthesis of arachidonic acid metabolites such as prostaglandins and thromboxanes that facilitate the process of inflammation [12,22]. Diclofenac inhibit the enzyme cyclo-oxygenase that is important in the metabolism of arachidonic acid. Acetylsalicylic acid is important in pain prevention [9]. In comparing the NSAIDs with opioids in pre-emptive way, they both confirmed their beneficial effect preoperatively than postoperatively [14]. The common side effects following Diclofenac Sodium administration includes: nausea, vomiting, headaches and gastrointestinal discomfort [14]. Visual analogue scale is the most common and the most severe one in assessing pain quality among patients [23]. It is important to differentiate between measurement of pain and experimental pain where in experimental pain the pain is measured in terms of intensity of stimulus [24].

Conclusion

The current systematic review of the literature indicates the early postoperative hours; Diclofenac is effective in minimizing the pain resulting from the extraction of impacted mandibular third molars when administered preoperatively. It is possible to perfectly make a minimum postoperative pain by a previous per oral or systemic single-dose regimen of Diclofenac. However, we should take into consideration the pharmacokinetics/dynamics properties of NSAIDs and the medical status of the patient.

Conflict of Interest

None.

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