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## Efficacy of ibuprofen versus meloxicam in post-surgical pain control after lower third molar surgery

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#### Abstract

Post-surgical pain is a direct consequence of the surgical event, being closely related to inflammation after treatment, both manifesting itself in parallel. Nonsteroidal anti-inflammatory drugs have been considered the analgesic therapy of choice.

**Objective:** To compare the analgesic effectiveness of ibuprofen against meloxicam after surgical intervention to remove the lower third molar.

**Materials and Methods:** A total of 30 patients were assigned to the two treatment groups: 15 from to ibuprofen group and 15 to the meloxicam group. The first dose was administered at the end of the surgery and the necessary tablets were given to complete the 3-day drug treatment regimen, as well as 1 sublingual ketorolac tablet as rescue medication. Postoperative pain reduction was evaluated making phone calls to evaluate pain by using the numerical scale of pain at 24, 48, 72 hours and 7 days postoperatively.

**Results:** Meloxicam is more effective over time, showing stable analgesic levels and less pain than the ones in ibuprofen group. However, its maximum effect takes longer, which explains that some patients required rescue medication in the first postoperative hours.

**Conclusions:** Due to its analgesic, anti-inflammatory and antipyretic effect, we can consider meloxicam as a good alternative in postoperative pharmacological treatment. It is suggested the use of some other drug that achieves pharmacological synergy to optimize results or to use meloxicam based on preventive analgesia models.

Keywords: Ibuprofen, meloxicam, postsurgical pain, third molar

### Introduction

After performing third molar surgeries, patients experience a clinical picture characterized by pain, edema, and trismus, which limits them in performing their routine activities; pain being one of the most prevalent side effects and produces a considerable degree of fear in patients. Pain control arising from invasive interventions in the buccal cavity is a common clinical problem. It is known that the mismanagement of this postoperative symptom exerts a negative influence on the physical, mental and social health of patients [1].

Therefore, post-surgical pain secondary to the extraction of third molars is the most studied model in oral surgery. This type of pain is a consequence of nociceptive stimulation after surgical aggression, muscle spasms, nerve injuries and in general all the actions involved during the operative act. Thus, pain and inflammation are intimately related, manifesting themselves in parallel. According to the literature, the pain after surgical intervention of these dental organs is usually moderate to severe, developing mostly in the first 24 hours reaching its peak at 3-8 hours postoperatively <sup>[2, 3, 4]</sup>.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) have been shown to be effective for the treatment of mild to moderate postoperative pain, with first-line analgesic therapy considered for included third molar surgery. They inhibit the synthesis of prostaglandins and thromboxanes, reducing their activity, by blocking cyclooxygenase enzymes. Of these, it is known that it occurs in two isoforms, COX-1 that is expressed in a stable and continuous way

in most of the cells of the organism, responsible in addition to physiological functions and COX2, isoform undetectable in basal conditions in most tissues, mediator of responses to pathological processes, such as inflammation, pain and fever <sup>[5]</sup>. As a result of the fact that there is a wide variety of analgesics available, it has become necessary to know those that provide better analgesia with a small number of adverse effects. That said, in the present study the analgesic effectiveness of two non-steroidal anti-inflammatory drugs after surgery of the lower third molar was evaluated with the aim of evaluating the efficiency of two analgesics in the postoperative treatment of this procedure. For this study, a non-selective inhibitor, Ibuprofen, was selected, and the other is a COX-2 preferred inhibitor, Meloxicam.

### Materials and Methods Sample

It is represented by 30 male and female patients aged between 18 and 60 years who required surgery of the lower third molar for various dental indications and went to the maxillofacial clinic of the Faculty of Universidad Autónoma de Coahuila, Torreón Unit.

### **Inclusion criteria**

Patients between 18 and 60 years of age who signed the informed consent sheet, who did not present any systemic disease (ASAI) or presented mild to moderate systemic disease, without functional limitation (ASAII). With the ratio of the lower third molar with respect to the ascending branch of the jaw and the second molar found in class I and II according to classification of Pell and Gregory. With relative depth of the lower third molar in the bone found in position A and B according to classification of Pell and Gregory. Position of the lower third molar in relation to the longitudinal axis of the second molar found in a mesioangular, horizontal,

vertical and distoangular direction according to winter's classification. Patients who required unilateral inferior third molar exodontia surgically in which minimal flap and osteotomy should be performed.

### **Exclusion criteria**

Patients in whom the administration of the drugs under study was contraindicated, patients who are already medicated previously with any steroidal or non-steroidal analgesic, as well as opioids, patients with drug addiction. Patients who have used a drug that interacts with the study drugs. Patient with poorly controlled associated pathology such as: cardiopathy, coagulation disorders, thyroid alterations, etc.

### **Assignment to treatment**

The allocation of medications was in 2 groups divided equally randomly, who received in the immediate postoperative period:

- 1. Flexiver® Meloxicam tablets 7.5 mg, 1 tablet every 12 hours for 3 days.
- 2. Dolprofen® Ibuprofen tablets 600 mg, 1 tablet every 8 hours for 3 days.

Post-surgical pharmacological therapy was complemented with amoxicillin 500 mg, 1 capsule every 8 hours for 7 days and in cases where the patient was allergic, clindamycin 300 mg was chosen, 1 capsule every 8 hours for 7 days. Antibiotic was prescribed according to the case of the patient.

In addition, a sublingual tablet of ketorolac of 30 mg, used as rescue medication, was delivered. It was specified that this drug would only be administered if strictly necessary and notifying it immediately, as well as checking the time at which it was required. Postoperative indications were given verbally and in writing.

### **Procedure**

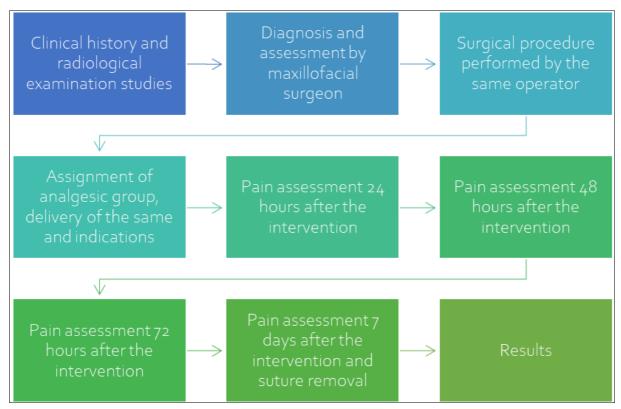


Fig 1: Research protocol diagram. (Own creation)

### Research protocol diagram. (Own creation) Pain assessment

Total consumption of analgesics either meloxicam, ibuprofen and/or ketorolac was recorded. To assess the intensity of the pain, the patient was questioned about their level of discomfort before starting the procedure and immediately after finishing so that they became familiar with the format and took as a reference the degree of discomfort of each of the patients.

The first pain control was performed in the immediate postoperative period. The following pain control shots are performed at 24, 48 and 72 hours after taking the drug by

telephone. In the same way, records of postoperative complications or adverse effects were kept.

Pain assessment was performed using a numerical verbal scale, where 0 is the absence of pain and 10 is the maximum pain imaginable. According to the patient's criteria, the values corresponding to pain assessments were assigned in all categories.

Considering that the parameters to be assessed are totally subjective and for statistical reasons, the values of the numerical scale were categorized to unify assessments of each patient. For this, the following categories were assigned by self-authorship:

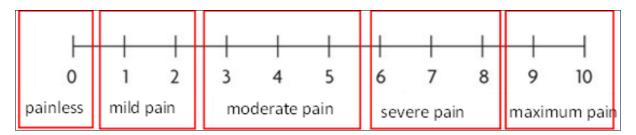


Fig 2: Pain assessment scale. (Own creation)

### Results

The results of this research were concentrated in tables, obtained with the statistical program SPSS, IBMTM 2018. Surgical extraction of the lower third molar was performed in a total of 31 patients between 18 and 56 years, with an average of 25 years and weight in kilograms of between 48 and 86 kg with an average of 66.50 kg. Of these, 1 patient was eliminated due to postoperative complication (paresthesia). That said, our total sample was 30 patients, of which 11 men represented 36.7% and 19 women representing 63.3%.

In the first pain assessment, which corresponds to the 24 postsurgical hours, a higher percentage of patients undergoing third molar extractions and receiving analgesic therapy with meloxicam, had no pain (4 cases) or had mild pain (9 cases); compared to those who were being treated with ibuprofen, of those who had no pain (4 cases), or had mild pain (4 cases). The rest of the patients with meloxicam reported moderate pain at 24 hours (1 case) or severe (1 case) against those in the ibuprofen group where more patients reported moderate pain (3 cases) and severe pain (4 cases).

Regarding the intensity of pain at 48 hours after taking the analgesic, most patients in the meloxicam group maintained a pain level at 0 (8 cases), some others reported mild pain (6 cases) and the remaining patient manifested moderate pain (1 case). On the other hand, those in the ibuprofen group reported not feeling pain or mild pain in a smaller amount (4 and 5 cases respectively), and the rest reported moderate or intense pain (5 and 1 case respectively).

In the 72 hours after surgery and administration of the analgesic, 11 of the patients treated with meloxicam had no pain compared to 5 of the patients who were on ibuprofen treatment, 4 of the patients in the meloxicam group and 6 of the ibuprofen patients manifested mild pain. In the rest of the categories, only 3 cases of moderate pain and 1 of intense pain were recorded, said belonging to ibuprofen. There were no complications associated with the surgical procedure and none of the patients reported adverse effects associated with the medications.

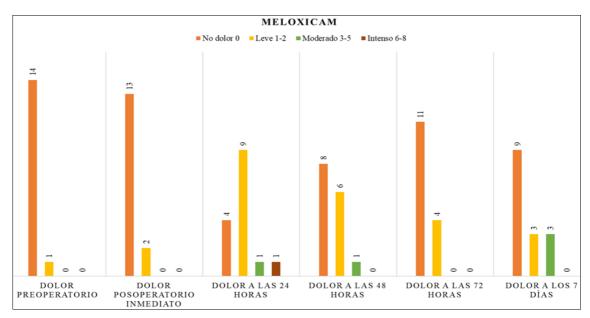
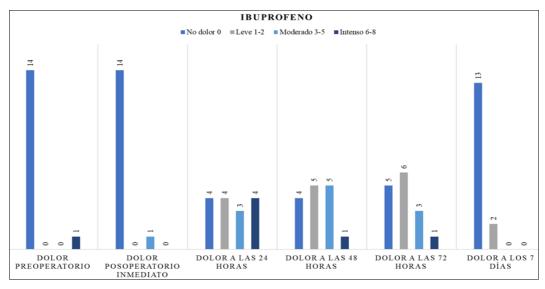


Fig 3: Results pain level with meloxicam group in preoperative pain level, immediate postoperative, at 24, 48, 72 hours and 7 postoperative days. Total, shows 30. (Own creation)



**Fig 4:** Results pain level in ibuprofen group in preoperative pain level, immediate postoperative, at 24, 48, 72 hours and 7 postoperative days. Total, shows 30. (Own creation)

However, 53.3% of the patients included in the study (16 cases) reported sublingually placing the rescue drug, against 46.7% (14 cases) of those who only administered orally the analgesic indicated according to randomization of the study. It should be noted that of the 53.3% of patients (16 cases) who confirmed having required the rescue medication for having felt very intense pain, 10 patients belonged to the meloxicam group and 6 to the ibuprofen group.

The hours after the procedure where patients considered it necessary to go to the rescue medication were counted, obtaining that in the meloxicam group 8 of 10 patients required greater analgesia in a time less than 12 hours after surgery, having as a more repeated schedule that of 4 hours after the procedure (4 cases). On the other hand, from the ibuprofen group it was reported that the need for rescue medication was more frequent after one postoperative day, with the 72 hours after the most repetitive response (2 cases). Our study agrees with the literature found on the pharmacokinetics of each drug, especially the onset of action and the maximum concentration of each of them, was key to the evolution of our patients. Knowing the pharmacology of the medicines used is of vital relevance for decision-making in the dental field.

El analgésico meloxicam demostró ser más eficaz al paso de los días que ibuprofeno, con el inconveniente de que su inicio de acción es más lento por vía oral, lo que explica el mayor uso de medicación de rescate en las primeras horas postquirúrgicas. Cabe destacar que la incidencia de mayor dolor está estimada en función del umbral del dolor e impresiones subjetivas personales.

### Discussion

The analgesic effect of both meloxicam and ibuprofen has been evaluated in some previous clinical studies compared to other NSAIDs in third-molar surgery. Meloxicam has been compared fewer times than ibuprofen in oral surgery models. In a clinical trial by De Menezes and Cury (2010), 100 mg of nimesulide per day was compared to 7.5 mg of meloxicam twice daily, both for 5 days in the control of pain, inflammation, and trismus after removal of the retained third molar. The results obtained indicated adequate and similar analgesic effects in both drugs, with slight greater efficacy in the nimesulide group in control of inflammation and trismus. Two years later, Rafael Linard and colleagues conducted

research on the effect of partially COX-2 inhibitory NSAIDs in third-molar surgery model. 100 gr of nimesulide or 7.5 gr of meloxicam were administered every 12 hours for 2 days, obtaining that nimesulide demonstrated greater efficacy in pain control due to the lower number of rescue medication and lower levels of pain <sup>[6,7]</sup>.

In this research we agree with a previous comparative study between ibuprofen, meloxicam and diclofenac sodium carried out by Carlos A. Puhueyestewa-Sarango and collaborators in 2017, where pain after surgical extraction in third molars class I position A was evaluated in 15 patients. It was observed that in the diclofenac group the pain values were higher even on the third day, compared to the ibuprofen group where pain manifested itself in the first 24 and 48 hours, decreasing considerably on the third day. However, a significant difference was found in the meloxicam group, where patients manifested very mild pain at 24 hours, noticing its absence at 48 and 72 hours [8].

Similarly, we agree with the clinical trial conducted by Steven E. Christensen and colleagues (2018), where the levels of analgesic effectiveness of meloxicam were higher than those of ibuprofen after surgery of the lower third molar. Notably, this study was based on intravenous administration of meloxicam <sup>[9]</sup>.

In the present study, meloxicam exhibits a significant analgesic effect during the postoperative week compared to ibuprofen. The group of patients who received meloxicam showed greater intensity of postoperative pain in the first 4-12 hours following the intervention than in the 12-24 hours; these values decreased continuously during the following follow-up sessions. This result is consistent with the pharmacokinetics of the drug, since after oral administration, maximum plasma concentrations are reached at 4.9 hours, experiencing a second gastrointestinal recirculation, observing a second peak of maximum concentration at 12-14 hours. [10].

### Conclusion

In oral surgery, an inflammatory process is set in motion that has as fundamental symptoms the swelling of soft parts associated with different degrees of trismus and a painful picture of the intervened area. The minimization of these manifestations is directly reflected in the improvement of patients' quality of life, as well as a high degree of satisfaction with treatment. This study tries to contribute to the scientific

evidence and clinical experience to add protocols that help us unify criteria and serve as a guide.

Based on the clinical experience acquired and based on the literature, it was concluded:

- 1. Meloxicam is more effective over time, showing stable analgesic levels, however, the plasma concentration takes longer to reach its peak than ibuprofen (five hours) which explains the greater number of patients who placed the rescue medication sublingually.
- 2. Ibuprofen takes less time to take effect and reach maximum blood concentrations (orally, one to two hours) but its analgesic effect takes longer to establish itself even after 48 post-surgical hours.
- 3. Due to its indication for moderate acute pain, analgesic effect, anti-inflammatory action and reduced side effects, we can consider meloxicam as a good pharmacological alternative for oral surgical interventions. It is suggested to use a drug that achieves pharmacological synergy to optimize results especially the first 4-12 postoperative hours or to use it based on the model of preventive analgesia or analgesic premedication, in which it would be administered before the procedure.
- 4. Our hypothesis was correct, and the objectives of the study were achieved.

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