

# The use of analgesics and anti-inflammatories in an oral surgery service in Medellín, Colombia, 2013-2015

## Uso de analgésicos y antiinflamatorios en un servicio de cirugía bucal en Medellín, 2013-2015

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### ABSTRACT

**Introduction:** dental surgical procedures trigger an inflammatory response, for which dental practitioners prescribe analgesic and anti-inflammatory medications using pharmacological guidelines that require knowledge on the use of medicines in a given environment. The aim of the present study was to identify the analgesics and anti-inflammatory drugs most commonly prescribed at the oral surgery service of the Universidad de Antioquia School of Dentistry. **Methods:** this retrospective descriptive study reviewed the clinical records of the oral surgery service in the period January 2013-August 2015. A total of 1,177 records were reviewed, and 709 were selected for analysis. **Results:** 53.1% of the drugs prescribed were non-selective Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Ibuprofen was formulated in 26.7% of all cases, followed by nimesulide with 24.1% and the combination of acetaminophen plus meloxicam with 10.2%. This same prescription pattern was observed in patients reporting no additional relevant medical history. In the case of gastric history, nimesulide was the drug of choice. 84% of all procedures were surgical extractions of third molars, with ibuprofen 600 mg postoperative for three days as the main therapeutic scheme. **Conclusion:** ibuprofen, nimesulide, and the combination acetaminophen plus meloxicam were the main analgesics and anti-inflammatory drugs prescribed in this study, according to medical and surgical records.

### Keywords:

analgesics, anti-inflammatory drugs, medical prescriptions, oral surgical procedures

### RESUMEN

**Introducción:** la realización de procedimientos quirúrgicos odontológicos desencadena una respuesta inflamatoria, por la cual el profesional prescribe medicamentos analgésicos y antiinflamatorios teniendo como apoyo guías farmacológicas cuya construcción requiere del conocimiento del uso de los medicamentos en un determinado entorno. El objetivo del presente estudio consistió en identificar los analgésicos y antiinflamatorios más prescritos en el servicio de cirugía bucal de la Facultad de Odontología de la Universidad de Antioquia. **Métodos:** estudio descriptivo retrospectivo en el que se revisaron las historias clínicas del servicio de cirugía bucal en el período comprendido entre enero del 2013 y agosto del 2015. De una revisión de 1.177 registros se incluyeron 709 para el análisis de la información. **Resultados:** el 53,1% de los medicamentos prescritos fueron AINEs no selectivos, el ibuprofeno fue formulado en el 26,7% de los casos, seguido de la nimesulida (24,1%) y la combinación acetaminofén más meloxicam (10,2%). Este mismo patrón de prescripción se apreció cuando el paciente manifestó no tener ningún antecedente médico de relevancia; en el caso de referir antecedentes gástricos, la nimesulida fue el fármaco de elección. El 84% del total de procedimientos fue la exodoncia quirúrgica de terceros molares, en el cual el ibuprofeno de 600 mg posoperatorio durante tres días fue el principal esquema terapéutico. **Conclusión:** el ibuprofeno, la nimesulida y la combinación acetaminofén más meloxicam fueron los principales analgésicos y antiinflamatorios prescritos en este estudio según los antecedentes médicos y el procedimiento quirúrgico.

### Palabras clave:

analgésicos, antiinflamatorios, prescripciones de medicamentos, procedimientos quirúrgicos orales

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## INTRODUCTION

Inflammation is a protective response of the host and is critical in healing; it consists of the release of chemical mediators of plasma or cellular origin. Some of these, such as vasoactive amines, cytokines, reactive oxygen species, nitric oxide, arachidonic acid (AA) metabolites, and neuropeptides induce a vascular and cellular reaction which clinically appears with cardinal signs of inflammation: edema, heat, erythema, pain, and loss of function.<sup>1-3</sup>

Dental surgical procedures such as extraction, implants, and orthognathic surgery trigger the appearance of inflammatory signs with varying levels of intensity depending on the extent of soft and hard tissue manipulation during surgery.<sup>4</sup> Thus, the greater the tissue harm and operation time, the greater the inflammation in the tissues surrounding the surgical area.<sup>5</sup>

In order to reduce the expression of the inflammatory process and postoperative pain in procedures like third-molar surgery, the oral surgeon usually prescribes nonsteroidal anti-inflammatory drugs (NSAIDs), followed by steroids and opioids.<sup>4</sup> Due to their mechanism of action, opioids have a powerful analgesic effect but lack anti-inflammatory activity, while NSAIDs and steroidal anti-inflammatory drugs help control both pain and post-surgical inflammation by inhibiting specific enzymes involved in the synthesis of AA metabolites.<sup>4,6</sup>

NSAIDs suppress the cyclooxygenase pathway (COX), both the COX-1 isoenzyme that primarily mediates physiological processes, and the COX-2, primarily involved in the inflammatory response.<sup>7-9</sup> The inhibition of either enzyme leads to the classification of NSAIDs according to their COX selectivity

profile into non-selective and selective COX-2.<sup>10,11</sup> Non-selective NSAIDs affect both COX-1 and COX-2, while selective COX-2 have a strong affinity for COX-2. As a result of these inhibitory reactions, the synthesis of eicosanoids involved in physiological and pathological functions is blocked, and this is related to the adverse effects of the diverse NSAIDs.<sup>5</sup>

Several adverse effects are associated with the intake of NSAIDs, mainly gastrointestinal and hematological problems, renal alterations, and skin and mucous membranes reactions.<sup>5</sup> Gastrointestinal effects are more marked with the intake of non-selective NSAIDs; while these effects decrease with COX-2 selective NSAIDs, the risk of thrombus formation, myocardial infarction, and stroke generally increase.<sup>5</sup> Bone healing is also affected by the inhibition of processes like the differentiation of osteoblast mesenchymal cells.<sup>12,13</sup>

Steroid anti-inflammatory drugs inhibit the inflammatory response by blocking phospholipase A<sub>2</sub>, which in turn alters the pathway of cyclooxygenase and lipoxygenase, leading to the reduction of leukotrienes and prostaglandins. This mechanism results in a decrease in capillary dilation, leukocyte migration, and phagocytosis, and an overall suppression of all stages of the inflammatory response.<sup>5</sup> In addition, long-term systemic effects may appear after prolonged consumption, including Cushing's syndrome and adrenal-cortisol insufficiency.<sup>5,14,15</sup>

The onset of adverse effects is dependent on factors such as concentration and length of therapy, with risks increasing when there is chronic use.<sup>16</sup> The manifestation of such effects can be therefore prevented by prescribing the minimum effective dose of NSAIDs, conducting therapies of the

shortest possible time, and assessing each patient's individual risks.<sup>17</sup>

Because of the implications of prescribing analgesics, clinicians need to rely on evidence-based information,<sup>16</sup> as empirical therapeutic strategies can produce subtherapeutic effects<sup>5</sup> in addition to the abovementioned adverse effects.

It is critical for dental practitioners to count on information strategies such as pharmacological guidelines and scientifically-supported analgesic protocols to support their prescriptions.<sup>18-20</sup> In order to develop such strategies, it is first necessary to know the use of medicines in a given health environment.<sup>21</sup>

In consequence, the aim of this study is to identify the anti-inflammatory analgesics most commonly prescribed at the oral surgery service of the Universidad de Antioquia School of Dentistry, regarding different dental surgical procedures and patient's systemic records.

## METHODS

This was a retrospective descriptive study classified as a risk-free research project according to Resolution 8430/93 of Colombia's Ministry of Health and Social Protection. This project was carried out taking into account the handling of information contained in clinical records in accordance with Resolution 1995/99 and Act 1581 of 2012.

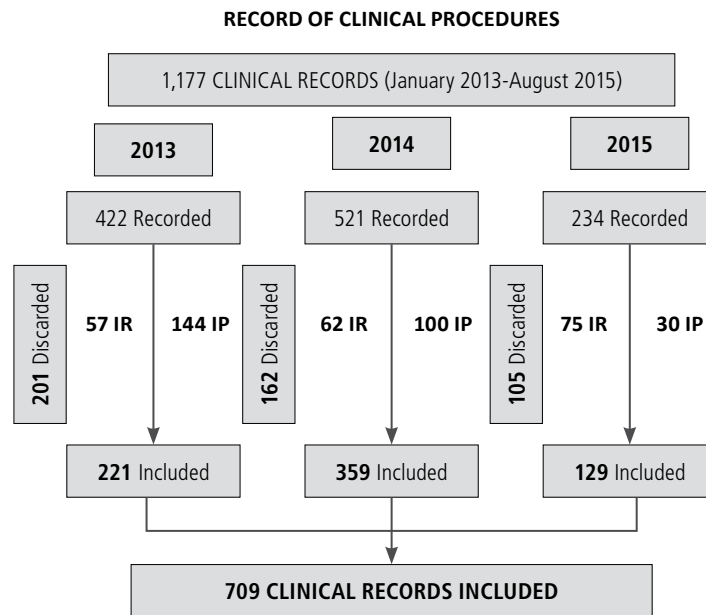
The process of sample selection involved the review of surgical records of the oral surgery service of the Universidad de Antioquia

School of Dentistry, corresponding to patients subjected to any type of surgical procedure from January 2013 to August 2015. The inclusion criteria considered the full completion of all items in the medical records and the presence of the institution's surgical procedure as an annex, in addition to complete pharmacological prescription, providing the analgesic/anti-inflammatory name, dose, route and time of administration, and duration of therapy. All records failing to meet these criteria were excluded. The process of reviewing the medical records was conducted by two of the authors, who were previously calibrated.

Of 1,177 procedural records obtained during the study period, 709 were included for analysis. Figure 1 shows the process of selection of medical records included in the study. The most common cause for exclusion of records was incomplete data on drug prescription.

The study variables were: personal medical records (which were grouped per affected system), age, sex, clinical staff in charge of procedure and prescription (student and professor), procedure performed, name of anti-inflammatory, type of analgesic/anti-inflammatory according to mechanism of action, generic or brand-name drug, dose, route and time of administration, and duration of therapy.

Information on prescribed analgesic drugs and patients' medical records were collected in a Microsoft Excel spreadsheet (version 2010; Microsoft Corporation, Redmond, Washington). The data were summarized using absolute and relative frequencies, and central trend measures such as average and standard deviation were used.



**Figure 1.** Clinical records selection process

IR: Incomplete Clinical Records: fail to fill out all items in the medical record and the annex of surgical procedure

IP: Incomplete Prescription: fail to specify analgesic/anti-inflammatory name, dose, route and time of administration, or duration of therapy

## RESULTS

709 procedural records were included, corresponding to 556 patients, most of them female. Each patient’s pharmacological prescription and surgical procedure were processed by a student supervised by a professor, for a total participation of 209 students and 11 professors. A total of 937 medical records were reported, as some patients referred up to three records. Most patients reported no relevant history, followed by respiratory and gastric disorders (Table 1).

**Table 1.** Characteristics of the study population

Characteristics		n	%
Sex	Female	351	63.1
	Male	205	36.9
	<b>Total</b>	<b>556</b>	
Age (years) Average ± SD		22.9±9.2	
Medical history	No history	262	28.0
	Respiratory disorders	141	15.0
	Gastric disorders	103	11.0
	Nervous system disorders	99	11.0
	Endocrine/metabolic	97	10.0
	Other medications	70	7.5
	Allergies	47	5.0
	Anti-inflammatory treatment	22	2.3
	Other medical histories	96	10.2
	<b>Total</b>	<b>937</b>	

The “Other medications” group includes patients currently treated with non-inflammatory drugs because of their medical histories, including antihypertensive, anti-glycemic, and acne control medications (3 patients on Isoface®). And the “Other medical histories” group includes alterations that were reported less frequently, such as cardiovascular or renal conditions, or history of hepatitis (4 cases).

Table 2 shows—from higher to lower frequency—the 891 analgesic/anti-inflammatory drugs that were prescribed. Non-selective NSAIDs (53.1%) represent most of the prescriptions; in contrast, corticosteroids were formulated in only 5 cases (third-molar surgical extraction) dexamethasone (3 cases), Diprospan®, and dexamethasone. There were no cases of opioids as single prescription, and the generic form of drugs was the most frequently prescribed (88.1%).

**Table 2.** Analgesic/anti-inflammatory drugs and main doses prescribed at the oral surgery service of the Universidad de Antioquia School of Dentistry, 2013-2015

Type of anti-inflammatory	Medicines	n	%	Dose		
				mg	n	
Non-selective NSAIDs	Ibuprofen	221	24.8	600	137	
	Meloxicam	117	13.1	7.5	91	
	Advil Max®	63	7.1	400	63	
	Naproxen	24	2.7	500	16	
	Injected diclofenac	15	1.7	75	15	
	Diclofenac sodium	14	1.6	50	14	
	Diclofenac retard	9	1.0	100	9	
	Advil®	5	0.6	200	5	
	Ketoprofen	2	0.2	100	2	
	Motrin®	2	0.2	800	1	
	Ponstan®	1	0.1	500	1	
	COX2 preferential NSAIDs	Nimesulide	215	24.1	100	215
		Nimesulide MK®	1	0.1	100	1
Peripheral-antipyretic analgesics	Acetaminophen	162	18.2	500	162	
	Dolex®	7	0.8	500	7	
	Adorem®	2	0.2	500	2	
Multimodal therapy	Dolex forte®	6	0.7	*	6	
	Winadeine F®	8	0.9	*	8	
	Sinalgen®	1	0.1	*	1	
COX2 Selective NSAIDs	Arcoxia®	6	0.7	120	6	
	Celecoxib	5	0.6	200	3	
Steroidal analgesic/anti-inflammatory	Dexamethasone	1	0.1	8	1	
	Diprospan®	1	0.1	7	1	
	Betamethasone	3	0.3	8	2	
<b>Total medicines</b>		<b>891</b>				

\* Dolex Forte®: acetaminophen 500mg/cafeine 65 mg; \* Winadeine F®: acetaminophen 500 mg/codeine 30 mg; \* Sinalgen®: acetaminophen 325 mg/hydrocodone 5 mg

As for prescription time, all medicines were prescribed postoperatively, except for one case (surgical extraction of third molars), in which ibuprofen was administered preoperatively. The main route of administration was the oral (97.8%), with the intramuscular route used in only 20 cases, 5 of which were corticosteroids and the others were diclofenac. The duration of therapy ranged from 1 to 10 days; the drugs were mainly prescribed for three days (596 cases),

followed by one day (168 cases) and five days (62 cases).

A total of 709 prescriptions were given for the same number of surgical procedures. Patients were given one (531 cases), two (174 cases) or three medicines (4 cases). The main form of prescription was ibuprofen as a single drug in 189 patients, followed by nimesulide with 171 cases, and the combination acetaminophen plus meloxicam in 72 patients.

**Table 3.** Therapeutic scheme most used in the main surgical procedures at the oral surgery service of the Universidad de Antioquia School of Dentistry, 2013-2015

Procedure	Drug	Dose		Duration		
		n	mg	n	days	n
<b>Surgical extraction of third molars</b> n=596	Ibuprofen	155	600	96	Three	80
	Nimesulide	149	100	149	Three	133
	Acetaminophen + Meloxicam	67	500 7.5	67 56	Three Three	64 50
<b>Surgical extraction of third molars + simple extraction</b> n=44	Ibuprofen	15	600	10	Three	8
	Nimesulide	10	100	10	Three	8
	Acetaminophen + Meloxicam	2	500 7.5	2 1	Three Three	2 1
<b>Simple extraction</b> n=12	Ibuprofen	4	600	2	Three	2
	Nimesulide	3	100	3	Three	2
	Acetaminophen + Meloxicam	1	500 7.5	1 1	Three Five	1 1

Regarding the surgical procedures performed at the oral surgery service, 22 types of procedures were recorded, of which 84.0% were surgical extractions of third molars, corresponding to 596 of the 709 procedures, followed by the surgical extraction of third molars plus simple extraction, with 44 cases, and simple extraction, with 12 records. Other procedures (57 cases) were less often reported, and include dental implants, biopsies, and other minor oral surgical procedures.

Concerning the prescription form per the three most common surgical procedures, the drug most highly prescribed was 600 mg ibuprofen, followed by 100 mg nimesulide, and the combination acetaminophen plus meloxicam of 500 mg and 7.5 mg respectively. All three medicines were prescribed post-surgically, via oral administration, and for a period of 3 days, except in one case of meloxicam in a simple extraction, which was prescribed for 5 days.

Regarding the patients' medical history (no history, and respiratory, nervous or endocrine/metabolic system alterations), the prescription pattern was maintained, with ibuprofen as the main prescribed analgesic, followed by nimesulide and the combination acetaminophen plus meloxicam. Since this pattern varied in patients with gastric disorders, nimesulide was the main medicine of choice in these patients.

As for patients who were under active medical treatment with some analgesic/anti-inflammatory, the post-surgical prescription shows that of the total patients, only one who was using Winadeine F was given the same medicine for pain management after surgery. One patient treated with the brand-name NSAID Advil Max<sup>®</sup> was prescribed generic ibuprofen, and two out of three patients who were taking acetaminophen continued a post-surgical scheme with 200 and 600 mg ibuprofen only.

## DISCUSSION

Of the total medications prescribed after the various surgical procedures in this study, NSAIDs were the most commonly formulated (78.5%), especially non-selective NSAIDs (53.1%), while steroid drugs accounted for 0.6% of prescribed drugs, and opioids alone were not prescribed in either case. In a survey conducted by Universidad Autónoma de Nayarit, 92.9% of 113 surveyed dentists admitted not using steroidal analgesics and only 0.9% of participants prescribe opioid analgesics in their dental practice.<sup>22</sup>

NSAIDs are effective analgesics following oral surgery;<sup>23</sup> these drugs, just like acetaminophen, are considered first line of pain control in dentistry.<sup>24</sup> Acetaminophen is indicated for the management of mild

to moderate pain and is one of the safest analgesics if used under therapeutic doses: 500 to 1,000 mg every 4 to 6 hours, with a maximum consumption of 4,000 mg per day.<sup>25</sup> Considering the maximum daily dose, the FDA suggested lowering it to 3,250 mg, and reducing the maximum individual dose from 1,000 mg to 650 mg.<sup>26</sup>

Due to their adverse effects, corticosteroids are not routinely used in dentistry and are only recommended in cases of complex surgical procedures, where there is moderate to severe significant surgical trauma, or the patient is at risk of excessive edema,<sup>5</sup> such as deeply impacted teeth, large teeth with weakened coronal structure or very divergent roots located inside dense bone, cases of multiple extraction with extensive alveolar reshaping, block resection, and other equally extensive procedures.<sup>27</sup> These medications are used in specific situations in which the pain is of inflammatory origin, in the absence of infection, and when the patient's medical history does not show contraindications.<sup>24</sup>

On the other hand, opioids are powerful analgesics, but due the high incidence of adverse effects when prescribed individually, they should not be considered as first line of pain control, but for the management of intense pain. Synergistic therapy<sup>28</sup> with acetaminophen is a better alternative in patients in which adequate analgesia is not achieved with the first lines of management or in NSAID-intolerant patients, in order to reduce adverse effects.<sup>24</sup>

From high to low, Ibuprofen, nimesulide and the acetaminophen plus meloxicam combination were the three main analgesic prescriptions in this study. This same order was observed in the prescription following the three main surgical procedures in this

study: surgical extraction of third molars, surgical extraction of third molars plus simple extraction, and simple extraction.

The data for this study comes from the School of Dentistry's surgical procedures room, where simple extractions are not usual as a single procedure; this is why it only accounted for 1.7% of cases. Despite simple extractions being the most common dental surgical practice,<sup>18</sup> the literature review shows few studies on the effectiveness of analgesics following this procedure.<sup>18,29,30</sup>

Regarding pain after simple extractions, it was found out that on the night of the extraction day there is a peak of pain in 81.8% of patients, with pain decreasing after days 1 and 5 post-surgery.<sup>29</sup> This validates the importance of pain management following a simple extraction, even in the presence of a less invasive procedure. In the present study, medications were prescribed for 3 to 5 days following simple extractions (see Table 4), in line with the scientific evidence that suggests analgesic prescription during the first week after a simple tooth extraction.<sup>29</sup>

The surgical extraction of third molars, which was the main procedure in this study (84.0%), is the most common surgical procedure performed in oral surgery,<sup>31</sup> triggering signs and symptoms such as pain, inflammation, and loss of function,<sup>32</sup> usually controlled with narcotic analgesics, nonsteroidal anti-inflammatory analgesics (NSAIDs), corticosteroids and combinations of these.<sup>5</sup>

600 mg ibuprofen for a three-day period was the main scheme in third-molar surgical extractions, while corticosteroids were only prescribed in five cases of such surgical procedure. This is in line with the consideration of ibuprofen as the first line of acute pain management. In addition,

ibuprofen has proven to be very effective in managing moderate pain, at a concentration of 400 to 600 mg every 6 hours.<sup>24</sup>

Although corticosteroids are potent modulators of inflammation,<sup>33</sup> when comparing the pharmacological efficacy of an NSAID (ibuprofen) with a corticosteroid (dexamethasone) after surgical extraction of third molars, previous studies have shown that using 600 mg ibuprofen preoperative, prolonging the scheme every 6 hours for a week, has a better long-term effect in reducing PGE2 (in urine and saliva), compared to a single intraoperative dose of 8 mg of intravenous dexamethasone. The combination of the two schemes leads to a slight improvement of post-surgical clinical signs and symptoms, but it is not a statistically significant improvement compared to the single ibuprofen scheme.<sup>32</sup>

100 mg nimesulide over three days was the second most prescribed therapeutic scheme in this study, followed by the combination of 500 mg acetaminophen plus 7.5 mg meloxicam. Both nimesulide and meloxicam have similar capacities to control post-surgical pain caused by the surgical extraction of impacted third lower molars; however, nimesulide is more effective than meloxicam in the control of inflammation.<sup>34</sup>

The consumption of nimesulide has been associated with hepatotoxicity, so its market was suspended in countries like Spain and Finland in 2002.<sup>35-37</sup> In 2004, following a study on the safety of nimesulide, the European Medicines Agency (EMA) determined that the risk-benefit profile of this medicine was favorable. However, although the risk of liver damage with the consumption of nimesulide and other NSAIDs is small, the risk remains higher for nimesulide.<sup>38,35</sup> Therefore, the EMA



Committee for Medical Products for Human Use (CHMP) recommended restricting the use of Nimesulide to acute pain, as a second line of management, for a treatment period of up to 15 days. In addition, it recommends removing the pharmaceutical presentation of 200 mg nimesulide from the market, restricting its use to 100 mg twice a day and only in patients over 12 years of age.<sup>39</sup>

In Colombia, regarding the use of nimesulide, the National Institute for Surveillance of Drugs and Foods (Instituto Nacional de Vigilancia de Medicamentos y Alimentos, INVIMA)<sup>40</sup> recommends using it for a maximum period of 15 days as a second line of management and only in the treatment of acute pain. The institute is unclear on the recommendation given by the CHMP regarding the maximum dose of 100 mg.

In consequence, nimesulide is a NSAID that—prescribed under the criteria stipulated by the CHMP—offers effective anti-inflammatory results following procedures such as third molar surgical extraction, under a 100 mg scheme for three days, in which the benefits outweigh the risks.

It is also important to keep in mind the patients' medical history when prescribing nimesulide, because elderly women and patients being treated with more than one potentially hepatotoxic drug are two groups with a high risk of drug-induced liver damage.<sup>20,41</sup> Therefore, prevention is highly important for careful prescribing, avoiding simultaneous administration of more than one hepatotoxic drug (particularly in high-risk patients) and even more so in patients with prior history associated with liver damage.<sup>41</sup>

In this study, three patients reported being under Isoface® (Isotretinoin), a medicine that

has proven to cause alterations in hepatic enzymes.<sup>42</sup> Of these three patients, only one was given nimesulide plus diclofenac as post-surgical prescription.

When evaluating the time of prescription of the most commonly used therapeutic schemes in the three main surgical procedures, it was observed that analgesics like ibuprofen were always prescribed postoperatively. While the issue of pre-surgical or post-surgical administration of medicines is controversial, it has been found out that there are no statistically significant differences in pain reduction, inflammation, and trismus with administration of 600 mg ibuprofen one hour before surgical extraction of third lower molars, compared to administration of the same drug immediately after the procedure.<sup>43</sup>

Although the oral was the main route of drug administration in this study, corticosteroids (5 cases) were always prescribed parenterally and distal to the surgical site, with the intramuscular being the most common route of administration because of a faster effect compared to the oral route.<sup>33</sup> Similarly, when comparing the intramuscular route with the submucosal administration of a corticosteroid such as dexamethasone—long used in oral surgery due to its powerful mechanism of action and long-lasting half-life—,<sup>44</sup> it was found out that some authors suggest concentrations of 8 to 12 mg preoperative via intramuscular route, in order to achieve better results,<sup>27</sup> while 4 mg dexamethasone submucosally administered is an effective strategy in the management of pain, inflammation, and trismus following surgical extraction of third molars, with results comparable to the intramuscular administration of this drug, taking into account that the latter is dependent on

blood flow at the administration site<sup>5</sup> and is more uncomfortable for patients.<sup>45</sup>

At this point, the clinician should conduct an individual risk-benefit assessment for each patient. For corticosteroids, special attention should be paid to aspects like adverse effects, which usually appear after taking the drug in high doses, for long periods (longer than two weeks),<sup>24</sup> or for a combination of both factors. This is the case of a 0.75 mg dose of dexamethasone administered for two to three weeks, which can suppress the hypothalamic-pituitary-adrenal axis.<sup>46</sup> However, it has been determined that a single dose of glucocorticoid, even a large one, has virtually no harmful effects, and short therapies for up to a week, in the absence of contraindications related to the patient's medical history, are unlikely to be harmful.<sup>47,48</sup>

This study identified 22 patients receiving anti-inflammatory drugs at the time of surgery. This is an important aspect during prescription due to the risk of gastrointestinal damage associated with NSAID treatments, dependent on factors like dose, combination of more than one NSAIDs, simultaneous use of aspirin, concomitant use of corticosteroids, and patients treated with anticoagulants or antiplatelet agents.<sup>23</sup>

Another side effect associated with the consumption of non-selective NSAIDs is inhibition of platelet aggregation as a result of the reduction of thromboxane A<sub>2</sub> synthesis, thereby altering hemostasis.<sup>47</sup> Five patients in this study were taking ibuprofen at the time of surgery; it is unknown for how long they had been doing so, but apparently an earlier consumption three days prior to surgery does not increase the postoperative bleeding in extraction of third molars.<sup>50</sup>

In addition, two patients were under Acetylsalicylic acid. Regarding the bleeding risk in these patients, it has been suggested that procedures like dental extractions can be performed under a low dose of Aspirin® (75-300 mg/day) alone.<sup>51,52</sup> Similarly, a daily dose of 100 mg of aspirin does not increase bleeding during tooth extraction, and therefore these therapies should not be discontinued prior to such dental procedures, as local hemostatics are sufficient for bleeding control.<sup>51,53</sup> It has also been reported that suspending the daily aspirin use in patients under this medication increases the risk of cardiovascular disorders during the first month after suspension, and therefore the recommendation is not to discontinue the daily use of aspirin before procedures like dental extractions.<sup>51,54</sup>

In evaluating patients' baseline analgesic regimen and post-surgical prescriptions, one patient who was previously under the acetaminophen plus ibuprofen combination was asked to stop this pharmacological combination and was prescribed 800 mg ibuprofen only after surgical extraction of third molars. In this regard, a critical analysis of studies found out that the combination therapy of ibuprofen plus acetaminophen is more effective than administering these drugs individually in the management of acute postoperative pain in dentistry.<sup>55</sup> This was even observed when administering doses of 400 mg ibuprofen and 1,000 mg acetaminophen.<sup>56</sup> In this scenario, some authors recommend the combination of 400 mg ibuprofen plus 500 mg acetaminophen every six hours in cases of moderate to very severe pain.<sup>55</sup>

On the other hand, concerning the comparison of optimal doses of ibuprofen plus acetaminophen prescribed individually in the control of pain after third molars

surgery, a systematic review concluded that ibuprofen at doses of 400 mg has an analgesic effect higher than 1,000 mg acetaminophen, considering that these doses are the most frequently used in clinical practice, and that the results of the study refer to single postoperative doses of these drugs.<sup>57</sup> In contrast, another study found out that after surgical extraction of third molars, 1,000 mg acetaminophen prescribed every six hours produce an analgesia comparable to 600 mg ibuprofen administered every six hours.<sup>58</sup> The present study found out that no such therapy was maintained in two patients who were under acetaminophen at the time of third molar surgery; instead, one patient was prescribed 200 mg ibuprofen and the other 600 mg ibuprofen post-surgically.

Regarding other procedures such as simple extractions, no statistically significant differences in pain control have been found when comparing the effectiveness of 500 mg Acetaminophen and 400 mg ibuprofen, with both medications administered orally three times a day postoperatively for three days. Therefore, the literature suggests that acetaminophen is a safe and effective alternative in the management of pain after simple extraction with respect to NSAIDs such as ibuprofen of common use.<sup>30</sup>

Regarding analgesic preferences according to medical history, in patients with respiratory disorders the preference for analgesic schemes is equal to the general recommendations found in this study, so that a non-selective NSAID such as ibuprofen was the main choice; however, evidence indicates that this type of drug increases the risk of bronchospasm in asthmatic patients and therefore the use of COX-2 selective

NSAIDs is safer in this population group.<sup>59</sup> In contrast, in patients with a gastric history, the main prescribed analgesic was nimesulide, a COX-2 selective drug, which helps prevent gastric alterations and possible lack of adherence to treatment.

Finally, the dental practitioner has a wide range of drugs for analgesic/anti-inflammatory purposes. A rational prescription should be promoted, taking into account different aspects related to the drugs (pharmacodynamics, pharmacokinetics) and patients (medical history, type of procedure, and the like), leading to an individualized prescription for each patient.

## LIMITATIONS

Several clinical records had to be excluded from the study for different reasons (Figure 1), suggesting the need for a careful handling of clinical records, which are important not only for clinical decision-making during patient follow-up, but also for research.

## CONCLUSION

The most prescribed anti-inflammatory analgesics in the oral surgery service at the Universidad de Antioquia School of Dentistry in the period January 2013-August 2015 were ibuprofen, followed by nimesulide and acetaminophen plus meloxicam. The same order of preference was observed in the post-surgical prescription of third molars extraction and in patients with no medical history.

## CONFLICTS OF INTEREST

One of the authors (MCMP) is part of the Thematic Coordinators of *Revista Facultad de Odontología Universidad de Antioquia*, but transparency in the editorial processing of the manuscript has been guaranteed since she did not participate in such process.

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