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Pharmacological management of orthodontic pain

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ABSTRACT

Pain associated with orthodontic treatment, which is both frequent and challenging, primarily arises following procedures such as the placement of interproximal elastic separators and the installation of archwires. This pain is often due to inflammation of the periodontium, leading to discomfort. Effective pharmacological management is essential to enhance patient comfort throughout orthodontic treatment. Nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen are commonly employed due to their proven efficacy and safety profiles. These medications help reduce both inflammation and pain, thereby improving patient tolerance of orthodontic procedures. When selecting an analgesic, it is important to consider factors such as the intensity of pain, pre-existing medical conditions, and potential drug interactions. Careful and supervised use of these medications helps minimize risks and optimizes patient comfort during orthodontic care.

Keywords: pain; pain management; orthodontics.

INTRODUCTION

The definition of pain constitutes an unpleasant sensorial and emotional experience closely linked to tissue damage, weather it is current or bound to happen (1). In the context of orthodontic treatments, its presence stands as one of the most relevant and inevitable situations in the course of dental movement (2). This frequent symptom originates from some orthodontic procedures, starting from the initial phase, such as the placement of interproximal separator elastics, to the installation of archwires and their subsequent activations, including the action of orthopedic appliances and even the delicate process of braces debonding (3).

This phenomenon has consequences that go beyond the physical, impacting significantly patients' daily activities, presenting difficulties to chew, alterations in their sleep patterns, headaches, and discomfort in the facial area (4). The implications of this painful manifestation do not end here, since they can lessen the

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patient's ability to fully cooperate with the orthodontic treatment, becoming in some cases a determining factor to stop the process (3, 5). It is worth highlighting that, besides the physical effects, orthodontic pain can also be an essential demotivation factor in individuals who initially seek to undergo orthodontic treatment (6). These considerations remark the importance of thoroughly exploring pharmacological strategies for pain management in orthodontics, with the aim to optimize the patient experience and the therapy efficacy.

The purpose of this study is to offer a literature review on the pain associated to orthodontic treatments and the pharmacological approaches recommended for its management. To achieve a comprehensive understanding of the topic, a thorough search in the PubMed database was done, by selecting original and review articles published between 2002 and 2020.

CLASSIFICATION OF PAIN IN ORTHODONTICS

The classification of pain in orthodontics, proposed by Burstone (1962), is based on two main parameters that help to understand precisely this sensation in response to orthodontic procedures. These factors are essential to evaluate and categorize pain in this context (3).

The first parameter is related to the magnitude of pressure put on the teeth and the sensation experienced by the patient. According to this association, pain is classified in three different degrees: i) first degree, which is not detected by the patient until the orthodontist manipulates the teeth, which implies a delayed perception; ii) second degree, which manifests when the patient clenches their teeth firmly or during situations of intense chewing; and, iii) third degree, which presents the highest intensity of the three degrees, reaching a level that hinders the chewing of foods of usual consistency (3).

The second classification parameter is based on the time pain appears. Here, there are two categories: i) immediate, which is associated to the sudden imposition of pressure on the teeth; and ii) delayed, which reflects the hyperalgesia of the periodontal ligament, manifesting after the orthodontic procedure (3).

PATHOPHYSIOLOGY OF PAIN IN ORTHODONTICS

Pathophysiology of pain in orthodontics presents an intricate relationship between dental movement caused by orthodontic treatment and pain. Both are biological processes linked by a common mechanism: the local inflammation that triggers a series of events at a vascular, cellular and chemical level in the periodontium (1).

From a vascular perspective, an alteration in blood pressure occurs, causing local ischemia, which, in turn, creates an acidic environment interpreted as a pain signal by the ASIC3 receptor, a hydrogen-sensitive ion channel. Pain signals are transmitted to trigeminal neurons, which release neurogenic mediators, such as substance P and calcitonin gene-related peptide (CGRP), in the central nervous system (CNS), in the trigeminal nucleus, and the peripheric nervous system, at the level of the periodontal tissues. Mediators foster vasodilation, increase local inflammation and stimulate prostaglandin (PG) production (1).

In addition, acidosis induces epithelial cells and fibroblasts to secrete nitric oxide, increasing vascular permeability and allowing the migration of leukocytes (neutrophils, lymphocytes, and monocytes), as well as cells responsible for secreting inflammatory mediators, chemokines, and cytokines which amplify pain signals and local inflammation (1).

At the cellular level, the increase of vascular permeability increases the number of leukocytes in tissues, including periodontal and macrophage mastocytes, which secrete mediators such as the tumor necrosis factor alfa (TNF-α), and histamine, facilitating the recruitment of more leukocytes in the periodontal tissue. At a chemical level, inflammatory cells release inflammatory mediators, cytokines and chemokines, such as interleukin 1 (IL-1), interleukin 6 (IL-6), the tumor necrosis factor alfa (TNF-α), and interferon gamma (INF-γ). These mediators have a joint role in bone remodeling, stimulating osteoblast and osteoclast activity. In addition, PGs bind to sensory nerve endings, while the macrophage colony-stimulating factor (M-CSF) promotes the conversion of monocytes into macrophages and the recruitment and differentiation of osteoclasts. The vascular endothelial growth factor (VEGF) stimulates neovascularization and bone remodeling (1).

Pain signals travel through the nervous system, being processed by first, second, and third-order neurons before they reach the somatosensory cortex. It is worth noting that pain perception varies among individuals and it has an emotional component related to the limbic system, which can influence its perception (1).

PAIN-RELATED PROCEDURES DURING ORTHODONTIC TREATMENT

At the orthodontic level, thorough research on pain-related procedures has been done, with especial emphasis on the placement of interproximal separators and the insertion of alignment and levelling arches. The insertion of interproximal separators, preliminary stage before the placement of bands, aims to create interproximal space of 0.25 mm for bands that on mean are 0.16 mm thick. Among the different types of interproximal separators, widely used elastomeric materials create a space of 0.45 mm (7). In general, this is the first procedure in the orthodontics treatment, and it is relevant to consider that the anxiety levels of a patient can increase, which influences pain perception. This one tends to increase over time, reaching the highest intensity after 24 hours, and then gradually decreases toward the seventh day (8).

On the other hand, the pain related to the insertion of the first arches, corresponding to the alignment and levelling phase, manifests predominantly at the level of the incisors and canines. This type of ailment manifests approximately 2 hours after the procedure, reaching its highest intensity after 24 hours and lasting for three days, decreasing progressively until the seventh day (4, 6, 9). It is worth remarking that there were no significant differences in the intensity of the pain perceived neither in relation to the gauge of the nickel-titanium arches (0.014" y 0.016"), the type of braces (conventional and self-ligating), nor in the different types of nickel-titanium arches (conventional, superelastic and thermoelastic) (6, 10, 11).

ORTHODONTIC PAIN MANAGEMENT

Currently, an urgent need has been identified to establish a pain management protocol in the field of orthodontics, particularly on the first day of treatment when patients tend to experience discomfort with greater intensity, as supported by scientific literature (12). Four main approaches have been outlined to address orthodontic pain: pharmacological, mechanical, acupuncture and low-level laser; out of which the first one stands out as a fundamental pillar and it is recognized as the method of choice or gold standard (13).

Within pharmacological therapy, nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol emerge as the most frequently used and most effective medicine. NSAIDs have particularly shown their efficacy at reducing inflammation and, therefore, the pain related to orthodontic dental movement. On the other hand, paracetamol, having a well-established safe and efficacy profile, becomes a relevant therapeutic option (14).

PHARMACOLOGICAL MANAGEMENT OF ORTHODONTIC PAIN

Oral inflammation, a complex phenomenon triggered by a variety of factors including mechanical manipulation in orthodontic procedures, can trigger the release of pain mediators, thereby exacerbating the perception of discomfort in patients. In this context, the NSAIDs emerge as fundamental therapeutic agents in the strategy to manage orthodontics-associated pain. Their main mechanism of action focuses on the inhibition of PG synthesis, bioactive compounds derived from fatty acids that play an essential role in the modulation of pain, inflammatory response, and fever. By interfering with the biosynthesis of these molecules, NSAIDs cause a significant reduction of the sensitivity and excitation of peripheral nerve fibres, resulting in a notable attenuation of dental pain (15).

These therapeutic effect of NSAIDs is attributed to their interaction with the isoforms of cyclooxygenase (COX), crucial enzyme in the process of converting arachidonic acid to PG. Among these isoforms, COX-1, ubiquitous in its cellular presence, is responsible for PG production, which maintains homeostasis in physiological conditions. In contrast, COX-2, labeled as pro-inflammatory, is expressed in an inducible manner in response to stimuli such as cytokines, growth factors, and endotoxins at the site of cellular injury. This isoform is also found in specific tissues as a constitutive form, such as the kidney and the brain, where it actively participates in the regulation of their functioning. Lastly, COX-3, identified in the vascularization of the CNS, plays a main role in the creation of fever and pain at a central level, acting independently from inflammatory processes (15, 16).

It is important to point out that the COX inhibition mechanism can vary depending on the NSAIDs in question, leading to two main categories: non-selective inhibitors of COX isoforms, also known as traditional NSAIDs; and selective inhibitors of COX-2, known as COXIBS (16).

Both paracetamol and ibuprofen have been established as primary analgesic agents due to their efficacy and safe profile. Paracetamol, known by its analgesic action, inhibits COX-3 activity in the CNS in conditions of low peroxide levels, which lowers their peripheric

anti-inflammatory effects, and, in turn, limits the incidence of gastrointestinal and cardiovascular side effects. On the other hand, ibuprofen, an NSAID that has demonstrated its efficacy for mild to moderate pain relief, has been proved to be as efficacious as paracetamol, or a superior drug, in a dose of 200-400 mg every 4 to 6 hours, maintaining a low-risk profile for side effects. However it is imperative to acknowledge that increasing the dose to 600 mg can elevate the risk of adverse reactions significantly (14, 15).

Furthermore, the timing of analgesic administration is crucial to maximize its effectiveness (17). Pre-operative administration, one hour before the orthodontic procedure, followed by a post-operative dose 6 to 8 hours later, has been shown to optimize pain control, as opposed to prescribing only pre- or post-procedure doses. This regimen allows the appropriate absorption of the drug before PG production, mitigating the subsequent inflammatory response (12, 13, 17). Both ibuprofen and paracetamol have shown significant differences regarding their analgesic effectiveness, but it is crucial to adjust to the recommended dose: in case of patients older than 12 years old, the ibuprofen dose is 400 mg every 4 to 6 hours, with a daily limit of 2400 mg; while for paracetamol, 500 mg to 1 g are recommended every 6 to 8 hours, not exceeding 4 g a day. Both medications have an mean lifespan of about 2 hours, factor that must be taken into account when designing the dose regimen (15, 18) (table 1).

Table 1. Summary of the pharmacological management protocol for orthodontic pain in adults and adolescents (12 years of age and older).

Drug	Recommended dose	Administration	Maximum dose	Efficacy	Side effect risks	Half-life
Ibuprofen	200-400 mg every 4-6 hours	Pre-operative (1 hour before) and post-operative (6-8 hours later)	2400 mg/day	High efficacy for mild to moderate pain	Low for a standard dose, gastrointestinal toxicity	~2 hours
Paracetamol	500 mg to 1 g every 6-8 hours	Pre-operative (1 hour before) and post-operative (6-8 hours later)	4 g/day	High efficacy for mild to moderate pain	Low when adhered to recommended dose, hepatotoxicity	~2 hours

Finally, analgesic treatment protocols for pediatric patients should include ibuprofen at a dose of 4-10 mg/kg every 6-8 hours, without exceeding 40 mg/kg in 24 hours; or paracetamol at 10-15 mg/kg every 6-8 hours, with a maximum dose of 50 mg/kg in 24 hours (19) (table 2).

Table 2. Summary of the pharmacological management protocol of orthodontic pain in children (12 years old and under).

Drug	Recommended dose	Administration	Maximum dose	Efficacy	Side effect risks
Ibuprofen	4-10 mg/kg every 6-8 hours	Pre-operative (1 hour before) and post-operative (6-8 hours after)	40 mg/kg in 24 hours	High efficacy for mild to moderate pain	Low for a standard dose, gastrointestinal toxicity
Paracetamol	10-15 mg/kg every 6-8 hours	Pre-operative (1 hour before) and post-operative (6-8 hours after)	50 mg/kg in 24 hours*	High efficacy for mild to moderate pain	Low when adhered to recommended dose, hepatotoxicity

*DIGEMID Alert (issued by the Peruvian General Directorate of Medicines, Supplies, and Drugs) nº 43, 2009 (Peru).

DISCUSSION

Pain management in orthodontics represents an essential component of patient care since said sensation is a common experience associated to orthodontic treatment. This subjective and multifaceted experience emerges as a result of the activation of nociceptive mechanisms during dental movement induced by orthodontic forces. Despite the advances in orthodontic techniques, pain continues to be one of the main concerns of patients, and a challenge for clinicians (9, 20).

In the context of pharmacological management of orthodontic pain, NSAIDs have a crucial role, acting through COX inhibition, a key enzyme in PG synthesis, which are essential pain and inflammation mediators. However, it is fundamental to accurately evaluate their role in modulating the pain response, especially considering their impact on bone remodelling, which is a vital process in dental movement.

Scientific evidence indicates a duality in NSAIDs action in orthodontics. These medications are effective to alleviate pain associated to orthodontic treatments, but they are also capable to influence dental movement. Studies have shown that medicine, such as ibuprofen and diclofenac, can decrease significantly the magnitude of dental movement in orthodontics. This means that, although NSAIDs are beneficial for pain management, they could also impact the speed of said dental movement. This influence is an important consideration for dental health professionals, since it can alter the timing of the established orthodontic treatment. Even though clinical relevance of this effect is still a subject of debate and active research, it is crucial for planning and effective application of orthodontic treatments (4, 21).

Acetaminophen stands out as a valuable alternative, with a relatively high safety profile and an action mechanism that could be less detrimental to orthodontic dynamics. Literature suggests that, in animal models, paracetamol provides pain relief without significantly altering dental movement, which could represent an advantage over the NSAIDs in certain clinical contexts. However, the need for caution in extrapolating these results to human practice is recognized, and the importance of more rigorous research is emphasized in order to support analgesic prescription guidelines in orthodontics (22).

It is pertinent to highlight the absence of significant differences in analgesic efficacy between ibuprofen and paracetamol, and the need to adhere to recommended doses in order to mitigate the possibility of side effects. The timing in the administration of these medications, before and after orthodontic procedures, is presented as an optimized strategy for pain management, enabling early medication absorption and a more efficient intervention in the inflammatory cascade (17).

Paracetamol presents only analgesic and antipyretic effects, and inhibits the COX enzyme in the CNS, reducing gastrointestinal and cardiovascular side effects, typical of NSAIDs. This profile makes it adequate for patients who are allergic to NSAIDs. However, excessive use can cause hepatic damage, so it must be administered carefully. Ibuprofen, a conventional NSAID, is effective for mild to moderate pain, with lower risk of side effects in low doses. However, high doses can increase the risk of gastrointestinal complications, due to the inhibition of PG production, which impacts the protection of the gastric mucosa. For high risk patients, it can be taken with gastroprotective agents (15).

CONCLUSIONS

Effective pain management associated to orthodontic treatments is crucial to improve patient experience, and to guarantee a comfortable recovery. The main strategy focuses on analgesic administration, being paracetamol and ibuprofen those that stand out for their efficacy and safety profile. Clinical evidence suggests that pre-operative analgesic administration, preferably one hour before the procedure, followed by additional doses between 6 and 8 hours later, optimizes pain management. Not only does this proactive regime alleviates its intensity, but it also decreases the probability of post-procedure complications, enabling a more fluid recovery and a better quality of life for the patient during the orthodontic treatment. This approach, based on evidence, highlights the importance of careful planning in pain management as a comprehensive part of orthodontic treatment, thereby ensuring satisfactory results for both the patient and the professional.

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