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# HOW MEDICATIONS AFFECT ORTHODONTIC TOOTH MOVEMENT

Altea Kuduz<sup>1</sup>, Vildana Džemidžić\*<sup>2</sup>, Alisa Tiro<sup>2</sup>

\*Corresponding author

Vildana Džemidžić, PhD  
University of Sarajevo – Faculty  
of Dentistry with Clinics  
Department of Orthodontics  
71000 Sarajevo,  
Bosnia and Herzegovina  
Email: vdzemidzic@hotmail.com;  
vdzemidzic@sf.unsa.ba  
Phone: ++387 33 214 249

<sup>1</sup> Dr. Simon Haug & Kollegen – Zahnheilkunde – Metzingen, Germany

<sup>2</sup> University of Sarajevo – Faculty of Dentistry with Clinics, Department of  
Orthodontics, Sarajevo, Bosnia and Herzegovina

### ABSTRACT

Correction of orthodontic irregularities includes orthodontic tooth movement. The action of force initiates a series of biomechanical processes of bone remodeling leading to tooth movement. Different medications can affect orthodontic tooth movement - inhibiting (decrease tooth movement) or stimulating (increase tooth movement). Knowledge of medications effects is of particular importance to clinicians. The purpose of this review is to explain the mode of action of certain medications and to show their influence on orthodontic tooth movement.

**Keywords:** orthodontics, tooth movement, medications

## Introduction

Correction of orthodontic irregularities includes orthodontic tooth movement. By the action of the force, a series of biomechanical processes of bone remodeling are initiated leading to tooth movement [1].

The process of orthodontic tooth movement begins when the orthodontic force applied to the crown of the tooth is transmitted through the root to the periodontal ligament and alveolar bone thus causes changes in the activity of these structures cells. Bone remodeling is a process of bone formation on tension side and bone resorption on pressure side [2]. During orthodontic tooth movement, the remodeling process is associated with the influence of mediators that trigger inflammatory processes in the initial stages of orthodontic tooth movement - cyclic adenosine monophosphate (cAMP), prostaglandins, interleukins, cytokines. Since different medications can affect the level of prostaglandins and other mediators, pharmacological interventions can thus modify the response to the application of orthodontic force [3].

Many orthodontic patients consume vitamins, hormonal preparations, certain medications for the prevention or treatment of various diseases. Thus, it is necessary to know the mechanism of their action and effects on orthodontic tooth movement.

The purpose of this review is to explain the mode of action of certain medications and show their influence on orthodontic tooth movement. This can serve as a quick reminder for clinicians when managing therapy in patients using certain medications or supplements.

Considering the large number of medications that can affect orthodontic tooth movement, the first part will describe the influence of non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, vitamin D3, calcium, bisphosphonates and anticonvulsants.

## 1. Nonsteroidal anti-inflammatory drugs (NSAIDs)

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly used drug groups. They have analgesic, antipyretic and anti-inflammatory effect, and are used in the therapy of various diseases such as rheumatoid arthritis, osteoarthritis, gout, as well as for the prevention of cardiovascular diseases [4]. The main mechanism of action is based on the inhibition of prostaglandin synthesis by blocking cyclooxygenase (COX) – COX-1 and COX-2 enzymes [5]. Since prostaglandins play an important role in orthodontic tooth movement processes, it is clear that the use of drugs that block their synthesis will affect tooth movement. The most important groups of NSAIDs that differ in their chemical composition are: salicylates, arylalkanoic acids, arylpropionic acids (profens), oxicams and coxibs [3].

### 1.1. Salicylates (Aspirin)

Acetylsalicylic acid is the most widely used NSAID. It inhibits both types of COX thus directly inhibits prostaglandin synthesis. Clinically, this is manifested by slower orthodontic tooth movement in patients who have undergone long-term therapy with acetylsalicylic acid. Salicylates inhibit the synthesis of prostaglandins, influence the differentiation of osteoclasts and thereby reduce bone resorption [4].

One of the experiments conducted on rats showed that non-steroidal anti-inflammatory analgesics, such as aspirin and ibuprofen, reduce the number of osteoclasts, probably by inhibiting prostaglandin secretion, which significantly reduces orthodontic tooth movement. To the contrary, acetaminophen did not affect orthodontic tooth movement in rats, and this analgesic could be used in the treatment of pain caused by orthodontic tooth movement [6].

Therefore, before starting orthodontic therapy, it is necessary to consider the possibility of excluding the use of salicylates if this will not affect

the course of the disease for which this drug is prescribed.

### **1.2. Arylalkanoic acids (Diclofenac, Indomethacin)**

Indomethacin has a strong analgesic, anti-inflammatory and antipyretic effect, and in higher concentrations it prevents platelet aggregation. It is used in patients with rheumatic diseases because it reduces pain, joint swelling and morning stiffness. It is a specific inhibitor of prostaglandin [7]. The results of several studies conducted on experimental animals – rats [8], pigs [9], cats [10] - showed a significant decrease of tooth movement after the application of indomethacin, regardless of the magnitude of the applied orthodontic force.

Diclofenac is among the most commonly used NSAID drugs used in the treatment of rheumatoid arthritis, spondylitis, toothache, post-traumatic and postoperative inflammatory conditions. The mechanism of action consists in the inhibition of prostaglandin synthesis by inhibiting COX-1 and COX-2 enzymes [11]. Carlos et al. observed that after 2 local applications of diclofenac injection (10mg/kg) there was a complete inhibition of molar movement in rats [12].

### **1.3. Arylpropionic acids (Ibuprofen, Flurbiprofen, Naproxen)**

Numerous studies have established that ibuprofen has a similar effect on orthodontic tooth movement as other drugs from the NSAID group [6, 13, 14]. A study examining the movement of rat incisors by applying a force of 25 or 35 CN and after the administration of ibuprofen in a dose of 30 mg/kg, showed a significant reduction in the rate of orthodontic tooth movement [6].

The mechanism of action is based on the inhibition of prostaglandin synthesis due to the blockade of the COX enzyme. This leads to a reduction in the differentiation and activation of osteoclasts, which will lead to a significant reduction in tooth movement and thus prolongation of orthodontic therapy [15].

### **1.4. Coxib (Celecoxib, Rofecoxib, Valdecoxib)**

Coxibs are a specific group of NSAID that selectively inhibit the COX-2 enzyme and are commonly used in the treatment of osteoarthritis and acute and chronic pain of other causes [4].

The results of studies, mostly conducted on experimental animals, have shown different effects of coxib on orthodontic tooth movement. Several studies observed that bone resorption was inhibited by celecoxib administration and concluded that COX-2-dependent prostaglandin synthesis is critical for bone resorption [16], resulting in reduced tooth movement after orthodontic force application [17]. De Carlos et al. compared the effects of rofecoxib, celecoxib and parecoxib on orthodontic tooth movement, and determined that celecoxib and parecoxib had no effect on orthodontic tooth movement [18].

NSAIDs are the most commonly used analgesics to control pain and discomfort, specifically ibuprofen and acetylsalicylic acid. These two medications have shown that they mostly lead to a decrease in prostaglandin E and osteoclast levels, and therefore slow down orthodontic treatment. However, in low doses, NSAIDs have little or no effect. Although all experiments show similar results, their effect on orthodontic displacement is not uniform. However, based on experiments and evidence, it is concluded that NSAIDs are inhibitors of prostaglandin synthesis thus decreasing orthodontic tooth movement.

## **2. Paracetamol (acetaminophen)**

Paracetamol (acetaminophen) has pronounced analgesic and antipyretic effects with no anti-inflammatory effect. Unlike NSAIDs, which inhibit COX-1 and COX-2 enzymes, paracetamol inhibits the third isoform COX-3, which is found exclusively in the brain and spinal cord. Thus, paracetamol has minimal effects on prostaglandin synthesis [3].

Tests of the effect of paracetamol on orthodontic tooth movement in rabbits and rats showed that there is no effect on the rate of

movement of incisors and molars [3, 19]. Since paracetamol does not affect the rate of tooth movement, both studies recommend that paracetamol should be the medication of choice for reduction of pain associated with orthodontic tooth movement.

### 3. Vitamin D (1,25 dihydroxycholecalciferol)

The active metabolite of vitamin D is 1,25 dihydroxycholecalciferol. It regulates the level of calcium and phosphate in the serum, then stimulates bone deposition and inhibits the release of parathyroid hormone (PTH) and has an important role in the immune system.

The effect of vitamin D on orthodontic tooth movement has been studied in numerous studies. Kale et al observed that local application of vitamin D accelerates tooth movement in rats, and the assumption is that this effect is the result of balanced processes of bone resorption and apposition caused by vitamin D [20]. Intra-ligament injections of vitamin D metabolites cause an increase in osteoclastic activity thus leading to an increase in bone resorption producing an increase in tooth movement during orthodontic therapy [21]. A study conducted by Tehranchi et al. showed that patients with lower serum vitamin D concentrations did not show greater root resorption after completion of fixed orthodontic therapy [22].

### 4. Calcium

Calcium is a mineral necessary for various physiological processes such as muscle contraction, heart rhythm regulation, fluid balance and enzyme regulation. Dietary recommendations for calcium intake for children aged 4–8 years is 800 mg/day and for adults between 1000 and 1300 mg/day. It is often prescribed as a dietary supplement in order to prevent certain diseases (osteoporosis) [15].

The influence of dietary calcium on orthodontic tooth movement was investigated in dogs whose diets were high and low in calcium. The research results showed that those whose diet was low in calcium had significantly faster tooth movement compared to the group whose diet was rich in calcium [23].

Thyroid and parathyroid hormones, sex hormones and vitamin D play an important role in the regulation of calcium levels in the body. A special group of drugs that affect calcium homeostasis are bisphosphonates [24].

### 5. Bisphosphonates

Bisphosphonates have a strong inhibitory effect on bone resorption and are successfully used in the treatment of osteoporosis, Paget's disease and bone tumors. Bisphosphonates are incorporated into the bone matrix, and they are specific in that their half-life is 10 years or more, so they can affect bone metabolism for many years after stopping the medication [4]. Considering the possible effects of different bisphosphonates on orthodontic tooth movement, studies have shown that both alendronate and clodronate inhibit key factors mediating tooth movement.

Liu et al. applied clodronate to the subperiosteal region of a molar exposed to orthodontic force in rats and concluded that local application of clodronate not only reduces orthodontic tooth movement, but also reduces the number of osteoclasts and root resorption [25]. Local periosteal application of clodronate shows an inhibitory effect on tooth movement and with a shorter application interval even at lower doses [26].

### 6. Anticonvulsants

Anticonvulsants are drugs that stop and prevent an epileptic attack, but do not act on the cause of the convulsions. The main mechanism of their action is an increase in inhibitory and a decrease in

excitatory transmission in the central nervous system, stabilization of the neuron membrane, slowing down of synaptic transmission [7].

Phenytoin causes gingival hyperplasia due to excessive proliferation of gingival collagen fibers, including the interdental papilla which significantly complicates orthodontic tooth movement [27].

Akhoundi et al. examined the effect of carbamazepine and valproic acid on orthodontic tooth movement in rats, and found that these drugs can reduce bone density which will cause accelerated orthodontic tooth movement [28].

Due to changes in bone metabolism and the consequent acceleration of orthodontic tooth movement, as well as an increased risk of gingival hyperplasia, patients using anticonvulsants should be monitored more often.

Today, there are many more adults and older patients who seek orthodontic treatment, either for aesthetic reasons or as a pre-prosthetic treatment. Considering that most of these patients have some chronic disease and therefore consume certain medications on a daily basis, it is necessary to know the mechanism of action of these medications as well as their possible side effects influences on orthodontic tooth movement. Knowing the effects of medications on orthodontic tooth movement is important for planning orthodontic treatment, as well as to predict possible difficulties for patients that can be expected during treatment. In addition, the importance of the medical history of each patient and data on the consumption of certain medications that can affect orthodontic treatment should be emphasized.

## Conclusion

Different medications can affect orthodontic tooth movement - inhibiting or stimulating, which should be taken into account before starting orthodontic treatment in patients who consume medications daily. It is important to know the effects of the following medications:

- Aspirin has an inhibitory effect on orthodontic tooth movement.
- Acetaminophen (Paracetamol) does not affect the rate of tooth movement and therefore this should be the analgesic of choice for managing pain associated with orthodontic tooth movement.
- Vitamin D has a stimulating effect on orthodontic tooth movement.
- Reduced intake of calcium accelerates tooth movement.
- Bisphosphonates have an inhibitory effect on orthodontic tooth movement and can therefore prolong the duration of orthodontic treatment.
- Phenytoin makes orthodontic tooth movement more difficult, while carbamazepine and valproic acid accelerate orthodontic tooth movement.

## Declaration of interest

The authors declare no conflict of interest.

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