

## ANALYSIS OF EFFECT OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON TEETH AND ORAL TISSUES DURING ORTHODONTIC TREATMENT. REPORT BASED ON LITERATURE REVIEW

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**Abstract:** In view of high availability and diversity of non-steroidal anti-inflammatory drugs (NSAIDs) on Polish market it is important for orthodontists to be aware of NSAID effect on the range of orthodontic tooth movement as well as the risk of root resorption in the moved teeth and other adverse effects, which might occur within oral cavity. The disadvantages of NSAID non-selective inhibition of COX include common oral inflammatory conditions, gingival bleeding, and disturbances of salivary secretion. Both, the selective and non-selective COX inhibitors, meloxicam excluded, used to alleviate the pain of orthodontic tooth movement, impede the movement of teeth. Paracetamol, explicitly indicated by most authors as the safest NSAID, seems to be the drug of choice in view of no influence on the range of tooth movement, the risk of root resorption or other adverse effects within oral cavity.

**Key words:** orthodontic tooth movement, NSAIDs, root resorption, non-steroidal anti-inflammatory drugs, NSAID adverse effects

All over the world in the last century and in Poland within the last 20 years, orthodontics, the field of dentistry concerned with treatment of malocclusion and correction of teeth position, has been developing rapidly. The wide assortment of removable dental braces was expanded with fixed appliances attached to teeth for the entire treatment period with no possibility to take them out and back into the mouth. This advancement allowed precise positioning of teeth with forces of low value but constant effect.

### Orthodontic tooth movement

Gradual dislocation of teeth during orthodontic treatment is possible owing to resorption and apposition of teeth. Application of orthodontic force to a tooth changes its position in the alveolus and creates pressure against blood vessels within the area. After a short period of time, due to deformation of fibroblasts and osteoblasts, prostaglandins and interleukin

$1\beta$  are secreted to the periodontal pocket. Cytokines and nitric oxide are also released as well as other cellular activity regulators (1). The substances induce degradation of type I collagen, which results in bone resorption. The most significant inflammation mediator seems to be prostaglandin E, which stimulates activity of osteoclasts and osteoblasts. (2, 3)

The process described above is usually associated with pain occurring within the first several days following appliance fixation as well as after subsequent follow-up visits. In view of the fact, often use of analgesics becomes necessary to alleviate the pain related to teeth movement. Because of that pain, the patient usually chooses a medication from the large group of analgesics, which may be purchased over the counter in any pharmacy and even grocery shops. The task of the orthodontist attending the particular case is to indicate the drug which is going to be the safest for the patient and will not adversely affect orthodontic treatment. (4, 5).

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### Effect of non-steroidal anti-inflammatory drugs

NSAID mode of action consists in inhibition of prostanoid synthesis through blocking an enzyme called cyclooxygenase (COX) during transformation of arachidonic acid (Fig. 1). Aspirin as well as other classical NSAIDs inhibit synthesis of COX-1 and COX-2 at the same time, which reduces the number of prostaglandins (including PGE<sub>2</sub>), thromboxanes (inhibited aggregation of platelets), and prostacyclins (PGI<sub>2</sub>) that play an important role in normal physiological processes (6, 7). Introducing selective inhibitors of COX-2 (induced cyclooxygenase responsible for blocking proinflammatory prostaglandin production), such as coxibs, allowed elimination of serious gastro-intestinal (intestinal perforation, gastric ulceration) and urino-genital (renal failure) adverse effects. The discussed drug class is not homogenous showing different routes of metabolism in the body as well as diverse properties (6).

The influence of analgesics on orthodontic treatment may be as follows: first of all they may affect the process of tooth movement as well as the grade of root resorption. Secondly, adverse effects of the medications may hamper the patient's adaptation to the appliance exacerbating oral inflammatory conditions as well as dry mouth symptoms, which contributes to mucous membrane abrasions (4).

The purpose of this work was a comparison of NSAIDs most commonly used by patients during orthodontic treatment in regard of their safety and adverse effects within the oral cavity.

### MATERIALS AND METHODS

Analgesics used to alleviate orthodontic pain were divided into groups.

Based on data from the medicinal product characteristics, oral adverse effects like xerostomy, oral inflammation, taste disorders or gingival bleeding, were summarized in Table 1.

The table was expanded with data considering the effect of the drugs on the range of orthodontic tooth movement as well as the quantity and size of resorption undermining the roots of moved teeth. The data were obtained from articles published after 1990 available in Medline database.

Inclusion criteria for articles included the following:

1. Experimental study.
2. Study group/groups and control group undergoing the same procedure.
3. Use of a drug during orthodontic tooth movement.
4. Study material of human or animal origin.
5. Exact description of dosing.
6. English-language article.

### RESULTS

The results were compiled and summarized in Table 1 (7-19).

The least toxic NSAID is ibuprofen; however, ibuprofen inhibits orthodontic tooth movement. A majority of non-selective COX inhibitors (aspirin, diclofenac) induce decreased range of this movement through reduction of the number of osteoclasts (10). However, studies conducted in rats by Gonzales et al. (9) indicated no effect of aspirin on the range of tooth movement and the risk of root resorption. As it was demonstrated by Kameyama in the studies conducted in rats (8), aspirin may also inhibit resorption undermining the roots, which is an irreversible process damaging the tooth (8). The risk

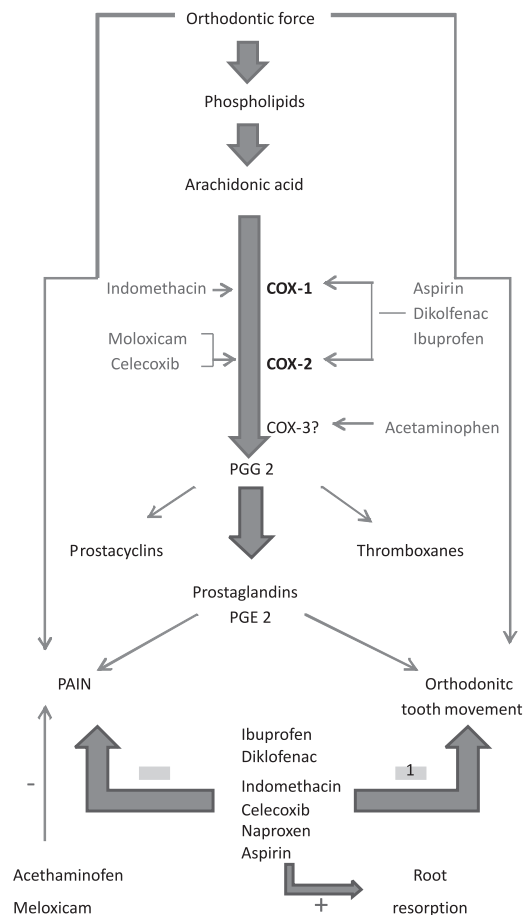


Figure 1. Mechanism of analgesic effect of NSAIDs in tooth movement resulting from orthodontic forces.

Table 1.

	Effect on orthodontic tooth movement	Xerostomy	Taste disorders	Aphthous stomatitis	Ulcerative stomatitis	Gingival bleeding	Root resorption	Mode of action	Reference
<b>Carboxylic acid derivatives</b>									
Acetylsalicylic acid (Aspirin)	Inhibiting	None	None	None	None	Yes, rarely	Less significant	Non-selective COX-1 and COX-2 inhibitor	8-10
Arylacetic acids									
Diclofenac	Inhibiting	No	Yes	Common	Yes/No	Yes/No		Non-selective COX-1 and COX-2 inhibitor	11, 12
Indomethacin	Inhibiting	None	None	None	?	None		Selective COX-1 inhibitor	13
Naphthaleneacetic acid (Naproxen)	Inhibiting	Yes	None	None	Yes	None		Inhibition of hormones responsible for pain	14
Arylpropionic acid Ibuprofen	Inhibiting	Yes	No	No	Very rare	Yes/No		Non-selective COX-1 and COX-2 inhibitor	10, 15, 16
<b>Non-acidic compounds</b>									
Coxibs ( Celecoxib)	Inhibiting	No	Rare	No	Rare	No	Less significant	Highly selective COX-2 inhibitor	9, 12, 17, 18
Oxicams (Meloxicam)	None	No	No	No	Rare	Yes/No	None	Selective COX-2 inhibitor	9
Pyrazolones (Pyralsgina)	?	Yes	No	No	Common	Yes/No		Inhibition of COX in CNS	
<b>Aniline derivatives</b>									
Paracetamol	None	No	No	No	No	No	None	Mode of action not fully known	9, 10, 15, 19

of root resorption in teeth moved orthodontically is also lower with highly selective COX-2 inhibitors (celecoxib). At the same time, the drug's effect on the tooth under orthodontic force is inhibitory and leads to either extension of treatment period or an increase of force values (9). However, the study conducted by de Carlos in 2007 states that the use of celecoxib does not affect the time of teeth moving and using rofecoxib in the study inhibited the movement completely (17). Meloxicam seems to be a considerably safer selective COX-2 inhibitor but with long-term use it may cause gingival bleeding as well as ulcerative stomatitis (9). In view of orthodontic treatment, such adverse effects may affect patient's adaptation to the appliance and brackets constantly irritating the surrounding tissues may increase the incidence of such effects. Pyralginum (metamizole sodium) is another drug with few oral adverse effects. Pyralginum inhibits COX effect on the central nervous system but there are no studies assessing its influence on incidence and risk of root resorption as well as its influence on the range of orthodontic tooth movement.

Many authors explicitly indicate acetaminophen (paracetamol) as the safest and recommended drug to alleviate pain during orthodontic treatment (9, 10, 15, 16, 19). Lack of dangerous adverse effects provides paracetamol with number one position among analgesics used in pregnant women and small children. Moreover, paracetamol does not affect the range of tooth movement nor does it increase the risk of root resorption in the moved teeth (9, 10, 15, 16). Since it is not associated with any oral adverse effects, it will not negatively influence the process of becoming accustomed to the appliance (20). Stabile and Stuani in their work draw a conclusion that short-term, two-day use of celecoxib does not affect tooth movement and may constitute an alternative treatment for acetaminophen (21).

## DISCUSSION

Considering the increasing number of drugs, analgesics included, which are available on the market, orthodontists have to constantly expand their knowledge of the medications' possible influence on the duration of orthodontic treatment as well as their adverse effects (4, 5).

In case of drugs contributing to root resorption, the use of self-ligating brackets may be considered, which will allow using less forces due to reduced friction. Moreover, expected duration of treatment should be prolonged and orthodontic forces reduced or used in intervals.

Other adverse effects occurring in the oral cavity should also be considered. Although they do not directly influence duration of orthodontic treatment or condition of dental roots, they may lead to inferior adaptation to the presence of the appliance in the oral cavity or cause chronic gingival conditions. As a result, the orthodontic treatment may have to be suspended and in extreme cases it may produce a need to change the drug to one that would not cause symptoms mentioned above (4, 5).

It is significant that studies of experimental nature are based on different animal material. Different species as well as varied research methodologies may indicate a slightly different response to the same drugs used in the studies (20). Another variable is the dose of medication used. Apparently different doses of drugs may affect or not the risk of dental root resorption as well as the range of movement of the tooth under orthodontic forces (9). Moreover, a question arises, whether the NSAID mode of action is reduced to COX synthesis only or do the drugs also influence other substances and biological response of the body leading to a determined clinical outcome (7, 11, 22).

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