INTRODUCTION

Orthodontic tooth movement is basically a biologic response towards a mechanical force. The movement is induced by the prolonged application of controlled mechanical forces, which create pressure and tension zones in the periodontal ligament and alveolar bone, causing remodeling the tooth sockets.1,2

Orthodontists often prescribe drugs to manage pain from force application to biological tissues, manage temporomandibular joint problems and tackle fungal and viral infections throughout the course of treatment. A recent review of pharmaceuticals commonly used in orthodontic practice, provided an insight into the dosage, pharmacological actions and side effects of these agents.3

Apart from these drugs, patients who consume vitamins, minerals, and other compounds, for the prevention or treatment of various diseases, can also be found in every orthodontic practice. Some of these drugs may have profound effects on the short and long term outcomes of orthodontic treatment. However, in many cases little is known on the nature of this interaction between specific drugs and orthodontic tissue remodeling, thereby increasing the risk of negative effects.4

Orthodontists need to know the pharmacology of drugs that can change bone physiology because they can hinder treatment and increase morbidity.

INFLUENCE OF DRUGS ON ORTHODONTIC TOOTH MOVEMENT

FIDAN ALAKUS SABUNCUOGLU, DDS, PhD
ELCHIN ESENLIK, PhD

ABSTRACT

The objective of the review was to outline the mechanisms of action and effects of some commonly used drugs on tissue remodeling and orthodontic tooth movement. International literature from 1960-2010 on this topic was searched from Medline.

A thorough knowledge about the drugs is mandatory for the dental professionals dealing with patients under orthodontic treatment.

Key words: Drugs, Influence, Orthodontic Tooth Movement

Drugs that promote or retard orthodontic tooth movement

1 Promoter drugs: These agents basically enhance bone resorption. They couple with the secondary and primary inflammatory mediators and enhance tooth movement. They are prostaglandin5, leucotriens6 cytokines7, vitamin8, osteocalcin9 and corticosteroids.10

Prostaglandins and analogs

Remodeling activities associated with inflammatory reactions induced by mechanical stimuli form the biological basis for orthodontic tooth movement. Certain eiconsanoids (PGs and leucotrienes) released from paradental cells in sites of compression and tension have significant stimulatory effects on bone remodeling. This finding led researchers to inject PGs locally at the site of orthodontic tooth movement, to enhance the bone remodeling process, and thereby enhance the pace of tooth movement. Yamasaki et al11 found an increased number of osteoclasts in rats alveolar bone after local injection of PGE1. A similar regimen in human subjects increased significantly the rate of canine and premolar movement.12

Apparently, PGs act by increasing the number of osteoclasts, and by promoting the formation of ruffled borders, thereby stimulating bone resorption. Among the PGs that had been found to affect bone metabolism (E1, E2, A1, and F2-alpha), PGE2 stimulated osteoblas-
tic cell differentiation and new bone formation, coupling bone resorption in vitro.\textsuperscript{13} This indicates that although they enhance the tooth movement process, their side effects are very serious to consider its clinical use. Recent trends are directed toward combining local anesthetics with PGs, in order to reduce pain while injected locally. Research in this regard is still in its preliminary phase.

2 \textbf{Suppressor agents:} These agents basically reduce bone resorption.

\textit{Non-steroidal anti-inflammatory drugs:} Non-steroidal anti-inflammatory drugs (NSAIDs) are little used in orthodontic treatment as clinical and experimental studies have demonstrated that they diminish the tooth movement\textsuperscript{14} through inhibition of the periodontal inflammatory response caused by the activation. Since NSAIDs are freely available over the counter, patients should be advised not to take these drugs during orthodontic treatment, without the dentist’s knowledge. One drug of choice for the patients under orthodontic treatment is acetaminophen whose mode of action is central rather than peripheral. Other drugs having effect on orthodontic tooth movement are described in Table 1.

\textit{Bisphosphonates:} This class of pharmacological agents selectively inhibits osteoclasts. It has been used to treat bone metabolism disorders such as osteoporosis, bone diseases and bone pain from some types of cancer. Laboratory studies have demonstrated that orthodontic tooth movement can be inhibited by the topical application of bisphosphonates. Further studies are required before these drugs can be used in clinical orthodontic therapy. Orthodontists should also be aware of their interactions. In 2005, Schwarz reported an important case of female orthodontic patient who was being medicated with Zometa to control bone metastases related to breast cancer. At the time the patient began treatment with this drug, when the premolar spaces were about one-third closed, all orthodontic movement stopped.\textsuperscript{15,16,17,18}

\textit{Echistatin and RGD peptides:} Another approach made recently was local injection of echistatin and arginine-glycine-spartic acid (RGD) peptides on rats to prevent tooth movement, thereby enhancing anchorage. Dolce et al\textsuperscript{21} made the first attempt in this aspect and reported that ELVAX-40 (a non-biodegradable, non-inflammatory, sustained release polymer) could be used to deliver integrin inhibitors like echistatin and RGD peptide agents (known to perturb bone remodeling), to reduce tooth movement at a local level. Recent research has even demonstrated decrease in root resorption following orthodontic force application after administration of echistatin.\textsuperscript{22} Further research is progressing in this area at different laboratories worldwide. It is clear from the ongoing discussion that up till now no well-established means are available to promote or retard orthodontic tooth movement in clinical setting.

\textit{Acetaminophen:} Acetaminophen (paracetamol) a weak COX-1 and COX-2 inhibitor that also reduces urinary prostaglandin levels after systemic administration, has shown no effect on orthodontic tooth movement in quinea pigs and rabbits. Comparative studies and our clinical experience have demonstrated that acetaminophen is effective for controlling pain and discomfort associated with orthodontic treatment.\textsuperscript{23}

\textit{Sex hormones:} Estrogen is considered the most important hormone affecting bone metabolism in women. It inhibits the production of cytokines involved in osteoclastic activation and bone resorption, such as interleukin-1, tumor necrosis factor-a. Miyajima and colleagues\textsuperscript{24}, in 1996, attributed a female patient’s slow turnover of alveolar bone to her menopausal status and...
to the estrogen supplement she had been taking for three years. The inhibitory effect of androgens on bone resorption has been demonstrated, but their influence on orthodontic tooth movement has not been clarified.

Parathyroid Hormone: Parathyroid hormone (PTH) is produced by the parathyroid glands to regulate serum calcium concentration. In the kidneys, PTH increases renal calcium reabsorption and stimulates the excretion of urinary phosphate. In bone PTH can induce a rapid release of calcium, but also mediates longer term changes by acting directly on osteoblasts and indirectly on osteoclasts. PTH affects osteoblasts’ cellular metabolic activity, gene transcriptional activity, and multiple protease secretion. Its effects on osteoclasts occur through the production of RANKL, a protein that plays a crucial role in osteoclast formation and activity.25

Thyroid Hormones: Thyroid hormones play an essential role in the normal growth and development of vertebrates. They enhance the response to growth hormone, stimulate cartilage growth and differentiation, and promote bone maturation and resorption. In bone remodeling, they act directly by stimulating the action of osteoclasts but they also have an indirect effect through growth factors that are closely related to bone metabolism, such as insulin-like growth factor I (IGH-1), which is produced locally in bone cells by the action of thyroid hormones. The clinical applications of these drugs still need to be clarified.27

Vitamin D: In 1988, Collins and Sinclair demonstrated that intraligamentous injections of a vitamin D metabolite, 1,25-dihydroxycholecalciferol (1,25D), caused an increase in the number of osteoclasts and the amount of tooth movement during canine retraction with light forces in cats. Similar results were observed that local application of vitamin D enhanced the rate of tooth movement in rats; according to the authors, this effect was due to the well-balanced bone turnover induced by vitamin D.26

CONCLUSION

A thorough knowledge the drugs is mandatory for the dental professionals dealing with orthodontic patients. There are more chances for the patients to take NSAIDs inadvertently. This might slow down the rate of orthodontic tooth movement, which will eventually increase the total treatment period.

<table>
<thead>
<tr>
<th>Non-steroidal-anti-Inflammatory Drugs</th>
<th>Effect on Bone Metabolism</th>
<th>Effect on Tooth Metabolism</th>
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<tr>
<td>Aspirin</td>
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<tr>
<td>Diclofenae</td>
<td>Bone resorption –</td>
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<td>Ibuprofen</td>
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<td>Indometacin</td>
<td>Bone resorption –</td>
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<tr>
<td>Celecoxib</td>
<td>Bone resorption (in vitro) –</td>
<td>Tooth Movement –</td>
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<tr>
<td>Corticosteroids</td>
<td>Bone resorption + (chronic use)</td>
<td>Tooth Movement +</td>
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<tr>
<td>Bisphosphonates</td>
<td>Bone resorption –</td>
<td>Tooth Movement –</td>
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<tr>
<td>Acetaminophen</td>
<td>Unproven</td>
<td>No Influence</td>
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</tbody>
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**Table 1: Effects of Drugs on Induced Tooth Movement**
REFERENCES


8. MK Collins et al: the local use of vitamin D to increase the rate of orthodontic tooth movement AJODO 1988;94:278-84.


26. MK Collins et al. The local use of vitamin D to increase the rate of orthodontic tooth movement AJODO 1988;94:278-84.

