ROLE OF DRUGS IN ORTHODONTIC TOOTH MOVEMENT

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ABSTRACT

There is no drug with out any side effect or adverse reaction, adverse drug reaction is an unwanted or harmful reaction experienced following the administration of a drug or combination of drugs under normal conditions of use and suspected to be related to the drug. Hence in dentistry even the orthodontist also should pay a close attention to the drug consumption history of each and every patient. Since many drugs have shown inhibitory effect on tooth movement. The purpose of this article is to describe the drugs which are commonly affecting the rate of tooth movement.

Keywords: Adverse effects, Drugs, Orthodontic tooth movement.

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

Apart from drugs users, 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.²

Orthodontists should take proper medical history of the patient and also should know the effect of drugs on the tooth movement, because many drugs have shown the retarded 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 prostaglandin,³ leucotriens,⁴ cytokines,⁵ vitamin,⁶ osteocalcin,⁷ and corticosteroids.⁸

Prostaglandins and analogs

Remodeling activities associated with inflammatory reactions induced by mechanical stimuli form the biological basis for orthodontic tooth movement. Certain eicosanoids (PGs and leucotrienes) released from parodontal cells in sites of compression and tensions 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 al 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.\textsuperscript{9}

**Relaxin**

Relaxin has been known for decades as a pregnancy hormone. It is released just before child birth to loosen the pubic symphysis, so that the relaxed suture will allow widening of the birth canal for parturition. It has also been shown to have effects on a multitude of other physiological processes, including the regulation of vasotonus, plasma osmolality, angiogenesis, collagen turnover, and renal function. Relaxin’s influence on soft tissue remodeling and on several mediators that stimulate osteoclast formation and this has attracted attention from orthodontics researchers.\textsuperscript{10}

**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 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.\textsuperscript{10}

**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.\textsuperscript{11}

**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.\textsuperscript{10}

**II Suppressor agents:** These agents basically reduce bone resorption.

**Non-steroidal anti-inflammatory drugs:**

Investigation into the mechanisms involved in the transduction of mechanical forces into biological responses began in the 1970s. Harell and colleagues, in 1977, observed the synthesis of prostaglandins from osteoblasts like cells cultured on orthodontic screws, which had been cemented to the bases of Petri dishes. In an interesting practical application of these findings, Yamasaki and colleagues, in 1980, found that indomethacin, a non-steroidal cyclooxygenase 1 and 2 (COX-1 and COX-2) inhibitor, reduced bone resorption and orthodontic tooth movement in rats. These authors also demonstrated that the local injection of prostaglandin E-1 and E-2 into the submucosa overlying orthodontically treated teeth doubled the rate of tooth movement, both in monkeys and in humans.

Because prostaglandins appear to be important in the process of tooth movement, it has been suggested that the use of over-the-counter NSAIDs by orthodontic patients can significantly alter the efficacy of tooth movement. Recently, Jerome and colleagues showed that Celebrex (Registered trademark of Pfizer, Inc., New York, NY) administered in rats during the application of orthodontic forces did not interfere with tooth movement and
appeared to offer some protection against root resorption.\textsuperscript{10,12,13}

**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{14,15,16}

**Corticosteroids:** The increasing use of glucocorticoid therapy for many inflammatory and autoimmune diseases should alert clinicians to the variations from normal bone turnover that may be caused by this steroid. In animal experiments, high doses of glucocorticoid have actually made the animals osteoporotic. In 2004, however Kalia and colleagues evaluated the rate of tooth movement in rats during short and long term corticosteroid therapy. They demonstrated that bone remodeling seemed to slow down in acute administrations, whereas the rate of tooth movement increased in chronic treatment. Clinically these results suggest that it is possible to treat patients undergoing corticosteroid therapy with a minimum adverse effect. Patients who are within the short term phase of drug use may be advised to postpone orthodontic treatment or because their bone turnover will be delayed, should be scheduled for appliance adjustments at long intervals.\textsuperscript{17}

**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 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. 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.\textsuperscript{18}

**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 guinea pigs and rabbits. Comparative studies and our clinical experience have demonstrated that acetaminophen is effective for controlling pain and discomfort associated with orthodontic treatment.

**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, 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.\textsuperscript{19}

**CONCLUSION**
Orthodontists should be aware that many patients use drugs on a daily basis, and all these
drugs have therapeutic effects, as well as side effects, that may inhibit orthodontic forces. Therefore close attention should be given to the drug consumed by each and every patient during the course of orthodontic treatment. These drugs may slow down the rate of orthodontic tooth movement, which will eventually increase the total treatment duration.

REFERENCES