INFLUENCE OF DRUGS ON ORTHODONTIC TOOTH MOVEMENT

[1]FIDAN ALAKUS SABUNCUOGLU, DDS, PhD
[2]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*

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.

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[5], leucotriens[6] cytokines[7], vitamin[8], osteocalcin[9] 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 al[11] found an increased number of osteoclasts in rats alveolar bone after local injection of PGEI. 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-

[1]**Corresponding author:** Dr Fidan Alakus Sabuncuoglu, Department of Orthodontics, Faculty of Dentistry, Erzurum Marasal Cakmak Military Hospital, Erzurum, Turkey. Email: fidansabuncuoglu@yahoo.com. Tel: +90 442 529 2665, Fax: 90 442 529 2660

[2] Department of Orthodontics, Faculty of Dentistry, University of Suleman Demirel, Isparta, Turkey

tic cell differentiation and new bone formation, coupling bone resorption in vitro.[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 Suppressor agents: These agents basically reduce bone resorption.

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[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 acetaminorphen whose mode of action is central rather than peripheral. Other drugs having effect on orthodontic tooth movement are described in Table 1.

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.[15,16,17,18]

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 glucocorticosteroids have actually made the animals osteoporotic. In 2004, however Kalia and colleagues[19] 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 effects. 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.[20]

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[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.[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.

Acetaminophen: Acetominophen (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.[23]

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[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 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]

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.[28,29] 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 have attracted attention from orthodontics researchers.

Vitamin D: In 1988, Collins and Sinclair demonstrated that intraligamentous injections of a vitamin D metabolite, 1,25-dihydroxycholecalciferaol (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 1: EFFECTS OF DRUGS ON INDUCED TOOTH MOVEMENT

Non-steroidal-anti-Inflammatory Drugs	Effect on Bone Metabolism	Effect on Tooth Metabolism
Aspirin	Bone resorption –	Tooth Movement –
Diclofenae	Bone resorption –	Tooth Movement –
Ibuprofen	Bone resorption –	Tooth Movement –
Indometacin	Bone resorption –	Tooth Movement –
Celecoxib	Bone resorption (in vitro) –	Tooth Movement –
Corticosteroids	Bone resorption + (chronic use)	Tooth Movement +
Bisphosphonates	Bone resorption –	Tooth Movement –
Acetaminophen	Unproven	No Influence

REFERENCES

1 Reitan K. Biomechanical principles and reactions. In: Graber TM, Swain BF, editors. Current orthodontic concepts and techniques, 3rd ed. Philadelphia: WB Saunders Co; 1985.

2 Terranova, VP, Nishimura F. Periodontal ligament cells are chemotactic to fibroblast collagenase. J Dent Res 1996;75: 993-1001.

3 Burke SP, German DS. A brief review of pharmaceuticals commonly used in orthodontic practice. Orthod Cyber J. [www document]. URL http://www.oc-j-com/2-99/drug.htm.

4 Isaacson RJ. Your patients are on drugs. Angle Orthod 2000;70:iv (Editorial).

5 Yamaski et al: clinical application of PGE 1 upon orthodontic tooth movement AJODO 1984;Jun:508-18.

6 Abbash Mohamed et al: Leucotriens in orthodontic tooth movement AJODO 1989;95:231-37.

7 Laurariwasaki et al: Tooth movement and cytokines in gingival crevicular fluid and whole blood in growing and adult subjects AJODO;2005:128;483-91.

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

9 Yasuhiro Kobayashi et al: Effect of local administration of Osteocalcin on experimental tooth movement angle ortho 1998;68:259-66.

10 Michael B. Ashcraft: the effect of corticosteroids induced osteoporosis on orthodontic tooth movement AJODO 1992;102:310-19.

11 Yamasaki K, Shibata Y, Furihara T. The effect of prostaglandins on experimental tooth movement in monkeys (maccaca fuscata). J Dent Res 1982;61:1444-46.

12 Yamasaki K. Shibata Y, Imai S, Tani Y, Shibasaki Y Furihara T. Clinical application of prostaglandin E1 (PGEI) upon orthodontic tooth movement. Am J Orthod Dentofacial Orthop 1984;85:508-18.

13 Gustafson T, Eckerdal O, Leever DL, Sanfeld JL, Montgomery P, Dvidovitch Z. Prostaglandin E2 (PGE2) levels in alveolar bone of orthodontically treated cats. J Dent Res 1977; 56: 407-15.

14 Yamasaki K, Miura F, Suda T. Prostaglandin as a mediator of bone resorption induced by experimental tooth movement in rats. J Dent Res 1980;59:1635-42.

15 Sandy JR, Harris M. Prostaglandins and tooth movement. Eur J Ortho 1984;6:175-82.

16 Kehoe MJ, Cohen SM, Zarrinnia K, Cowan A. The effect of acetaminophen, ibuprofen and mispprostol on prostaglandin E2 synthesis and the degree and rate of orthodontic tooth movement. Angle Orthod 1996;66:339-49.

17 Nase JB, Suzuk JB. Osteonecrosis of the jaw and oral bisphosphonate treatment. J Am Dent Assoc 2006;137: 1115-59.

18 ADA Council on Scientific Affairs. Dental management of patients receiving oral bisphosphonate therapy. J Am Dent Assoc 2006;137:1144-50.

19 Kalia S, Melsen B, Verma C. Tissue reaction to orthodontic tooth movement in acute and chronic corticosteroid treatment. Orthod Craniofac Res 2004;7:26-34.

20 Verma C, Hartig LE, Kalia S, Melsen B. Influence of steroid drugs on orthodontically induced root resorption. Orthod Craniofac Res 2006;9:57-62.

21 Dolce C, Vakani A, Archer L, Morris-Wiman JA, Holliday LS. Effects of echistatin and an RGD peptide on orthodontic tooth movement. J Dent Res 2003;82:682-86.

22 Talic NF, Evans C, Zaki AM. Inhibition of orthodontically induced root resorption with echistatin, an RGD-containing peptide. Am J Orthod Dentofacial Orthop 2006;129:252-60.

23 Graf P, Glatt M, Brune K. Acidic non-steroidal anti-inflammatory drugs accumulating in inflamed tissue. Experientia 1975;31:951-53.

24 Miyajima K, Nagahara K, Iizuka T. Orthodontic treatment for a patient after menopause. Angle Orthod 1996;66:173-78.

25 Potts JT, Gardella TJ. Progress, paradox and potential. Parathyroid hormone research over five decades. Ann NY Acad Sci 2007;1117:196-208.

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

27 Shiraz M, Dehpour AR, Jafari F. The effect of thyroid hormone on orthodontic tooth movement in rats. J Clin Pediatr Dent 1999;23:259-64.

28 Yan Y, Cai J, Fu P, Layfield S, Ferraro T, Kumagai J, et al. Studies on soluble ectodomain proteins of relaxin (LGR7) and insulin 3 (LGR8) receptors. Ann NY Acad Sci 2005;1041:35-39.

29 Sherwood OD. Relaxin's physiological roles and other diverse actions. Endocr Rev. 2004;25:205-34.