Wonders to Orthodontics - Drugs and Hormones.
Sukhpal Kaur¹, Riponjot Singh²
¹Senior lecturer, Dept. of Orthodontics and Dentofacial Orthopaedics, Desh Bhagat Dental College and Hospital, Muktsar, Punjab, India.
²Second Year Dental Hygiene Student, Georgian College of Applied Arts and Technology, Barrie, Canada.

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ABSTRACT
In orthodontic treatment force is applied on tooth which is further transmitted to the adjacent investing tissues leading to some mechanical, chemical and cellular events in these tissues, resulting in tooth movement. Medications can reach these tissues through blood circulation and can change the events taking place in these tissues, thereby affecting orthodontic tooth movement. Their effect may be inhibitory or additive. This review will discuss the different views by various authors regarding the effects of drugs and hormones on orthodontic treatment.

Keywords: Prostaglandins; periodontal ligament; frontal resorption.

INTRODUCTION
Orthodontic tooth movement is a unique process where a solid object (tooth) is made to move through a solid medium (bone). Orthodontic treatment involves the use and control of forces acting on teeth and associated structures.¹ If prolonged pressure is applied to a tooth, tooth movement will occur as the bone remodels. On application of light force, areas of pressure in direction of tooth movement and tension areas on opposite side are formed around the tooth. Blood vessels of periodontal ligament (PDL) compressed on pressure side and dilated on tension side within 3 to 5 seconds resulting in alteration of blood flow and oxygen tension. This changed environment leads to production of primary and secondary chemical messengers like prostaglandins, cytokines, cAMP and cGMP etc which stimulate cellular activity and cell differentiation (osteoblasts and osteoclasts). Osteoclasts remove bone on pressure side, allowing tooth movement. This bone resorption is called as frontal bone resorption. Osteoblasts form bone on tension side and also remodel resorbed bone on pressure side.²

Prostaglandins
Prostaglandins (PGs) mediate the inflammatory response in PDL following orthodontic force application, facilitating tooth movement. They stimulate bone resorption by increasing the number of osteoclasts and activating already existing osteoclasts and also stimulate root resorption, decreased collagen synthesis and increase cyclic AMP. A lower concentration of PGE 2 increases tooth movement and higher concentration leads to root resorption.³,⁴ A Human study reported two times faster tooth movement with administration of local injection of prostaglandins.⁵ The side effect of local injection of PGs is hyperalgesia due to release of noxious agents.³ Nonsteroidal anti-inflammatory drugs (NSAIDs) which inhibit PG synthesis and decrease tooth movement.⁴,⁶ Acetaminophen has no effect on orthodontic tooth movement as it does not inhibit or slightly inhibits PG synthesis.⁷ Rofecoxib completely inhibited orthodontic tooth movement in rats, whereas celecoxib and parecoxib did not.⁸,⁹ But some studies found that Celecoxib suppress
tooth movement and root resorption while aspirin, acetaminophen and meloxicam do not affect tooth movement.\[^{10}\]\(^{10}\) Although celecoxib administration did not affect the number of osteoclasts, the osteoclast activity might be reduced, which could explain the inhibition of tooth movement observed in the celecoxib-treated animals.\[^{11}\]\(^{11}\) Another study found that aspirin and ibuprofen decrease tooth movement whereas acetaminophen has no effect on tooth movement.\[^{12}\]\(^{12}\) Sandy and Harris found that flurbiprofen inhibit the appearance of osteoclasts but had no significant effect on tooth movement but Sakas found that flurbiprofen reduces rate of orthodontic tooth movement.\[^{13}\]\(^{13}\),\[^{14}\]\(^{14}\) So effects of NSAIDs on orthodontic tooth movement are still controversial.

**Corticosteroids**

They inhibit intestinal calcium absorption which leads to direct inhibition of osteoblastic function and increase bone resorption, so they increase the rate of tooth movement but there is decreased stability of tooth movement as bone formation is less due to inhibition of osteoblastic function.\[^{15}\]\(^{15}\),\[^{16}\]\(^{16}\) Yamane et al found lower amount of tooth movement after hydrocortisone administration at a dose of 10 mg/kg/day for 7 days in rats and Davidovitch et al showed slower tooth movement in cats treated with cortisone acetate (12.5 to 25 mg/day).\[^{17}\]\(^{17}\),\[^{18}\]\(^{18}\) Treatment with trimacrolone acetonide is associated with increased tooth movement in rabbits due to increased resorptive activity in the alveolar bone.\[^{19}\]\(^{19}\) Another study on rats reported that prednisolone treatment did not affect the magnitude of orthodontic tooth movement as compared to control group. These differences may be explained by variations within animal species studied, forces used to move teeth, duration of the experiment, dosage and time interval of administration, and potency of the steroid used.\[^{20}\]\(^{20}\)

**Vitamin D**

Vitamin D is a fat-soluble vitamin that promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of bone. It is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts.\[^{21}\]\(^{21}\),\[^{22}\]\(^{22}\) Intraligamentary injections of vitamin D metabolite, 1,25-dihydroxy cholecalciferol, increases the number of osteoclasts and amount of tooth movement during canine retraction with light forces.\[^{23}\]\(^{23}\) Kale et al observed that local application of vitamin E enhanced the rate of tooth movement in rats due to the well-balanced bone turnover induced by vitamin D.\[^{24}\]\(^{24}\) Another human study demonstrated that dose of 25 pg calcitriol, produces 51% faster canine movement as compared to controls without any damaging effect on surrounding tissues.\[^{25}\]\(^{25}\)

**Thyroid hormone**

Thyroxine and calcitonin hormones are produced by thyroid gland. Thyroid hormones are recommended for the treatment of hypothyroidism and used after thyroidectomy in substitutive therapy. Thyroxine administration increases bone resorption and reduces bone density.\[^{26}\]\(^{26}\) It enhances osteoclastic activity in rats by stimulating the prostaglandins and makes orthodontic tooth movement significantly faster as compared to control group.\[^{27}\]\(^{27}\),\[^{28}\]\(^{28}\) A case report of 11 year old girl showed sudden increase in orthodontic tooth movement of impacted canine at certain periods which coincided with hyperthyroid periods. This indicated possible relationship between the serum level of thyroid hormone and the rate of orthodontic tooth movement.\[^{29}\]\(^{29}\)

**Bisphosphonates**

Bisphosphonates are powerful inhibitors of bone resorption which are commonly used for the prevention and treatment of osteoporosis, osteopenia and some tumor diseases. These affect bone metabolism so it is said to have an influence on orthodontic tooth movement.\[^{30}\]\(^{30}\) They have strong affinity to the solid phase surface of calcium phosphate, leading to inhibition of Hydroxyapatite aggregation, dissolution and crystal formation. Bisphosphonates prevent osteoclastic development from hematopoietic precursors, and produce osteoclast inhibitory factor so decrease orthodontic tooth movement.\[^{31}\]\(^{31}\),\[^{32}\]\(^{32}\) Keles et al found that use of pamidronate in mice, decrease osteoclasts on compression side and reducing tooth movement by 34%.\[^{33}\]\(^{33}\) Orthodontic treatment is possible in patients taking low dose of bisphosphonates for short periods (low risk patients). But in high risk patients treatment is not predictable and has more side effects like longer treatment duration, decreased tooth movement, incomplete space closure and poor root parallelism.\[^{34}\]\(^{34}\) Bisphosphonates investigated to use them in orthodontic treatment to enhance retention, to increase anchorage ability of teeth, to decrease inflammatory root resorption expected during orthodontic treatment.\[^{35}\]\(^{35}\),\[^{36}\]\(^{36}\),\[^{37}\]\(^{37}\)

**Immunosuppressant**

These drugs are used to treat autoimmune disorders and to prevent graft rejection during organ transplantation. Studies have demonstrated that Cyclosporine reduces bone volume, number of osteoblasts and increases osteoclasts.\[^{38}\]\(^{38}\),\[^{39}\]\(^{39}\),\[^{40}\]\(^{40}\) Tacrolimus also induced bone loss both in human beings and in experimental animal models.\[^{41}\]\(^{41}\) When patients taking these drugs require orthodontic treatment, in the initial stage of medications usage, it may be advised to delay orthodontic treatment, as there would be less bone remodeling, or orthodontic activation appointments should be scheduled at longer intervals. Long term
mediation therapy may accelerate tooth movement, thus orthodontic appliances must be adjusted customarily, or with greater frequency.\[42\]

**Estrogens**

These are female sex hormones that present in three forms; estradiole, estrone and estriole. Estrogens enhance bone formation by stimulating bone forming activity of osteoblasts and inhibit tumour necrosis factor.\[43\] interleukin 1a and 6 which are involved in bone resorption.\[44,45\] Thereby these are going to affect orthodontic tooth movement. Celebi et al reported orthodontic tooth movement association with ovarian activity. PGE2 and interleukin 1 are increased in ovariectomized and anestrous cat groups resulting in greater tooth movement.\[46\] Orthodontic tooth movement is faster and root resorption is less in ovariectomized female rats and oocytectomized male rats.\[47\] Xu X et al also found that tooth movement is faster when estrogen levels are low. Therefore orthodontic treatment should be planned according to menstrual cycle.\[48\] Another study showed association of tooth movement with ovulation and menstruation. Orthodontic tooth movement would be faster if orthodontic force applied during menstruation as estrogen levels are low at this time and tooth movement would decrease during ovulation. So this study suggested that orthodontist may accelerate tooth movement by doing activation of orthodontic appliances during menstruation. This method will be safer and effective for female patients.\[49\]

**CONCLUSION**

Drugs and hormones can be beneficial or detrimental to tooth movement that is accelerating or decelerating the tooth movement. Therefore within the sphere of ethics and safety these can make miraculous difference to the orthodontic treatment.

So knowledge of medication of patient undergoing orthodontic treatment is very crucial and medication history should be considered as integral part of orthodontic diagnosis.

**REFERENCES**