**Review Article**

# DRUG INDUCED ORTHODONTIC TOOTH MOVEMENT- A REVIEW

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ABSTRACT:
Orthodontic tooth movement is basically a biologic response towards a mechanical force. It is challenge to orthodontist as orthodontic treatment may cause irritation among adults plus increasing risks of caries, gingival recession, and root resorption and to reduce the time duration is need of the hour. In recent time several drugs have been devised to alter the rate of orthodontic tooth movement. Present review article is an attempt to discuss various drugs and their pharmacological action which promote or suppress orthodontic tooth movement.
Key words: Orthodontic tooth movement, Osteoclast, Bone resorption, Root resorption

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## 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] Today, it is still very challenging to reduce the duration of orthodontic treatments. It is one of the common deterents that faces orthodontist and causes irritation among adults plus increasing risks of caries, gingival recession, and root resorption.

Several studies have been conducted in recent time to study the application of drugs to accelerate the tooth movement. Orthodontists need to know the pharmacology of drugs that can change bone physiology because they can hinder treatment and increase morbidity. Present review article has focused to discuss pharmacological action of various drugs which can accelerate or hinder orthodontic tooth movement.

## METHODS OF ACCELERATING TOOTH MOVEMENT

There are three phases of tooth movement: the initial phase, which is characterized by rapid movement after the application of force; followed by a lag period, where little or no movement and the last phase, where gradual or sudden increase of movement occurs.[3]

The early phase of tooth movement involves acute inflammatory responses characterized by leucocytes migrating out of blood capillaries and producing cytokines, which stimulates the excretion of prostaglandins and growth factors.[4]

The acute phase is followed by the chronic phase that involves the proliferation of fibroblast, endothelial cells, osteoblasts, and alveolar bone marrow cells remodeling process.[5]

## DRUGS PROMOTING TOOTH MOVEMENT

**Prostaglandins (PGE):** They are a group of chemical messengers belonging to the family of

hormones called eicosanoids. It acts by regulating the synthesis of cyclic AMP in many tissues. Cyclic AMP is responsible in controlling the action of various hormones. This allows prostaglandin to affect a wide range of cellular and tissue functions. Prostaglandins are responsible in stimulating contraction of the smooth muscles of the uterus, affects blood flow, sleep cycle and also response to hormones such as adrenaline and glucagon. It also plays a role in elevating body temperature, which leads to inflammation and pain. According to Klein and Raisz[6], Raisz et al[7], 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 osteoblastic cell differentiation and new bone formation, coupling bone resorption in vitro.[8]

**Thyroid hormones:**

Thyroxin and calcitonin are hormones produced by thyroid gland. Thyroxine (T4) is a prohormone that can be converted to its active form tri-iodothyronine (T3). This active form of thyroxine is very important in metabolism of cells and plays a vital role in physical development and growth. Administration of thyroxine will lead to increase in bone remodeling, increase in bone resorption activity and reduces bone density.[9,10]

Thyroxin produces interleukin 1 (IL-IB),a type of cytokine which involves in bone formation through osteoclastic reaction. Studies on rat have been conducted to determine the relationship between exogenous thyroxine and tooth movement. Results show that there was a significant increase in orthodontic movement compared to the control.[11]

**Vitamin D3:**

Vitamin D3 has also attracted the attention of some scientist to its role in the acceleration of tooth movement; 1,25 dihydroxycholecalciferol is a hormonal form of vitamin D and plays an important role in calcium homeostasis with calcitonin and parathyroid hormone (PTH).

Another set of investigators[12] has made an experiment where they have injected vitamin D metabolite on the PDL of cats for several weeks; it was found that vitamin D had accelerated tooth movement at 60% more than the control group due to the increasement of osteoclasts on the pressure site as detected histologically. A comparison between local injection of vitamin D and PGEs on two different groups of rats was also investigated. It was found that there is no significant difference in acceleration between the two groups. However, the number of osteoblasts on the pressure side which was injected by vitamin D was greater than on the PGE2 side. This indicates that vitamin D may be more effective in bone turnover.[13]

**Nitric Oxide:**

Akin[14] et al in 2004 evaluated the role of nitric oxide in orthodontic tooth movement in Sprague-dawley rats. They concluded that multinuclear osteoclasts, Howship's lacunae, capillary vascularization, and orthodontic tooth movement were significantly increased in nitric oxide synthase precursor group as compared to nitric oxide synthase inhibitor.

**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, Kalia[15] 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 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 and clinicians should expect a faster rate of tooth movement with more alveolar bone loss in patients with a long-term steroid therapy, as in chronic asthmatics.

**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 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.[16]

**Bisphosphonates:**
Bisphosphonates are synthetic class of pyrophosphate analogues and they are powerful inhibitors of bone resorption. Bisphosphonates are widely used in treating osteoporosis, Paget's disease, bone metastases, and bone pain from some types of cancer.[17,18] They act by inhibiting the osteoclastic activity and decreasing the number of osteoclasts.[19]
This leads to inhibition of orthodontic tooth movement and hence delays orthodontic treatment. Few studies have been reported on the effect of bisphosphonates in orthodontic tooth movement. All showed a dose-dependent decrease in the rate of OTM, with either topical or systemic administration of bisphosphonates. Topical application of bisphosphonates is also said to be very useful in anchoring and retaining teeth under orthodontic treatment. Long term, use of bisphosphonate is very dangerous. They can cause osteonecrosis, especially in the alveolar bones of maxilla and the mandible.[20]

**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,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.[21]

**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.[22]

**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 have attracted attention from orthodontics researchers.[23]

**Immunosupressants:**
The orthodontist may frequently encounter patients that require prolonged immunosuppressive therapy and orthodontic treatment. Immunosupressants that affect cytokine synthesis (glucocorticoids, cyclosporin-CsA, tacrolimus-FK506 and Sirolimus-RAPA) interfere in bone metabolism and may influence tooth movement. Usually, patients in the initial stage of these medications usage may be advised to delay orthodontic treatment, as there would be less bone remodeling, or orthodontic activation appointments should be scheduled at longer intervals. On the other hand, long term

medication therapy may accelerate tooth movement, thus orthodontic appliances must be adjusted customarily, or with greater frequency.[19]

**Cyclosporine:**

It increases gingival hyperplasia. In most patients the greatest changes in the gingival occurs in first six months of cyclosporine therapy. Severe gingival hyperplasia, make orthodontic treatment, and maintenance of oral hygiene difficult. Treatment should be started or resumed after surgical removal of excessive gingival tissues once there is good oral hygiene. Whenever possible, fixed appliances should be kept to a minimum period with brackets, and avoiding the user of cemented bands. Removable appliances in these cases are not recommended, due to improper fit.[24,25]

**Anti Histamines:**

Histamine (H(1)) receptor antagonists are widely used drugs for treatment of allergic conditions. Although histamine was shown drugs may have varying effects on orthodontic tooth movement.[26]

**Drinking coffee,**

Yi J, et al conducted a study to analyse the effect of coffe on tooth movement. As a daily habit of many people, can be an effective accelerator of tooth movement with little side effect for caffeine can break the calcium balance in bone tissue and directly inhibit the development of osteoblasts, leading to temporary decreased bone mineral density and consequently inducing faster orthodontic tooth movement. Much effort has been made to explore therapies to shorten orthodontic treatment period with limited success. Daily coffee consumption may be a promising approach to enhance orthodontic tooth movement for its reversible effect on bone mineral density and calcium balance.[27]

## CONCLUSION

Bone metabolism allows orthodontic tooth movement. Anything that affects this may either promote or inhibit tooth movement. In some cases this may be beneficial, for example, by increasing stability after active treatment has concluded; or be detrimental, for example by slowing down the rate of space closure following extractions. An understanding of a patient's medications is crucial.

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