**REVIEW ARTICLE**

# Effects of Drugs in Orthodontic Tooth Movement: A Review

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(Kakadiya A, Tandon R, Bhardvaj M, Chandra P. Effects of Drugs in Orthodontic Tooth Movement: A Review. *www.journalofdentofacialsciences.com*, 2014; 3(4): 13-17.)

## Introduction

Systemic or local application of medications and the intake of dietary supplements, such as vitamins and minerals, intentionally or unintentionally may have an impact on orthodontic tooth movement and orthodontic treatment[1].

Usually the effects are mainly two categories of effects: those related to general bone physiology in terms of bone density, bone mineralization, bone turnover rate, and osteoclast differentiation; and clinical side effects induced by medications, such as gingival hyperplasia, xerostomia, and external root resorption[2].

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**Table 1: List of promoter and suppressor drugs**

| Drugs Stimulating Orthodontic Tooth Movement (Promoter drugs) | Drugs Inhibiting Orthodontic Tooth Movement (Suppressor drugs) |
|---|---|
| • Prostaglandins<br>• Para thyroid hormone<br>• Vitamin D<br>• L – arginine | • Calcitonin<br>• Bisphosphonates<br>• Corticosteroids<br>• Estrogens<br>• NSAIDS<br>• Anti cancer drugs<br>• Anti rheumatoid arthritis drugs<br>• Fluorides |

## Prostaglandins

Archidonic acid is metabolized by cyclooxygenase pathway resulting in prostaglandins production[3]. Prostaglandins are important to orthodontic treatment since they mediate the inflammatory response in the PDL following orthodontic force application, facilitating tooth movement. Prostaglandins have been linked with bone resorption as well as bone apposition[4,5].

Prostaglandins play an important role in inflammation. Furthermore, they have an effect on smooth muscle cells, platelet aggregation, peripheral nerve endings, and calcium homeostasis. Synthetic prostaglandin analogues, such as misoprostol, are used for various conditions, including prevention of peptic ulcers[2].

Experiments have shown that PG's may be mediators of mechanical stress during orthodontic tooth movement. They stimulate bone resorption, root resorption, decreased collagen synthesis and increase cyclic AMP. They stimulate bone resorption by increasing the number of osteoclasts and activating already existing osteoclasts. A lower concentration of PGE2 (0.1-1microgram) appears to be effective in enhancing tooth movement. Higher concentration leads to root resorption. Systemic administration is reported to have better effect than local administration[1,2,].

1st human study done by Yamasaki et al (1984)[6] and 2nd by Patil AK et al (2005)[7] clearly depicted that orthodontic tooth movement was achieved approximately twice faster if accomplished by local injection of prostaglandins.

The main side effect associated with local injection of PGs is hyperalgesia due to the release of noxious agents[1].

**Vitamin D**

Vitamin D is collective name given to anti-rachitic substances synthesized in the body and found in dietary sources activated by UV radiation[5]. 1,25 dihydroxycholecalciferol is the most active hormonal form of vitamin D. It regulates calcium and phosphate serum levels by promoting their intestinal absorption and reabsorption in the kidneys. Furthermore, it promotes bone deposition and inhibits PTH release. It also plays a role in the immune response by promoting immunosuppression[2].

In 1988, Collins and Sinclair demonstrated that intraligamentous injections of a vitamin D metabolite, 1,25-dihydroxycholecalciferol, caused an increase in the number of osteoclasts and the amount of tooth movement during canine retraction with light forces in cats[8]. Similar results were observed by Takano-Yamamoto and colleagues in 1992[9].

In 2004, Kale and colleagues observed that local applications of vitamins enhanced the rate of tooth movement in rats due to the well-balanced bone turnover induced by vitamin D[10].

Stimulatory action of vitamin D on osteoblasts can help stabilize orthodontic tooth movement. In 1976, Bran and colleagues reported that rats treated with vitamin D showed increased bone formation on the pressure side of the periodontal ligament after application of orthodontic forces. In 2004, Kawakami observed an increase in the appositional rate on alveolar bone after orthodontic force application; they suggested that local application of vitamin D could intensify the re-establishment of supporting alveolar bone, after orthodontic treatment[11].

**Parathyroid Hormone**

PTH is secreted by the parathyroid glands. Its main effect is an increase in the concentration of calcium in the blood; consequently, it stimulates bone resorption[12]. More recently, Soma and colleagues observed an increased rate of tooth movement in rats treated with PTH, whether administered systemically[13] or locally[14]. These results indicate that orthodontists should take note of patients

being treated with PTH-for example, in cases of severe osteoporosis[15].

**Estrogen**

Estrogen is considered to be the most important hormone affecting the bone metabolism in women. It inhibits the production of various cytokines which are involved in bone resorption by stimulating osteoclast formation and osteoclast bone resorption. It also inhibits osteoblast's responsiveness to PTH. Estrogens do not have any anabolic effects on bone tissue; they directly stimulate the bone forming activity of osteoblasts[1]. Studies have shown that estrogens decrease the velocity of tooth movement[16]. Estrogen supplementation was used to over overcome postmenopausal problems might slow down the rate of OTM[12].

**Corticosteroids**

Corticosteroids are a class of steroid hormones, produced in the adrenal cortex. They are involved in many physiologic systems, such as stress response, inflammatory and immune responses, carbohydrate metabolism, protein catabolism, and blood electrolyte levels[2]. Evidence indicates that the main effect of corticosteroid on bone tissue is direct inhibition of osteoblastic function and thus decreases total bone formation. Decrease in bone formation is due to elevated PTH levels caused by inhibition of intestinal calcium absorption which is induced by corticosteroids[1]. Corticosteroids increase the rate of tooth movement, and since new bone formation can be difficult in a treated patient, they decrease the stability of tooth movement and stability of orthodontic treatment in a general[17].

**Bisphosphonates**

There are two classes of bisphosphonates: nitrogen containing and non-nitrogen containing bisphosphonates. They act on different pathways, but their final effect is the same. They all inhibit bone resorption, although their effectiveness differs considerably. They are used primarily for the prevention and therapy of osteoporosis, Paget's disease, bone metastases, and bone pain from some types of cancer[18,19]. Studies have shown that bisphosphonates inhibit orthodontic tooth movement and delay the orthodontic treatment[20]. A serious drawback of long-term use of bisphosphonates is that they can cause osteonecrosis, especially in the alveolar bones of the maxilla and the mandible[19].

**Calcitonin**

Calcitonin is a peptide hormone secreted by thyroid in response to hypocalcaemia .It is produced by parafollicular 'C' cells of thyroid. Synthesis and secretion of Calcitonin is regulated by plasma calcium concentration. Rise in plasma calcium increases, while fall in plasma calcium decreases Calcitonin release. Calcitonin inhibits proximal tubular calcium and phosphate reabsorption by direct action on kidney. Calcitonin is used in the treatment of hypercalcemia, osteoporosis and paget's disease of bone. Calcitonin inhibits bone resorption by direct action on osteoclasts, decreasing their ruffled surface which forms contacts with resorptive pit. It also stimulates the activity of osteoblasts. Because of its physiological role, it is considered to inhibit the tooth movement; consequently, delay in orthodontic treatment can be expected[1, 3].

**Fluoride**

Fluoride is one of the trace elements having an effect on tissue metabolism. Fluoride increases bone mass and mineral density, and because of these skeletal

actions, it has been used in the treatment of metabolic bone disease, osteoporosis. Even a very active caries treatment with sodium fluoride during orthodontic treatment may delay orthodontic tooth movement and increase the time of orthodontic treatment. Soudium fluoride has been shown to inhibit the osteoclastic activity and reduce the number of active osteoclasts[21].

**Paracetamol**

Paracetamol (acetaminophen) is a commonly used analgesic. It lacks anti-inflammatory properties. Therefore, it does not belong with NSAIDs, although their chemical structures are comparable. Other important differences are that paracetamol has almost no effect on blood clotting and no detrimental effects on the stomach lining. These differences are related to its mode of action[2,3]. Paracetamol does not affect the rate of OTM with low dosages, studies suggest that it should be the analgesic of choice for managing pain associated with orthodontic therapy[22,23].

**Table 2: Effects of various drugs and systemic factors on induced tooth movement**

| *DRUGS* | Effects on bone metabolism | Effects on tooth movement |
|---|---|---|
| **Non Steroidal Anti Inflammatory Drugs** | | |
| Aspirin | Decrease bone resorption | Decrease tooth movement |
| Diclofenac | Decrease bone resorption | Decrease tooth movement |
| Ibuprofen | Decrease bone resorption | Decrease tooth movement |
| Indomethacin | Decrease bone resorption | Decrease tooth movement |
| Celecoxib | Decrease bone resorption | No influence |
| **Paracetamol** | Unproven | No influence |
| **Corticosteroids** | Increase bone resorption | Increase tooth movement |
| **Bisphosphonates** | Decrease bone resorption | Decrease tooth movement |
| **Prostaglandins** | Stimulate bone resorption | Enhancing tooth movement |
| **Interleukin Antagonist** | Reduced bone remodeling | Reduced tooth movement |
| **Anti Cancer drugs** | Produce damage to precursor cells involved in bone remodeling process | Complicating tooth movement |
| **Leukotrienes** | Stimulate bone resorption | Enhancing tooth movement |
| **Flourides** | Inhibit osteoclastic activity | Decrease tooth movement |
| **L – Arginine** | Increased bone remodeling | Increase tooth movement |
| ***SYSTEMIC FACTORS*** | | |
| **Para thyroid hormone** | Increase bone resorption | Increase tooth movement |
| **Thyroid hormone** | Increase rate of bone remodeling | Increase tooth movement |
| **Vitamin D** | Increase rate of bone remodeling | Increase tooth movement |
| **Estrogen** | Decrease bone resorption | Decrease tooth movement |
| **Calcitonin** | Inhibit bone resorption | Inhibit tooth movement |
| **Androgen** | Decrease bone resorption | Unproven |
| **Relaxin** | Increase bone resorption | Increase tooth movement |
| **Dietary Calcium (Low diet)** | Increase bone resorption | Increase tooth movement |

**Table 3: Teratogens affecting dentofacial development**

| Teratogens | Effects |
|---|---|

| Teratogens | Effects |
|---|---|
| Aminopterin | Anencephaly |
| Aspirin | Cleft lip and palate |
| Cigarette smoke | Cleft lip and palate |
| Cytomegalovirus | Microcephaly, Hydrocephaly and Micropthalamia |
| Dilantin | Cleft lip and palate |
| Ethyl alcohol | Central midface deficiency |
| Mercaptopurine | Cleft palate |
| Rubella virus | Micropthalamia, Cataracts and Deafness |
| Thalidomide | Malformations similar to Craniofacial microsomia and Treacher Collins syndrome |
| Toxoplasma | Microcephaly, Hydrocephaly and Micropthalamia |
| X- radiation | Microcephaly |
| Valium | Similar to Craniofacial microsomia and Treacher Collins syndrome |
| Vitamin D excess | Premature suture closure |
| cis Retinoic acid | Similar to Craniofacial microsomia and Treacher Collins syndrome |

## Conclusion

Orthodontists must know that teeth move at different rates and every individual has differing responses to orthodontic treatment. Many of these differences are caused by changes in bone remodeling process by various drugs and systemic factors.

Orthodontists should assume that many patients are taking prescription or medications regularly. The orthodontist must identify these patients by carefully questioning them about their medication history and their consumption of food supplements and it should consider a part of every orthodontic diagnosis.

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