Drug Induced Orthodontic Tooth Movement: A Comprehensive Review

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Abstract
Remodeling of the paradental tissues facilitates orthodontic tooth movement in response tomechanical forces. During orthodontic treatment, the application of sustained force on teeth which guides to tooth mobility processes that ultimately lead to alveolar bone remodeling. The present review highlights the significance for orthodontists to get a full list of all the medications being taken by every patient scheduled to undergo orthodontic treatment.

Keywords: *Movement, Orthodontic, Tooth*

Introduction

During orthodontic treatment, the application of sustained force on teeth which guides to tooth mobility processes that ultimately lead to alveolar bone remodeling. These biochemical processes involve a multitude of cellular and molecular networks. Pharmacological agents have the potential to interfere with the biochemical processes which govern tooth movement during, and stability after, orthodontic treatment. As a result, the possibility to accelerate/enhance Orthodontic Tooth Movement (OTM)where needed (such as in areas of space closure) and to halt tooth movement where desired (to provide anchorage or to ensure positional tooth stability during the initial retention period) has attracted considerable interest in the field.[1- 3]

Drugs

Tenoxicam

In a previous study, Athirst et al investigated the effect of Tenoxicam in controlling pain and its influence on orthodontic tooth movement of the upper canine in 36 patients who had an orthodontic indication for bilateral retraction of the upper canine teeth. Group A patients received one tablet of 20 mg of Tenoxicam 45 minutes before the orthodontic activation process and one tablet of placebo after activation. Group B patients received the opposite treatment, and Group C received one tablet of placebo 45 minutes before the procedure and one tablet of placebo just afterward. Subsequently, after 30 days interval, there was no statistically significant difference in orthodontic tooth movement between the 3 groups, but patients in groups A and B had lower pain intensity than in those in group C. Thus, Tenoxicam when used only once daily was shown to be effective for pain control, without having a significant influence on orthodontic tooth movement.[4]

Calcitriol (Vitamin D3)

Al Hasini et al conducted a randomized control trial (RCT) on 15 patients who required bilateral maxillary canine retraction were randomly allocated into three groups, each treated with a specific dose of vitamin D3 (15 µg, 25 µg and 40 µg, respectively). In the experimental side, a specific dose of Calcitriol was injected locally in the distal side of the canine, while the control side received 0.2 ml of vehicle. As a result, the experimental site in groups 1 and 3 showed about 10% higher clinical net rate of canine movement compared to the control site. In group 2, the experimental site demonstrated 51.0% increase in OTM movement compared to the control site. This suggests that locally injected calcitriol, in a specific dose is cost-effective in increasing orthodontic tooth movement in humans without any side effect.[5]

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 osteoblastst. Studies have shown that estrogens decrease the velocity of tooth movement. Estrogen supplementation was used to over overcome postmenopausal problems might slow down the rate of OTM.[6]

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. 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. 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 general.[6]

Acetaminophen

Paracetamol (acetaminophen) was first identified in the late nineteenth century and it was available in the UK on prescription in 1956, and over-the-counter in 1963. Since then, it has become one of the most popular antipyretic and analgesic drugs worldwide, and it is often also used in combination with other drugs. The lack of a significant anti-inflammatory activity of paracetamol implies a mode of action which is distinct from that of the non-steroidal anti-inflammatory drugs. Yet, the Cochrane Systematic Review, 2004 concluded that paracetamol was effective against the postoperative pain in adults. Acetaminophen (paracetamol) is effective for controlling pain and discomfort associated with orthodontic treatment.[7]

Fluorides

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. Sodium fluoride has been shown to inhibit the osteoclastic activity and reduce the number of active osteoclasts.[8]

Bisphosphonates

A research study conducted by Igar et al 16 implicates that, Bisphosphonates (BPNs) can inhibit orthodontic tooth movement and delay the orthodontic treatment. On topical application these are very useful in anchoring and retaining the teeth position during the fixed orthodontic therapy. They also suggest that BPNs have a strong chemical affinity to the solid-phase surface of calcium phosphate leading to inhibition of hydroxyapatite aggregation, dissolution, and crystal formation. Other important functions of Bisphosphonates (BPNs) are as follows: It cause a rise in intracellular calcium levels in osteoclastic-like cell line, prevention of osteoclastic development from hematopoietic precursors, production of an osteoclast inhibitory factor and reduction of osteoclastic activity.

Thyroid hormones

Some evidences suggest that the orthodontic tooth movement is accelerated when the patients are under thyroxine medication.[17] Reduced dosage with short-term thyroxine administration are reported to decrease the frequency of “force-induced” root resorption. Decrease in root resorption may be correlated to a change in bone remodeling process with a reinforcement of the protection of the cementum and dentin to “force-induced” osteoclastic resorption. Administration of Thyroxin leads to increased bone remodeling, bone resorptive activity with reduced bone density. Increase in interleukin-1 (IL-1B) production induced by thyroid hormones at low concentrations affects the bone tissue by cytokine stimulated osteoclast formation and osteoclastic bone resorption.

Relaxin

Relaxinis also known as a pregnancy hormone which are just released before the child birth to loosen the pubic symphysis, so that the relaxed suture will allow widening of the birth canal for parturition. In 2005, Liu et al showed that the administration of relaxin accelerates the early stages of orthodontic tooth movements in rats. [18]Stewart et al also used gingival injections of Relaxin to relieve rotational memory in the connective tissues of maxillary lateral incisors which have been rotated orthodontically. Nicoziset al also suggested that Relaxin might be used as an adjuvant during the fixed orthodontic therapy, for rapid remodeling of gingival tissue during extraction space closure, elevation of stability and during orthopaedic expansion in non – growing patients, by reducing the tension of the stretched soft tissue envelope, particularly the expanded palatal mucosa, after orthognathic surgery.

Echistatin and RGD peptides

Recent study on rats to prevent tooth movement evokes that, local injectionof integrin inhibitors like echistatin and RGD (Arginine–Glycine–Aspartic acid) peptides enhances anchorage. Current research

has also demonstrated that after the administration of Echistatindecreased the root resorption following orthodontic force application.[19]

Anticancer drugs

Current analysis clearly stated that patients who had been on chemotherapy with busulfan/cyclophosphamide belong to the risk group for orthodontic treatment which causes damage to precursor cells involved in bone remodeling process, thereby complicating and slowing down the tooth movement.[20]

Immunosuppressant drugs

Immunosuppressant drugs administered to patients with chronic renal failure or kidney transplants has encountered some difficulty during orthodontic treatment. These drugs consumed for prevention of graft rejection like cyclosporine A to produce severe gingival hyperplasia, making the orthodontic treatment and maintenance of oral hygiene difficult. These fixed appliances should be kept to a minimum period of time with brackets by avoiding the cemented bands and also the removable appliances in these cases are not recommended due to improper fit.[21]

Mechanism& Discussion

Several theories about orthodontic tooth movement have been proposed, and all of them present the bone resorption as one of the biological effects. In the first half of the twentieth century there was already concern about the action mechanism and the events triggered by the applied force on the dental crown. The pressure-tension theory was based on the vitality of the periodontal ligament, i.e., the stimulation applied to the ligament did not involve or require stimulation coming from other structures such as the alveolar bone, for instance. The collagen fibers and the vascular system were essential for the development of this phenomenon.[9, 10]

The orthodontic tooth movement is characterized by a multiple biological process involving sequential reactions of the periodontal tissue in response to biomechanical forces. Two regions can be observed in the periodontal ligament, the tractionzone and the compression zone. New bone is deposited in the alveolar wall on the traction side when light or heavy mechanical forces are applied. On the compression side, under light force, the alveolar bone is directly resorbed by osteoclasts located in Howship's lacunae.[11]

When the force exerted on the tooth has enough strength to fully occlude the vessels and block the blood supply before the engagement of the osteoclasts, sterile necrosis is produced in the area. Due to the acellular and avascular aspect, this region is called hyaline. The tooth movement will not happen until the alveolar bone is resorbed, the hyaline areas are removed and the ligament restored. Role of vitamin D3 and Corticosteroids in OTM still remains unclear. Some authors have reported that it promotes tooth movement but there are also studies that demonstrate bone formation after application of these drugs. So, it is important to have more clinical trials on determining the exact role of Vitamin D3 and Corticosteroids in orthodontic tooth movement. Bisphosphonates are drugs which also effect the calcium homeostasis. It is known for its role in inhibiting tooth movement. They are used in cases of prevention of orthodontic relapse but it should be used with great caution because of its severe side effects on long term use. Hormones also play an important role in tooth movement. Hormones such as thyroxin is known to increase the rate of tooth movement by directly stimulating the action of osteoclast.Calcitonin and Estrogen have the opposite effect on tooth movement. It is very important to know if the patient is under any oral contraceptive pills containingestrogens, which inhibits tooth movement.[12- 16]

Conclusion

Orthodontists have long observed that teeth move at different rates and individuals differ in their response to treatment. Some of the differences are caused by change in bone remodeling induced by drugs and systemic factors. All the drugs reviewed have therapeutic effects as well as side effects that influence the cells targeted by orthodontic forces. The value of a thorough medical history is increasingly significant as young and old alike are exposed to a greater range of therapeutic agents.

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