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Influence of Drugs on Orthodontic Treatment: A Review

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ABSTRACT

Background: Orthodontic tooth movement is basically a biologic response towards a mechanical force. Tooth movement is the key principle behind any orthodontic treatment. Orthodontic tooth movement is mainly a biological response towards 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.

Keywords: Orthodontic tooth movement, Osteoclast, Bone resorption, Root resorption.

INTRODUCTION

Tooth movement is the key principle behind any orthodontic treatment. Orthodontic tooth movement (OTM) is mainly a biological response towards mechanical force. It is induced by the prolonged application of controlled mechanical force on the tooth, which eventually causes remodeling of the tooth socket by creating pressure and tension zones in the alveolar bone and periodontal ligament[1]. 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[2]. The classical theory of tooth movement suggests that the cellular reactions are simply the result of differential pressure induced in the periodontal ligament, and that the response to force is confined to the cellular elements of the ligament and the endosteal marrow spaces[3]. Strains of periodontal cells, bone-related cells, and extracellular matrix play a key role in orthodontic tooth movement (OTM) [4]. This strain forms changes in gene expression in the cells by interactions between the cells and the extracellular matrix, whereby integrins play an important role[5]. Various cell-signaling pathways are activated, ultimately leading to stimulation of periodontal ligament metabolism, and localized bone resorption and bone deposition[4, 6]. These interactions are regulated by local factors such as cytokines (IL-1), and growth factors, as well as by systemic factors such as parathyroid hormone, vitamin D, estrogen, or caicitonin[7].

Drugs that alter or interfere with the inflammatory process will therefore have an effect on the tooth movement. 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 effects of pharmacological action of various drugs which can accelerate or hinder orthodontic tooth movement.

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DRUGS PROMOTING TOOTH MOVEMENT:

Prostaglandins (PGE):

Prostaglandins (PGE) 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[1, 2].

Prostaglandins play an important role in promoting bone resorption. It is believed that, prostaglandins promote resorption by stimulating cells to produce cyclic AMP, which is a very important chemical messenger for bone resorption[8, 9]. Introduction of prostaglandins in controlling the rate of tooth movement were first attempt in 1982, where the rate of orthodontic tooth movement and the possible side effects on gingival tissues in monkeys was studied[10, 11]. Studies on humans were conducted in 1984, effects of PGE1 administration on orthodontic tooth movement where studied.

The author reported that, the rate of tooth movement was doubled compared to control sides[12]. In India, Bhalajhi and Shetty conducted a study on the effect of exogenous administration of PGE2 in young rabbits. The study concluded that, there was a significant increase in the rate of tooth movement clinically, and microscopically there were increase in the number of osteoclasts and resorption of lacunae. But there was a frequent need of administration of the drug as PGE2 gets metabolized rapidly in the lungs[13].

Leukotrienes:

Leukotrienes are a type of eicosanoid which is a product of arachidonic acid conversion and are the only eicosanoids that are formed independently from cyclooxygenase (COX). They are produced when arachidonic acid is metabolized by lipoxygenase enzymes. Leukotrienes also play an important role in Inflammation, allergies, and diseases such as asthma. These conditions can be cured by using leukotriene inhibitors which block leukotriene receptors hence counteracts their effects. Examples of medication are montelukast and zafirlukast[1]. According to Mohammed AH et al. 1989, leukotrienes causes increase in orthodontic tooth movement, through bone remodeling whereas, leukotrine inhibitors work the other way round[14]. Therefore, the use of leukotriene inhibitors can delay orthodontic treatment, leukotrienes can be used in future clinical applications that could result in increasing tooth movement.

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)[1, 2]. Thyroxin administration lead to increased bone remodeling, increased bone resorptive activity, and reduced bone density. Effects on bone tissue may be related to the augmentation of interleukin-1 (IL-1B) production that thyroid hormones induce at low concentrations, cytokine stimulate osteoclast formation and osteoclastic bone resorption. The speed of orthodontic tooth movement increased in patients undergoing such medication[15]. 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[16]. The thyroid hormone increases the speed of orthodontic tooth movement in patients undergoing such medication. Low dosage and short-term thyroxine administration are reported to lower the frequency of "force-induced" root resorption. Decrease in resorption may be correlated to a change in bone remodeling process and a reinforcement of the protection of the cementum and dentin to "force-induced" osteoclastic resorption [17].

Vitamin-D:

Vitamin D and its active metabolite, 1,25, 2(OH)D3, together with parathyroid hormone (PTH) and calcitonin, regulate the amount of calcium and

phosphorus levels. Vitamin D receptors have been demonstrated not only in osteoblasts but also in osteoclasts precursors and in active osteoclasts[18]. Vitamin D3 has also attracted the attention of some scientist to its role in the acceleration of tooth movement; 1, 25 dihydroxy-cholecalciferol is a hormonal form of vitamin D and plays an important role in calcium homeostasis with calcitonin and parathyroid hormone (PTH)[2]. Collins et al in 1988 [23], demonstrated that local application of vitamin D3 improves the rate of tooth movement in rats. This effect was due to the well-balanced bone turnover induced by vitamin D3. So more studies have to be conducted in determining the exact role of Vitamin D3 in orthodontic tooth movement[19].

Corticosteroids:

Adrenal cortex is a part of the adrenal gland, which is responsible for production of androgen (sex hormone) and corticoid hormones. According to their biological effects, corticoid can be classified as glucocorticoid (cortisol) and mineralocorticoid (aldosterone) [1]. A low dose (1mg/kg body weight) decreases orthodontic tooth movement by suppressing osteoclastic activity. At high dose (15mg/kg body weight) it increases osteoclastic activity thus produces more rapid orthodontic tooth movement and subsequent relapse. The main effect of corticosteroid on bone tissue is direct inhibition of osteoblastic function and thus the decrease of total bone formation[20]. Glucocorticoids are prescribed for various inflammatory and autoimmune conditions, including rheumatoid arthritis, dermatitis, allergies, and asthma. They are also used as immunosuppressive medications after organ transplantation. Corticosteroids acts by preventing the formation of prostaglandins by influencing the arachidonic acid pathway. An endogenous protein, lipocortin formed by steroids acts by blocking the activity of phospholipase A2, thus inhibits the release of arachidonic acid which in return influences the synthesis of prostaglandin, leukotrienes or thromboxanes. Corticosteroids also act by reducing the release of lymphokines, serotonin and bradykinin at the injured site[15, 20].

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They play a vital role in inhibiting the intestinal calcium absorption, which leads to direct inhibition of osteoblastic function, and increase in bone resorption[15,20,21]. In 2004, Kalia and colleaguesevaluated the rate of tooth movement in rats during short and long term corticosteroid therapy. They concluded that bone remodeling seemed to slow down in acute administrations, whereas the rate of tooth movement increased in chronic treatment.

This suggest that orthodontic treatment should be postponed in patient undergoing short term corticosteroids whereas, patient with long term corticosteroid therapy treatment can be continued with minimal adverse effect and more extensive retention may be helpful in retaining these teeth if the dentist decides to proceed with the orthodontic treatment[22].

Nitric Oxide:

Akin et al in 2004 evaluated the role of nitric oxide in orthodontic tooth movement in Spraguedawley 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[23].

Cytokines:

Cytokines are small proteins that are identified as mediators of bone resorption. One cytokine, Interferon (IFN)-γ, acts as a bone resorption inhibitor that is opposite to other cytokines. Leukotrienes are a type of eicosanoid which is a product of arachidonic acid conversion and are the only eicosanoids that are formed independently from cyclooxygenase (COX) [15]. According to Mohammed AH et al leukotrienes causes increase in orthodontic tooth movement, through bone remodeling whereas, leukotrine inhibitors work the other way round. Therefore, the use of leukotriene inhibitors can delay orthodontic treatment, leukotrienes can be used in future clinical

applications that could result in increasing tooth movement[29].

SUPPRESSOR AGENTS: These agents basically reduce bone resorption.

Non-steroidal anti-inflammatory drugs:

Non steroidal Anti-Inflammatory Drugs or generally called as NSAIDS is a very common drug in pain control. They have analgesic, antipyretic, and anti-inflammatory effects, and are prescribed for many conditions, such as rheumatoid arthritis, osteoarthritis, gout, dysmenorrhea, headache, migraine, and postoperative pain, as well as for the prevention of cardiovascular diseases and colorectal cancer[1]. 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[2]. Several studies were conducted in determining the effect of NSAIDs in orthodontic tooth movement. All the studies revealed that there was some amount of retardation in the rate of orthodontic tooth movement[24].

Sex Hormones:

Sex hormones play a role of bone metabolism. Estrogen has a direct effect on bone. It preserves calcium in bone by suppressing the activation frequency of bone remodeling. The remodeling activation will increase when menopause starts and the result is rapid bone loss leading to symptomatic osteoporosis. Estrogen directly stimulates the bone-forming activity of osteoblasts, so it is reasonable to expect a slower rate of orthodontic tooth movement[25]. Oral contraceptive pills contains estrogen, when taken by younger woman for a long span, it can influence the rate of tooth movement. Therefore, it is extremely important for the dentist to consider this factor during history taking and treatment planning in females[1,25].

Bisphosphonates:

Bisphosphonates are synthetic class of pyrophosphate analogues and they are powerful inhibitors of bone resorption. Bisphosphonates (BPNs) have strong chemical affinity to the solid-phase surface of calcium phosphate; this causes inhibition of hydroxyapatite aggregation, dissolution, and crystal formation. Bisphosphonates are widely used in treating osteoporosis, Paget's disease, bone metastases, and bone pain from some types of cancer. They act by inhibiting the osteoclastic activity and decreasing the number of osteoclasts. This leads to inhibition of orthodontic tooth movement and hence delays orthodontic treatment[1,26,27].

Topical application of bisphosphonates is also said to be very useful in anchoring and retaining teeth under orthodontic treatment. Long term, use of bisphosphonate are very dangerous. They can cause osteonecrosis, especially in the alveolar bones of maxilla and the mandible[28].

Anti-Convulsant:

Valporic acid has a potential to induce gingival bleeding even with minor trauma making orthodontic maneuvers difficult. Phenytoin induces gingival hyperplasia due overgrowth of gingival collagen fibers, which involves the interdental papilla, making application of orthodontic mechanics difficult and difficulty in maintaining oral hygiene. Gabapentin produce xerostomia, making oral hygiene maintenance difficult during orthodontic treatment[15].

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[30, 31].

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[32].

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[33].

Immunosuppressants:

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[2,34].

CONCLUSION

As more and more chemical analogues are being used in the form of new drugs to avoid resistance, today's clinicians should mandatorily update his knowledge on the clinical efficacy of the new drugs as well as the beneficial and harmful effects on human tissues . Bone metabolism allows orthodontic tooth movement. Anything that affects this may either promote or inhibit tooth movement. It is always advisable for a dentist to confirm with the family physician or the concerned physician for fitness of the patients who undergo orthodontics involving tooth movement. Orthodontists should assume that many patients are taking prescription or over-the counter medications regularly. An understanding of a patient's medications is crucial.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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