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Review Article: Effects of Medication on Orthodontic Tooth Movement

Dr. Mahaja Maharoof[1], Dr. Hashim ali[2], Dr. Govind Hari[3],
[1]*Post Graduate student, Kannur Dental College, Anjarakkandy, Kerala*
[2]*Head of the Department, Department Of Orthodontics, Kannur Dental College*
[3]*Post Graduate student, Kannur Dental College, Anjarakkandy, kerala*
CorrespondingAuthor: Dr. Mahaja Maharoof

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I. INTRODUCTION

Orthodontics is a specialty of dentistry, work mainlyusingbiomechanical principles of moving teeth that can correct dental malrelation and malformations of the jaws and face to correct and restore a functional, stableandaesthetic dentition. Orthodontic treatments are mainly to correct dental displacements, using either fixed or removable systems. Mostly the alveolar bone needs to be remodelled. Dentofacialorthopedics treatments also include the control and modification of jaw positions and facial growth by controlling the growth sites in the maxilla and mandible. An applied force to the crown of a tooth is transmitted through the root of the tooth to the periodontal ligament and alveolar bone. According to the applied force direction, there will be areas of pressure and tension on these supporting structures [1].

For the movement of tooth, there must be resorption of alveolar bone in response to this stress, and deposition of bone in the opposite

Side to retain tooth in that moved position. The classical theory of tooth movement suggests that the cellular reactions are simply the result of differential pressure applied in the periodontal ligament, and the response to the applied force is confined to the cellular elements of the periodontal ligament and the endosteal marrow spaces [2,3]]. Many experiments have suggested that altered physical stress in the bone changes the solubility of the hydroxyapatite crystals, which in turn induces the osteoblastic and osteoclastic activity which results in bone remodelling [4, 5].

Davidovitch, Krishnan V and Yamasaki et al concluded in their studies that the rate of orthodontic tooth movement can be altered by administrating certain drugs locally or systemically. Drugs used in orthodontics can be broadly classified into two major groups, promoter agents and suppressor agents. Promoter drugs are agents that act with inflammatory mediators and enhance tooth movement,examples; Prostaglandin, Leukotrienes, Cytokines, Vitamin D, Osteocalcin, and Corticosteroids. Suppressor agents are drugs which reduces bone resorption e.g.; Nonsteroidal anti-inflammatory agents and bisphosphonates [6, 7]. Most of the patients who undergo orthodontic treatment may be on medication for different medical conditions, as an orthodontist we must take a proper history of medication that may influence the orthodontic mechanics.

Effects of drugs on the orthodontic tooth movement can be summarized as:

NSAIDS: Analgesic is a drug that selectively relieves pain by acting on the CNS or peripheral pain mechanisms, without significantly altering consciousness. NSAIDs are a relatively weak inhibitor of PG synthesis. The whole process is controlled by inhibition of COX activity, leading to altered vascular and extravascular matrix remodeling, causing a reduction in the pace of the tooth movement [3, 8]. A recent study reported that Nabumetone, a drug belonging to NSAID group reduces the amount of root resorption along with control of pain from intrusive orthodontic forces without affecting the degree of tooth movement [1, 8].

THERAPEUTIC USES

- ❖ Inflammation
- ❖ Pain
- ❖ Fever
- ❖ Fetal circulatory system
- ❖ Systemic mastocystosis
- ❖ Niacin tolerability
- ❖ Bartter syndrome
- ❖ Cancer chemoprevention

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ACETAMINOPHEN: Paracetamol is available in the market under different trade names in simple or complex preparations combined with an additional active substance obtainable only by prescription (with tramadol). Paracetamol (acetaminophen) was first identified in the late nineteenth century, since then it is the most widely used analgesic. It has become one of the most popular antipyretic and analgesic drugs worldwide, and it is often used in combination with other drugs. As paracetamol does not have significant anti-inflammatory activity, a mode of action which is distinct from that of the non-steroidal anti- inflammatory drugs, So it does not have any adverse effects on orthodontic tooth movement [1,8]. Acetaminophen (paracetamol) can be used safely for controlling pain and discomfort associated with orthodontic treatment [8]

VITAMIN-D: Vitamin D metabolite, dihydroxycholecalceferol (1, 25, (OH) 2D3), along with parathyroid hormone (PTH) and calcitonin, plays a major role in calcium metabolism and maintain the amount of calcium and phosphorus levels in blood. . Vitamin D is actually a hormone rather than a vitamin; it is synthesized in mammals and, under ideal conditions, probably is not required in the diet. Vitamin D receptors have been demonstrated not only in osteoblasts but also in osteoclast precursors and in active osteoclasts [9, 10]. Intra ligamentary injection of vitamin D showed increased number of osteoclasts and easy tooth movement: studies done by Collin and Sinclair 1988.

BISPHOSPHONATES: Bisphosphonates (BPNs) have strong chemical affinity to calcium phosphate; also has an inhibitory effect on hydroxyapatite aggregation, dissolution, and crystal formation. Bisphosphonates cause a rise in intracellular calcium levels in osteoclastic-like cell line, reduction of osteoclastic activity, prevention of osteoclastic development from hematopoietic precursors, and production of an osteoclast inhibitory factor. Studies have shown that BPNs can inhibit orthodontic tooth movement and delay the orthodontic treatment. Topical application of BPNs could be helpful in anchoring and retaining teeth under orthodontic treatment [11, 12]. They are used as a medication in conditions like osteoclast mediated bone resorption, including steroid-induced osteoporosis, Paget's disease, breast and prostate cancer and hypercalcemia.

CORTICOSTEROIDS: These are anti-inflammatory and immunosuppressive agent in treatment of a many chronic medical disorders. At low dose (1mg/kg body weight), it 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 then ultimately cause relapse [13,14]. Increased level of corticosteroid causeselevated parathyroid hormones, which reduces intestinal absorption of calcium and reduces osteoblastic bone formation.

THERAPEUTIC USES

- ❖ Rheumatic Disorders
- ❖ Renal Diseases
- ❖ Allergic Disease
- ❖ Bronchial Asthma and Other Pulmonary Conditions
- ❖ Infectious Diseases
- ❖ Ocular Diseases
- ❖ Skin Diseases
- ❖ Gastrointestinal Diseases

THYROID HORMONES: Thyroid hormones are used for the treatment of hypothyroidism and are recommended after thyroidectomy as asubstitutive therapy. Thyroxin administration lead to increased bone remodeling, increased bone resorptive activity, and reduced bone density. The speed of orthodontic tooth movement increased in patients undergoing such medication. It has been reported that low-dosage and short- term administration of thyroxin lower the frequency of force induced root resorption. Decrease in root 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 [15, 16]. Calcitonin has the opposite effects, which decreases the intestinal calcium and renal calcium absorption. In bones, calcitonin inactivates osteoclasts and hence inhibits bone resorption and activates bone formation.

SEX HORMONES: Sex hormones play a role of bone metabolism. Estrogen preserves calcium in bone by suppressing the frequency of bone remodeling. Once the menopause is attained, the reduced level of estrogen result is rapid bone loss leading to symptomatic osteoporosis. Estrogen directly stimulates the bone- forming activity of osteoblasts, so it has an effect of lowering the amount of orthodontic tooth movement. Androgen also inhibits bone resorption and stimulates the growth of the muscular system. Thus, the excessive use of these drugs by athletes, to achieve better athletic scores, may increase the duration of the orthodontic treatment [17, 18]

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PARATHYROID HORMONES: The main function of parathyroid hormone is to maintain a normal level of calcium level, along with thyroid and vitamin D. Many Studies have shown that thyroid and parathyroid glands plays a major role in calcium metabolism and calcification of teeth.

No evidence of calcium withdrawal has been reported from the fully formed tooth due to deficiency of parathyroid. Its effects on osteoclasts occur through the production of RANK-L Receptor activator of nuclear factor kappa -B legend), a protein playing a crucial role in osteoclasts' formation and activity. In 1970s, animal studies demonstrated that PTH could induce an increase in bone turnover that would accelerate orthodontic tooth movement. More recently, an increased rate of tooth movements has been observed in rats treated with PTH, whether administered systemically or locally. These results indicate that orthodontists should take note of patients being treated with PTH, as for example, in cases of severe osteoporosis [19].

Parathyroid hormone affects both bone resorption and formation process. If PTH appears around bone cells, the effect of bone will be resorption. By contrast, low level of PTH results in bone formation. When the calcium level in blood decreases, PTH will stimulate osteoclastic activity to increase calcium and phosphate absorption in the gut, and decrease calcium excretion and tubular phosphate reabsorption in the kidney. This plays a role as regulator of calcium homeostasis by PTH [20, 21]

PROSTAGLANDINS AND ANALOGS:

Experiments have shown that PGs have been released in response to applied orthodontic force. They stimulate bone resorption, root resorption, decrease collagen synthesis, and increase cyclic AMP. They stimulate bone resorption by increasing the number of osteoclasts and activating the existing osteoclasts. A lower concentration of PGE2 appears to be effective in enhancing orthodontic tooth movement. Higher concentration leads to root resorption. Systemic administration is reported to have better effect than local administration. Researchers have shown the increased rate of tooth movement by local application of prostaglandin as compared to control group [22,23].

INSULIN: Insulin is a polypeptide hormone secreted by the beta cells of the Langerhans islets of the pancreas. A normal non-obese man secretes approximately 50U/day, with a basal plasma insulin concentration of 10-50 microns/ml. Its main function is to maintain the blood glucose level. Insulin deficiency produces a condition called diabetes mellitus, while its excess leads to hypo-glycemia. Diabetes mellitus is diagnosed in 3-4% of the population treated in our day-to-day orthodontic practice. It is very important to have a thorough medical history taken prior to orthodontic diagnosis and treatment planning. The orthodontists should have a basic knowledge and understanding of this disease and of its impact on the oral cavity, as well as of its consequences upon the dental treatment. Patient should be advised to have good diet and medical control prior to begin the treatment and well informed on the oral complications induced by diabetes mellitus [24,25].

CYCLOSPORINE:Itincreases gingival hyperplasia. In most patients the first six months of cyclosporine therapy is very crucial, having the severe gingival hyperplasia, make orthodontic treatment, and maintenance of oral hygiene very difficult. Treatment should be started only 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 [26]. Patients should be informed well about their oral complication and difficulties they may have to face because of improper oral hygiene, as they are on those medications prior to treatment.

ANTI CONVULSANTS:Valporic acid has a potential to induce gingival bleeding even with minor trauma making orthodontic treatment 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. In these cases, clinician should be aware of possible difficulties during Treatment period, and discuss it with the patients and or parents and educate them so that adequate measures to maintain oral hygiene are followed [27, 28].

ALCOHOL: Long term ingestion of alcohol on daily basis may have very destroying effects on many tissues and organ systems, including skeletal system. Alcoholism may lead to severe complications, such as liver cirrhosis, neuropathies, osteoporosis, and spontaneous bone fractures. Circulating ethanol inhibits the activation of

vitamin D3 in liver, thus disturbing calcium homeostasis. All these lead to increased level of PTH, changing the balance of cellular function towards the constant resorption of mineralized tissues, which leads to increased root resorption in order to maintain normal levels of calcium in blood. It was found that chronic alcoholics receiving orthodontic treatment are high risk of developing severe root resorption during course of orthodontic treatment [29].

II. DISCUSSION

This review of literature summarizes the effects of various medications, that orthodontic patients may be undergoing treatment for various disorders. As described by Krishnan V and Davidovitch Z, these groups of drug have an effect on OTM. Some of these drugs are promoter drugs where it promotes orthodontic tooth movement, but others have an inhibitory effect. Orthodontic tooth movement is always accompanied by alveolar bone remodeling. The remodeling of bone is a process that starts with resorption followed by deposition. The activation period is about 10 days. There are cells recruitment, differentiation, proliferation and migration in this period followed by resorption. The resorption period takes 21 days that occurs by osteoclast activity [6, 7].

Acute inflammatory response is mediated in the early phase of orthodontic tooth movement.Inflammatory mediators play a major role in the process that associated with alveolar bone resorption and deposition. Orthodontic forces can induce the bone remodeling process by release of the local mediators, such as prostaglandins, cytokines and growth factors which play an important role in bone remodeling. PGE2 has been involved in bone remodeling and recognized as a potent stimulator of bone resorption [22,23].Studies have shown that some drugs can affect tooth movement by local or systemic intake, many showing the usage of pharmacologic agents to induce bone resorption and deposition for control of tooth movement. Studies by Yamasaki et al reported that local injection of prostaglandin to stimulate tooth movement in rats. Other pharmacologic agents such as calcitonin, and 1, 25(OH) 2 D3can also induce tooth movement [22, 23].NSAIDs can inhibit the synthesis of prostaglandins which is an important mediator of bone resorption. So, it is important that the patient does not take NSAIDs such as aspirin or other related compounds for long periods of time during orthodontic treatment [8].

The safest analgesic that can be suggested to patients is paracetamols. Paracetamol also known as acetaminophen is a type of analgesic, which does not have any anti-inflammatory effect.so it doesn't have any adverse effect on orthodontic tooth movement. Orthodontists should be aware of the patients who under short- and long-term therapy with COX-2 inhibitors because these drugs can decrease the rate of orthodontic tooth movement. Acetaminophen acts at the central nervous system and does not stimulate PGs synthesis, so it does not interfere with the orthodontic tooth movement. The numbers of osteoclasts in the pressure areas are not decreased, and the bone regeneration does not change by acetaminophen. So, it is a drug of choice that orthodontists should recommend to their patients for relieving the discomfort during orthodontic treatment [6, 7, 8, 30].

III. CONCLUSION

As more and more chemical analogues are being used in the form of new drugs to avoid resistance, today's orthodontist should have updated knowledge about the clinical efficacy of the new drugs as well as the mechanism of action of these drugs on human tissues. It is always advisable for a dentist to confirm with the general physician for fitness of those patients who seek orthodontic treatment involving tooth movement.Orthodontists should assume that many patients are taking prescription or over-the counter medications regularly. The orthodontist must identify these patients by taking a proper history of medication and their consumption of food supplements; should be considered as a part of orthodontic diagnosis

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