DRUGS OF SYSTEMIC DISORDER AND ORTHODONTIC TOOTH MOVEMENT; A LITERATURE BASED RANDOM STUDY

*Siddharth Sonwane¹, B. Sunil Kumar², Shweta RK³, Ashok Satyanarayan⁴, Jagdish⁵ and BoscoThomas⁶

¹Department of Orthodontics, Mansarovar College of Dental Sciences, Bhopal, MP State India
²Department of Orthodontics, HKES’s S. N. Dental College, Gulbarga, Karnataka 585105, India
³Department of Oral and Maxillofacial Surgery, Government Dental College, Nagpur, Maharashtra State, India
⁴Department of Periodontics, Mansarover Dental College, Bhopal, MP State India
⁵Department of Orthodontics, VSDC Sangli, Maharashtra India
⁶Department of Orthodontics, People’s College of Dental Sciences, Bhopal, MP State India

*Author for Correspondence

ABSTRACT

Cellular activity generally decreases with age, and there is evidence of decreased rates of bone remodeling in old age. On the other hand, orthodontic tooth movement requires remodeling of periodontal tissues, especially alveolar bone. Apart from age changes it has been seen that rate of orthodontic tooth movement reduces due to medication. Medications might have an important influence on the rate of tooth movement, and information on their consumption is essential to adequately discuss treatment planning with patients. For many years, the rate of OTM and the medication consumed by orthodontic patients apparently were not considered issues. In the clinical orthodontic literature, only isolated case reports have been mentioned. This review article gives a comprehensive knowledge on effects of drugs on orthodontic tooth movements

Key Words: Cellular, Drugs, Remodeling, Periodontal Tissues, Tooth

INTRODUCTION

The principal trigger for orthodontics tooth movement (OTM) is probably strain of the periodontal ligament cells, bone-related cells, and the extracellular matrix. This strain leads to changes in gene expression in the cells by interactions between the cells and the extracellular matrix, whereby integrins play an important role. Various cell-signaling pathways are activated, which ultimately lead to stimulation of periodontal ligament turnover, and localized bone resorption and bone deposition. In most cases, these reviews distinguish 2 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.

This information is important for clinicians in communications with patients, because many patients use prescription and over-the-counter medications, as well as dietary supplements daily. Consequently, these substances can affect both the rate of OTM and the expected duration of treatment.

MATERIALS AND METHODS

Our search was mainly concentrated on PubMed from dated September 2011 with English words our key words were drugs used in orthodontics or effect of drugs in orthodontic tooth movements. We searched for 119 articles. General information on the medications and their effects on various mediators in this review is mainly web-based information derived from the following Internet sites (October 2007): http://en.wikipedia.org, www.nlm.nih.gov/medlineplus, www.rxlist.com, and www.drugs.com. References to these web sites were omitted in the text.
Our inclusive criteria remained
Most of the article taken, described on animal experimental bases.
Clear dosage information given articles were given priority.
Review article describing comprehensive note on the side effects of drugs during orthodontic tooth movements.
Adequate information on technical measurements of tooth movements.

RESULTS
The total number of articles found through pubmed was 116. Hand searching identified 11 more references. Application of the inclusion criteria resulted in 29 articles used for data extraction and subsequent review.

DISCUSSION
Pain is an unpleasant, sensory and emotional experience associated with an actual or potential damage or described in terms of such damage. Orthodontic tooth movement basically involves the coupling effect of bone remodelling – resorption and deposition resulting in a painful experience for the patients. Eicosanoids
These are signaling molecules made by oxidation of twenty-carbon essential fatty acids, (EFAs). They exert complex control over inflammation or immunity, and act as messengers in the central nervous system. There are four families of eicosanoids—the prostaglandins, prostacyclins, the thromboxanes and the leukotrienes, derived from arachidonic acid by various enzymatic conversions. Cyclooxygenases (COX) play a pivotal role for the conversion to thromboxanes, prostacyclins, and prostaglandins.

Leukotrienes
Leukotrienes are fatty molecules of the immune system that contribute to inflammation in asthma and allergic rhinitis. Leukotriene antagonists are used to treat these diseases cause inhibition of leukotrienes synthesis. This have an impact on bone remodeling, mainly it inhibit bone resorption, affects OTM.

Thromboxanes
These are potent vasoconstrictors and facilitate platelet aggregation, by acting on thromboxane receptors, and couple with receptors G protein. Under inflammatory conditions increased amount of thromboxanes seen in the oral cavity, especially in deep periodontal pockets. NSAIDS Inhibits thromboxanes synthesis affects rate of OTM.

Prostacyclins
They act as vasodilators and prevent platelet aggregation. Synthetic prostacyclin (epoprostenol) or analogues such as iloprost are used for the treatment of ischemic conditions and pulmonary arterial hypertension. Administration of the prostacyclin analogue iloprost and the thromboxanes analogue increases the synthesis of prostaglandins, thereby indirectly affecting the rate of OTM.

Prostaglandins
Prostaglandins Play an important role in inflammation; also have an effect on smooth muscle cells, platelet aggregation, peripheral nerve endings, and calcium homeostasis. Synthetic prostaglandins are analogues, used in various conditions, including prevention of peptic ulcers and induction of labor. Deflection in rate of orthodontic tooth movement depends upon dose; however the final result is positive, i.e. Increase rate of OTM.

NSAIDS
The non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently used and the drug of choice for the control of pain following mechanical force application to teeth. They act primarily on peripheral pain mechanisms but also in CNS to raise pain threshold, by inhibiting the enzyme cyclo-oxygenase.
Research Article

(COX), which modulates the transformation of prostaglandins (PGs) from arachidonic acid in the cellular plasma membrane23,24,25. These drugs are classified as:

a) Non selective COX inhibitors (traditional NSAIDs)
   1) Salicylates: Aspirin
   2) Propionic acid derivatives: Ibuprofen, naproxen
   3) Anthranilic acid derivative: Mephenamic acid
   4) Aryl-acetic acid derivatives: Diclofenac, Aceclofenac
   5) Oxicam derivatives: Piroxicam, Tenoxicam
   6) Pyrrolo-pyrrole derivative: Ketaorolac
   7) Indole derivative: Indomethacin
   8) Pyrazolone derivatives: Phenylbutazone, Oxyphenbutazone

b) Preferential COX-2 inhibitors
   Nimesulide, Meloxicam, Nabumetone

NSAIDs are the most important class of prostanoidsynthesis inhibitors. They have analgesic, antipyretic, and anti-inflammatory effects. Most frequently used in 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 cancer26,27. Prescription of NSAIDS can be divided into three types, Short term, long term, and incidentally prescription. For chronic diseases such as rheumatoid arthritis, osteoarthritis, and gout, relatively high doses are prescribed for a long period of time. For the prevention of cardiovascular problems and colorectal cancer, long-term prescriptions are also given, but at a low dose. For pain and headache, NSAIDs are taken incidentally. This should be considered in evaluating the effects of NSAIDs on OTM26,27,28.

All NSAIDs have more or less similar effects and mechanisms of action. They suppress the production of all prostanoids (thromboxanes, prostacyclins, and prostaglandins) because of their inhibition of COX-1 and COX-2, which are essential enzymes in the synthetic pathways of the prostanoids. Thus reduce rate of OTM26,27,28.

Arylalkanoic Acids
Administration of a single dose of Indometacin orally at 5 mg per kilogram per day reduces bone turnover, suggesting a decrease in OTM rate28.

Arylpropionic Acids
Oral administration of ibuprofen 30 mg per kilogram twice a day, the rate of OTM decreased significantly. On the other hand, no inhibitory effect was found at a low dose (10 mg per kilogram per day) of flurbiprofen on OTM28,29.

Oxicams
No experimental data are available from the literature on the effects of oxicams on the rate of OTM28,29,30.

Coxibs
Only 1 study is available on the effects of selective COX-2 inhibitors on the rate of OTM28,29,30.

Other Analgesics
Paracetamol
The most potent, oftenly used analgesic; chemical structure simulates s to NSAIDS, lacks in lacks anti-inflammatory properties. Therefore, it does not belong with NSAIDs. Most elegant feature is that it does not have any effect on blood clotting and no detrimental effects on the stomach lining. Mode of action is
by blocking third isoform, COX-3, which is expressed only in the brain and the spinal cord. As a consequence, paracetamol has minimal effects on prostaglandin synthesis\textsuperscript{30,31}. The studies have revealed that on administration of 500 mg per kilogram per day, paracetamol does not affect the rate of OTM, suggest that it should be the analgesic of choice for managing pain associated with orthodontic therapy\textsuperscript{30,31}.

\textbf{Corticosteroids}

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\textsuperscript{30,31,32}. There are two types of corticosteroids they are as follows: Glucocorticoids, Mineralocorticoids.

\textbf{Glucocorticoids}

Glucocorticoids are involved in the control of carbohydrate, fat, and protein metabolism, but they also have anti-inflammatory properties, also involved in bone physiology, but their mode of action is not yet completely elucidated. It was recognized that osteoblasts and osteoclasts can express glucocorticoid receptors; this expression is influenced by proinflammatory factors, such as IL-6 and IL-11\textsuperscript{30,31,32}. 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\textsuperscript{30,31,32,33}.

Mode of action is blocking of phospholipase A2 and the suppression of the synthesis of both COX-1 and COX-2. This leads to inhibition of the synthesis of prostaglandins and leukotrienes.

\textbf{Mineralocorticoids}

These are aldosterone, control mainly electrolyte and water levels by promoting sodium retention in the kidneys\textsuperscript{30,31,32,33}.

Only a few authors have examined the effects of glucocorticoids on OTM, and revealed that the therapeutic use of cortisone, prednisolone, and methylprednisolone have considerable effect on OTM\textsuperscript{30,31,32,33}.

Cortisone acetate dosage of 15 mg per kilogram per day led to a significant increase in the rate of OTM. Also, the relapse rate was faster in the experimental group than in the control animals. Prednisolone was administered at 1 mg per kilogram per day led to an increase in the rate of OTM. However, in another experimental group without an induction period, methylprednisolone had no effect on the rate of OTM\textsuperscript{30,31,32,33}.

\textbf{Calcium and Calcium Regulators}

\textbf{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.

Pathologic PTH conditions might involve hypoparathyroidism and hyperparathyroidism. Hypoparathyroidism leads to a shortage of active PTH. The most commonly used therapy is the administration of vitamin D or calcium supplementation. In primary hyperparathyroidism, overproduction of the hormone stimulates bone resorption, reduces renal clearance of calcium, and increases intestinal calcium absorption; these result in increased serum calcium levels.

Teriparatide is a recombinant form of the active (1 through 34) fragment of PTH, used to treat advanced osteoporosis. Daily injections of teriparatide stimulate new bone formation, leading to increased bone mineral density. A significant stimulation of the rate of OTM , dosage of teriparatide injections.

\textbf{Thyroid hormones}

The thyroid produces 2 hormones: thyroxine and calcitonin. Thyroxine (T4) is a prohormone that can be converted to its active form tri-iodothyronine (T3). This active hormone influences the activity and
metabolism of all cells and it plays an vital role in physical development and growth. 0.003% thyroxin was added to the drinking water, a significant increase in the rate of OTM was found. In many ways, calcitonin has the opposite effects of those inherent to PTH; calcitonin decreases intestinal calcium absorption, osteoclast activity in bone, and renal calcium reabsorption. It is used to treat postmenopausal osteoporosis, hypocalcemia, and Paget’s disease, and it might be beneficial in osteoarthritis.

Although calcitonin is involved in bone remodeling and calcium homeostasis, but no experimental data available to exhibit role of calcitonin on the rate of OTM.

Estrogens Estrogens are female sex hormones that occur naturally in 3 forms. The first and most prominent form of estrogen is estradiol, which is produced from menarche to menopause. The second form is estrone, produced after menopause. The third form, estriole, is expressed primarily during pregnancy. The relationship between the decrease of estrogens after menopause and the development of osteoporosis is well established.

Estrogen supplementation was used to over come postmenopausal problems might slow down the rate of OTM. However, no experimental studies are available. 1,25 dihydroxycholecalciferol (vitamin D3) 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.

1,25 (OH) 2D3 deficiencies can result from inadequate intake combined with inadequate sunlight exposure, eventually leading to impaired bone mineralization, rickets, and osteoporosis. Furthermore, it can lead to increased susceptibility to high blood pressure, periodontal disease, affective disorders, and auto-immunediseases. Systemic administration of 1,25(OH) 2D3 in dosages as low as 0.25 X10 mol can stimulate the rate of OTM.

Conclusion
Orthodontists should assume that many patients are taking prescription or over-the-counter 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.

REFERENCES


Research Article


Research Article


