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REVIEW ARTICLE

ACCELERATORS OF ORTHODONTIC TOOTH MOVEMENT: A BOON - REVIEW ARTICLE

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ABSTRACT

In today's world, shorter treatment duration with consequent lower costs are important to all patients, particularly to adults who have been increasingly seeking treatment. It is challenging to reduce the duration of orthodontic treatments and it is one of the common deterents that an orthodontist faces. A number of attempts have been made to create different approaches both preclinically and clinically in order to achieve quicker results which can be categorized as Biological, Physical and Surgical. The surgical approach is the most frequently used clinically and most tested with known predictions and stable results. However, it is invasive, aggressive and costly. Piezocision technique is one of the newest techniques and has good clinical outcome and is considered the least invasive in the surgical approach. This article reviews different methods of accelerating Orthodontic tooth movement.

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INTRODUCTION

Orthodontics has steadily evolved from a technique-oriented profession to a comprehensive specialty that incorporates aspects of all fields of medicine during last few years. Orthodontic tooth movement (OTM) is a biological process characterized by periodontal ligament and alveolar bone remodeling in response to an orthodontic force which promotes extensive cellular and molecular changes in the periodontium. Orthodontic tooth movement differs markedly from physiological dental drift or tooth eruption which is a slow process but in contrast the Orthodontic tooth movement is rapid and is uniquely characterized by the creation of compression and tension regions in the periodontal ligament (Nimeri, 2013). Orthodontic treatment time ranges between 21 to 27 and 25 to 35 months for nonextraction and extraction therapies, respectively (Skidmore, 2006 and Vu *et al*., 2008). In today's world, with hectic schedules, travel and job issues, this treatment timing seems to be very long to adult patients and discourages them from undergoing the treatment. However, adult patients typically require longer treatment time due to slower metabolism in comparison to younger patients (Ong *et al*., 2002). Accelerating the rate of tooth movement is desirable to orthodontists because treatment duration has been associated with an increased risk of gingival inflammation, decalcification, dental caries, and especially, root resorption.
A number of attempts have been made to create different approaches both preclinically and clinically in order to achieve quicker results. Most attempts can broadly be categorized into biological, physical, biomechanical, and surgical approaches.

- ***Biological approach***: Prostaglandin E (PGE), Cytokines - lymphocytes and monocytes-derived factors, receptor activator of nuclear factor Kappa B ligand (RANKL) and macrophage colony-stimulating factor (MCSF).
- ***Physical approach***: Direct electric currents, Pulsed electromagnetic field, Static magnetic field, Resonance vibration and Low level laser.
- ***Surgical technique***: Interseptal alveolar surgery, Osteotomy, Corticotomy, Piezocision technique etc.

Biological Methods of Accelerating Orthodontic Tooth Movement (Figure 1)

Although current clinical systems in Orthodontics use mechanical forces to induce bone remodeling, several

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researchers have suggested that there might be ways to increase cellular activity with agents more potent than mechanical forces alone (Krishnan *et al*., 2006).

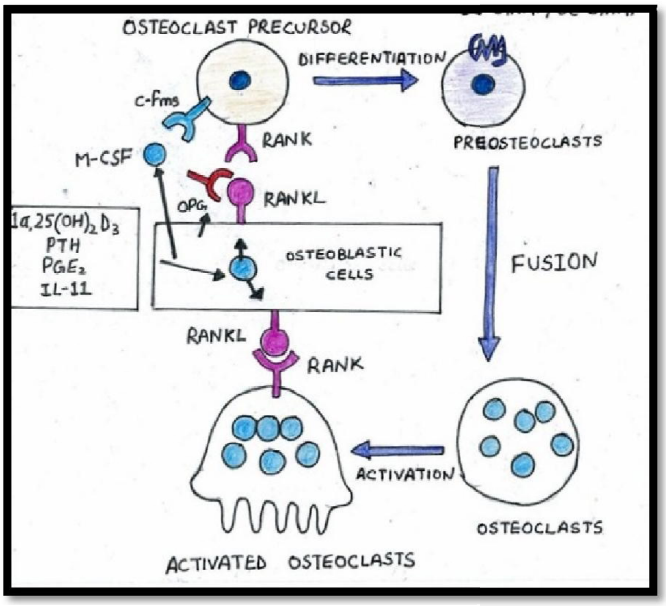

Figure 1. Biological methods to accelerate orthodontic tooth movement

Effect of cytokines on tooth movement: Cytokines are extracellular signalling proteins directly involved in the bone remodeling and inflammatory process during orthodontic tooth movement, which act directly or indirectly, to facilitate bone and periodontal ligament cells differentiation, activation, and apoptosis. The receptor activator of nuclear factor-B ligand (RANKL) and macrophage colony-stimulating factor (M-CSF) expressed by osteoblast and apoptotic osteocyte are the most important proinflammatory cytokines responsible for recruitment, differentiation, activation, and survival of osteoclasts (Krishnan *et al*., 2006). Tumor necrosis factor (TNF) is another proinflammatory cytokine that is involved in bone resorption and acute as well as chronic inflammation. Like TNF, IL-1 (alpha and beta) is a proinflammatory cytokine that is highly expressed on the pressure side of periodontal ligament of humans and animals and the adjacent alveolar bone in the early stages of orthodontic tooth movement (Ildeu Andrade Jr, 2014). Other cytokines, such as IL-6, IL-8, and IL-11 also stimulate alveolar bone resorption during orthodontic tooth movement by acting early in the inflammatory response. These cytokines can be enhanced by, or can act synergistically with TNF and IL-1. Analysis of cytokine levels in GCF may also be helpful in monitoring the biological activities in the periodontium during the retention period, which could provide information about possible relapse (Iwasaki *et al*., 2009).

Effect of Prostaglandins on tooth movement: Prostaglandins (PGs) are inflammatory mediators that act on nearby cells to stimulate bone resorption by increasing directly the number of osteoclasts. Yamasaki, was among the first to investigate the effect of local administration of prostaglandin on rats and monkeys (Yamasaki, 1984). In the field of Orthodontics, the forces applied to move the teeth cause local inflammation and as a result lymphocytes, monocytes and macrophages infiltrate into the inflammatory tissue where the prostaglandins are released. The secretion of prostaglandins appears to be regulated by a feedback mechanism, since prostaglandins are believed to inhibit adenylcyclase activity above a certain concentration. Patil *et al* in 2005, performed a clinical assay on 14 patients who were injected for three days with a dose of 1 g of PGE1 (3 g in total), using lidocaine as a vehicle substance in the distal buccal area of canines retracted with Niti open coils and concluded that following a minimal dose of PGE1 an increase in the rate of movement was evident compared to the control group (Domínguez, 2014). A study was carried in 2004 by Gurton *et al* to compare the effects of PGI2 and TxA2 analogs and inhibitors on orthodontic tooth movement and it was found that PGI2 and TxA2 analogs increased the number of multinuclear osteoclasts, osteoclastic bone resorption, and rate of orthodontic tooth movement (Gurton, 2004).

Effect of Vitamin D on tooth movement: Vitamin D is a steroid hormone that has specific receptors in many target organs and tissues (Krishnan and Davidovitch, 2006; Hussain, 2011). In particular, the active form of vitamin D (1,25-dihydroxycholecalciferol henceforth referred to as 1,25DHCC), is one of the most potent stimulators of osteoclastic activity known. It also is involved in the formation of osteoclasts from precursor monocytes and may produce these effects at much lower doses than other hormones such as prostaglandins (Batmaraj, 2014 and Gameiro, 2007). Collins and Sinclair as well as Kale *et al*. have reported that the local administration of vitamin D increases the rate of tooth movement in cats[15] and rats[16] respectively and emphasized that administration of vitamin D results in a good balance between deposition and resorption of bone and well-modulated bone turnover compared to prostaglandin administration.

Effect of Relaxin on tooth movement: *Relaxin* has been known as a pregnancy hormone. It is released just before childbirth to loosen the pubic symphysis, so that the relaxed suture will allow widening of the birth canal for parturition. Relaxin's influence on soft-tissue remodelling and on several mediators that stimulate osteoclast formation has attracted attention from orthodontic researchers (Meikle, 2006). In 2005, Liu and colleagues showed that the administration of human relaxin might accelerate the early stages of orthodontic tooth movement in rats (Liu, 2005). In 2000, Nicozisis and colleagues demonstrated that the presence of relaxin abolished the integrity of sutures in vitro (McGorray, 2012). These authors suggested that relaxin might be used as an adjunct to orthodontic therapy, during or after tooth movement, for promotion of stability; for rapid remodelling of gingival tissue during extraction space closure or for orthopaedic expansion in non-growing patients, by reducing the tension of the stretched soft-tissue envelope particularly the expanded palatal mucosa, after orthognathic surgery. Whether these findings will hold true in clinical practice remains to be investigated.

Effect of Thyroid Hormones on tooth movement: Thyroid hormones play an essential role in the normal growth and development of vertebrates. In bone remodelling, they act directly by stimulating the action of osteoclasts but they also have an indirect effect through growth factors that are closely related to bone metabolism such as insulin-like growth factor I (IGF-I), which is produced locally in bone cells by the action of thyroid hormones (Batmaraj, 2014). More recently, Vazquez- Landaverde and colleagues showed that low doses of thyroid hormones may have a protective effect on root surfaces, either during orthodontic treatment or in patients who present spontaneous root-resorptive lesions. The clinical applications of these drugs still need to be clarified (Gameiro, 2007).

Effect of Nitric oxide on tooth movement: Nitric oxide is released from macrophages and osteoclasts during cell to cell interactions and acts as a cytotoxic molecule to kill intracellular microorganisms and tumor cells. Because NO elevates the amount of cGMP, the second messenger in the bone remodeling cycle, it was suggested that NO may raise the rate of orthodontic tooth movement leading to altered orthodontic treatment duration (Shirazi *et al*., 2002). 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 and hence they increase orthodontic tooth movement (Singh, 2015).

Effect of Gene Therapy on tooth movement: RANKL is a membrane bound protein on the osteoblasts that bind to the RANK on the osteoclasts and causes osteoclastogenesis. Osteoprotegerin (OPG), protoagonist of RANKL is a decoy receptor produced by osteoblastic cells, which compete with RANK for RANKL binding. The biologic effects of OPG on bone cells include inhibition of terminal stages of osteoclast differentiation, suppression of activation of matrix osteoclasts, and induction of apoptosis. Thus, bone remodeling is controlled by a balance between RANK/ RANKL binding and OPG production. It was demonstrated that the transfer of RANKL gene to the periodontal tissue induced prolonged gene expression for the enhancement of osteoclastic activity and acceleration of tooth movements in rats (Roychodhury, 2015). In indirect Gene therapy, target cells are harvested from the patient and then reinserted. It is advantageous for being able to accurately select a particular cell as the protein delivery vehicle. The indirect method has been effectively used to target articular cartilage, spine and human metacarpophalangeal joints (Ildeu Andrade Jr, 2016). Numerous reports have described the pharmacological acceleration of orthodontic tooth movement through local gene transfer which has two advantages. First, it maintains local effective concentration and prolonged protein expression, regardless of blood circulation. Second, protein expression occurs at a local site, thereby avoiding systemic effects. When comparing corticotomy surgery and RANKL gene transfer to periodontal tissue as two methods that might substantially reduce orthodontic treatment time, RANKL gene transfer demonstrated higher efficacy than standard surgical methods (Kanzaki, 2006).

Physical Methods of Accelerating Orthodontic Tooth Movement: Another approach in accelerating tooth movement is by using device-assisted therapy. The concept of using physical approaches came from the idea that applying orthodontic forces causes bone bending and bioelectrical potentials to develop.

Effect of Direct electric current on tooth movement: According to Davidovitch, mechanical stress induced electric potential in the bone may be signal to activate the cells that participate in the remodeling process. Also, the electrical stimulation in conjunction with mechanical force can increase the rate of tooth movement (Maheshwari, 2015). Kim *et al* revealed that electric current was capable of accelerating orthodontic tooth movement (Long, 2013). This technique was tested only on animals by applying direct current to the anode at the pressure sites and cathode at the tension sites, thus, generating local response and acceleration of bone remodelling. Further, development of the direct electric device and the biocatalytic fuel cells is needed to be done so that these can be tested clinically (Nimeri, 2013).

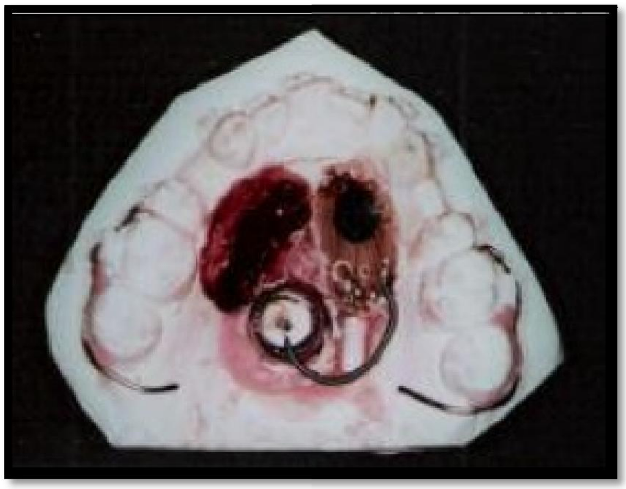

Figure 2. Electromagnetic device used for pulsed electromagnetic field

Effect of Pulsed Electromagnetic Field on tooth movement **(Figure 2)**: Recently, magnets and pulsed electric magnetic fields (PEMFs) have been used as medicine, particularly in orthopedics. The effect of electric currents in bone was examined by Fukada and Yasuda in 1957, and they hypotheized that electricity is produced when bone is stressed (Fukada *et al*., 1957). This phenomenon, termed *piezoelectricity,* results from tension and compression in bone which generate voltages of opposite polarity. The electric currents generated within the alveolar bone by orthodontic forces are thought to provide the signal for the directionality of the response (that is, either resorption or deposition occurring during the remodeling process), whereas, the generalized enhancement of cellular activity is a function of the magnetic field strength. In another study, Darendeliler *et al* in 2007 suggested that the PEMF induced vibration enhance the effect of mechanical and magnetic forces on tooth movement (Showkatbakhsh *et al*., 2010 and Darendeliler *et al*., 2007).

Effect of vibration on tooth movement: It is well known that mechanical stimuli have an important role in bone tissue metabolism. The types of vibration include: whole-body vibration, pulsed electromagnetic field driven vibration, resonance vibration, mechanical vibration.[29]Studies that involve whole-body vibration have been done in both animals and humans. Nishimura *et al*. looked at the effects on orthodontic tooth movement in rats utilizing resonance vibration (vibration with a continuously changing frequency) applied to the dentition and found that the amount of tooth movement in the vibration group was significantly greater (15%). Ultrasonic vibration has also been studied for its effects on orthodontic tooth movement. Ohmae *et al*. looked at 5 adult male beagle dogs where they bilaterally extracted maxillary first premolars and they found a significantly greater amount of tooth movement in the teeth exposed to ultrasonic vibration (Dobie, Thomas, 2013 and Al–Sayagh, 2014). Low-intensity pulsed ultrasound (LIPUS) is a form of physical energy that can be delivered into living tissues as acoustic intensity waves. Studies indicate that LIPUS accelerates the differentiation pathway of mesenchymal stem cells in the osteogenic lineage via activated phosphorylation of MAPK (mitogen-activated protein kinase) pathways, up-regulation of cyclo-oxygenase-2 (COX-2), prostaglandin E2 (PGE2), altering the OPG/RANKL ratio in the microenvironment and stimulating the production of bone morphogenetic proteins.

Effect of Low level laser on tooth movement: The acronym "laser" is commonly used terminology for "Light Amplification by Stimulated Emission of Radiation". It is a device that emits light through a process of optical amplification based on the stimulated emission of elec-tromagnetic radiation (Camachoa, 2010). A study by Coombe *et al* demonstrated that low-level laser therapy (LLLT) stimulates cellular proliferation and differentiation of osteoblast lineage nodule-forming cells, especially in committed precursors, resulting in an increase in the number of differentiated osteoblastic cells as well as in bone formation (Genc, 2013). Furthermore, recent studies showed that low-energy laser irradiation accelerated orthodontic movement of human teeth (Sousa *et al*., 2014).

Surgical Methods of Accelerating Orthodontic Tooth Movement: Several surgical approaches that have been tried in order to accelerate tooth movement. It is a clinically effective technique used for adult patients, where duration of orthodontic treatment may be critical.

Effect of Corticotomy on tooth movement : Over the past 10 years, corticotomies have become a popular means of increasing the rate of tooth movement. In corticotomy, the cortical layer is cut or perforated to the depth of the medullary bone which is preserved. During bone healing process, a re-gional acceleratory phenomenon (RAP) takes place in the periodontium (Baloul *et al*., 2011). RAP is a natural localized reaction of soft and hard tissues in response to an injury, and is associated with increased perfusion, bone turnover and decreased bone density. The animal studies showed that corticotomies provide three times as many osteoclasts, three times greater bone apposition rate and a twofold decrease in calcified trabecular bone (Hoogeveen, Jansma, and Ren, 2014 and Mathews, 2013). Corticotomy-assisted orthodontic treatment is quite invasive as it requires extensive flap elevation and bone surgery. Taken all together, there is twice as much tooth movement with than without corticotomies. However, this window of opportunity used to accelerate tooth movement is limited to 2-3 months, in which 4-6 mm of tooth movement might be expected (twice as much the normal rate), (Ren, 2007). Nevertheless, further controlled clinical trials are needed to determine the actual effects of corticotomies.

Effect of Distraction Osteogenesis on tooth movement : Interseptal alveolar surgery or Distraction Osteogenesis is divided into distraction of PDL or distraction of the dentoalveolar bone (Fleming, 2015). From surgical treatments of craniofacial skeletal dysplasia, this concept was later adapted in relation to the rapid tooth movement (George *et al*., 2014). In the rapid canine distraction of PDL, the interseptal bone distal to the canine is undermined surgically at the same time of extraction of the first premolars, thus, this will reduce the resistance on the pressure site (Lv *et al*., 2009). Rapid canine distraction of the dentoalveolar bone is done by the same principle of the distraction of PDL, with the addition of more dissection and osteotomies performed at the vestibule. In all the studies done, both techniques accelerated tooth movement with no evidence of significant root resorption, ankylosis and root fracture. Liou in 1998 reported 9 out of 26 teeth showed positive vitality (Iseri *et al*., 2005) while Sukurica in 2007 reported that 7 out of 20 showed positive vitality after the sixth month of retraction. So, there are still some uncertainties regarding this technique (Sayin, 2004).

Effect of Piezocision on tooth movement: In the late 1990s, the Wilcko brothers added the alveolar augmentation to the corticotomies and developed the Accelerated Osteogenic Orthodontics (AOO) procedure and claiming that the orthodontic treatment time could be reduced by 75% in majority of the orthodontic cases. In 2009 Dibart *et al* described a new minimally invasive procedure that they called as Piezocision (Aylikci, 2013). This technique combines micro-incisions limited to the buccal gingiva that allow the use of a piezoelectric knife to give osseous cuts to the buccal cortex and initiate the regional acceleratory phenomenon (RAP) without involving palatal or lingual cortex. The procedure allows for rapid tooth movement without the downside of an extensive and traumatic surgical approach while maintaining the clinical benefit of a bone or soft-tissue grafting concomitant with a tunnel approach.

Effect of Corticision on tooth movement: ‘‘Corticision’’ was introduced as a supplemental dentoalveolar surgery in orthodontic therapy to achieve accelerated tooth movement with minimal surgical intervention. In this technique, a reinforced scalpel is used as a thin chisel to separate the interproximal cortices transmucosally without reflecting a flap. According to Young-Guk Park, this is a minimally invasive technique to induce accelerated tooth movement by stimulating osteoblasts and bending alveolar bone that has been surgically separated (Huang, 2014).

Conclusion

The administration of exogenous biological molecules to accelerate tooth movement during orthodontic treatments has been intensively tested on animal experiments. However, clinical trials on humans are limited since they must be administered occasionally by local injections to avoid systemic applications that can be painful and cause discomfort to the patients. In the physical approach, the low level laser therapy is the most promising method; however, contradictory results were shown. The surgical approach is the most frequently used clinically and most tested with known predictions and stable results. However, it is invasive, aggressive and costly. Piezocision technique is one of the newest techniques in accelerating tooth movement and it has good clinical outcome and is considered the least invasive in the surgical approach. In general, all these techniques had draw backs and uncertainties that made them clinically inacceptable. However, there has been a rapid increase in the interest levels of product companies to enhance the effects of biology in orthodontics. These new approaches have the potential to be the next frontier for orthodontics and its resources.

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