Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 28s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Biomarkers In Orthodontic Tooth Movement

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Cite this paper as: Dr. Sagarika Manmohan, Dr. Lokesh N K, Dr. Vaishnavi S, Dr. Keerthana L Bharadwaj, Dr. Nag Nachiket Patil, (2025) Biomarkers In Orthodontic Tooth Movement, *Journal of Neonatal Surgery*, 14 (28s), 656-661

ABSTRACT

Orthodontic tooth movement is a complex process of various mechanisms bringing about remodeling changes in periodontium, alveolar bone and gingiva. This process occurs as a response to the mechanical forces applied onto the teeth by orthodontic appliances which gets transmitted to the alveolar bone, periodontal ligament and gingival tissue. These tissues undergo adaptive changes and result in movement of the teeth to their desired positions. The exact mechanisms of the changes occurring at cellular level is of great interest and importance in modern orthodontic practice. The orthodontists can better understand the mechanisms of action and the significance of various biomarkers to have clear insight into the phases of tooth movement, site and nature of force applied and its impact on the alveolar tissues, the response of the tissues to forces applied on the teeth and the continuous process of bone remodeling even after cessation of active orthodontic tooth movement. the gingival crevicular fluid (GCF) is a medium of study of these processes as it contains concentrations of biomarkers that reflect the underlying process of tissue adaptation. GCF can be collected from patients using filter paper strips, gingival washings, platinum loops and micropipettes. Analyzing the GCF can reveal its composition and the various biomarkers present in it. The orthodontist can use this to understand the intricate details of bone remodeling and make proper choice of mechanical force application to shorten orthodontic treatment time and avoid adverse effects of improper force application

Keywords: *Biomarkers, orthodontic tooth movement, bone remodeling, gingival crevicular fluid*

1. INTRODUCTION

Orthodontic tooth movement occurs as a result of the bone resorption around the tooth root due to the application of orthodontic force on the tooth crown.

Orthodontic force is a controlled and carefully regulated mechanism to bring about the desired tooth movement in an efficient and physiologically compliant manner

The orthodontic force results in a process of bone remodeling to allow for the movement of teeth which is a complex and continuous process of resorption and deposition.

Bone resorption is mediated by a series of enzymes and cell markers which can trigger the reaction to orthodontic force that

is expressed by the interplay between the alveolar bone, the periodontal ligament and the cells.

Orthodontic treatment needs periodontal health, oral hygiene, and optimal orthodontic forces to be considered for optimal success.[1]

Biomarkers can provide a deeper understanding into phases of tooth movement, sites of mechanical loading and tissue response to the orthodontic forces applied. This can help clinicians apply mechanical forces accurately to guide tooth movement while avoiding adverse effects of improper or excessive stress application..

2. MECHANISM OF TOOTH MOVEMENT

Tooth movement by orthodontic forces occurs due to remodeling changes in the alveolar tissue surrounding the tooth.

It is primarily an inflammatory change that is characterized by the action of inflammatory cell factors.

Two processes involved in orthodontic tooth movement (OTM) are compression of periodontal fibres and alveolar bone on one side (pressure side) and stretching of the fibres on the other side (tension side).

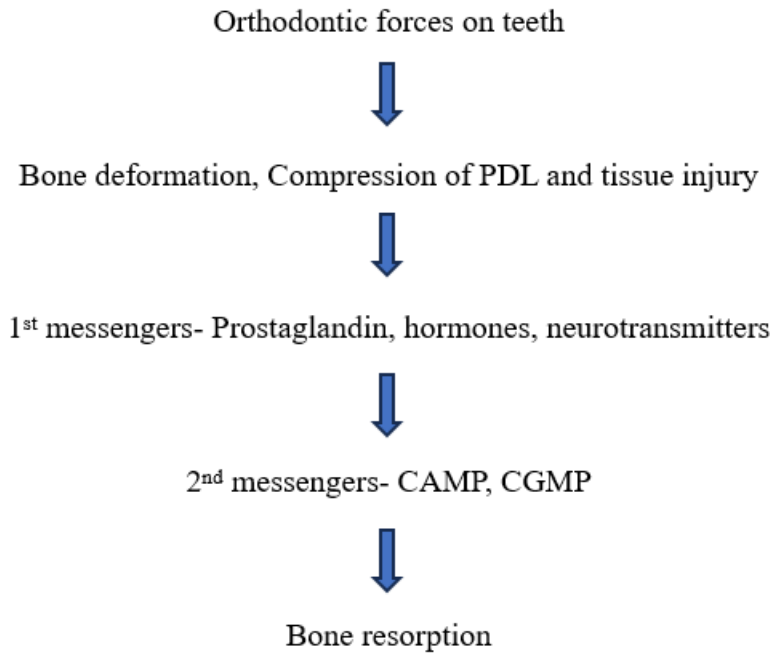

Figure 1: flowchart explaining the sequence of events occurring in the alveolar bone following the application of orthodontic force

The compression of the periodontal tissue leads to the resorption of bone directly adjacent to the compressed tissue. The tension or stretching on the opposite side leads to the deposition of new bone. These two processes occur simultaneously in the same tooth. The periodontal ligament undergoes this compression and tension leading to the extravasation of blood vessels and inflammatory cells are released to the site. There is recruitment of osteoclasts and osteoclast progenitor cells. The amount and rate of resorption and deposition of bone is carefully controlled by the respective regulatory mediators.

The orthodontic force changes the vascularity of the periodontal tissue which leads to signalling molecules being released. This generates a cellular response from the osteocytes and osteoclasts which facilitate the bone deposition and resorption.[2]

Phases of orthodontic tooth movement

Burstone, in 1962, suggested three phases of tooth movement.[3]

1. Initial phase
2. Lag phase
3. Post lag phase

The initial phase is characterised by the rapid movement of teeth in the periodontal space. Usually, it occurs with 24 hours to two days of inducing the orthodontic force.[4]

In this stage the expression of inflammatory mediators is brought about by the initial application of force to the tooth and its

subsequent movement within the alveolar bone socket.

The lag phase follows the initial phase wherein the tooth movement rate decreases due to the formation of hyalinised bone which hinders the tooth movement. The hyalinisation of compressed periodontal tissue occurs by the constriction of the vessels on the resorption side and it leads to a layer of necrosed tissue. Until this tissue is removed by the cells the tooth movement will be minimal or may be entirely stopped. The necrotic tissue is removed by macrophages, foreign body giant cells and osteoclasts within twenty to thirty days.[4]

The third phase is the post lag phase wherein the tooth movement rate increases, usually occurring forty days after the initial force application.

Chemical mediators of tooth movement

a. Inflammatory mediators
    i. Prostaglandin-e
    ii. Neuropeptides
b. RANKL and OPG
c. Tumour necrosis factor
d. Interleukin-1
e. Transforming growth factor- β -1
f. Insulin like growth factor
g. Enzymes and enzyme inhibitors
    i. Cathepsin b
    ii. Acid and alkaline phosphatase
    iii. Matrix metalloprotein

PROSTAGLANDIN E

It plays the role of mediating inflammatory response by activating the osteoclastic cells. It stimulates the osteoclasts and formation of ruffled border leading to bone resorption. The pressure and tension sides have been found to show significantly elevated levels of PGE1 and PGE2 during OTM in a study performed by Dudic et al (2006).[5] Prostaglandins mediate osteoclast formation by enhancing RANKL expression.

Yamasaki et al showed the effect of prostaglandin E injection in experimental tooth movement in rats and found that PGE1 or PGE2 when injected in the gingiva shows an increased amount of osteoclast formation and bone resorption within 24 hours of administration.[6]

RANKL and OPG

Receptor activator of nuclear factor- kappa ligand is a regulator of osteoclast formation. RANKL can bind the RANK receptor on the osteoclastic precursor cells. These cells then differentiate to mature into osteoclastic cells and thus the bone resorption is promoted. RANKL is a key player in the bone remodeling process along with RANK and OPG.

Osteoprotegerin is the decoy receptor that competes with the RANK and RANKL for binding to the osteoclastic precursors. It is produced by the osteoblastic cells when bone resorption is not desired, thus it competes with RANK and inhibits the bone resorption process. Al-Ansari et al in 2015 said that the levels of OPG must be less at the compression site to allow for bone resorption during OTM.[7]

Kanzaki et al reported that the inhibition of RANKL activity by introducing OPG is beneficial in certain situations such as to prevent movement of anchor teeth during orthodontic treatment.[8]

TUMOUR NECROSIS FACTOR

This is a pro-inflammatory cytokine, having a stimulatory effect on the bone resorption and causing acute or chronic inflammation. TNF- α can promote the differentiation of progenitor cells into osteoclastic cells, and has been shown to be increased in PDL and alveolar bone during OTM.[9-12]

In 2004, Ogasawara et al performed experiments on rats (19) and in 2006, Basaran et al found in humans that there was increase in TNF- α levels in the periodontal tissue due to orthodontic tooth movement.[13]

TNF- α has several direct and indirect effects on the bone remodeling namely activation as well as inhibition of osteoclastogenesis. It works through activation of two receptors namely TNF-receptor type 1 which enhances osteoclastogenesis, and TNF-receptor type 2 which inhibits it.[14]

Additionally, TNF-α indirectly acts on the process of imflammatoy response by inducing certain mediators which in turn induce osteoclast recruitment and bone resorption.[15-16]

INSULIN LIKE GROWTH FACTOR

It is one of the growth factors, a hormone responsible for the regulation and expression of growth hormone in the body. It has been shown to play a role in bone remodeling by Hu et al in 2016. It was found that when recombinant growth hormone was administered to rats and mechanical tooth movement was initiated, there were more number of insulin like growth factor-1 positive osteoclasts in the periodontal tissue, supporting the theory that IGF plays a role in tooth movement.[16]

INTERLEUKIN

They are inflammatory cytokines that promote osteoclast action and enhance bone resorption while inhibiting bone deposition. They act by attracting leukocytes and stimulating the endothelial cells, fibroblasts and osteoclasts to promote bone resorption.[17]

Interleukin-1 (IL-1) is involved in not just survival but also the activation of osteoclastic cells. IL-1β is a physiological form of IL-1 that is secreted by many cells mainly monocytes. Stimuli applied to these cells, such as mechanical trauma, triggers the production of the inflammatory cytokines.[13]

TRANSFORMING GROWTH FACTOR β -1

TGF is one of the growth factors whose role in orthodontic tooth movement is still under review. TGF- β1 levels in Gingival crevicular fluid during orthodontic treatment was measured at various time intervals. It was found that TGF- β1 levels significantly increased 7 days after mechanical load application. Thus, it was suggested that pro-inflammatory cytokines levels are increased during orthodontic force application and they are involved in bone resorption. Monitoring the levels of these cytokines can serve as markers for the period of orthodontic tooth movement.[18]

ENZYMES and ENZYME INHIBITORS

CATHEPSIN B

Cathepsin B, is an intracellular lysosomal cysteine proteinase that plays an important role in intracellular proteolysis. It can degrade extracellular components such as collagen.[19]

It has been shown in studies that cathepsin B plays a vital role in the initiation of inflammatory processes. In a study by Sugimoto et al, cathepsin B levels in GCF were found to have a positive correlation with the occurrence of orthodontic tooth movement. The periodontal tissues in the cases undergoing orthodontic tooth movement showed no sign of severe inflammation despite this elevation in the level of cathepsin B. It was thus hypothesised that the increase in cathepsin B level may be involved in the tissue response to the mechanical stress applied on the tooth, which causes extracellular matrix degradation.[19]

Additionally, the level of cathepsin B when compared between patients undergoing active orthodontic tooth movement and patients in the retention phase of therapy, was discovered that cathepsin B levels were elevated in the group undergoing active tooth movement and decreased steadily in the retention group. Thus, it was surmised that the cathepsin B level can indicate the stability of the tooth movement but further research must be undertaken to prove the reliability of cathepsin B in orthodontic tooth movement.[20]

ACID AND ALKALINE PHOSPHATASE

Alkaline phosphatase (ALP) enzyme is a glycoprotein that has a role to play in the mineralization process in bone, cementum and calcifying cartilages.[21]

Acid phosphatase (ACP) is also an enzyme thought to be involved in bone remodeling, especially in bone resorption as it shows increased levels of acid phosphatase in osteoclasts and macrophages.[22]

A longitudinal study by Farahani et al[23] evaluated the ALP and ACP levels in GCF at three different points in orthodontic treatment. They found that the ALP and ACP activities can reflect the metabolic changes in periodontium and the ALP can sufficiently indicate sites of bone deposition. ACP was found to be less sensitive than ALP but it can adequately indicate site of bone resorption during orthodontic tooth movement.

MATRIX METALLOPROTEINS

MMPs are chemokines, which are the protein molecules that are regulated by the enzyme matrix metalloproteinases. The MMPs along with cathepsin are responsible for the degradation of organic component of bone, while osteoclasts degrade the inorganic bone via acids. They denature the collagen structure of the bone to facilitate resorption. MMP has been seen to increase significantly soon after initial application of orthodontic force, but soon reduces after removal of force.[24-25]

3. CONCLUSION

Various biomarkers have been proposed to provide a way to analyse and understand the complex system of the remodeling and adaptive changes that occur in the periodontal tissues and structures when subjected to mechanical force from orthodontic forces. These enzymes and molecules can help clinicians to understand the cellular level of changes that take place during orthodontic tooth movement and basic bone remodeling procedure. Many biomarkers are also easy to procure from GCF of patients. A clear insight into the biomarkers and their role in metabolic changes in bone and periodontium will improve the clinician's control over each step of the orthodontic treatment, treatment planning, the patient's prognosis as well as decrease undesired consequences of orthodontic force application

REFERENCES

[1] Kumar AA, Saravanan K, Kohila K, Kumar SS. Biomarkers in orthodontic tooth movement. J Pharm Bioallied Sci. 2015

[2] Krishnan V, Davidovitch Z. Cellular, molecular, and tissue-level reactions to orthodontic force. Am J Orthod Dentofacial Orthop 2006;129:469

[3] Smith RJ, Burstone CJ. Mechanics of tooth movement. Am J Orthod. 1984 Apr;85(4):294-307

[4] Asiry M, Biological aspects of orthodontic tooth movement: A review of literature. Saudi Journal of Biological Sciences, 2018

[5] Dudic A, Kiliaridis S, Mombelli A, Giannopoulou C. Composition changes in gingival crevicular fluid during orthodontic tooth movement: Comparisons between tension and compression sides. Eur J Oral Sci 2006;114:416-22

[6] Yamasaki K, Miura F, Suda T. Prostaglandin as a mediator of bone resorption induced by experimental tooth movement in rats. J Dent Res. 1980 Oct;59(10):1635-42.

[7] Alansari S, Sangsuwon C, Vongthongleur T, Kwal R, chneh Teo M, Lee YB, Nervina J, Teixeira C, Alikhani M. Biological principles behind accelerated tooth movement. In Seminars in Orthodontics 2015 Sep 1 (Vol. 21, No. 3, pp. 151-161).

[8] Kanzaki H, Chiba M, Takahashi I, Haruyama N, Nishimura M, Mitani H. Local OPG gene transfer to periodontal tissue inhibits orthodontic tooth movement. J Dent Res 2004;83:920-5

[9] Davidovitch Z, Nicolay OF, Ngan PW, Shanfeld JL. Neurotransmitters, cytokines, and the control of alveolar bone remodeling in orthodontics. Dent Clin North Am 1988;32:411-35.

[10] Saito S, Ngan P, Saito M, Kim K, Lanese R, Shanfeld J, et al. Effects of cytokines on prostaglandin E and cAMP levels in human periodontal ligament fibroblasts in vitro. Arch Oral Biol 1990;35:387-95.

[11] Alhashimi N, Frithiof L, Brudvik P, Bakhiet M. Orthodontic tooth movement and de novo synthesis of proinflammatory cytokines. Am J Orthod Dentofacial Orthop 2001;119:307-12.

[12] Alhashimi N, Frithiof L, Brudvik P, Bakhiet M. Orthodontic movement induces high numbers of cells expressing IFN-gamma at mRNA and protein levels. J Interferon Cytokine Res 2000;20:7-12.

[13] Başaran G, Ozer T, Kaya FA, Kaplan A, Hamamci O. Interleukine-1beta and tumor necrosis factor-alpha levels in the human gingival sulcus during orthodontic treatment. Angle Orthod. 2006

[14] Barcelos LS, Talvani A, Teixeira AS, Vieira LQ, Cassali GD, Andrade SP, et al. (2005). Impaired inflammatory angiogenesis, but not leukocyte influx, in mice lacking TNFR1. J Leukoc Biol 78:352-358.

[15] Garlet GP, Cardoso CR, Campanelli AP, Ferreira BR, Avila-Campos MJ, Cunha FQ, et al. (2007). The dual role of p55 tumour necrosis factor-alpha receptor in Actinobacillus actinomycetemcomitans-induced experimental periodontitis: host protection and tissue destruction. Clin Exp Immunol 147:128-138.

[16] Hu YJ, Liu WT, Wang YL, He H. [Effects of recombinant human growth hormone on local expression of insulin-like growth factor- during orthodontic tooth movement]. Zhonghua Kou Qiang Yi Xue Za Zhi. 2016;51(6):374-8.

[17] Sabatini M, Boyce B, Aufdemorte T, Bonewald L, Mundy GR. Infusions of recombinant human interleukins 1 alpha and 1 beta cause hypercalcemia in normal mice. Proc Natl Acad Sci U S A 1988;85:5235-9

[18] Almotareb FL, Al-Shameri BHH, Al-Najhi MMA, Al-dossary OAI, Al-Shamahy HA. (2023) Increase of Transforming Growth Factor-Beta 1 in Gingival Crevicular Fluid during Human Orthodontic Tooth Movement. J Oral Med and Dent Res. 4(2):1-09.

[19] Mort JS, Buttle DJ. Cathepsin B. Int J Biochem Cell Biol. 1997 29(5):715-20.

[20] Seung-Hoon Rhee, Junghee Kang, Dong-Seok Nahm, Cystatins and cathepsin B during orthodontic tooth movement, American Journal of Orthodontics and Dentofacial Orthopedics, Volume 135, Issue 1, 2009,

[21] Yamaguchi M, Shimizu N, Shibata Y, Abiko Y. Effects of different magnitudes of tension-force on alkaline phosphatase activity in periodontalligament cells. J Dent Res. 1996; 75: 889–894.

[22] Burstone MS. Histochemical demonstration of acid phosphatase activity in osteoclasts. J Histochem Cytochem. 1959; 7: 39–41.

[23] Farahani M, Safavi SM, Dianat O, Khoramian Tusi S, Younessian F. Acid and Alkaline Phosphatase Levels in GCF during Orthodontic Tooth Movement. J Dent (Shiraz). 2015 Sep;16(3 Suppl):237-45.

[24] Cantarella G, Cantarella R, Caltabiano M, Risuglia N, Bernardini R, Leonardi R. Levels of matrix metalloproteinases 1 and 2 in human gingival crevicular fluid during initial tooth movement. Am J Orthod Dentofacial Orthop 2006;130:568

[25] Redlich M, Reichenberg E, Harari D, Zaks B, Shoshan S, Palmon A. The Effect of Mechanical Force on mRNA Levels of Collagenase, Collagen Type I, and Tissue Inhibitors of Metalloproteinases in Gingivae of Dogs. J Dent Res. 2001;80(12):2080–4.

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