

ASSESSMENT OF BIOMARKERS OF ORTHODONTIC TOOTH MOVEMENT WITH FIXED APPLIANCES-ORIGINAL RESEARCH

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ABSTRACT

Background: Several important biomarkers have been identified clinically and in animal studies that mediate orthodontic tooth movement. The present study was conducted to assess biomarkers of orthodontics.

Materials & Methods: 28 patients requiring orthodontic treatment of both genders were divided into 2 groups of 14 each. Group I was vibrational and fixed appliance group and group II was fixed appliance group only. Collection of unstimulated whole saliva in a sterile test tube was done and the targeted biomarkers such as IL1b and IL18 were analyzed using ELISA assay test.

Results: Group I had 5 males and 9 females and group II had 6 males and 8 females. Irregularity index at time point T0 was 8.4 in group I and 9.6 in group II, at T1 was 5.2 in group I and 5.7 in group II, at T2 was 2.1 in group I and 2.3 in group II and at T3 was 1.0 in group I and 0.8 in group II. The difference was significant ($P < 0.05$). The mean pain score value at T0 was 40.2 in group I and 34.2 in group II, at T1 was 16.5 in group I and 14.5 in group II and at T2 was 28.1 in group I and 40.7 in group II. The difference was significant ($P < 0.05$). The mean IL-1B level at T0 was 41.5 and 82.5, at T1 was 26.3 and 57.4, at T2 was 29.7 and 106.3 and at T3 was 26.8 and 131.5. The mean IL-8 level at T0 was 265.4 and 250.5, at T1 was 190.7 and 178.2, at T2 was 198.2 and 261.5 and at T3 was 296.4 and 385.2 in group I and II respectively. The difference was significant ($P < 0.05$).

Conclusion: There was no difference in the expression of biological markers of bone remodeling between both groups.

Key words: biological markers, orthodontics, IL-8

Introduction

On average, comprehensive orthodontic treatments last approximately 21-27 months in non-extraction cases and 25-35 months when extractions are considered in the treatment plan.¹ Longer treatment time has been associated with multiple detrimental effects such as white spot lesions, root resorption, gingival inflammation and dental caries. Additionally, increased treatment time often leads to the exhaustion of the patient's compliance.² It is then in the patient's and in the clinician's interest to identify methods to increase the speed and efficiency of treatment. It has been estimated that normal tooth movement occurs at a rate of 0.8-1.2 mm/month.³

The application of mechanical vibration to the dentition has also been hypothesized to increase the rate of tooth movement by affecting the expression of key biological factors involved in bone remodeling.^{4,5} Several important biomarkers have been identified clinically and in animal studies that mediate orthodontic tooth movement. Among these, the osteoprotegerin (OPG)/receptor activator of nuclear factor kappa-B ligand (RANKL) system in bone modelling has been mentioned in studies performed on animals and recently on humans during orthodontic treatment.⁶ Matrix metalloproteinases (MMPs) play a key role in collagen breakdown, tissue modelling, and degradation of the extracellular matrix.⁷ Multiple studies have shown increased expression of certain metalloproteinases during orthodontic treatment. Lastly, tumour necrosis

factorialpha (TNF- α) and interleukins are cytokines that increase with orthodontic force application in rats and human.^{8,9} The present study was conducted to assess biomarkers of orthodontics.

Materials & Methods

The present study comprised of 28 patients requiring orthodontic treatment of both genders. The consent was obtained from all enrolled patients.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of 14 each. Group I was vibrational and fixed appliance group and group II was fixed appliance group only. All patients were bonded with passive self-ligating brackets featuring 0.022”X0.025” slot and MBT prescription from second premolar to second premolar as well as a bonded tube on first molars. At the bonding appointment (T0), an 0.014” Cu-NiTi wire was inserted on the lower arch and was kept until the T2 appointment. At T2, bracket position was assessed and repositioning was performed. At this same appointment, the wire was changed for 0.014”X0.025” Cu-NiTi. All subjects were seen for orthodontic adjustments every 5-6 weeks. Collection of unstimulated whole saliva in a sterile test tube was done and the targeted biomarkers such as IL1b and IL18 were analyzed using ELISA assay test. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Distribution of patients

Groups	Group I	Group II
Method	vibrational and fixed appliance	fixed appliance
M:F	5:9	6:8

Table I shows that group I had 5 males and 9 females and group II had 6 males and 8 females.

Table II Irregularity index at each time points

Time points	Group I	Group II	P value
T0	8.4	9.6	0.82
T1	5.2	5.7	0.74
T2	2.1	2.3	0.95
T3	1.0	0.8	0.97

Table II, graph I shows that irregularity index at time point T0 was 8.4 in group I and 9.6 in group II, at T1 was 5.2 in group I and 5.7 in group II, at T2 was 2.1 in group I and 2.3 in group II and at T3 was 1.0 in group I and 0.8 in group II. The difference was significant (P< 0.05).

Graph I Irregularity index at each time points

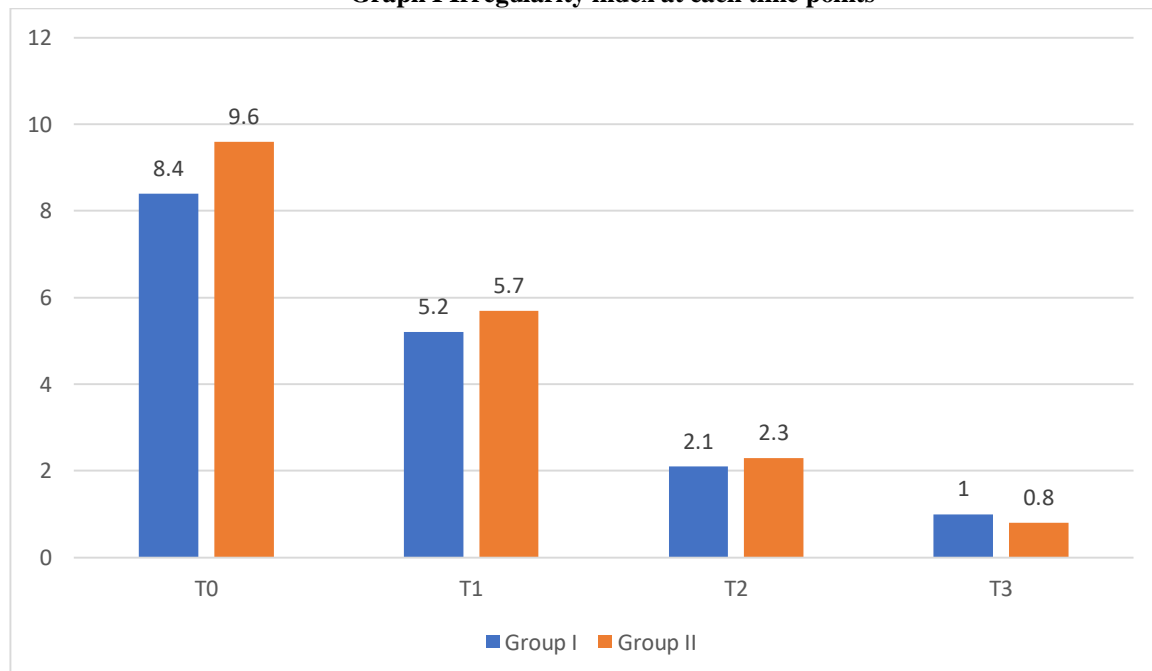


Table III Pain scores in both groups

Time points	Group I	Group II	P value
T0	40.2	34.2	0.08

T1	16.5	14.5	0.91
T2	28.1	40.7	0.02

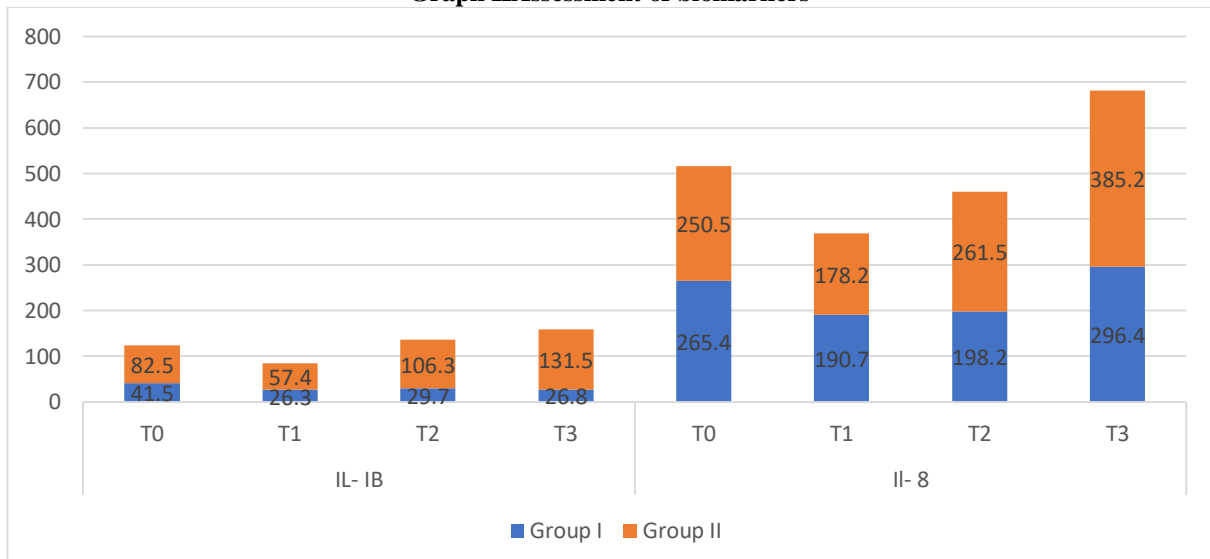
Table III shows that mean pain score value at T0 was 40.2 in group I and 34.2 in group II, at T1 was 16.5 in group I and 14.5 in group II and at T2 was 28.1 in group I and 40.7 in group II. The difference was significant ($P < 0.05$).

Table IV Assessment of biomarkers

Biomarkers	Time points	Group I	Group II	P value
IL- IB	T0	41.5	82.5	0.05
	T1	26.3	57.4	0.02
	T2	29.7	106.3	0.01
	T3	26.8	131.5	0.03
IL- 8	T0	265.4	250.5	0.91
	T1	190.7	178.2	0.12
	T2	198.2	261.5	0.17
	T3	296.4	385.2	0.05

Table IV, graph II shows that mean IL- IB level at T0 was 41.5 and 82.5, at T1 was 26.3 and 57.4, at T2 was 29.7 and 106.3 and at T3 was 26.8 and 131.5. The mean IL- 8 level at T0 was 265.4 and 250.5, at T1 was 190.7 and 178.2, at T2 was 198.2 and 261.5 and at T3 was 296.4 and 385.2 in group I and II respectively. The difference was significant ($P < 0.05$).

Graph II Assessment of biomarkers



Discussion

It has been successfully demonstrated that pro-inflammatory cytokines have an important role throughout bone modelling of the alveolus during orthodontic tooth movement.^{10,11} The present study was conducted to assess biomarkers of orthodontics.

We found that group I had 5 males and 9 females and group II had 6 males and 8 females. Ogasawara research focusing on tumor necrosis factor alpha (TNF- α) and interleukins concentration have shown increased values when orthodontic force was applied. Basaranet al¹² using gingival crevicular fluid instead of saliva. This difference in 26 the protocol could affect some biomarker detection, especially ones found to be expressed in lower concentrations in the GCF.

We found that irregularity index at time point T0 was 8.4 in group I and 9.6 in group II, at T1 was 5.2 in group I and 5.7 in group II, at T2 was 2.1 in group I and 2.3 in group II and at T3 was 1.0 in group I and 0.8 in group II. Ren et al measured a panel of proinflammatory cytokines (IL1 β , IL-6, IL-8 and TNF- α) during tooth movement of short and long durations and found large variation in the results for each biomarker. Floréz-Moreno et al¹³ investigated salivary levels of RANKL, OPG, and the RANKL/OPG ratio during orthodontic tooth movement.

We found that mean pain score value at T0 was 40.2 in group I and 34.2 in group II, at T1 was 16.5 in group I and 14.5 in group II and at T2 was 28.1 in group I and 40.7 in group II. We found that mean IL- IB level at T0 was 41.5 and 82.5, at T1 was 26.3 and 57.4, at T2 was 29.7 and 106.3 and at T3 was 26.8 and 131.5. The mean IL- 8 level at T0 was 265.4 and 250.5, at T1 was 190.7 and 178.2, at T2 was 198.2 and 261.5 and at T3 was 296.4 and 385.2 in group I and II respectively. Reiss et al¹⁴ investigated the effect of supplemental vibratory

force on biomarkers of bone remodelling during orthodontic tooth movement, the rate of mandibular anterior alignment (RMAA), and compliance with a vibration device. Forty patients between the ages 15–35 undergoing fixed appliance treatment that presented to a university orthodontic clinic were randomly allocated to supplemental use of an intraoral vibrational device (n = 20, AcceleDent®) or fixed appliance only (n = 20). Salivary multiplex assay was completed to analyse the concentration of selected biomarkers of bone remodelling before treatment (T0) and at three following time points (T1, T2, T3), 4–6 weeks apart. Irregularity of the mandibular anterior teeth and compliance was assessed at the same trial time points. No difference in the changes in salivary biomarkers of bone remodelling and RMAA between groups at any time point over the trial duration was observed. No correlation was found between changes in irregularity and biomarker level from baseline to another time point. Lastly, there was no association between RMAA and compliance with the AcceleDent® device.

Conclusion

Authors found that there was no difference in the expression of biological markers of bone remodeling between both groups.

References

1. Bildt, M.M., Bloemen, M., Kuijpers-Jagtman, A.M. and Von den Hoff, J.W. (2009) Matrix metalloproteinases and tissue inhibitors of metalloproteinases in gingival crevicular fluid during orthodontic tooth movement. *European Journal of Orthodontics*, 31, 529–535.
2. Capelli, J., Kantarci, A., Haffajee, A., Teles, R.P., Fidel, R. Jr. and Figueredo, C.M. (2011) Matrix metalloproteinases and chemokines in the gingival crevicular fluid during orthodontic tooth movement. *European Journal of Orthodontics*, 33, 705–711.
3. Takahashi, I., Nishimura, M., Onodera, K., Bae, J.W., Mitani, H., Okazaki, M., Sasano, Y. and Mitani, H. (2003) Expression of MMP-8 and MMP-13 genes in the periodontal ligament during tooth movement in rats. *Journal of Dental Research*, 82, 646–651.
4. Ogasawara, T., Yoshimine, Y., Kiyoshima, T., Kobayashi, I., Matsuo, K., Akamine, A. and Sakai, H. (2004) In situ expression of RANKL, RANK, osteoprotegerin and cytokines in osteoclasts of rat periodontal tissue. *Journal of Periodontal Research*, 39, 42–49.
5. Başaran, G., Ozer, T., Kaya, F.A., Kaplan, A. and Hamamci, O. (2006) Interleukine-1beta and tumor necrosis factor-alpha levels in the human gingival sulcus during orthodontic treatment. *The Angle Orthodontist*, 76, 830–836.
6. Leethanakul, C., Suamphan, S., Jitpukdeebodindra, S., Thongudomporn, U. and Charoemratrote, C. (2016) Vibratory stimulation increases interleukin-1 beta secretion during orthodontic tooth movement. *The Angle Orthodontist*, 86, 74–80.
7. Navazesh, M. and Kumar, S.K.; University of Southern California School of Dentistry. (2008) Measuring salivary flow: challenges and opportunities. *Journal of the American Dental Association* (1939), 139(Suppl), 35S–40S.
8. Little, R.M. (1975) Theirregularity index: a quantitative score of mandibular anterior alignment. *American Journal of Orthodontics*, 68, 554–563.
9. Grant, M., Wilson, J., Rock, P. and Chapple, I. (2013) Induction of cytokines, MMP9, TIMPs, RANKL and OPG during orthodontic tooth movement. *European Journal of Orthodontics*, 35, 644–651.
10. Holliday, L.S., Vakani, A., Archer, L. and Dolce, C. (2003) Effects of matrix metalloproteinase inhibitors on bone resorption and orthodontic tooth movement. *Journal of Dental Research*, 82, 687–691.
11. Ogasawara, Y., Yoshimine, T., Kiyoshima, I., Kobayashi, K., Matsuo, A., Akamine and H. Sakai, "In situ expression of RANKL, RANK, osteoprotegerin and cytokines in osteoclasts of rat periodontal tissue," *Journal of Periodontal Research*, vol. 39, no. 1, pp. 42-49, 2004.
12. Basaran, T., Ozer, F., Kaya, A., Kaplan and O. Hamamci, "Interleukine-1beta and tumor necrosis factor-alpha levels in the human gingival sulcus during orthodontic treatment," *Angle Orthodontist*, vol. 76, pp. 830-836, 2006.
13. Flórez-Moreno, G.A., Isaza-Guzmán, D.M. and Tobón-Arroyave, S.I. (2013) Time-related changes in salivary levels of the osteotropic factors sRANKL and OPG through orthodontic tooth movement. *American Journal of Orthodontics and DentofacialOrthopedics*, 143, 92–100.
14. Reiss S, Chouinard MC, FriasLanda D, Nanda R, Chandhoke T, Sobue T, Allareddy V, Kuo CL, Mu J, Uribe F. Biomarkers of orthodontic tooth movement with fixed appliances and vibration appliance therapy: A pilot study. *European Journal of Orthodontics*. 2020 Aug;42(4):378-86.