ORIGINAL RESEARCH

Gingival Crevicular Fluid Turnover Markers in Premenopausal *vs* Postmenopausal Women receiving Orthodontic Treatment

[1]Anusha Bitra, [2]B Jhansi Rani, [3]Sanket S Agarkar, [4]Anuj S Parihar, [5]Gopinath P Vynath, [6]Shekhar Grover

ABSTRACT

Background: Orthodontic treatment is one of the commonly used dental treatments. Orthodontic forces act on the bone by modulating the biomolecules, chiefly the osteoprotegerin (OPG), osteopontin (OPN), receptor activator of nuclear factor kappa-B (RANK), and RANK ligand (RANKL) (OPG ligand). Hormonal changes are known to cause marked alteration in the levels of these biomolecules. Hence, we planned this study to evaluate the response of bone biomarkers in the gingival crevicular fluid (GCF) in postmenopausal women undergoing fixed orthodontic therapy.

Materials and methods: This study included assessment of 50 subjects who underwent orthodontic treatment from June 2012 to July 2016. All the patients were divided into two study groups with 25 patients in each group: premenopausal group and postmenopausal group. Similar orthodontic wires were used for controlling the forces applied in subjects of both the study groups and their GCF levels of RANKL, and OPN was assessed at baseline and 24 hours after the activation of orthodontic forces. All the results were compiled, assessed, and analyzed by Statistical Package for the Social Sciences software version 16.0. Chi-square test, Student's t-test, and Mann–Whitney U test were used for the assessment of the level of significance.

Results: The mean values of RANKL and OPN in the premenopausal and postmenopausal groups were found to be 241.52 and 317.15 pg/µL respectively. The mean values of RANKL at baseline in the premenopausal and postmenopausal groups were found to be 7.15 and 3.84 pg/µL respectively. Nonsignificant results were obtained while comparing mean OPN and RANKL level alteration in between the two study groups.

Conclusion: The mean alterations in the GCF levels of bone biomarkers are similar for both premenopausal and postmenopausal women.

Clinical significance: For women with either premenopausal or postmenopausal status, orthodontic treatment appears to be equally safer.

Keywords: Menopause, Orthodontic, Receptor activator of nuclear factor kappa-B ligand.

[1,2]Department of Orthodontics and Dentofacial Orthopaedics Drs Sudha and Nageswara Rao Siddhartha Institute of Dental Sciences, Vijayawada, Andhra Pradesh, India

[3]Department of Orthodontics, Dr. D. Y. Patil Dental College & Hospital, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India

[4]Department of Periodontology, RKDF Dental College and Research Centre, Bhopal, Madhya Pradesh, India

[5]Department of Periodontics, Malabar Dental College & Research Center, Edappal, Kerala, India

[6]Department of Public Health Dentistry, Maulana Azad Dental College & Hospital, New Delhi, India

Corresponding Author: Shekhar Grover, Department of Public Health Dentistry, Maulana Azad Dental College & Hospital, New Delhi, India, Phone: +919501544877, e-mail: drshekhargrover@gmail.com

INTRODUCTION

One of the consequences of the application of intentional mechanical force to the dentition is the orthodontic tooth movement. In response to the orthodontic forces, bone formation and resorption occurs on the tension and compression side of the bone respectively. When orthodontic forces are applied on a tooth, the following essential biological reactions occur, which are:

- Formation of bone,
- Resorption of bone, and
- Iatrogenic resorption of root.[1]

Bone remodeling occurs by the action of bone resorbing cells—osteoclasts—and by bone forming

cells—osteoblasts—which further results in bodily or axial movement of the tooth. Bone remodeling is affected by many body hormones, which include sex steroids, parathyroid hormone, and growth hormone, 1,25-dihydroxyvitamin D3. Action of most of these occurs by mediating through a number of local factors produced by them, which act on bone cells.[2,3]

Osteoprotegerin, OPN, RANK, RANKL, etc., are the main biomarkers that control the physiological bone remodeling.[4] Literature quotes paucity of data that has established the influence of hormonal status in premenopausal and postmenopausal women and their effect on orthodontic tooth movement and bone remodeling.[5] Hence, we planned this study to evaluate the response of bone biomarkers in the GCF in postmenopausal women undergoing fixed orthodontic therapy.

MATERIALS AND METHODS

The present study was conducted in the Department of Orthodontics and Periodontology of the Dental Institute and included assessment of 50 subjects who fulfilled the inclusion and exclusion criteria and underwent orthodontic treatment from June 2012 to July 2016. Ethical approval was taken from the Institutional Ethical Committee, and written consent was obtained from all the subjects after explaining in detail the entire research protocol. Inclusion criteria for the present study included:
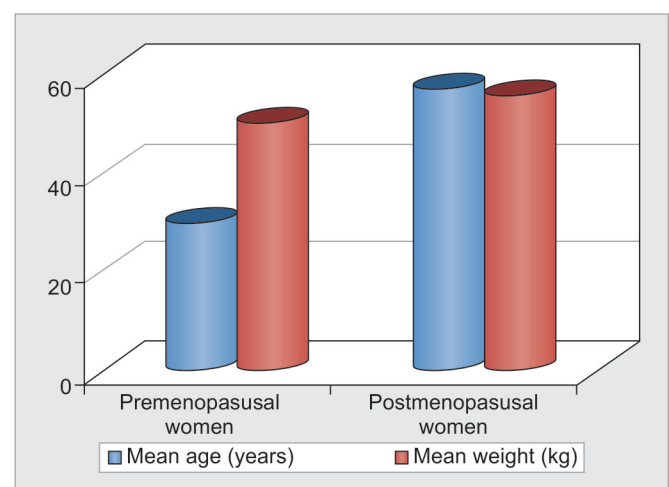
- Patients more than 22 years of age,
- Patients with more than four anterior and posterior teeth,
- Patients who appeared for complete follow-up examination,
- Patients without history of any type of systemic illness,
- Patients without history of any bony lesion,
- Patients without any known drug allergy,
- Patients with negative history of usage of nonsteroidal anti-inflammatory drugs, steroids, or other anti-inflammatory drugs in the past 1 month,
- Patients who were not on any type of hormonal replacement therapy.

After meeting the inclusion and exclusion criteria, a total of 50 patients were selected and were divided into two study groups with 25 patients in each group. Group I included premenopausal subjects, which were taken as controls, and group II included postmenopausal subjects that were taken as a subject group. Only those cases were considered as postmenopausal which had surgical or natural menopause as reported by medical reports.[6,7] All the subjects were subjected to equivalent orthodontic forces on the day of collection of the GCF sample. The malocclusion status was assessed in all the patients and discrepancy index was found to be equivalent among all

the subjects in both the groups.[5] Similar orthodontic wires were used for controlling the forces applied in subjects of both the study groups. Routine activation situations were intentionally chosen for bringing consistency in the results. Before the activation of orthodontic treatment, samples were collected from the GCF of all the subjects and were denoted as B_0. This value indicated the baseline value. After activating the orthodontic treatment, collection of second samples of GCF was done from the similar sites 1 day after the baseline and was denoted as B_1. Skilled and experienced periodontists were employed for collection of GCF samples. For the purpose of collection of GCF, Periopaper (BVM Meditech Private Limited, India) strips were utilized. After the collection of the GCF samples, sterile polypropylene vial was used for the collection of the Periostrips. All the strips were transported to the laboratory where they were processed and analyzed. All the results were compiled, assessed, and analyzed by Statistical Package for the Social Sciences software version 16.0. Chi-square test, Student's t-test, and Mann–Whitney U test were used for the assessment of the level of significance; $p < 0.05$ was taken as significant.

RESULTS

In this study, we observed that the mean age of the subjects in the premenopausal and postmenopausal groups were 30 and 57 years respectively (Graph 1). In the premenopausal and postmenopausal groups, the mean values of OPN at baseline were found to be 241.52 and 317.15 pg/μL respectively. The mean values of RANKL at baseline in the premenopausal and postmenopausal groups were found to be 7.15 and 3.84 pg/μL respectively (Table 1). We observed significant difference while comparing the OPN and RANKL levels between the two study groups at baseline ($p < 0.05$). The mean levels of OPN and RANKL in the premenopausal and postmenopausal groups at B_1

Graph 1: Demographic details of the subjects in both the groups

Table 1: OPN and RANKL mean concentrations in subjects of both the study groups at B_0

Parameter	Premenopausal women	Postmenopausal women	p-value
OPN (pg/µL)	241.52	317.15	0.02*
RANKL (pg/µL)	7.15	3.84	0.03*

*Significant

Table 2: OPN and RANKL mean concentrations in subjects of both the study groups at B_1

Parameter	Premenopausal women	Postmenopausal women	p-value
OPN (pg/µL)	540.97	492.73	0.01*
RANKL (pg/µL)	12.16	10.58	0.26

*Significant

Table 3: OPN and RANKL mean concentrations in subjects of premenopausal women at B_0 and B_1

Parameter	B_0	B_1	p-value
OPN (pg/µL)	241.52	540.97	0.04*
RANKL (pg/µL)	7.15	12.16	0.02*

*Significant

Table 4: OPN and RANKL mean concentrations in subjects of postmenopausal women at B_0 and B_1

Parameter	B_0	B_1	p-value
OPN (pg/µL)	317.15	492.73	0.03*
RANKL (pg/µL)	3.84	10.58	0.04*

*Significant

Table 5: OPN and RANKL alteration in concentrations at two different time intervals in subjects of premenopausal and postmenopausal women

Parameter	Premenopausal women	Postmenopausal women	p-value
Alteration in OPN concentration (pg/µL)	299.45	175.58	0.07
Alteration in RANKL concentration (pg/µL)	5.01	6.75	0.41

*Significant

were found to be 540.97, 12.16, 492.73, and 10.58 pg/µL respectively (Table 2). We observed significant difference while comparing the mean OPN concentrations between the two study groups at B_1 ($p < 0.05$). While comparing the alteration in mean OPN and RANKL levels in the premenopausal group at different time intervals, it was found to be significant ($p < 0.05$) (Table 3). We also observed significant difference in comparing the alteration in mean OPN and RANKL levels in the postmenopausal group at different time intervals ($p < 0.05$) (Table 4). Table 5 summarizes the OPN and RANKL alteration in concentrations at two different time intervals in subjects of premenopausal and postmenopausal women. We did not observed any significant difference while comparing mean OPN and RANKL level alteration between the two study groups at different time intervals ($p > 0.05$).

DISCUSSION

The branch of dentistry that is concerned with the treatment of malocclusion is orthodontics. Parallel with the treatment execution, orthodontic therapy is associated with certain adverse effects. These effects can be either patient-related or dentist-related. In context to root resorption and other adverse effects, not much understanding exists in relation to their occurrence and pathogenesis.[8-10]

Osteoblasts and osteoclasts are the principal cells involved in the bone remodeling process which causes movement of teeth inside the bone. Past studies in the literature have shown that some amount of alteration do occur in the GCF levels of various bone biomarkers (RANKL, OPN) under the influence of active orthodontic treatment.[11-13] Hence, we planned this study to evaluate the response of bone biomarkers in the GCF in postmenopausal women undergoing fixed orthodontic therapy.

In this study, we observed similar alterations occurring in both premenopausal and postmenopausal women in the GCF biomarker levels, in reaction to the active orthodontic forces (Tables 1 and 2). This confers that in both premenopausal and postmenopausal women, orthodontic forces have a similar effect, and therefore orthodontic treatment in all these patients can be carried out in similar manner irrespective of their biological status. Our results were in correlation with the results obtained by Smuthkochorn et al,[5] who also observed similar findings in their study. In both the study groups individually, we observed similar significant alteration in the levels of biomarkers at different time intervals (Tables 3 and 4). The GCF bone biomarker turnover was comparatively evaluated between premenopausal and postmenopausal subjects who were subjected to fixed orthodontic therapy. Smuthkochorn et al[5] evaluated and assessed the GCF levels at two different time intervals. They analyzed a total of 28 female patients and divided them into two study groups. First group was of premenopausal patients and included 16 women, while the second group included 12 postmenopausal patients. They assessed RNAKL and OPN levels in the GCF in these patients at two different time intervals; baseline, and 24 hours after orthodontic force activation. They observed a significant alteration in the baseline values of RANKL and OPN in between the subjects of two study groups. They also observed a significant elevation in the values of both the markers in both the study groups with time. From the results, they concluded that significant amount of security exists with orthodontic force activation.

Bone density alteration around the teeth in patients undergoing orthodontic treatment was assessed by

Yu et al.[14] They used dental cone beam computed tomography for assessing the bone density changes. They assessed these changes in the anterior maxillary arch at different time intervals as follows: T0, T1, and T2. They used Friedman test for evaluating the alteration in the bone density around the teeth. They observed significant difference from the time interval of T0 to T1 in terms of bone density. They concluded that bone density alterations do occur with time in patients undergoing orthodontic treatment. While evaluating the alteration in the biomarker levels in the two time intervals between the two study groups, we observed nonsignificant results (Table 5). Earlier also, the authors reported similar findings in their study.[5] Pizzo et al[15] evaluated the periodontal parameters in female subjects with postmenopausal status receiving hormone replacement therapy (HRT). They assessed a total of 991 postmenopausal women and divided them into two study groups. First group consisted of 52 patients and included subjects who were on HRT, while the other groups consisted of subjects who were not on HRT and included 39 subjects. They assessed probing pocket depth (PD) and clinical attachment level (CAL) in those patients. They also evaluated gingival bleeding on probing. They did not observe any significant difference in the values of PD and CAL between the two study groups. In the HRT-positive groups, they observed significantly lower amount of visible plaque in comparison to the subjects of the control group. From the results, they concluded that long-term HRT does not influence the periodontal parameters and status of postmenopausal women.

CONCLUSION

No difference is observed while comparing the mean alteration in the levels of biomarkers in the GCF in premenopausal and postmenopausal women. Therefore orthodontic treatment appears to be equally safer for both premenopausal and postmenopausal subjects.

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