Gingival crevicular fluid bone turnover biomarkers: How postmenopausal women respond to orthodontic activation

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Introduction: Bone turnover associated with orthodontic tooth movement is evidenced by increased bone turnover markers in gingival crevicular fluid (GCF). Postmenopausal women have an increased concentration of serum bone turnover markers. The filtrate of this serum makes up GCF, but little is known of the bone turnover around teeth in this cohort. The objective of this investigation was to compare the GCF bone turnover markers in premenopausal vs postmenopausal women receiving orthodontic treatment at baseline and at orthodontic activation. **Methods:** Twenty-eight women were enrolled in the study and separated into 2 groups: premenopausal (16) and postmenopausal (12). Bone turnover was evaluated by GCF at baseline and 24 hours after orthodontic appliance activation. GCF concentrations of RANKL and OPN were measured using ELISA. Baseline and change in concentrations were compared between groups. **Results:** Baseline RANKL and OPN were significantly different between the premenopausal and postmenopausal groups ($P < 0.05$). Both markers increased significantly from baseline to 24 hours after orthodontic appliance activation in both groups ($P < 0.05$). However, the response to orthodontic activation was not significantly different between groups. **Conclusions:** Although postmenopausal women have a different bone turnover profile at baseline than do their premenopausal counterparts, there is no difference in their response to orthodontic activation. This confers a level of security associated with orthodontic activation. Future studies are warranted to construct biomarker curves throughout orthodontic therapy. (Am J Orthod Dentofacial Orthop 2017;152:33-7)

According to the American Association of Orthodontists, the numbers of adult patients increased by 14% from 2010 to 2012.[1] A record high of 1.2 million adult patients was reached, of whom 56% were women.[1] With women living longer and more vibrant lives than ever before, we can expect a continued increase in the demand for ideal smiles. This opens the door to questions comparing orthodontic treatment vs other restorative treatments as a means to obtain a more ideal esthetic result. Although the number of women having orthodontic treatment continues to rise, the biology required to answer questions about moving teeth in this demographic group remains largely understudied, particularly between premenopausal and postmenopausal women. It is well known that as ovarian estrogen production ceases, in skeletal bone remodeling, if osteoclastic action outpaces osteoblastic action, net skeletal bone loss occurs and osteoporosis happens. Bone turnover markers, such as receptor activator of nuclear factor kappa-B (RANKL) and osteopontin (OPN), are increased in serum when osteoporosis is present.[2,3] Investigations have reported that orthodontic tooth movement is associated with a change in gingival crevicular fluid (GCF) concentration of these bone turnover markers as well.[4] These bone turnover markers signal osteoclastic action during bone remodeling during orthodontic tooth movement and would be evident at activation.

RANKL and OPN concentration have been shown to significantly increase after 24 hours of orthodontic

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activation.[5,6] Differences in bone turnover markers after orthodontic activation have also been noted in the literature between the sexes and between juveniles and adults.[7] However, bone turnover markers after orthodontic activation have not been defined for postmenopausal women. This is relevant, since after menopause women have greater concentrations of bone turnover markers in serum, which are responsible for greater skeletal bone turnover.

The purpose of this study was to elucidate GCF bone turnover marker response in premenopausal vs postmenopausal women receiving orthodontic treatment.

MATERIAL AND METHODS

One hundred ten women were screened for this case controlled prospective investigation. The investigation was approved by the investigational review board of Case Western Reserve University in Cleveland, Ohio. Twenty eight women were enrolled after meeting the inclusion criteria. Inclusion criteria were the following: (1) current patient with fixed orthodontic appliances at our Department of Orthodontics clinic, (2) with 2 or more anterior teeth and 2 or more posterior teeth, and (3) available to be retested 24 hours later. The exclusion criteria were (1) less than 21 years of age; (2) use in the past 30 days of NSAIDS, steroids, or other anti-inflammatory medications or supplements (such as arnica); (3) under hormone replacement or bone sparing medication therapy; (4) bleeding on probing score greater than 10% of sites in the mouth; (5) plaque score above 30%; (6) systemic inflammatory condition (eg, rheumatoid arthritis, Sjogren's syndrome); and (7) being in orthodontic treatment for less than 2 months. The participants were divided into 2 groups, premenopausal (control) and postmenopausal based on self-reports of surgical or natural menopause.[8,9] A board-certified periodontist (L.P.) was an active participant in this study at all levels. Both groups had equivalent numbers of orthodontic malocclusions, and the activation performed on the day of the sample collection was of equivalent force. The equivalency of the maloccusion was assessed by using the American Board of Orthodontics Discrepancy Index, which is common practice in our clinic. All patients in this project had Discrepancy Index scores between 10 and 20, with equivalent distributions in both groups. The equivalency of the force applied was controlled by using similar wires and at all times fully engaging the bracket with an o-tie. No stainless steel tie was needed for full engagement. All situations represented an average orthodontic activation force. No subjects were outliers or extremes in the bell curve in that regard.

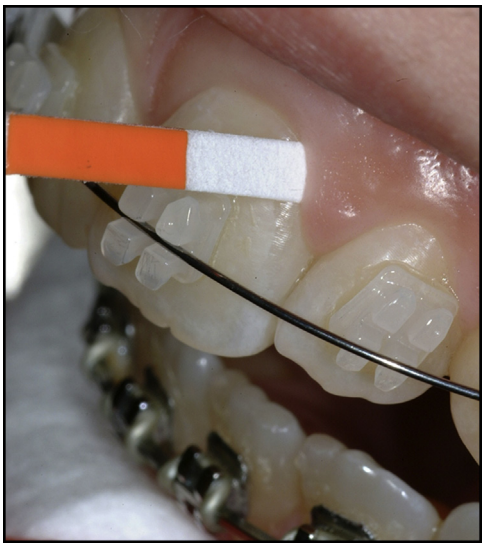

Fig. GCF collection: teeth were wiped with gauze before cleaning by the patient, and moisture was controlled with cotton rolls. Periopaper was gently inserted into the sulcus to absorb the GCF.

For consistency, we purposely chose to test routine activation situations.

Baseline GCF samples were obtained from the subjects just before orthodontic activation of the dentition (T0). Orthodontic activation was defined as placing new elastic ties or ligating a metal wire with full engagement into the bracket slot. GCF samples were collected again at identical sites, exactly 24 hours later (T1) to control for circadian changes. All GCF samples were collected by 2 trained investigators (S.S., C.J.). Periopaper (Oraflow, Smothtown, NY) strips were used for GCF collection. With the collection area isolated with air and cotton rolls, each strip was inserted into the sulcus for approximately 60 seconds or until saturation of the apical third of the strip (Fig). Four strips, 2 anterior and 2 posterior teeth, were used to collect GCF fluid from each patient. All 4 strips were combined and stored in a sterile polypropylene vial and considered to be 1 sample; this pooled sample provided an overall patient-centered response rather than a site-specific response. The samples were placed in a dry-ice cooler (sublimating temperature of dry ice is −79°C to −109°C) for transport and then transferred into a larger storage freezer, which maintained a constant −80°C temperature. Once all samples had been collected, they were transferred for laboratory processing and analysis. GCF collection following this protocol has been validated, extensively published, and is not subject to investigator calibration.[6,10-12]

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