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Evaluation of inflammation during fixed orthodontic treatment

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ABSTRACT

Objective: The aim of this study was to assess effects of fixed orthodontic therapy on high-sensitivity C-reactive protein (hs-CRP) level, CBC parameters and levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), urea, creatinine, sodium (Na), potassium (K), calcium (Ca), total protein (TP), and albumin (Alb).
Design: Blood samples (7 ml) were drawn at baseline, on days 1 and 7, and three months after placement of braces in the study group, while only one blood sample was drawn at baseline in the control group. Serum hs-CRP levels were measured by nephelometric method. Friedman two-way variance analysis was used to assess values with skewed distribution obtained at baseline, on days 1 and 7, in the third month. Wilcoxon rank sign test was performed if median values were unequal.
Results: During measurement periods, there were significant increases in hs-CRP level, WBC count and neutrophil count while a significant decrease in Na level ($p < 0.05$). K level was significantly decreased on the day 1. No significant differences were detected in other biochemical parameters evaluated.
Conclusion: Elevation in serum hs-CRP levels and neutrophil: lymphocyte ratio within first 3 months indicates that a systemic immune response develops against therapy in patients undergoing fixed orthodontic therapy.

1. Introduction

Currently, fixed orthodontic therapy is the most preferred therapeutic modality for treatment of malocclusions that affect mastication and facial appearance (Liu et al., 2014). Although successful outcomes are achieved by orthodontic therapy, orthodontic appliances can affect subgingival microbial composition and inflammatory reactions can develop in gingival tissues of patients particularly at early periods of therapy (Kim et al., 2012; Liu, Zhang, Wang, Guo, & Xiao, 2013; Martha, Mezei, & Janosi, 2013).

The most hazardous condition that causes systematic passage of chemical particles in orthodontics is braces left in the mouth for approximately two years (Kloukos, Pandis, & Eliades, 2013). Prolonged stay of these braces leads plaque accumulation and enhances enzymatic activation, particularly salivary esterase. The braces can hinder complete oral hygiene, promoting an inflammatory process (Boncuk, Cehreli, & Polat-Ozsoy, 2014; Dubey, Jalili, & Garg, 1993; Martha et al., 2013).

High-sensitivity C-reactive protein (hs-CRP) is a plasma protein and acute phase reactant that is synthesized by the liver. CRP is the first inflammation and tissue damage marker identified. CRP and other acute phase molecules are generally found in lower amounts in plasma; however, they may show dramatic increases within 72 h in the presence of tissue injury or infection. hs-CRP is the gold standard molecule that can be tested comprehensively in the assessment of inflammation (hs-CRP2) (Kalra, Pradeep, Priyanka, & Kumari, 2013; Pepys & Hirschfield, 2003).

Systemic elevation in C-reactive protein (CRP), is a mechanism that can explain response to oral stimulus. These stimuli can develop as a result of periodontal inflammation or systemic spread of oral bacteria. Periodontal inflammation can result from plaque accumulation due to orthodontic appliances as well as aseptic

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necrosis due to orthodontic forces or combination. In case of the great orthodontic force a hyalinized zone which is an area of focal aseptic necrosis, occurs in the compressed periodontal ligament (PDL). Also an indirect resorption occurs in the tension side (Danesh et al., 2004; MacLaine, Rabie, & Wong, 2010; Rossi, Whitcomb, & Lindemann, 1996).

Previous studies suggested that release of cytokines (IL-1β, TNF-α, etc.) occurs in tissue response to mechanical stimuli at early phases of orthodontic tooth movement. IL-1β and TNF-α may be transported into the systemic circulation and stimulate hepatocytes in the liver to produce C −reactive protein (CRP) (Saadi & Ghaib, 2013). This mechanical stress can lead to development of acute inflammatory reactions in periodontal tissues, which promote tooth movement and biological processes, resulting in bone resorption (Sandy, Farndale, & Meikle, 1993).

Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP) are mainly found in the liver and assessed in the diagnosis of hepatic diseases. These enzymes are evaluated in the early diagnosis and prognosis of PDL inflammation (Ozmeric, 2004). Complete blood count (CBC) parameters are most commonly present at the initial inflammatory response (Martin & Leibovich, 2005).

The literature includes a limited number of studies about elevated levels of circulating inflammation markers by the response to periodontal inflammation due to orthodontic tooth movement. The present research aimed to study changes in hs-CRP level, CBC parameters, and levels of AST, ALT, GGT, ALP, urea, creatinine, sodium (Na), potassium (K), total protein (TB), calcium (Ca), and albumin (Alb) over time. This study may help to elucidate whether inflammation caused by orthodontic therapy and orthodontic appliances causes a toxic reaction in patients' livers and kidneys.

2. Materials & methods

This study was approved by an institutional ethics committee at 28.03.2014. The patients and controls were randomly chosen from among patients presented to the orthodontics clinic. The study group consisted of 37 patients scheduled for fixed orthodontic therapy, while the control group consisted of 40 patients without a need for orthodontic therapy. Overall, 77 patients were included in the study. There were 16 women (mean age 14,59 ± 2,16 years) and 21 men (mean age 14,86 ± 2,13 years) with mean age of 14,75 ± 1,89 years in the study group, and 21 women (mean age 13,75 ± 2,12 years) and 19 men (mean age 13.45 ± 2,31 years) with mean age of 13.68 ± 2,09 years in the control group. Eligibility criteria were lack of systemic disease, no drug use within the last four months, lack of gingivitis or periodontitis, and good oral care. The control group was comparable to the study group regarding sex, age, geographic location, and social characteristics.

Visible plaque index (VPI), gingival bleeding index were used for the measurement of the state of oral hygiene (Ainamo & Bay, 1975).

Plaque: The visible plaque index (VPI) was recorded as "1" when there was visible plaque and "0" when there was no plaque accumulation on the mesio-buccal tooth surface. Gingivitis: GBI for the gingival margin at the mesio-labial surfaces was assessed with 0.5 mm diameter periodontal probe which lightly inserted into the gingival crevice parallel to the long axis of the tooth with minimum axial force. Bleeding was recorded as 1, and no bleeding as 0.

The patients had "0" VPI and GBI scores were included in the study.

All cases in the study group had Class I malocclusion and were treated using straightwire fixed appliances. The slot size of Roth metal brackets (Dentaurum equilibrium 2, Phorzeim, Germany) was 0.018-in. tooth extraction. Tooth extraction process was delayed until the end of the study process in 23 patients treated with extraction.

Blood samples were drawn at baseline, on days 1 and 7, and three months after placement of braces in the study group, while only one blood sample was drawn at baseline in the control group. Permission was obtained from the patients and their parents for receiving blood.

2.1. Laboratory analyses

Early morning venous blood samples were drawn from an antecubital vein and collected into EDTA vacutainer by a pediatric nurse. Blood samples were analyzed in an automated hematology-analyzer (Sysmex XN-1000, Japan) within the same day. Fasting venous blood samples were centrifuged at 1500g over 10 min to obtain supernatant, which was then divided into aliquots and stored at −80 °C until assays. In the sera obtained, ALT, AST, GGT, and ALP activities were studied by an enzymatic-kinetic method, while Ca, TP, and Alb levels were measured by spectrophotometric method and Na and K levels were measured by indirect ISE method by using an auto-analyzer (Architect c8000; Clinical Chemistry Analyzer, Abbott, USA). Serum hs-CRP levels were measured by nephelometric method (Beckman Coulter Immage Nephelometer, USA). Within-run and total% CV values were 5.0 and 7.5 for serum samples, respectively. Analytical range was 0.02–6.0 mg/dl.

2.2. Statistical analysis

Data were analyzed by MedCalc 12.7.4 (MedCalc Software bvba, Ostend, Belgium) statistic software. The Kolmogorv-Smirnove test was used to test normal distribution. All values except hs-CRP had normal distribution. Friedman test was used in hs-CRP value, while other biochemical parameters were analyzed with One-Way ANOVA. Wilcoxon rank signed test as post hoc test was used for non-parametric analysis and Duncan test was applied for parametric test. $p < 0.05$ was considered statistically significant.

3. Results

No significant difference was detected in biochemical parameters obtained at baseline between study and control groups. Table 1 presents hs-CRP and biochemical values obtained at the time points studied (baseline, day 1, week 1, and month 3). Significant differences were detected in hs-CRP ($p \leq 0.0001$) (Fig. 1, Table 1), Na ($p \leq 0.0001$), and K values ($p = 0.0002$), while no significant differences were detected in albumin, ALP, ALT, AST, Ca, creatinine, GGT, TP, and urea values among the time points studied ($p > 0.05$) (Table 1).

The Fig. 2 and Table 2 present changes in CBC parameters between baseline and month 3. Significant increases were detected in WBC ($p = 0.0040$) and neutrophil counts ($p \leq 0.0001$), while the lymphocyte count ($p = 0.0089$) decreased.

Base-line plasma levels of the hs-CRP were significantly lower than day 1 and month 3 levels of the hs-CRP. Base-line plasma levels of the Na were significantly higher than day 1 and month 3 levels of the Na, whereas levels of K were significantly higher than only day 1 plasma levels of K. Base-line plasma levels of the WBC and neutrophil counts were significantly lower than month 3 levels the WBC and neutrophil counts, whereas levels of lymphocyte count were significantly higher than month 3 plasma levels.

4. Discussion

Areas with plaque accumulation are at risk for gingival inflammation in orthodontic therapy. Bacterial plaque