

Clinical and Biological Study of Rheumatoid Arthritis Influence on Salivary Biomarkers in Patients with Periodontal Disease*

SUMMARY

Aim: The purpose was to identify if rheumatoid arthritis (RA) influenced levels of salivary biomarkers of periodontal disease. **Methods:** Biological assessments and periodontal examinations were performed in 15 patients with RA, 10 patients with chronic periodontitis and 11 healthy patients as controls. Unstimulated whole saliva samples were analysed for interleukin-1b (IL-1b) and tumour necrosis factor- α (TNF- α) concentrations. **Results:** The arthritis and healthy patients had significantly less oral disease than the periodontitis group but the arthritis group had significantly more sites bleeding on probing (BOP) than the control group. Salivary levels of IL-1b were significantly elevated in the periodontal disease group, and IL-1b was the only biomarker with significantly higher levels in the arthritis group compared with control group. Arthritis patients receiving anti-TNF- α antibody therapy had significantly lower IL-1b and TNF- α levels compared with arthritis patients not on the anti-TNF- α therapy and healthy controls, respectively. **Conclusion:** RA patients have higher levels of periodontal inflammation than healthy control group and also an increased BOP. Systemic inflammation appears to influence levels of selected salivary biomarkers of periodontal disease, and anti-TNF- α therapy significantly modified lowered salivary levels IL-1b and TNF- α levels in RA.

Keywords: Biomarkers; Interleukin-1b; Tumour Necrosis Factor- α ; Periodontal Disease; Rheumatoid Arthritis

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Introduction

The diagnosis of periodontal disease is generally based on the clinical detection of bleeding on probing (BOP), pocket depth (PD), clinical attachment loss (CAL) and plaque index (PI), as well as radiographic evidence of bone loss. Many studies have shown that constituents present in oral fluids (gingival crevicular fluid and saliva) can provide important additional diagnostic information for dental and general professionals. Systemic inflammation resulting from various chronic inflammatory diseases may confound the utility of the biomarkers. Whole saliva may contain serum-derived components like mediators of inflammation, collagen breakdown or products appearing due to bone remodelling, which are

elevated in serum of persons with conditions such as rheumatoid arthritis (RA), and could appear in saliva.

RA is a chronic inflammatory disorder that causes soft and hard tissue destruction similar to that shown in periodontal disease. Certain inflammatory mediators such as IL-1b, MMP-8 and TNF- α are elevated in the inflamed joints and serum of patients with RA and as a consequence, it is possible that persons with RA or other inflammatory processes in joints could have increased levels of these biomarkers in their saliva.

For this reason it seems possible to identify periodontal disease in patients with RA or at risk for RA and to test if RA influences levels of salivary biomarkers of periodontal disease. Therefore, the aim of this investigation was to identify whether RA influenced levels of salivary biomarkers of periodontal disease.

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Material and Methods

Biological assessments and periodontal examinations were performed on 15 patients with RA, 10 patients with chronic periodontitis and 11 healthy patients as controls. The groups were matched by age and gender. Examination and evaluation of patients was performed according to clinical observation sheet with periodontal specific (developed by the Department of Periodontology - Faculty of Medical Dentistry UMF "Gr. T. Popa", Iasi) based on clinical, extraoral and intraoral examination.

Unstimulated whole expectorated saliva samples were collected from each subject and analysed for interleukin-1b (IL-1b) and tumour necrosis factor- α (TNF- α) concentrations. Samples were thawed and analysed within 3 months of collection. Laboratory tests were performed, analysed and interpreted by BIODEV Medical Center collaborator - lecturer Dr Loredana Hurjui. The data were evaluated at the Periodontology Department, Faculty of Dental Medicine of Iasi and Rheumatology Clinic of Rehabilitation Hospital, Iasi.

Results

The arthritis and healthy groups had significantly less oral disease than the periodontitis group, but the arthritis group had significantly more sites with positive BOP than the control group.

Salivary levels of IL-1b were significantly elevated in the periodontal disease group, and IL-1b was the only biomarker with significantly higher levels in the periodontitis and RA groups compared with the control group (Fig. 1). The RA group had clinical findings less severe than the periodontitis group despite the salivary IL-1b levels being higher in the RA group, suggesting that salivary IL-1b was elevated due to systemic inflammation.

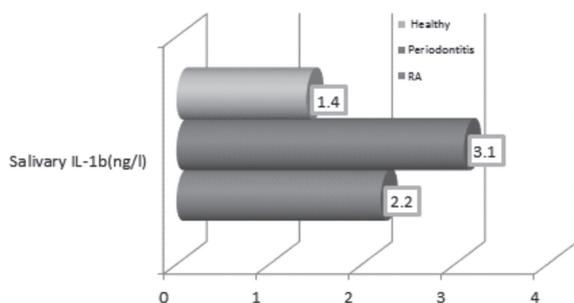


Figure 1. Salivary levels of IL-1b

IL-1b levels showed a positive correlation with the percent of PD more than 4mm and 5mm in the periodontitis group (Figs. 2 and 3).

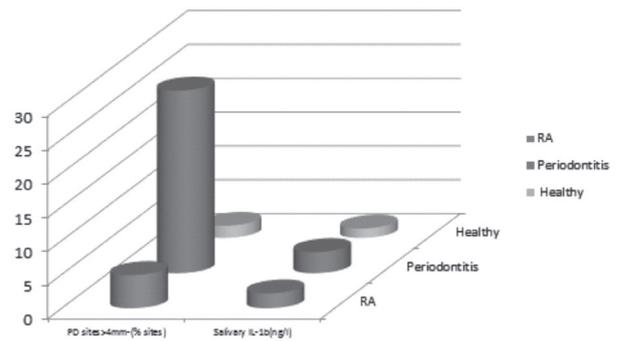


Figure 2. Salivary levels of IL-1b in correlation with the percent of PD sites > 4mm

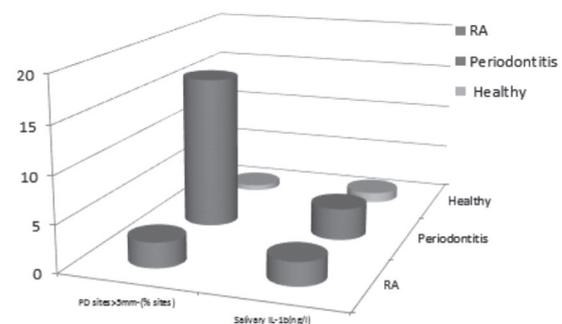


Figure 3. Salivary levels of IL-1b in correlation with the percent of PD sites > 5mm

Statistical analysis of TNF- α results in all groups of patients showed a significant difference between the group of patients with chronic periodontitis compared to RA patients and healthy controls (Fig. 4). Looking at the average values of TNF- α note that in the group of patients with chronic periodontitis were almost doubled than in the control group.

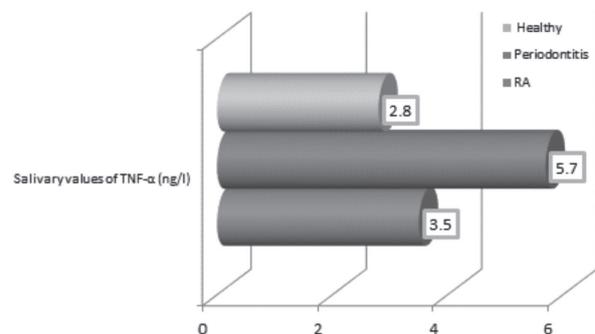


Figure 4. Salivary levels of TNF- α in all 3 groups

Arthritis patients receiving anti-TNF- α antibody therapy had significantly lower IL-1b and TNF- α levels compared to arthritis patients not on anti-TNF- α therapy and healthy controls, respectively.

Discussion

There are several inflammatory diseases that cause destruction of bone and its supporting connective tissue. The most prevalent of the disease that can cause destruction are rheumatoid arthritis (RA) and periodontal disease.

The periodontal diseases is a result of an imbalance between host inflammatory process and specific pathogenic bacteria residing in the gingival crevice. This observation and previous studies led to the hypothesis that there are susceptibility factors or risk factors that modulate patient susceptibility or resistance to destructive periodontitis.

Recent studies have shown that IL-1 gene markers were predictors for the specific serum levels of inflammatory markers, such as the severity of periodontal disease. These genetic variations might cause an imbalance between antagonistic inflammatory mediators and individual response influence to pathogens and treatment.

Levels of IL-1b and TNF- α were investigated because these salivary biomarkers have associations with biological aspects of periodontitis, and have been shown to be significantly elevated in subjects with periodontal disease compared to healthy controls.

This study investigated the influence of RA on salivary levels of biomarkers (IL-1b and TNF- α) associated with periodontitis. The effects were examined in 3 study groups (healthy persons, RA patients and adult patients with chronic periodontitis), hypothesizing that the salivary biomarker levels are altered in the presence of RA taking into account levels observed in groups with periodontal disease or in healthy persons.

We found that salivary levels of IL-1b were significantly elevated in the overall RA group compared with a control group with similar levels of periodontal disease, whereas TNF- α levels were not. As expected, we demonstrated elevations in concentrations of these salivary biomarkers in patients with periodontal disease compared to healthy controls.

Salivary levels of acute phase reactants were directly proportional to the severity of the disease, but were non-specific and could be elevated after any inflammatory process.

Conclusions

This study provides evidence that salivary IL-1b and TNF- α levels are clearly influenced by the local periodontal status, and selectively influenced by a systemic inflammatory condition, such as RA. RA patients had higher levels of periodontal inflammation

than healthy control group and also an increased BOP. Systemic inflammation appears to influence levels of the selected salivary biomarkers of periodontal disease; anti-TNF- α therapy significantly lowers the salivary levels of IL-1b and TNF- α in RA patients.

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