CLINICAL AND BIOLOGICAL STUDY OF RHEUMATOID ARTHRITIS INFLUENCE ON SALIVARY BIOMARKERS ON PATIENTS WITH PERIODONTAL DISEASE

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ABSTRACT

Aim Our purpose was to identify if rheumatoid arthritis (RA) influenced levels of salivary biomarkers of periodontal disease. **Methods** Biological assessments and periodontal examinations were performed on 15 patients with RA, 10 patients with chronic periodontitis and 11 healthy patients as control group. Unstimulated whole saliva samples were analysed for interleukin-1b (IL-1b) and tumour necrosis factor-α (TNF-α) concentrations. **Results** The arthritis and healthy groups had significantly less oral disease than the periodontitis group but the arthritis group having significantly moresites bleeding on probing (BOP) than control group. Salivary levels ofIL-1b were significantly elevated in the periodontal disease groupand 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 anti-TNF-α therapy and healthy controls, respectively. **Conclusions** RA patients have higher levels of periodontal inflammation than healthy control group and also an increased BOP. Systemic inflammation appears to influence levels of select salivary biomarkers of periodontal disease, and anti-TNF-α therapy significantly modify in lowers salivary levels IL-1b and TNF-α levels in RA.

Key words: salivary biomarkers, interleukin-1b, tumor necrosis factor (TNF-α), periodontal disease, rheumatoid arthritis

INTRODUCTION

The diagnosis of periodontal is generally based on the clinical detection of bleeding on probing (BOP), pocket depth (PD), clinical attachment loss (CAL), plaque index (PI) and radiographic evidence of bone loss. Many studies have shown that the constituents present in oral fluids (gingival crevicular fluid and saliva) can provide important complimentary diagnostic information for dental and general professionals. Systemic inflammation resulting from various chronic inflammatory diseases may confound the utility of the biomarkers. At some patients whole saliva contains serum-derived components, and mediators of inflammation, collagen break down or bone remodelling that 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 affect soft and hard tissue destruction similar to that shown in periodontal disease.

Certain inflammatory mediators such as IL-1b, MMP-8 and TNF-a are elevated in the inflamed joints and serum of patients with RA and as a consequence, is possible that persons with RA or other inflammatory arthritides could have increased levels of these potential biomarkers in their saliva. For

this reason we consider appropriate 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.

Aim: Our purpose was to identify if rheumatoid arthritis (RA) influenced levels of salivary biomarkers of periodontal disease.

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 control group. 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 –U.M.F "Gr. T. Popa" Iasi) based on clinical extra and intraoral examination.

Unstimulated whole expectorated saliva samples was collected from each subject and were 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, analyzed and interpreted in BIODEV Medical Center colaborator- lecturer dr. Loredana Hurjui.

The database consisted of selecting, testing, and evaluation was made in 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 having significantly more sites bleeding on probing (BOP) than 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 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 anti-TNF-α therapy and healthy controls, respectively.

Salivary levels ofIL-1b and TNF-a in those three groups are represented in figures below. Salivary IL-1b levels were significantly elevated in the periodontitis and RA group compared with the controls.

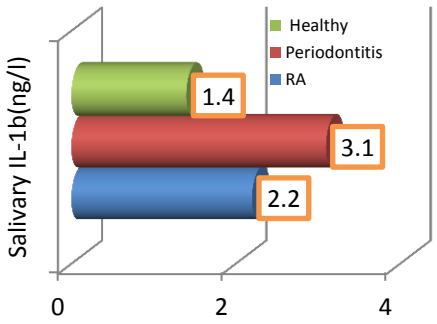

Figure 1. Salivary levels of IL-1b

The RA group had clinical measures 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. IL-1b levels showed a positive correlation with %PD sites >4 and >5mm in the periodontitis group.

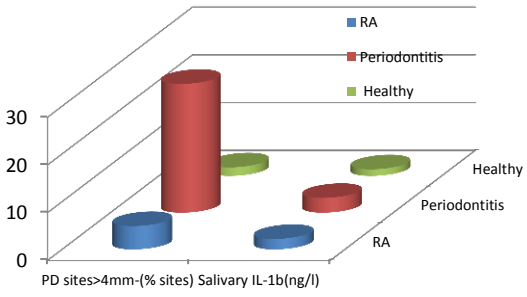

Figure 2. Salivary levels of IL-1b in

correlation with %PD sites >4mm

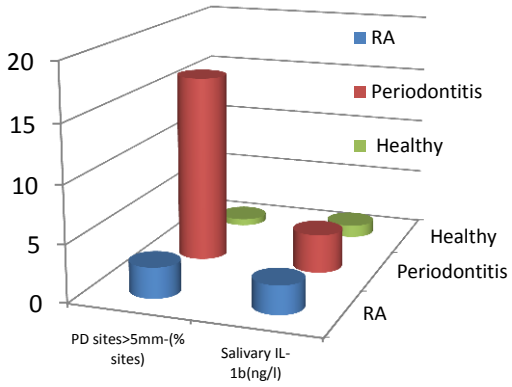

Figure 3. Salivary levels of IL-1b in correlation with %PD sites >5mm

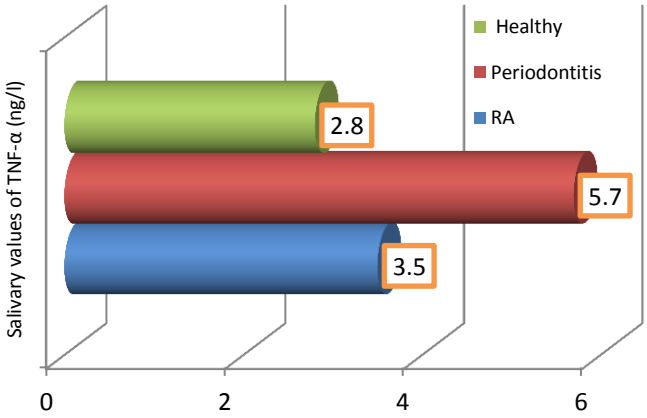

Figure 4. Salivary levels of TNF- αat all three goups

Statistical analysis of TNF-α results in the three groups of patients showed a significant difference between the group of patients with slightly chronic periodontitis and RA and patients with chronic periodontitis group without RA.

Looking at the average values of TNF-α note that in the group of patients with chronic periodontitis and RA values are almost double the control group of patients.

In the group of patients with chronic periodontitis periodontitis and TNF-α RA values were the highest recorded maximum value of 3.5ng / ml.

DISCUSSIONS

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 and periodontal disease.

This 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 observations 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 may cause an imbalance between antagonists inflammatory mediators and individual response influence to pathogens and treatment.

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

This study investigated the influence of RA on salivary levels of biomarkers (IL-1b and TNF-a) associated with periodontitis. The effects were examined using three study groups (healthy, RA and chronic adult periodontitis) considering that the presence of RA has an influence and the salivary biomarker levels are altered taking into accountt levels observed in the periodontitis or healthy groups.

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-a were not. As expected, we demonstrated elevations in the concentrations of these salivary biomarkers in patients with periodontal disease compared with healthy controls.

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

This study aimed to demonstrate the influence of a systemic inflammatory condition and its treatment on salivary biomarkers of periodontal disease.

4. This study provides evidence that salivary IL-1b and TNF-a levels are clearly influenced by the local periodontal status, and selectively influenced by a systemic inflammatory condition such as RA.
5. RA patients have higher levels of periodontal inflammation than healthy control group and also an increased BOP. Systemic inflammation appears to influence levels of select salivary biomarkers of periodontal disease, and anti-TNF-α therapy significantly modify in lowers salivary levels IL-1b and TNF-α levels in RA.

CONCLUSIONS

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