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The Effect of Periodontitis Treatment on Anti-DSDNA Titer in Patients with Systemic Lupus Erythematosus

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Abstract: - Aim: Systemic Lupus Erythematosus (SLE) and periodontitis are both inflammatory diseases. It has been revealed that may be an association exists between them. Inflammation in chronic periodontitis causes gingival erosion and alveolar bone destruction. According to available sources, chronic inflammation due to periodontal disease has a negative effect on Anti-dsDNA as one of the most important laboratory indicators of SLE. The aim of this research is to evaluate the effect of periodontal treatment on Anti-dsDNA titer in patients with SLE.

Materials and methods: The samples were selected from well controlled patients with SLE . In the initial visit, the laboratory factor "Anti-dsDNA" was recorded from the patients. Patients with periodontal disease were divided into case and control groups by block randomization method. For the case group, scaling was done with an ultrasonic device and oral health education was provided to all patients. The patients were asked to return 3 months after the periodontal treatment to evaluate the level of disease activity and the response to periodontal treatment. For data analysis, SPSS 18 program and Mann-Whitney non-parametric test was used.

Results: The average duration of the disease in this study was 6.89 ± 6.56 years. Comparison of the average Anti-dsDNA autoantibody titer before and after treatment in the intervention group considering that there was no normality between the data and there was a statistically significant difference between the average Anti-DsDNA titer before and after the intervention in the subject group.

Conclusion: Since the phase 1 of periodontal treatment as a modifiable risk factor has led to a significant change in Anti-dsDNA titer and this antibody is an indicator of disease flare, periodontal treatment is recommended separately from the reactivation of the disease and to promote the disease control.

Keywords: Systemic Lupus Erythematosus, periodontal disease, periodontal treatment, anti-dsDNA

I. INTRODUCTION

Systemic Lupus Erythematosus is an autoimmune disease in which deposition of high amounts of antibodies and vasculitis is evident in the pathophysiology of the disease. (1)

Periodontitis is an infectious-inflammatory disease which is generally caused by the bacteria (Treponemadenticola, Porphyromonasgingivalis, and Actinobacillusactinomycetemcomitans), and if it manifests as chronic inflammation, it causes gum recession and alveolar bone destruction (2, 3). The degree of inflammation in different patients depends on the degree of bacterial infection and the degree of functioning of the patient's immune system against inflammatory reaction. (4, 5)

The relation between collagen vascular diseases and periodontal disease as an inflammatory disease in the different sources are conflicting. In some studies that investigated the relationship between periodontal treatments in rheumatoid arthritis patients (6-8), positive results were obtained in such a way that improving the periodontal condition may change the disease activity index. In the case of SLE, a correlation between periodontitis and lupus is bi-directional. (9)

It has been stated that chronic inflammation due to periodontal disease may have a negative effect on the Systemic Lupus Erythmatous Disease Activity Index (SLEDAI) and also it has been revealed that periodontal treatment may improve SLE markers like Anti-dsDNA as one of them (10, 11). These are while the relation between periodontal treatment and SLEDAI K2000 is uncertain.

Treatment with corticosteroids and immunosuppressive may reduce inflammation by disrupting the microbial flora.(12, 13) In some articles, research has been done on the relationship between the treatment of periodontitis and the values of ESR (erythrocyte sedimentation rate) and CRP (C-), but few studies have been done on the relationship of periodontal treatment and Anti-dsDNA level as the most specific marker for SLE flare up.(12) Therefore, based on these conflicts and shortcomings, the present study designed to evaluate the periodontal treatment effects on Anti-dsDNA titer in patients with SLE.

II. MATERIALS AND METHODS

In this cross-sectional study with a descriptive and analytical approach, ethical approval was obtained from the ethics committee of Golestan University of Medical Sciences with the ethics code "IR.GOUMS.REC.1398.163" before the

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study. The result of this research is the part of the results of a clinical trial study in Golestan University of Medical Sciences on the relationship of SLEDAI in SLE and periodontal condition.

Before the study, everything about this study was explained to each patient to receive periodontal treatment voluntarily and written consent was obtained from them. Patients were free to exit from the study at any time they wished.

Sampling was simple and accessible. In this study, all patients with a lupus activity level greater than or equal to 2 according to the SLEDAI criteria(12) were referred from clinic of rheumatology, Sayadshirazi Educational-Therapeutic Center in Gorgan.

Inclusion criteria: All these patients were treated with prednisolone and hydroxychloroquine (according to the severity of the disease, the treatment dose was different for each patient) and their treatment plan did not change during the period of investigation and participation in this research project.

Exclusion criteria: Any change in the patient's treatment plan (increasing or reducing the treatment dose or adding another immunosuppressive drug), accompanying with rheumatoid arthritis or Sjogren's, being pregnant and breastfeeding, suffering from diabetes, and smoking, the presence of orthodontic appliances or removable prostheses. possibility of bone loss , Bone metabolic diseases (hyperparathyroidism, Paget's, etc.) , Aggressive periodontitis, , being treated with antibiotics in the last three months , having scaling in the last six months and non-cooperative patients who did not cooperate in controlling oral hygiene . Also using any of the following drugs caused the patient to leave the research. 1) Drugs that increase the volume of the gums (such as cyclosporine, calcium channel blockers, phenytoin), 2) History of warfarin use and the possibility of bleeding 3) Use of Phenytoin, Phenobarital, Carbamazepine, valproic acid, Clonazepam, Gabapentin, Topiramate.

In the initial visit, in the rheumatology clinic, the disease activity was assessed based on the SLEDAI criteria (for the other related study) and Anti-dsDNA laboratory factor was recorded (for this study).

Patients were divided into case and control groups as follows:

The case group consisted of patients with lupus who also had periodontitis, who were treated as follows:

Scaling was done with an ultrasonic scaler-D5 LED (made in China), a Currete, universal scaler pen, a cycle scaler pen and a dental probe, and then oral hygiene education was given to each patient.

The control group was lupus patients who had periodontitis but did not want to receive periodontal treatment for any reason. Necessary recommendations about oral and dental hygiene were given to each patient.

The patients of the case group were asked to return to the clinic about 3 months later to evaluate the level of response to periodontal treatment. The patients of the control group were also asked to return about 3 months later in order to evaluate the level of disease activity.

In the second visit, the SLEDAI checklist and the Anti-dsDNA test were completed again for each participant, and after being referred to the dental clinic, each patient in control group was evaluated in terms of response to periodontal treatment by examination. In all these stages, the type and dosage of the drug that the patient received for the treatment was not changed.

After data entry in SPSS 18 program, average, standard deviation, frequency and percentage were used to describe the data. Paired T-test, Wilcoxon test, Spearman's correlation coefficient and non-parametric Mann-Whitney test were used to compare the mean in 2 groups.

III. FINDINGS

In this study 40 patients were participated in the case group and 40 patients in the control group. In the case group, 2 patients and in the control group, 3 patients did not complete the study and were excluded from the study and the other patients were subjected to periodontal treatment. The average age of the patients in this study was 36.34 years. The lowest age of the patients was 14 years and the highest age of the patients were 75 years. The data related to the age of the patients were evaluated using the Wilk-Shapiro test in terms of normality of distribution, and it was concluded that the data did not have a normal distribution (P=0.002).

Among the studied patients, 7 (9.3%) were male and 68 (90.7%) were female. In the control group, 4 (10.5%) were male and 34 (89.5%) were female. There were women, and in the control group, 3 (8.1%) were men and 34 (91.9%) were women.

To compare the average titer of Anti-dsDNA autoantibody before and after the periodontal treatment in the case group because of unexistence of normality between the data, the Wilcoxon test was used to measure this goal.

Table1. Comparison of the average Anti-dsDNA autoantibody titer before and after the intervention in the case group

Component	**Average value**	**P value**
Comparison of the average autoantibody titer before and after the intervention	18/55	**0/000**

To compare the average autoantibody titer before and after the intervention in the case and control groups, the presumption of normality between the data was not established, so the Mann-Whitney non-parametric test was used to measure this goal.

Table2. Comparison of average autoantibody titer before intervention and after intervention in case and control groups

component	mean	**P value**
comparison of the average titer of autoantibodies before the intervention in the case and control groups	37/26	**0/767**
Comparison of the average titer of Anti-dsDNA autoantibodies after intervention in case and control groups	38/22	**0/928**
Comparison of the average autoantibody titer before and after the intervention in the case and control groups.	35/40	**0/000**

To investigate the relationship between Anti-dsDNA antibody titer and the duration of the disease, first the normality of both variables was measured and considering the abnormality of both variables, Spearman's correlation coefficient was used to measure this goal, and the result can be seen in Table3.

Table3. Relationship between Anti-dsDNA antibody titer and disease duration

	correlation coefficient	**p-value**
The relationship between Anti-dsDNA antibody titer and duration of disease	0/073	**0/536**

IV. DISCUSSION

SLE and periodontitis are two inflammatory diseases in which B lymphocytes play an important role in the pathogenesis of the disease by producing IgG2 immunoglobulin in genetically predispositioned individual. In periodontal disease, an inflammatory response is triggered by the confrontation between pathogenic bacteria in the supragingival and subgingival biofilm of the host, which ultimately leads to immune-related destruction of the tooth-supporting alveolar bone.

In recent years, it has been stated that periodontal disease can have an autoimmune component, which may indicate the connection of this disease with other autoimmune diseases.

Articles have shown the severity of periodontal disease in many patients with lupus, but contradictory results in terms of laboratory and clinical are still available. (15)

Since 1980, a relationship between lupus and periodontitis has been observed, and high values of the disease activity index (SLEDAI) are predictive of poor periodontal status, and periodontal treatment during 3 months may reduce SLEDAI. (16)

Fabbri pointed out the effectiveness of immunosuppressives during infection and also stated that immunosuppressives mask the clinical effect of infection. Infection is the trigger of autoimmune disease, so the activity of microorganisms and their products can have a stimulating effect on the autoimmune process. The expression of certain types of microRNAs by infected lymphocytes causes altered apoptosis and antigen presentation in the immune system and changes in endothelial CD34 cells, which ultimately trigger the autoimmune process. (17) In lupus and periodontal disease, high levels of beta 2 glycoprotein, FC immunoglobulin receptor and pro-inflammatory cytokines are seen; therefore the role of gene polymorphism in relation to lupus and periodontal disease is evident. In fact, the relationship between these two diseases has been detected in some genotypes. Like the examples related to invasive periodontitis in lupus patients (both systemic and cutaneous lupus). (15, 16, 18)

It has been stated that a correlation between periodontitis and lupus is bi-directional and sex predilection may affect the correlation. In the other words, estrogen/ progesterone imbalances may influence the association of periodontal disease and SLE and this needs more researches and investigations. (9)

The average duration of the disease in this study was 6.89 ± 6.56 years, the minimum duration of the disease was 6 months and the maximum was 28 years. The average duration of the disease was 4.85 years in the control group and 7.89 years in the case group. In examining the duration of the disease and the Anti-dsDNA autoantibody titer in the patients, no significant relationship was found between these two variables. Since the titer of this antibody is an indicator of the flare of the disease and not the parameters of the disease activity, it therefore shows the state of the disease within six months and this The duration was only a part of the duration of the person's illness, while the average incidence of the disease in the subjects under study was 6.89 ± 6.56. Therefore, Anti-dsDNA autoantibody titer cannot indicate an exact relationship between these two variables.

In some sources, an increase in susceptibility to periodontal disease is not seen in patients with lupus. In a recent systematic review and Meta analysis this was showed that SLE patients have moderately greater odds than controls but without worse periodontal parameters. (9)

Anti-dsDNA autoantibody is an indicator of the reactivity of the disease (flare) within six months. This index does not affect the activity of the disease, but it affects the immunological and clinical features of lupus and is a specific and diagnostic marker of lupus. This indicator is detected in less than half percent of healthy people and is detected rarely, but it is positive in 80% of patients and may be seen in the blood from 5 months before diagnosis. (18)

Both periodontitis and lupus are inflammatory diseases and the role of TLR4 in their development has been proven. These molecules are produced by specific pathogens during molecular processes and induce Anti-dsDNA production. By applying phase one periodontal treatment and eliminating bacterial agents, TLR4 production decreases, as a result, the occurrence of immunological reaction would be minimized and the production of anti-dsDNA autoantibodies will be also reduced. (16, 17)

In the current research, comparing the Anti dsDNA autoantibody titer before and after the intervention in the case group, we came to the conclusion that these values before and after the intervention had a significant difference, so that the phase one periodontal treatment can increase the Anti-dsDNA autoantibody levels (p value = 0). Also, the phase one of periodontal treatment can significantly change the Anti-dsDNA autoantibody levels before and after the periodontal treatment in the case and control groups (p value = 0).

From the periodontal treatment in this research, there was no significant relationship between periodontal-indices and Anti-ds DNA titer before and after the intervention, because the Anti-dsDNA titer is not related to disease activity and cannot be changed after periodontal treatment.

V. CONCLUSION

Since the phase 1 intervention of periodontal treatment as a modifiable risk factor has led to a significant change in Anti-dsDNA autoantibody titer values and also this antibody is an indicator of disease flare (reactivation), periodontal treatment may prevent reactivity of the SLE.

VI. REFERNCES

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