

THE EVALUATION OF THE EFFECTS OF NON-SURGICAL PERIODONTAL TREATMENT ON BLOOD PARAMETERS OF HEMATOCRIT, RBCS, HEMOGLOBIN, CRP (C-REACTIVE PROTEIN) AND LDL/VLDL AMONG PATIENTS WITH CHRONIC PERIODONTITIS

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ABSTRACT

Aim: Host inflammatory responses induce secretion of pro-inflammatory mediators such as CRP leading to systemic inflammation and as a result of that a situation that is called "anemia of chronic disease" will take place which is a secondary anemia to body immune responses. Also association between periodontal diseases and increasing of inflammatory mediators such as patients lipid profiles is approved.

Materials & Method: Among patients suffering from chronic periodontitis referred to periodontics department of dental school of medical sciences, University of Hamedan, 31 individuals were engaged in this study. Before and one month after treatment procedure, blood samples were taken and some blood parameters such as the amount of Red Blood Cells, Hemoglobin, Hematocrit, LDL, VLDL and CRP were assessed.

Results: The amount of hemoglobin and red blood cells one month after treatment procedure noticeably increased in comparison with the base line (p value for hemoglobin: 0.002, p value for red blood cells:0.006). Also hematocrit showed improvement in laboratory results (p = s0.002). About LDL/VLDL we discovered decrease in the amount of these risk factors (p value for LDL: 0.008 , p value for VLDL: 0.01). CRP were assessed qualitatively. In some patients this protein was not detectable that is pointing to improvement of inflammatory condition but overall changes were not meaningful statistically

Conclusion: According to the effect of inflammatory gingival diseases on blood parameters and lipid profile, treatment of such diseases can prevent cardiovascular diseases. CRP could be helpful in diagnosis, treatment and monitoring of inflammation and inflammatory diseases.

Key words: Chronic periodontitis, Red Blood Cells, Hemoglobin, Hematocrit, LDL /VLDL, CRP.

Introduction

Periodontitis is an infectious gingival disease that affects about 10% to 30% of the population and is caused by bacteria in the dental plaque that cause inflammatory response to periodontal injury. Inflammation causes the loss and attachment of the periodontal ligament and the creation of the pocket. Treatment of periodontitis is based on elimination of the causative agents and the main purpose of the periodontitis treatment is to prevent the development of this disease, which has different methods to achieve this goal,^{1,2} including nonsurgical and surgical procedures. The accumulation of plaque on the surface of the tooth and along the gingival margins cause inflammatory response in the host tissues. This reaction can be limited to coronal of junctional epithelium which is called Inflammation of the gingiva or gingivitis, or inflammation can extend to supporting tissues and structures (periodontium), leading to loss of connective tissue and supporting bone. This degradation can occur with either the toxic bacteria (especially the gram negative anaerobes) or the host's inflammatory response to these factors. The host's inflammatory response can cause the secretion of pro-inflammatory cytokines IL-1, TNF- α , IFN, and CRP,² which can increase systemic inflammation by increasing these cytokines. This condition can lead to the creation of a situation called "anemia associated with chronic disease" (ACD), which is infact secondary anemia to the immune response (due to a decrease in iron levels). The activation of the immune system causes a series of changes that

affects the reticuloendothelial system, and its effect can affect the amount of iron, proliferation of the precursor cells of the erythrocytes, and the life span of the red blood cells. As a result, in the early stages of periodontal disease, it can be prevented by the administration of appropriate and non-surgical treatment for this process of degeneration, which is systemic. Periodontitis is the most commonly reported localized dental disease, which is associated with many pathological conditions, such as gingival inflammation, destruction of periodontal fibers, tooth cements, and loss of alveolar bone and pocket formation.³ This disease is an infectious disease of the teeth supporting tissues that is caused by bacteria in the dental plaque, making inflammatory responses to periodontal tissue.¹ Gingivitis is the first stage of the onset of a disease that may lead to a more severe condition, such as periodontitis, periodontal abscesses, pain, tooth movement and drifting and eventually loss of teeth due to loss of supporting tissues.^{1,3} It should be noted that periodontal treatment is based on elimination of causative agents and the main purpose of the treatment is to prevent further progression of the disease, which is less invasive treatment, both in terms of treatment complications and costs to the patients.¹ Periodontitis is divided into two groups of aggressive periodontitis and chronic periodontitis. In both types of periodontitis, the supporting tissues of the tooth (periodontal attachments and alveolar bone) are invaded and damaged so that periodontal pockets can be created. The incidence of aggressive periodontitis is lower than

other periodontal diseases. It affects young people that can destroy the supporting structures of teeth. According to the latest classification by the American Academy of Periodontology (AAP) in 1999, the factors considered for aggressive periodontitis are: systemically healthy people, rapid attachment loss, and having a family history of aggressive periodontitis.

Early diagnosis is important in this disease, which often remains unrecognizable until the onset of serious symptoms.⁴ Chronic periodontitis is a disease that affects the supporting tissues of the teeth. The accumulation of bacterial plaque on the dental surfaces causes inflammation of the marginal tissues of the gingiva, which, if not treated, may lead to periodontitis, which is characterized by loss of supporting tissues of the teeth, loss of bone, and ultimately causing mobility and exfoliation of the teeth. The difference with aggressive periodontitis is higher age and the accumulation of plaque in chronic periodontitis. It is usually painless and has a slow progression. The first challenge is diagnosis and the second challenge is controlling the causative agents. In most cases, the disease can be controlled by non-surgical methods, such as the physical removal of bacterial masses and germs, by mechanical methods such as scaling and planning the root surface (SRP). The third challenge is preservative or supportive care that focuses on motivating the patient to maintain oral health and control the risk factors. The issues that should be considered in determining chronic periodontitis include probing depth, bleeding on probing, and clinical attachment levels. Examples of some criteria should be considered in treatment include: mechanical therapy, control of causative agents, examination of underlying diseases such as diabetes, psychiatric problems and smoking, the use of appropriate antibiotics, the use of low dose tetracycline, which is so-called host modulatory inhibits the collagen fibers destruction, and laser therapy is a supportive treatment.⁴ Chronic periodontitis is known to have an effect on the body due to its inflammatory nature, such as other inflammatory diseases, including changes in blood inflammatory factors and the occurrence of anemia. There are two view about anemia: either the disease induces anemia, or anemia increases the rate of tissue damage. Siegel *et al.* have shown that the occurrence of secondary anemia is due to periodontal disease. After non-surgical periodontal treatment, hemoglobin and hematocrit have been shown to increase in patients.⁵ Also, non-surgical treatments in patients with periodontitis increase the number of red blood cells (RBCs), and decrease the levels of acute phase proteins, such as C-RP, and also reduce LDL / VLDL in the blood. CRP is a serum protein produced during inflammatory diseases and returns to normal when inflammation is resolved.⁶⁻¹⁰

Similarly, Iwamoto and Nishimura (2003) also found that non-surgical periodontal treatments could reduce CRP and TNF- α in the blood and eventually reduce the risk of thrombosclerosis.⁶ Nonsurgical periodontal treatments (NSPTs) have been shown to reduce the probing depth and to improve the attachment level. The NSPT involves both

mechanical and chemical control and removal of plaque. The mechanical method refers to the supra and subgingival SRP by the sonic/ultrasonic instruments or manual. The chemical method also refers to the systemic or topical application of antibacterial agents. As soon as bacterial control and host infectious agents are performed, it is very important for the patient to take care of the disease to be controlled. Generally, mechanical therapy for periodontal infections is the first line of therapy. It has been shown that the binding of endotoxins to root cements is weak so makes the removal and shaving of a large amount of cements to eliminate endotoxins unnecessary. A study by Rahul⁷ showed that the number of erythrocytes and hematocrit levels were low in patients with periodontitis.

Another study by S. Latha *et al.*⁸ suggested that iron deficiency and microcytic anemia occur in periodontitis. In Khan NS *et al.*⁷ it was found that there was a significant reduction in blood parameters such as a decrease in the number of red blood cells with the progression of periodontitis. The results of Gokhale SR *et al.*¹⁰ study showed that patients with chronic periodontitis had lower levels of erythrocyte and hemoglobin than normal people. The results of the study by M.Anopama *et al.*¹¹ in 2014 also showed a significant increase in hemoglobin (Hb) and RBC and (packed cell volume) PCV after non-surgical periodontal treatment. A study by Kshitiz Parashar *et al.*¹² was performed to investigate the relationship between chronic periodontitis and anemia and this relationship was shown. This association was shown in a similar study by Niloofer Jenabian *et al.*¹³ According to A.R.Pradeep *et al.*¹⁴ which was performed to investigate the relationship between periodontal treatment and effect on anemia, periodontal treatment was effective in improving anemia status. In a cross-sectional study conducted by Venkata Naga Sri Harsha Anomolo *et al.*¹⁵ periodontal treatment was able to improve hematocrit and other blood-related conditions. Also, in a study by Anand PS and colleagues¹⁶ performed to investigate the relationship between generalized aggressive periodontitis and blood parameters, generalized aggressive periodontitis clearly causes lower levels of erythrocyte and hemoglobin than normal individuals. In a study performed by Chakroborty S. *et al* in 2014, patients with anemia experienced more periodontal degeneration.¹⁷ According to a study by Patel *et al* in 2014, chronic periodontitis, like other chronic conditions, can lead to anemia and non-surgical periodontal treatments improves the condition of anemia.¹⁸ In 2012, a study was conducted by Malhotra *et al.* According to the results of this study, individuals with periodontitis had lower amount of hemoglobin , red blood cells and hematocrit, which improved with non-surgical treatments such as SRP.¹⁹ In a study conducted by Yamamoto *et al.* In 2011, the relationship between the reduction of erythrocytes and progression of periodontal disease was noted.²⁰ In a study conducted by R.M.Sandi *et al* in 2014, there was a significant increase in cholesterol and LDL in chronic periodontitis patients.²¹ In 2013, Mahdiah Shojaee *et al.* Showed that chronic periodontitis as an infectious disease

could increase CRP in these patients.²² In 2015, Ahmed Tawfiq showed that nonsurgical chronic periodontitis treatment reduced serum CRP and LDL levels.²³

Materials & Method

The study was an interventional type and a clinical trial. This study was carried out in the periodontics department of Hamedan University of Medical Sciences and Health Services in the 2012-2013. To collect data, an information form containing the personal characteristics of each patient and the laboratory parameters to be considered in the first visit (before the treatment procedure) and on the second visit (one month after the completion of the procedure). In order to determine the sample size, consideration should be given to the measurement before and after the desired dispersal. For this, the formula has been used in proportion to the average estimate of a community. Considering the statistical power of 95%, the error level was 0.05 and the variance was equal to 0.22 and $dp = 0.93$ and the minimum sample size was considered 30.10 that was equal to 31. The inclusion criteria:

1. The patient is in the age range of 25 to 55 years.
2. The patients suffering from chronic periodontitis (Localized or generalized);
3. The patient has a pocket depth of at least 5 mm.
4. The patient has attachment loss of at least 3 mm.
5. The patient has bleeding during probing, or BOP +.

Exclusion criteria for the study:

1. History of antibiotic use in the past three months (also not to be taken during the study).
2. Taking of iron supplements over the past three months (iron supplements should not be taken during the study).
3. History of major trauma and oral surgery.
4. History of blood transfusion in the past 3 months (no blood transfusion during the study).

A total of 31 patients referring to the periodontics department of Hamedan University of Medical Sciences who studied the conditions mentioned above were included in the study. Prior to non-surgical periodontal treatment (SRP) in the laboratory, 5 ml of venous blood was prepared from the patient under an aseptic condition from antecubital fossa and blood was transferred to EDTA-containing tubes, and for the subjects in this design in the baseline line, was analyzed. After the preparation of the patient's blood test results, a non-surgical periodontal treatment (SRP) was performed by one person for all the cases and by ultrasonic apparatus in the specialized periodontology department of the dental school of Hamedan University of Medical Sciences with a technical characteristics of power input of 240-100 volts, Frequency 60-50 Hz, output power of 30-20 watts, water pressure of 0.01-0.5 mega pps, and dimensions of 375 x 11 x 11 x 375 mm belonging to woodpecker company, Supra and sub gingival SRP was done completely for teeth both jaws and complete brushing were performed. At the end, recommendations were given for not taking iron supplements, antibiotics and not doing

blood transfusion, as well as proper sanitation and using chlorhexidine 0.2% mouthwash twice a day for one month. After one month, blood samples were taken from the patient again, and then the results were compared with baseline results. After collecting data, the data was recorded by using descriptive statistics. A t-pair was used to examine the association and comparison of the results before and after the treatment. SPSS16 software was used to analyze the data and the significance level of tests was considered 5%.

Results

The aim of this study was to evaluate the effect of periodontal non-surgical treatment on changes in a number of blood-type factors in patients with chronic periodontitis including RBC, hemoglobin (Hb), hematocrit (Hct), LDL, LDLV and CRP. It should be noted, however, that during the study, the amount of triglyceride (TG) was also obtained and examined. An interventional study with follow up at the baseline and one month after non-surgical periodontal treatment was performed on 31 patients with chronic periodontitis. Of these, 19 men with an average age of 36.2 years (36.2 ± 10) with a minimum age of 25 and a maximum of 53 years old and 12 women with an average age of 48.6 years (48.6 ± 2.8) were at least 47 and maxed out 55 years. [Figure 1]

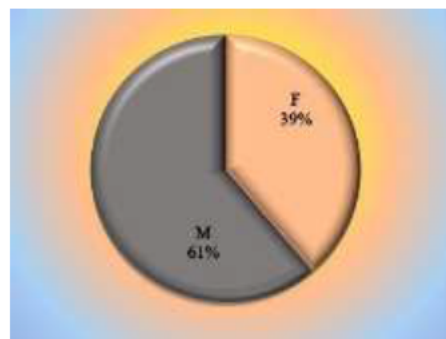


Figure1: Participants in the study

The amount of RBCs at the baseline and before treatment was moderate ($4.96 \pm 0.32 \times 10.6/\mu\text{L}$), which may be due to pro-inflammatory mediators such as IL-1, IL-6, and TNF. After the desired treatment, examination of the patients one month later showed an increase in the amount of red blood cells ($5.24 \pm 0.45 \times 10.6/\mu\text{L}$) ($p=0.006, CI=95\%$). [Table 1]

Total Number of patients	CI	p value	Second Visit	First visit	Blood parameters
31	95%	0.006	5.24±0.45	4.96±0.32	RBC($\times 10^6/\mu\text{L}$)
31	95%	0.002	15.19±0.79	14.62±1.01	Hb(g/dL)
31	95%	0.002	46.10±2.96	43.9±2.95	Hct(%)
31	95%	0.008	98.90±20.82	123.42±39.06	LDL(mg/dL)
31	95%	0.01	24.63±11.46	32.71±18.58	VLDL(mg/dL)
31	95%	0.03	123.42±57.65	154.68±92.81	TG(mg/dL)

Table 1- Results

Hemoglobin levels were also measured and increased one month later (15.19 ± 0.79 g/dL) relative to baseline (14.62 ± 1.01 g/dL) ($p=0.002$, $CI=95\%$). [Table 1]

In the case of hematocrit (Hct), the tests showed improvement in the condition one month after treatment and an increase in Hct was observed ($43.90\% \pm 2.95\%$ before treatment to $46.10\% \pm 2.96\%$ was observed one month after treatment). Since hematocrit is related to hemoglobin, this increasing is expected. ($p=0.002$, $CI=95\%$). [Table 1]

In this study, LDL and VLDL [Table 1] were also evaluated as factors affecting cardiovascular problems, indicating a relative improvement, or, in other words, a decrease in the level of these risk factors (LDL was 123.42 ± 39.06 mg/dl before treatment to 98.90 ± 20.82 mg/dL after treatment and the mean VLDL was 32.71 ± 11.46 mg/dl before treatment and 24.63 ± 46.6 mg/dL after treatment). p value for LDL and VLDL is 0.008 and 0.01 with $CI = 95\%$).

Patient's triglyceride (TG) changes were laterally evaluated for the purpose of calculating VLDL ($TG/5=VLDL$), and after one month of treatment, a decrease in this risk factor was also observed (92.81 ± 154.68 mg /dL before treatment to 123.42 ± 57.65 mg / dL after treatment ($p=0.03$, $CI = 95\%$). [Table 1]

In these patients, CRP, a pro-inflammatory mediator was evaluated qualitatively. In a number of patients, this protein was not isolated in the post-treatment test, indicating improvement in inflammatory conditions in these patients. In general, these changes were not statistically significant due to the small number of samples ($p = 0.1$). Of course, it should be noted that the measurement of CRP due to the lack of investigation of the presence of other inflammatory diseases in the patient can be misleading and is a weakness of this study.

Discussion

The main aim of this study was to find the effects of periodontal non-surgical treatment in chronic periodontitis patients on blood parameters such as red blood cells, hemoglobin, hematocrit, CRP, LDL/ VLDL. Among these parameters are RBCs and hematocrit levels, which decrease these elements can indicate anemia. Various studies in this field performed, including Hutter JW *et al.*²⁴ and Thomas B *et al.*²⁵ showed that patients with periodontitis had lower levels of erythrocyte, hematocrit, and hemoglobin. Agarwal *et al.*²⁶ as well as Gokhale¹⁰ showed this relationship. The present study, also reveals the relationship between chronic periodontitis and anemia. Low levels of hematocrit can be attributed to low levels of erythrocytes. Cartwright²⁷ stated there are 3 factors related in decreasing the amount of hematocrit and erythrocytes:

1. Reduced the survival of erythrocytes.
2. Bone marrow disorder reduces the amount of red blood cell.

3. Damage and defect of iron ion releasing from the reticuloendothelial system.

The specified inflammatory cytokines such as CRP mediators can play a role in suppressing the production of red blood cells in bone marrow, and the severity of anemia depends on the production of these cytokines. CRP for the first time detected by Tillet and Francis in 1930 in patients with pneumococcal pneumonia.²⁸ CRP can help diagnose, treat and monitoring inflammation and inflammatory diseases.²⁹ In this study, the relationship between CRP and inflammation in chronic periodontitis was expressed qualitatively. The effect of periodontal inflammatory disease control on CRP quality in patients who were initially CRP-positive, was shown after non-surgical periodontal treatment. It has been determined that chronic periodontitis affects the serum levels of LDL and VLDL. Finally, it should be noted the limitation of this study is insufficient assurance from accuracy of the patients in following all the orders were given to them for the maintenance phase.

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