The Relation between Periodontitis and Anemia Associated Parameters

Original Article

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Received: Aug 24, 2013
Accepted: Nov 10, 2013

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Abstract

Introduction: Periodontal disease, an inflammatory and infectious disease in adults and anemia associated with chronic infection, is one of the most common types of anemia. Considering the similarity of pathogens causing periodontal disease and anemia, this study aims to investigate the correlation between hematologic parameters associated with anemia and moderate chronic periodontitis.

Materials and Methods: This case-control study was systematically performed on blood samples of 60 healthy men. The control group consisted of 30 men who had healthy periodontium and the case group included 30 men with moderate chronic periodontitis. Clinical examination of patients was done using Williams periodontal probe and assessment of CAL, PPD, BOP and GI. Blood samples were collected at the Department of Periodontology, Babol school of Dentistry and evaluation of red Erythrocyte indices, Hemoglobin, Hematocrit, SI and TIBC was done. Data collected from clinical examinations and laboratory tests were analyzed by T-test, Pearson correlation coefficient and Spearman tests.

Results: Reduction of MCV, MCH, Hb, HCT, SI and TIBC factors were observed with increasing GI and CAL and BOP. There is no significant correlation between GI and CAL and BOP and MCHC factor. No Significant correlation exists between PPD changes and hematological factors associated with anemia.

Conclusion: A correlation was observed between some hematological parameters associated with anemia and moderate chronic periodontitis.

Keywords: •Anemia •Periodontitis• Iron •Hemoglobin •Erythrocyteindices

Introduction

Periodontitis is anti-inflammatory disease of the tooth supporting tissues leading to progressive destruction of PDL and alveolar bone with pocket formation, gingival recession or both[1] Chronic periodontitis which is more common in adults[2] is classified based on the amount of Clinical Attachment Loss (CAL) to three types: slight(1-2mm), moderate (3-4 mm) and sever (5mm or more).[3]

Routine laboratory evaluation of anemia is as follows: complete blood count (CBC) including Hb, HCT and erythrocyte indices, Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC) are discussed. Other important information are obtained through evaluation of reticulocyte count and iron stores by measuring serum iron (SI) and Total Iron Binding Capacity (TIBC) and Ferritin. Anemia is classified into 3 types based on dysfunction[4-6] One of the most common types of anemia found in hospitalized patients is anemia due to chronic infection(ACD=Anemia of Chronic Disease) that is found in inflammatory conditions, infections and tumors. This type of anemia occurs despite adequate iron stores and no bone marrow dysfunction.[7]

ACD is usually identified as normocytic or microcytic anemia.[8] As the level of SI and TIBC is low or normal, but high or normal Serum ferritin level is normal or high, ACD patients have a distinctive pattern regarding the Iron distribution. This change is due to Hepcidin hormone that regulates iron. It is produced by liver in response to inflammatory cytokines such as IL-6. Three mechanisms leading to decrease in Hb during inflammation:

1-Inflammatory cytokines causing suppression of erythroid proliferation in bone marrow.

2–Inflammatory cytokines preventing the release of erythropoitin from kidney.

3–Reduction in the life cycle of red blood cells.[4- 6 ,9]

There is a possible pathogenic relation between anemia and periodontal disease. In the pathogeneses of periodontal disease cytokines have a key role. Cytokines are proteins that attach to specific receptors on various target cells and cause transmission of intercellular signals. The low levels of these proteins affect different types of cells. Cytokines binding to cell surface receptors leads to initiation and exacerbation of intercellular changes and production of a group of materials and cell behavior changes, and eventually increase in cytokines secretion. Due to the positive feedback, this continuous changes cause inflammation.

Cytokines are produced by various inflammatory cells such as neutrophils, macrophages, lymphocytes and periodontal cells such as epithelial cells and fibroblasts. Cytokines are in conjunction with each other and do no intact alone. Cytokines can cause biological effects or tissue damages such as destruction of connective tissues and alveolar bones.

Bacteria that produce periodontal diseases cause stimulation of fibroblasts, keratinocytes and macrophages of periodontium. It leads to release of inflammatory cytokines such as TNF–α, prostaglandin E2 and interlukin1, 6 and 12.Following the release of these cytokines in blood, systemic effects occur. Among the effective cytokines in pathogeneses of periodontitis. IL-1β, TNF-α andIL-6 have the most important roles, respectively. IL-1β is known as one of the earliest and most important components of the immune response that is increase in periodontal disease and leads to secretion of mediators and inflammatory changes. IL-1β is produced by different cells such as monocytes, macrophages, neutrophils, fibroblasts,

Keratinocytes and osteocytes that release more neutrophil chemotaxis to the affected tissue (byIL-8secretion) and vascular in-

flammatory changes (by production of PGE2) in directly. The synergistic effects of PGE2, IL-1β and other inflammatory cytokines can lead to bone loss. Macrophages releaseIL-6 under the influence of TNF-α and IL-1β. IL-6 which increases in periodontal disease causes bone resorption. IL-1α is an intracellular protein which is made by necrotic cells and cannot be found in normal conditions.

The role of this interleukin in pathogeneses of periodontitis is unknown. TNF-α is one of the main components of immune response and plays an essential role in the neutrophils activity. TNF-α causes apoptosis of fibroblast cells and reduced tissue repair. These changes confirm the key role of TNF-α, IL-6, and IL-1β in the pathogeneses of periodontitis.[10-11] The main underlying reason for ACD, is previous chronic inflammation or infection. According to previous studies, increase of some inflammatory response cytokines such as TNF-α, interferon and IL-1 is observed in ACD. The whole process of the ACD can relate to these cytokines which leads to decreased RBC life span, and impaired development of erythroids.

In addition, it decreases erythropoietin response to anemia and abnormal iron store. Significant increase in TNF-α, IL-6, and IL-1β was observed in patients suffering from ACD that these cytokines prevent erythroid maturation. Cytokines interfere in the differentiation of erythroids.[12- 14]

Because of similar cytokines a role in pathogenesis of ACD and periodontitis, and also the role of periodontitis as a chronic infection, a relationship between these two diseases was proposed. In studies conducted by Yamamato et al.[15], Naik et al[16] and Gokhaleet al.[7] a significant correlation between periodontitis and anemia was found. Also, other studies by Pradeep et al[17] and Malhotra et al.[18] concluded that treatment of periodontal disease is associated with improving the anemic condition. According to the performed studies on the association between anemia and periodontal disease, the aim of this study was to determine the association between moderate chronic periodontitis and blood parameters associated with anemia.

Materials and Methods

This case-control study was performed on 60 men with systemic health and mean age of (25-50) years. The case group consisted of 30 men with moderate chronic periodontitis and mean age of 40.2 years. The control group included 30 men with clinically healthy periodontium and mean 38.5 years. The history of systemic diseases and recently taken medications were taken into consideration. Inclusion criteria are being male, age25- 50 years, and systemic health.

Exclusion criteria are females, and elderly subjects (over 50 years) because the aging process is associated with anemia.[19] Patients younger than 25 years because of the low incidence of periodontal disease.[1]

Patients with a history of diabetes, renal disease, cancer, fungal and respiratory disease, previous hospitalization, history of blood transfusion, blood donation in the past 3 months, and periodontal treatment, alcohol and tobacco use history.[5]Patients were assessed with regard to the consumed medicines such as aspirin, varfarin, Plavix, heparin, corticosteroids, lithium, phenytoin, methyldopa, NSAID, blood coagulation factors and the categories of drugs such as anti-blood pressure, antibiotics, anti-Arrhythmias, urinary tract drugs, penicillin and their derivatives. At the first step, written informed consent was obtained from patients and questionnaire was completed by the patient and researcher.

After selection of subjects, measurements of periodontium was performed using Williams probe. Periodontal parameters were as follows: Loe and Sillness Gingival

Index (GI) Clinical Attachment Loss (CAL), Periodontal Pocket Depth (PPD) and Ramfjord Index. In case of missing Ramfjord teeth, the replacement of absent teeth was done according to the pattern, showed in figure 1.[20]

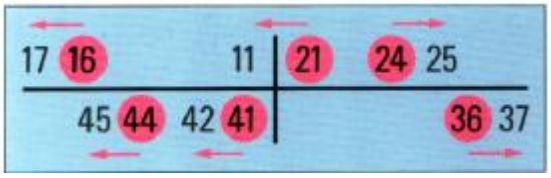

Figure1. Ramfjord teeth. Six teeth (red) could be taken as reposentative of the entire dentition. The substitutes for these six teeth are shown on the chart in gray

Patients with probing depth of less than 3 mm and healthy periodontium were included in the control group. The patients of case group had probing depth of more than 4mm or AL of more than 3 mm.

Muhlemann & Son GSBI were measured by periodontal probe. In presence of bleeding after 15 seconds, score 1 and in its absence, score 0 was recorded.[21]

After examinations, 5cc venous blood was taken from each subject, 1cc of that was maintained in CBC kit and 4cc was stored in clotting tubes for examination of TIBC and SI, and then immediately transferred to the labratory of Roohani hospital. Suffering from different degrees of anemia by most women after the age of 30, difficulty of allotting them to groups and their feature causing a big bias in the study lead to the inclusion of only men in this study. TIBCT and SI tests were performed by Hitachi electro-analyzer machine (model 912) and CBC was done by XS-800 fluorescence flow cytometry method By Sysmex.

Data obtained by clinical examinations and laboratory tests were analyzed using SPSS 17 software and T-test, Pearson correlation coefficient and Spearman test.

Results

The population of this study constituted 60 healthy men aged (25-50) years (mean age of case group 40.2 and mean age of control group 38.5). Periodontal health indices were compared in figure 2.

Hematologic indices were compared in table 1 between control group and moderate chronic periodontitis.

A statistically significant difference was observed in hematologic indices between the two groups (P<0.001). Only MCHC index showed no significant difference. Significant correlation was found between GI, CAL and BOP with MCV, MCH, Hb, HCT, SI and TIBC (P<0.001). Changes of Iron store are presented in figure 3.

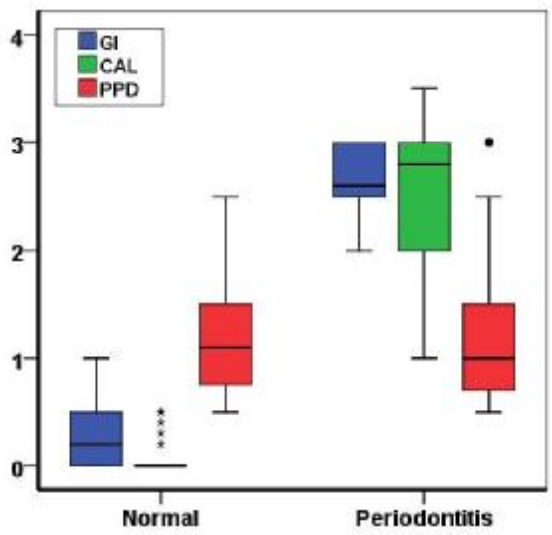

Figure 2. Comparison of periodontium health parameters between control group and moderate chronic periodontitis.

Table1. Comparison of hematologic parameters and Iron store

Parameter	Control	Periodontitis	P-value
MCV (Fl)	91.63±3.18	81.35±3.90	<0/001*
MCH (Pg)	29.40±0.71	28.05±0.65	<0/001*
MCHC (g/dL)	30.33±0.92	29.90±1.13	0/108
Hb (g %)	14.88±0.55	14.29±0.5	<0/001*
HCT (%)	49.09±2.06	42.96±1.36	<0/001*
SI(mcg/dL)	154.43±10.45	80.23±12.75	<0/001*
TIBC(mcg/dL)	402.17±10.94	297.77±12.44	<0/001*

* Significant

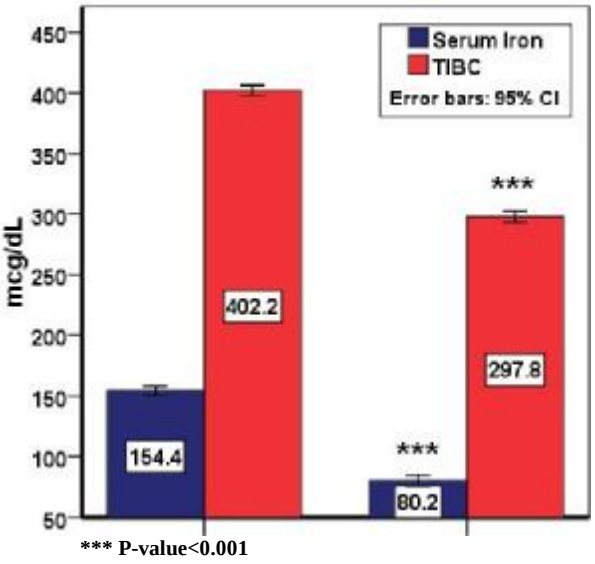

Figure3. Comparison of SI and TIBC between control group and moderate chronic periodontitis.

Only PPD and MCHC indices showed no significant correlation with any of the parameters. A significant correlation was found between GI increase and decrease of MCV, MCH, Hb, HCT, SI and TIBC (P<0.001). A significant correlation was found between BOP and CAL increase, and decrease of MCV, MCH, Hb, HCT, CAL, SI and TIBC (P<0.001). These correlations are showed on figure 4.

Figure 4. Correlation between hematological parameters and iron store and periodontal indices.

Discussion

The aim of this study was to investigate the association between blood parameters related to anemia and periodontal disease. Reduced MCV, MCH, Hb TIBC and HCT indices are symptoms of microcytic anemia and increased GI, CAL and BOP indices are associated with periodontitis. Since the MCHC is obtained from the ratio of $\frac{Hb}{HCT}$ (22) and in this study Hb and HCT both showed a decrease in the case group and increase in the control group, this ratio is constant and no significant difference was observed. Most studies showed similar results about some of the parameters. Only the study performed by Prakash et al. showed no significant relation between periodontitis and anemia.

Difference in results may be due to the cross sectional study done by Prakashet al. in both genders without considering the reduction of hematological parameters increase in females. Also the number of individuals in case and control groups was not

equal. The subjects of case group were not matched in terms of severity of periodontal disease.[23] Enhos et al. although rejected the anemia as one of the risk factors for periodontal disease, reported increase in hemoglobin level after phase I periodontal treatment in anemic patients.[2] Similar to this study, reduction in Hb and HCT associated with periodontitis was observed in Gokhale et al. Unlike the present study, no significant relationship between MCV and MCH changes and periodontitis was observed. Similar to the present study, the patients of case group showed a lower MCH level but probably because of sampling technique, laboratory conditions, the difference was significant. MCV of case group was in the normal range indicating a normocytic anemia.

Anemia due to chronic infection may present as normocytic and microcytic anemia.[7-8] Unlike the present study, Alijohani et al.(2009) indicated increased hemoglobin level in association with increased severity of periodontal disease This may be due to differences in case selection, In the study of Hind et al. periodontal patients with different intensity were selected and the number of samples in the groups was not equal. The number of individuals suffering from severe periodontitis was less than other groups and was conducted on samples of both sexes.[10] Naik et al. reported that anemia is associated with severe periodontitis showed a decrease in hemoglobin level in periodontal patients.

But unlike this study, significant reduction in MCHC changes were observed. The probable reason is that the reduction in Hb was evaluated but changes in HTC was not and apparently they did not in accordance with each other.

Probably the ratio of changes indicates reduction in MCHC. In the performed study, decrease in MCV or microcytic anemia was observed that matched with the decrease in iron stores. In Naik et al. decrease in MCV or microcytic anemia was observed. Since they did not have a reference to diet and iron level, it could be due to decrease in vitamin B_{12} or folic acid.[16] Zieblotz et al. in a study found correlation between increased Hb and HCT levels and periodontitis.

They identified periodontal inflammation as a cause of increased blood flow and hematological parameters.[24] Pradeep et al. in a similar study showed that decrease in Hb, MCV and MCH is associated to periodontitis, but they found a correlation between periodontitis and a significant reduction in MCHC. Probably similar to Naik et al. MCHC change is due to inappropriate change in Hb and HCT.[17] Difference in the results of some of these parameters may be due to different sampling techniques, different experimental conditions and devices, the number of subjects, assessment of sex, and time during the study. Yamamoto et al. found a significant relationship between periodontitis and anemia and found a correlation between CAL changes and anemia and also identified a relation between decrease in Hb and HCT level, and periodontitis.[15] Malhotra et al. revealed that decrease in HCT and Hb was significant in periodontitis and after the treatment and 3 months follow up of patients, they observed a significant increase in HCT and Hb but changes in MCV, MCH and MCHC were insignificant.[18]

Similar changes in the cytokines (TNF-α, IL-6 and IL-1β) in periodontal disease and ACD and also their mechanisms of action could be considered as a reason for the observed relationship between the reduced hemorrhagic parameters and chronic periodontal disease. Serum ferritin was not evaluated in this study because of the lack of financial support of council of research and technology of Babol University and it was a limitation of this study.

Conclusion

There was a relationship between blood parameters associated with anemia and moderate chronic periodontitis.

Acknowledgement

This study was supported by the council of research and technology of Babol University of Medical Sciences.

Authors appreciate Dr.Alireza Firoozjahi, the assistant professor and the laboratory technicians for their invaluable contribution in the laboratory process.

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