Assessment of non-surgical periodontal treatment combined with Low-Level Laser Therapy (LLLT) in chronic periodontitis patients suffering from Iron Deficiency Anemia (IDA)

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Abstract

Hence there are many chronic diseases known as catalyzers of destructive alterations in the periodontal complex, among them Iron Deficiency Anemia, the purpose of this study is to evaluate the assessment of non-surgical periodontal treatment combined with LLLT in chronic periodontitis patients suffering from IDA.

Subjects were selected from patients treated at the University Dentistry Clinical Center of Kosovo in Prishtina, included 63 participants suffering from Iron Deficiency Anemia only, followed by patients with IDA and any concomitant chronic condition and control group consisted of subjects with Chronic Periodontitis. (from October 1st, 2016 until March 31st, 2017). Patients suffering from Chronic Periodontitis were divided into three groups, suffering from IDA (Group A, 21 subjects), IDA and Chronic Disease subjects (Group B, 21 subjects) and the control group with normal iron values suffering from chronic periodontitis (Group C, 21 subjects). In this study we had also inclusion and exclusion criteria, Criteria for classifying Debris, Loe-Silness Gingival Index.LLLT adjusted to (660 nm, 10mW , 8 min/daily, in contact with gingiva); model continuously in the next five days. Blood samples were taken at baseline and at 2-month recall visit.

As far as the gender distribution between groups, it's evident that male subjects are dominant X(m)=39; n=63 in all groups (Chi=0.28; $p>0.05$). There was no significant difference regarding age discrepancy among subjects (F=11.6; $p<0.01$). IDA patients groups (A and B) have more tobacco users compare to overweight/obese group 40.9% (Chi=0.31, $p>0.05$).

The differences in GI, OHI-s and CAL values were statistically significant among groups at 2 months. A p value <0.05 was considered significant. IDA patients represented in group B showed higher values for PI ,GI and CAL. CPITN values are much higher in group B compare to group A and the control group C (Chi = 17.9; $p<0.05$).

Comparative data analysis of our measurements showed that root planning and scaling of periodontal pockets resulted in improved results for PI, GI, CAL after two months – compared to baseline measurement outcomes. Meanwhile, Hb and SI levels at baseline and after two months demonstrated weak correlation with periodontal parameters.

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Introduction

Periodontitis is a multifactorial inflammatory disease of periodontal tissues usually caused by extension of bacterial infection into subgingiva, which leads to the connective tissue destruction and alveolar bone loss. The essential objective of periodontal treatment is to decrease or eliminate the responsible perio-pathogens, by means of removing bacterial deposits from the tooth surface. Conventional mechanical debridement (ie, scaling and root planning [SRP]) is considered to be the gold standard for inflammatory periodontal disease treatment, which can cause an interim reduction in the levels of subgingival perio-pathogens.[1,2,3,4,5]

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Periodontal diseases are collectively the most common diseases known to mankind. Their classification is complex and takes into account the clinical presentation, age at diagnosis, rate of disease progression, and systemic and local factors that may increase risk. Periodontal diseases include gingivitis (in which the inflammation is confined to the gingiva, and is reversible with good oral hygiene) and periodontitis (in which the inflammation extends and results in tissue destruction and alveolar bone resorption). Tissue destruction in periodontitis results in breakdown of the collagen fibers of the periodontal ligament, resulting in the formation of a periodontal pocket between the gingiva and the tooth. 'Pocketing' is not evident on simple visual inspection, and assessment using a periodontal probe is essential. Periodontitis is a slowly progressing disease but the tissue destruction that occurs is largely irreversible. In the early stages, the condition is typically asymptomatic; it is not usually painful, and many patients are unaware until the condition has progressed enough to result in tooth mobility. The pockets deepen as a result of the further destruction of fibers of the periodontal ligament (referred to as attachment loss and the resorption of the alveolar bone that occurs in parallel with the progressing attachment loss. Advanced periodontitis is characterized by gingival erythema and edema, gingival bleeding, gingival recession, tooth mobility, drifting of teeth, suppuration from periodontal pockets, and tooth loss.[6,7,8,9]

Chronic diseases are well known catalyzers of destructive alterations in the periodontal complex. Diabetes has been unequivocally confirmed as a major risk factor for periodontitis. There is emerging evidence to support the existence of a two-way relationship between diabetes and periodontitis, with diabetes increasing the risk for periodontitis, and periodontal inflammation negatively affecting glycemic control.[10]

Oral lesions are common in patients with Inflammatory Bowel Disease and epidemiology data vary over a wide range of 5%-50% due to contradictory studies. Non-specific lesions in the oral cavity can also be the result of malnutrition and drugs. Malnutrition, followed by anemia and mineral and vitamin deficiency, affects the oral cavity and teeth. Furthermore, all of the drug classes that are applied for the treatment of inflammatory bowel diseases can lead to alterations in the oral cavity due to the direct toxic effects of the drugs on oral tissues, as well as indirect immunosuppressive effects with a risk of developing opportunistic infections or bone marrow suppression.[11,12,13]

Iron Deficiency Anemia (IDA) is a major health problem worldwide. Iron deficiency of nutritional origin is the most frequent cause of microcytic hypochromic anemia, but other conditions such as bleeding, gastro-intestinal malabsorption or Helicobacter pylori infection can lead to iron deficiency and anemia. Anemia is a global public health problem affecting both developing and developed countries and has major consequences for human health as well as social and economic development. It affects 24.8% of the world population. The burden of anemia varies with a person's age, sex, altitude, and pregnancy. The worldwide prevalence of anemia among adolescents is 15% (27% in developing countries and 6% in developed countries). Mutually, chronic periodontitis (CP) and iron deficiency anemia (IDA) induce oxidative stress in the body and cause an imbalance between reactive oxygen species and antioxidants. [14]

The World Health Organization defines anemia as a level of Hb below 13.0 g/dL in male adults, below 12.0 g/dL in female adults who are not pregnant, and below 11.0 g/dL in pregnant women. Hb levels may vary across age and race, so care must be taken, particularly in the interpretation of borderline values. Furthermore, smokers and inhabitants of higher altitudes may have higher baseline Hb levels, and participation in endurance sports may alter Hb levels. The amount of circulating iron bound to transferrin is reflected by the serum iron level. The serum iron reference range is 55–160 μg/dL in men and 40–155 μg/dL in women.[15, 16, 17, 18]

Subgingival irrigation was done using iodine. Elemental iodine or its derivatives [polyvinylpyrrolidone-iodine complex (PVP-iodine)] are probably the most broad-spectrum and potent antiseptics available. Dilute PVP-iodine may be able to kill Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis and other periodontal pathogens in vitro in as little as 15s of contact and bacteria and yeasts in vivo within 5 min of contact. [19, 20, 21, 22]

Materials and methods

Subjects were selected from patients treated at the University Dentistry Clinical Center of Kosovo in Prishtina, included 63 participants suffering from Iron Deficiency Anemia only, followed by patients with IDA and any concomitant chronic condition (Diabetes Type II, Rheumatoid Arthritis, Ulcerative Colitis or Celiac, COPD, Disease Cardiovascular Disease, etc.) and control group consisted of subjects with Chronic Periodontitis. (from October 1st, 2016 until March 31st, 2017).

All participants suffering from Iron Deficiency Anemia are selected based on the International Classification of Disease, 9th Revision [ICD – 9 – CM] (D50.-). Patients suffering from Chronic Periodontitis were divided into three groups, suffering from IDA (Group A, 21 subjects), IDA and Chronic Disease subjects (Group B, 21 subjects) and the control group with normal iron values suffering from chronic periodontitis (Group C, 21 subjects).

Inclusion criteria for participation of potential subjects in this study are:
- patients with IDA
- diagnosed chronic periodontal disease
- age 35 – 80, and
- having at least 20 remaining natural teeth were considered for the study.

Exclusion criteria are:
- no past or present history of malignant disease, particularly hematological malignancies
- patients who had hemolytic anemia or defined deficiency of vitamin B12 or folic acid
- not taking medication known to influence periodontal status, no past or present iron therapy
- not having history of any periodontal treatment in past 6 months.

In the beginning of the study data records for social status and smoking habit are noted. All patients who had history of smoking were heavy smokers (>20 cigarettes/day).

Community Periodontal Index of Treatment Needs (CPITN) as an epidemiological screening procedure for periodontal treatment needs in populations was presented and described by World Health Organization since 1978, named WHO 621 ("Trinity", with the Score 0 – 4).

Criteria for classifying Debris:
0 - No debris or stain present
1 - Soft debris covering not more than one third of the tooth surface, or presence of extrinsic stains without other debris regardless of surface area covered
2 - Soft debris covering more than one third, but no more than two third, of the exposed tooth surface.
3 - Soft debris covering more than two thirds of the exposed tooth surface.

Loe-Silness Gingival Index (GI) was utilized for four areas of the tooth then summed and divided by four to give the GI for the tooth, later adding the values of each tooth and dividing by the number of teeth examined, to assess the prevalence and severity of gingivitis in populations, groups and individuals.
Score 0 = Normal Gingiva
Score 1 = Mild inflammation - slight change in color, sight edema. No bleeding on probing.
Score 2 = Moderate inflammation – redness, edema, glazing. Bleeding on probing.
Score 3 = Severe inflammation – marked redness and edema, ulceration. Tendency toward spontaneous bleeding.
Clinical Attachment Level (CAL) - measured clinically from the base of the pocket – P
D to the cement-enamel junction - CEJ (in millimeters), using the formula PD + CEJ = CAL.

Measurements at baseline for OHI-s, GI and CAL are done using dental mirror and scaled periodontal probes. After baseline measurements, clinical parameters are noted and later all participants underwent a supragingival and subgingival full-mouth scaling and root planning (FRP), using hand instruments and ultrasonic devices under local anesthesia (SCANDONEST, Mepivacaine HCl 2%, Levonordefrin 1:20000, Septodont, USA). Pocket irrigation was done with 10% Povidon Iodine Solution, three times in 10 minutes (Viodin 10%, SQUARE Pharmaceuticals, Dhaka, Bangladesh), followed by copious irrigation with normal saline and adequate aspiration. Later, on the gingival part of the affected side LLLT was applied.

LLLT adjusted to (660 nm, 10mW, 8 min/daily, in contact with gingiva); model (Hager&Werken Laser HF "confort" V023-17, Duisburg, Germany) continuously in the next five days.

Blood samples were taken at baseline and at 2-month recall visit. Two milliliters of blood were collected using 22-gauge needle and 2 ml syringes, and immediately transferred to the

University Clinical Center of Kosovo Central Laboratory Department. The hemoglobin (Hb) and serum level of iron (SI) estimation was done by in a fully automated analyzer (Hitachi 911 Analyser, Hitachi Medical Corporation, Tokyo, Japan).

Results

As far as the gender distribution between groups, it is evident that male subjects are dominant X(m)=39; n=63 in all groups (Chi=0.28; p>0.05) (Table 1). There was no significant difference regarding age discrepancy among subjects (F=11.6; p<0.01). IDA patients groups (A and B) have more tobacco users compare to overweight/obese group 40.9% (Chi=0.31, p>0.05) (Table 2).

Variables	N=21 for each group			Test
	Group A	Group B	Group C	
Gender, n (%)				
Female	8 (38.1)	7 (33.3)	9 (42.8)	Chi=0.28, p>0.05
Male	13 (61.9)	14 (66.7)	12 (57.2)	
Age (years)				
Xb ± SD	53.3 ± 8.1	62.2 ± 9.5	64.0 ± 1.3	F=11.6, p<0.01
CV	15.20	15.27	2.03	
Smoking, n (%)				
Yes	9 (42.8)	11 (52.4)	8 (38.1)	Chi=0.31, p>0.05
No	12 (57.2)	10 (47.6)	13 (61.9)	

Xb-average
SD-standard deviation
CV-coefficient of variation applied for age and Hb/IS
Analysis of variance was used for Age and Hb/IS,
Chi square was used for Gender and Smoking

Table 1. Demographic characteristics applied for age and Hb/IS

Compared with baseline measurements, Root Planning and Scaling led to obvious reduction in the means of GI, OHI-s and CAL levels at 2 months follow up in both groups (Table 3). In view of the influence of baseline measurements, the analysis of covariance (ANOVA) was utilized to analyze the differences in periodontal indexes among all groups adjusted for the baseline covariates. The differences in GI, OHI-s and CAL values were statistically significant among groups at 2 months. A p value <0.05 was considered significant.

IDA patients represented in group B showed higher values for PI (2.8±0.4; CV = 27.8), GI (1.9 ±0.2; CV = 33.3) and CAL (6.1 ±1.3; CV = 29.3). CPITN values are much higher in group B compare to group A and the control group C (Chi = 17.9; p<0.05).

Variables	N=21 for each group			Test
	Group A	Group B	Group C	
Plaque Index				
Xb ± SD	2.3 ± 0.5	2.8 ± 0.4	1.7 ± 0.5	F=11.4, p<0.01
CV	21.7	27.8	29.4	
Gingival Index				
Xb ± SD	2.2 ± 0.4	1.9 ± 0.2	1.7 ± 0.6	F=7.1, p<0.01
CV	18.2	33.3	35.3	
Clinical Attachment Level				
Xb ± SD	5.1 ± 1.1	6.1 ± 1.2	3.9 ± 1.1	F=9.0, p<0.01
CV	21.6	29.3	28.2	
CPITN, n (%)				
2 - no pocketing	2 (9.5)	3 (14.1)	2 (9.5)	Chi=19.5, p<0.05
3 - shallow pockets	7 (33.4)	5 (24.8)	11 (52.4)	
4- deep pockets	12 (57.1)	13 (61.1)	8 (38.1)	

Xb-average
SD - standard deviation
CV - coefficient of variation
Chi - square test was used for CPITN.

Table 2. Dental health in all groups.

Comparative data analysis of our measurements showed that root planning and scaling of periodontal pockets resulted in improved results for PI, GI, CAL after three months – compared to baseline measurement outcomes. Meanwhile, Hb and SI levels at baseline and after two months demonstrated weak correlation with periodontal parameters. As far as the impact of baseline measurements, covariance analysis (ANOVA) was utilized to analyze differences in periodontal indexes in both groups adapted for baseline variables. Differences of PI, GI and CAL values were statistically significant between groups after two months. Whereas, p value <0.05 is considered significant.

There is no correlation between Hb and IS levels and tooth indexes, for both baseline and follow up measurements.

There is evidence that, for baseline measurement, there is moderate correlation between Hb and IS in addition to plaque index (r = 0.45, p <0.01), gingival index (r=0.39, p<0.01) and clinical attachment level (r=0.49, p<0.03).

There is weak correlation (between groups), for follow up measurement, between Hb and IS, and plaque index (r = 0.35, p <0.01), gingival index (r=0.32, p<0.05), while the correlation is moderate between Hb and IS, and clinical attachment level (r=0.49, p<0.01).

Measurement time (N=63)	*Plaque Index*	*Gingival Index*	*Clinical Attachment Level*
Baseline			
Hemoglobine (Hb g/dL)	0.45	0.39	0.49
Iron in Serum (IS µg/dL)	8.9 ±1.3 (49±14) -0.01	-0.01	-0.03
Follow up			
Hemoglobin (Hb g/dL)	0.35	0.32*	0.49
Iron in Serum (IS µg/dL)	9.1 ± 1.5 (54±9) -0.01	- 0.005	-0.15

Table 3. Pearson Correlation between blood parameters and tooth indexes (r), p<0.01

Discussion

Some literature data are confirming that presence of periodontal disease in patients suffering from IDA can be a potential threat for health. Worsened periodontal status has the potential to make worse the primary disease.[23, 24, 25, 26]

Chakraborty et al., in their original research paper stated that both chronic periodontitis (CP) and iron deficiency anemia (IDA) induce oxidative stress in the body and cause an imbalance between reactive oxygen species and antioxidants, such as superoxide dismutase (SOD), IDA-CP patients exhibited a higher gingival index, bleeding on probing, probing pocket depth, and percentage (%) of sites with a clinical attachment loss (CAL) of ≥6 mm (P<0.008) than CP patients. The mean salivary and serum SOD levels were significantly lower in the IDA-PH, CP, and IDA-CP patients than in the CG group (P<0.008). A significant positive correlation between salivary and serum SOD activity was observed in IDA (P<0.05); IDA patients with chronic periodontitis have more periodontal breakdowns than patients with chronic periodontitis. Serum and salivary SOD activity levels were lower in the IDA-PH, CP and IDA-CP groups than in the CG. Iron deficiency anemia influenced the serum SOD activity but did not seem to affect the salivary SOD activity in these patients.[27]

Khan et al., found that a significant negative correlation was observed between RBC, hemoglobin, PCV, MCV, MCH, and MCHC; data analysis showed a statistically significant decrease in red blood cell parameters with increase in different grades of periodontitis.[28]

The risk evaluation of specific biomarkers was also studied in our institution by Sllamniku et al, her results demonstrated that periodontal disease is associated with increased circulating concentrations of TNF- α, IL-1β, IL-6 and hs-CRP.[29] Another study conducted by Anumolu et al., revealed a decrease in Hb and erythrocyte counts and increase in white blood corpuscles counts in chronic periodontitis when compared to healthy controls and chronic generalized gingivitis group, on the other hand there was no statistically significant difference in MCV, MCH, MCHC, and ESR among the groups.[30]

In a 6 month follow up study Patel et al., in 50 patients had healthy periodontium and 50 patients had chronic periodontitis. Clinical parameters and red blood cell parameters of all the patients were assessed at baseline and 6 months after non-surgical periodontal therapy; from the presented study, it can be concluded that like any other chronic condition, chronic periodontitis can lead to Anemia of Chronic Disease (ACD). It also provides evidence that non-surgical periodontal therapy can improve the anemic status of patients with chronic periodontitis.[31] On the other hand, significant increase of Matrix Metalloproteinase 9 after short term LLLT in the GCF was noted in a study conducted by Ismaili et al, and furthermore this result could be associated with remodeling of extracellular matrix and stimulation of the regenerative processes.[32]

The findings from the clinical and hematological trial conducted by Kolte et al., confirmed the understanding that chronic infections such as periodontitis have systemic effects in terms of blood parameters, indicating anemia. The mean erythrocyte count for the control group was 4.32 ± 0.61 million/mm3, whereas the value for the test group was 4.09 ± 0.56 million/mm3 (P value 0.04). This decrease in the mean erythrocyte count was found to be statistically significant. Similarly, the MCHC percentage was found to be 31.64 ± 1.16 in the control group and 31.12 ± 1.35 in the test group. This decrease in the MCHC percentage was also found to be statistically significant (P value 0.03).[33]

Thought-provoking results were obtained in another representative study by Gunay et al, exploring periodontal status and total antioxidant status (TAS), ferritin levels of serum and gingival cervical fluid (GCF) in patients with thalassemia major. The systemic and local ferritin level of the

thalassemia major patient groups was seen to be high compared to the control group (healthy patients), and moreover no relationship was determined between periodontal parameters, which leads to the conclusion that TM is not a risk factor associated with periodontal disease.[34]

In another study performed by Prakash et al, showed that periodontal parameters were significantly higher (P≤.05) in periodontitis patients. Except for the Erythrocyte Sedimentation Rate (ESR), which was significantly higher (P=.03) in the mild periodontitis group than the control group, hematological and biochemical parameters were not significantly different (P>.05) among the study groups or between the control and study groups.[35] Associations between periodontal status and rheumatoid arthritis using comparative cross sectional study was completed by Suhaimi et al, demonstrating that there was significantly higher number of tooth loss in Rheumatoid Arthritis (RA) patients compared to non-RA (p=0.011). Tooth loss was significantly correlated with age of the subjects (r=0.630; p=0.0001) and duration of RA (r=0.457; p=0.009). No significant different found for periodontal parameters in between two groups (control group), in conclusion the authors using limited data demonstrated that rheumatoid arthritis may indirectly influence tooth loss.[36]

Correlation between stress-genic factors and periodontal disease was thoroughly studied in many research papers, Masulili et al investigated the relationship between academic stress with periodontal status and level of cortisol hormone, interleukin-1β (IL-1β) and interleukin-6 (IL-6) in gingival cervical fluid. In addition, this study was measured perceived stress and used The Dental Environment Stress (DES) and The Graduate Dental Environment Stress (GDES) questionnaire; periodontal condition using modified Russel periodontal index, and examined the levels of hormone cortisol, IL-1β and IL-6; at the dental profession students group the relationship between academic stress level to cortisol level showed significant differences (p=0,025), meanwhile IL-1β and IL-6 showed no significance.[37]

Smoking and tobacco consumption, to add on, further comprise a major environmental factor for periodontal disease. the mean RBC count in smokers came out to be 3.98 ± 0.18 while in nonsmokers came out to be 4.62 ± 0.27. Mean PCV level in smokers was 35.44 ± 1.45 and in nonsmokers was 40.54 ± 1.50, while mean MCV level in smokers was 85.41 ± 5.34 and in nonsmokers was 85.32 ± 5.68. MCV levels are the main determinants of some kinds of anemia.[38] In another comparable study related to smoking and periodontal disease Eid et al, evaluated the influence of smoking habit on the success of periodontal regeneration in treating intra-bony periodontal defects when using Platelet Rich Plasma (PRP) combined with Freeze Dried Bone Allograft (FDBA). Based on their results, clinical improvement, the amount of bone gain and the level of PDGF-BB were more in the non-smokers group, and consecutively smoking can impair the healing outcomes of periodontal regeneration.[39]

Conclusions

Within the limitation of this study, it can be concluded that Comparative data analysis of our measurements showed that root planning and scaling of periodontal pockets resulted in improved results for PI, GI, CAL after two months – compared to baseline measurement outcomes. Meanwhile, Hb and SI levels at baseline and after two months demonstrated weak correlation with periodontal parameters.

Declaration of Interest

The authors report no conflict of interest.

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