ORIGINAL RESEARCH

Evaluation of Systemic Markers Related to Anemia in Aggressive Periodontitis Patients before and after Phase I Periodontal Therapy: An Interventional Study

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Abstract

Aim: The main aim of the study was to evaluate the systemic markers related to anemia in generalized aggressive periodontitis (GAgP) patients before and after phase I therapy.

Materials and methods: Based on the inclusion criteria, 15 patients with GAgP were allocated to two groups, group A (before phase I periodontal therapy) and group B (after phase I periodontal therapy). After 3 months, clinical parameters and hematological parameters were reevaluated.

Results: The hematological parameters like hemoglobin (Hb) and red blood cell (RBC) counts were increased significantly after therapy in group B with a significant improvement in the plaque index score, gingival bleeding index score with a reduction of probing depth, and a gain in clinical attachment levels.

Conclusion: Within the limitation of this study, it could be concluded that GAgP was associated with reduced RBC parameters suggesting that it may tend toward anemia of chronic disease (ACD). Nonsurgical periodontal therapy (NSPT) not only reverses the periodontal health by reducing the inflammation but also improves the anemic status.

Clinical significance: Based on several studies, it was concluded that chronic periodontitis is associated with ACD. This study results indicate that like chronic periodontitis, aggressive periodontitis is also associated with reduced RBC and Hb count suggesting the risk for ACD. So when a patient is diagnosed to have any chronic infectious disease that might lead to ACD, then it is mandatory to treat that particular disease in order to reduce the infection so as to reverse the anemic status of an individual.

Keywords: Aggressive periodontitis, Anemia of chronic disease, Nonsurgical periodontal therapy.

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Introduction

Anemia of chronic disease (ACD) is defined as the anemia occurring in chronic inflammatory conditions which are not due to marrow deficiencies or other diseases and occur despite the presence of adequate iron that stores.[1] Periodontitis is one of the most common inflammatory diseases, like other chronic conditions, leading to anemia.[2] Periodontitis is an inflammatory disease of the supporting structures of the teeth.[3] Though the tissue destruction in periodontitis is confined to the periodontium, the microorganisms or their products invade the periodontal tissues through ulcerated pocket epithelium to reach the systemic circulation.[4] A large number of studies have proved the potential relationship between periodontal disease and several systemic conditions like cardiovascular disease, diabetes mellitus, adverse pregnancy outcomes, and obesity.[5] Researchers also suggested that periodontitis patients have altered blood cell counts when compared to healthy controls. Various studies have correlated the presence of anemia with chronic periodontitis. Lesser document is available for interrelationship between anemia and aggressive periodontitis. Aggressive periodontitis is distinguished from chronic periodontitis by the rapid rate of destruction, age of onset, alteration in the host immune response, composition of the subgingival microbiota, familial aggregation, and a strong racial influence.

Cartwright postulated three pathologic processes involved in the etiology of ACD:[6]

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- Shortened survival of erythrocyte,
- Failure of bone marrow in the production of red blood cell (RBC) to compensate demand (defective RBC production), and
- Impaired release of iron from the reticuloendothelial system.

The other pathways that have been presumed to cause ACD are aversion of iron traffic, reduced erythropoiesis, decreased response to erythropoietin, erythrophagocytosis, and invasion of bone marrow

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by tumor cells and pathogens.[7] The aim of the study was to evaluate the systemic markers related to anemia in generalized aggressive periodontitis (GAgP) patients before and after phase I therapy.

Materials and Methods

This is an interventional study which was conducted at the Department of Periodontology, Adhiparasakthi Dental College and Hospital, Melmaruvathur. A total number of 30 subjects were enrolled in the study with the age range of 18–40 years; after informing the study protocol, participants were asked to sign in the written informed consent. Clinical and blood parameters were measured at baseline. Out of 30 patients, 17 patients met the inclusion criteria (serum ferritin above 30 ng/dL). These 17 patients were allocated for nonsurgical periodontal therapy (NSPT) in that two patients failed to report for NSPT. So, a total of 15 patients were considered for investigation at baseline and 3 months after NSPT.

Group A: 15 subjects (GAgP, before phase I therapy)
Group B: 15 subjects (GAgP, after phase I therapy)

Inclusion Criteria

- Patients in the age-group of 18–40 years; individuals were included in the study if they had a probing depth and a clinical attachment level of ≥5 mm on at least eight permanent teeth, of which at least three were not permanent first molars or incisors (Classification of Periodontal Diseases and Conditions in 1999); and individuals with serum ferritin >30 ng/dL.

Exclusion Criteria

- Pregnant and lactating women; individuals with a history of any systemic disease, or any antibiotic therapy or under periodontal treatment during the 12 month period before the examination; smokers; and individuals with iron-deficiency anemia.

Clinical parameters recorded before and after phase I therapy were plaque index (Silness and Loe, 1964), bleeding index (Ainamo and Bay), probing pocket depth, and clinical attachment level. RBC parameters analyzed before and after phase I therapy were hemoglobin (Hb) concentration, total RBC counts, packed cell volume (PCV)/hematocrit (HCT), erythrocyte sedimentation rate (ESR), blood indices (mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), and serum ferritin.

Blood Sample Collection and Storage

After skin preparation, venous blood samples were obtained by venipuncture from the antecubital fossa under aseptic condition. After placing a tourniquet, 5 mL of blood was collected using a disposable syringe from the median cubital vein. The 2.5 mL of collected blood sample was transferred into a plain vacutainer for estimating serum ferritin levels, and the remaining blood sample was equally transferred into ethylenediaminetetraacetic acid (EDTA)-containing vial and sodium citrate-containing vial. The blood samples transferred into sodium citrate-containing vials were assigned to determine ESR while the blood samples collected in EDTA-containing vials were used for the estimation of hematological variables like Hb%, RBC count, PCV, and blood indices.

Statistical Analysis

The collected data were analyzed statistically through statistical package for social science (SPSS) software. The results of the normality tests Kolmogorov–Smirnov test and Shapiro–Wilk test revealed that except variable ESR, all other variables follow normal distribution, and ESR values do not follow normal distribution. Therefore, to analyze the data, both parametric and nonparametric methods were applied. For variables that follow the normal distribution, to compare mean values between pre-op and post-op, paired-samples *t*-test was applied. To compare pre-op and post-op ESR values, Wilcoxon signed-rank test was applied. To analyze the data, SPSS (IBM SPSS Statistics for Windows, version 22.0, Armonk, NY: IBM Corp. Released 2013) was used. Significance level was fixed as 5% ($\alpha = 0.05$).

Results

The obtained results were tabulated and the collected data were subjected to statistical analysis. The mean and standard deviation of all hematological parameters and clinical parameters in group A (pre-op) and group B (post-op) are presented in Tables 1 and 2, respectively.

Clinical parameters showed a statistically significant reduction from baseline to 3 months after NSPT.

Hematological parameters like Hb% and RBC count were found to have improved after phase I periodontal therapy in group B when compared to the baseline value. The mean baseline ESR value at 30 minutes and 1 hour was decreased postoperatively which was found to be statistically significant.

Discussion

The relationship between anemia and periodontitis was explored in the 20th century. Several studies reported the concept that anemia as an etiologic factor for periodontitis and periodontitis as a risk factor for anemia.[8–11] Meanwhile periodontal therapy also reduces inflammation, thereby improving anemic status

Table 1: Clinical parameters

Variables		*N*	*Mean*	*Std. dev*	*t value*	*p value*
Plaque index	Pre-op	15	1.04	0.068172	4.085	0.001
	Post-op	15	0.97	0.03751		
Bleeding index (%)	Pre-op	15	71.25	19.05725	11.485	<0.001
	Post-op	15	42.79	18.13282		
Probing depth	Pre-op	15	4.80	0.553551	13.344	<0.001
	Post-op	15	3.74	0.614341		
Clinical attachment level	Pre-op	15	5.12	0.562817	15.849	<0.001
	Post-op	15	3.98	0.609834		

Table 2: Hematological parameters

Variables		*N*	*Mean*	*Std. dev*	*t value*	*p value*
RBC count (million/cu mm)	Pre-op	15	4.48	0.54086	4.610	<0.001
	Post-op	15	4.98	0.61752		
Hb (%)	Pre-op	15	12.73	1.22915	4.740	<0.001
	Post-op	15	14.05	1.30395		
MCV (fL)	Pre-op	15	87.70	10.69	0.571	0.572
	Post-op	15	89.69	8.23		
MCH (pg)	Pre-op	15	28.27	2.07	−0.536	0.601
	Post-op	15	28.63	1.28		
MCHC (%)	Pre-op	15	29.99	5.32	0.530	0.600
	Post-op	15	30.89	3.86		
PCV/HCT (%)	Pre-op	15	44.82	8.2487	−1.000	0.334
	Post-op	15	47.69S	8.5280		
ESR (1 hour)	Pre-op	15	8.47	6.010		<0.001
	Post-op	15	4.07	2.549		

in periodontitis patients.[11–13] Case–control study reported that like chronic periodontitis, GAgP is also associated with a risk for anemia.[14] A longitudinal study was conducted to examine the systemic effect of nonsurgical therapy on white blood cell (WBC) count and differential blood count in GAgP patients and concluded that periodontal therapy may significantly reduce leukocyte counts in the patients with GAgP.[15]

Since aggressive periodontitis is presented with higher levels of circulating cytokines, such as interleukin-1 (IL-1), IL-6, IL-17, tumor necrosis factor-alpha (TNF-α), interferon-gamma (INF-γ), and other pro-inflammatory cytokines, which might lead to a low-grade systemic inflammation that would cause anemia, in order to treat ACD, it is better to eliminate the cause either systemic or local, thereby minimizing the treatment from invasive to conservative, untreated anemia may cause a critical issue in patients with chronic disease.[16] In the case of inflammatory diseases like periodontitis, periodontal therapy is one such possible way to control the inflammation and reverse the condition. Periodontal inflammation often causes bleeding from the gingiva; direct loss of blood from the gingiva might be a reason for reduced RBC count but evidence has not been substantiated. Few plausible mechanisms explained the decreased hematological parameters in periodontitis patients.[17]

Hence, this study was conducted to investigate whether aggressive periodontitis is associated with reduced erythrocyte count and Hb levels, and to investigate like chronic periodontitis, aggressive periodontitis also responds to phase I periodontal therapy.

The study results showed a significant reduction in the mean plaque index score from baseline to posttherapy (1.03 ± 0.06 to 0.96 ± 0.03) and a statistically significant reduction in the mean bleeding index percentage from baseline to posttherapy following the nonsurgical phase (71.25 ± 19.05 to 42.78 ± 1.13). This might be due to the elimination of local factors and the resolution of inflammation. So the reduction in bleeding index postoperatively would have improved the hematological variables. There was a significant reduction in the mean probing depth from baseline to 3 months after therapy (4.79 ± 0.55 to 3.74 ± 0.61). In the case of increased probing depth, the subgingival organism enters the bloodstream through ulceration of pocket epithelium that evokes low-grade systemic inflammation, which has been related to the suppression of erythropoiesis.[5] A significant gain in mean clinical attachment level (CAL) value was seen from baseline to 3 months after therapy (5.11 ± 0.56 to 3.97 ± 0.60) which might be due to mechanical debridement as it leads to the cessation of disease progression, hence resulting in a gain of attachment level. Following phase I therapy, all participants received oral hygiene instruction for home care plaque reduction; not only the clinical parameters but also the hematological parameters were found to be improved from baseline to posttherapy.

The blood investigation results showed a statistically significant increase in the mean RBC 4.48 ± 0.54 to 4.98 ± 0.61 and the mean Hb 12.73 ± 1.22 from baseline to posttherapy. The mean improvement in HCT (PCV) value from baseline to 3 months postoperatively 44.82 ± 8.25 to 47.69 ± 8.53 was not significant. The increase in the blood indices MCV, MCH, and MCHC values posttreatment was limited and not statistically significant. The values of the baseline blood indices were between normal or near-normal range that indicated the mild anemia was not due to iron or vitamin deficiency.

Reduced MCV and MCH values suggest microcytosis as seen in iron deficiency, and elevated levels suggest macrocytosis caused by vitamin deficiency. Hence, the normal MCV and MCH range in this study with minor increment posttherapy indicates this anemia to be normocytic as in ACD. Even though the Hb concentration at baseline was found to be reduced, the MCHC was not below the normal reference ranges in both the groups at baseline and posttherapy, indicating that Hb concentration per volume of packed red cells is normal. The normal MCHC reference range indicates normochromic anemia as seen in ACD.

Another valuable parameter indicating the underlying inflammatory process was the ESR value; the elevated ESR value at baseline suggested that aggressive periodontitis has an inflammatory component systemically and the reduction in ESR value after periodontal therapy over time suggested resolution of inflammation and inflammatory markers. ESR estimation is the oldest laboratory method that helps to monitor disease activity and reflects the systemic response of any chronic disease and results from a change in colloidal state of plasma that could be caused by variation in plasma proteins globulins and fibrinogens.[14]

Aggressive periodontitis patients have ESR elevated when compared to chronic periodontitis and healthy individuals. The mean change in ESR value at 1 hour from baseline to posttherapy

was statistically significant 20.87 ± 13.27–10.80 ± 7.173. This statistically significant reduction of ESR value posttherapy might be due to the reduction in the systemic disease activity.

The results indicated that the RBC count and Hb concentration were significantly increased after therapy with a significant decrease in ESR value and minimal increment was observed in PCV, MCH, MCV, and MCHC. Clinical parameters showed a statistically significant improvement after therapy. Few limitations of this present study were the relatively smaller sample size, and variables like socioeconomic status and stress were not elucidated.

Conclusion

The concept that periodontal diseases confined to tooth and supporting structures has been revised, as it can exaggerate to cause wide-ranging systemic effects. Aggressive periodontitis is also one of the clinical entities that can cause progressive destruction of periodontium and loss of alveolar bone. This might lead to increased levels of circulating pro-inflammatory cytokines. And, this low-grade systemic inflammation might cause depletion of RBC production and anemia to a milder extent when compared to other chronic inflammatory diseases like rheumatoid arthritis. A statistically significant improvement in the clinical parameters and blood parameters was observed after NSPT in the GAgP patients. A statistically significant decrease in the ESR was observed after therapy indicating a reduction in the systemic infection.

Within the limitations of this present study, it can be concluded that like other inflammatory diseases, aggressive periodontitis also exaggerates a mild systemic inflammation that might cause ACD and that like chronic periodontitis, GAgP also responds to NSPT and provides evidence in the improvement of anemic status.

Summary

Periodontal diseases confined to tooth and supporting structures have been revised, as they exaggerate to cause systemic effects. Aggressive periodontitis that can cause progressive destruction of periodontium might lead to increased levels of circulating pro-inflammatory cytokines; this low-grade systemic inflammation might cause depletion of RBC production and anemia, when compared to other chronic inflammatory diseases like rheumatoid arthritis. Treating periodontitis would result in the resolution of inflammation and improve the status of anemia.

Author Contribution

All authors have made substantial contributions to the conception and design of the study and have been involved in data collection and data analysis. All have been involved in data interpretation, drafting the manuscript, and revising it critically and have given the final approval of the version to be published.

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