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ORIGINAL ARTICLE

Associating Serum Iron and Magnesium Levels in Hypertensive and Chronic Periodontitis Patients: Do They have a Link?

[1]Nagaraj B Kalburgi, [2]Arati C Koregol, [3]TJ Jerin Mary, [4]Shivaraj Warad, [5]Tejaswini Annam, [6]Nitesh Kataria

ABSTRACT

Introduction: Micronutrients have been extensively studied in recent years; of these magnesium and iron are essential for a variety of physiologic functions. Activation of neutrophils is an early effect of hypomagnesemia, which, in turn, causes periodontal tissue destruction. Since magnesium also influences blood pressure regulation by vascular tone and reactivity, its altered levels could contribute to the pathophysiology of hypertension. Iron plays a key role in the formation of reactive oxygen species that causes peroxidative damage to tissues.

Aims and objectives: The present study is designed to estimate the levels of serum iron and magnesium in healthy, chronic periodontitis patients with and without hypertension.

Materials and methods: This study includes 90 subjects, age ranging from 18 to 65 years. They were categorized into three groups as group I: 30 periodontally healthy, group II: 30 chronic periodontitis, and group III: 30 chronic periodontitis with hypertension. Serum magnesium levels were determined using the modified xylidyl blue reaction method and serum iron levels using ferrozine method without deproteinization via photometry.

Results: Biochemical parameters showed mean serum iron levels in chronic periodontitis (59.17) to be significantly reduced as compared with the control group (76.90) and slightly increased in the chronic periodontitis with hypertension group (69.63). Serum magnesium levels were found to be significantly lower in the hypertensive group as compared with the chronic periodontitis and control groups.

Conclusion: Iron and magnesium have a link in the pathophysiology of periodontitis. Serum iron and serum magnesium levels were closely linked to periodontitis and hypertension.

Keywords: Hypertension, Micronutrients, Periodontitis, Peroxidative damage, Reactive oxygen species.

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[1]Professor and Head, [2,4]Professor, [3,5,6]Postgraduate Student

[1-6]Department of Periodontics, P.M. Nadagouda Memorial Dental College and Hospital, Bagalkot, Karnataka, India

Corresponding Author: Nagaraj B Kalburgi, Professor and Head, Department of Periodontics, P.M. Nadagouda Memorial Dental College and Hospital, Bagalkot, Karnataka, India, Phone: +919845092490, e-mail: drnagarajk@rediffmail.com

INTRODUCTION

Micronutrients are essential to execute a broad range of biochemical and physiological functions, so as to regulate the homeostatic processes. They function as coenzymes in key metabolic reactions, antioxidants in order to control the damage caused by reactive oxygen species, modulators of gene transcription, and cofactors for enzymes and structural components of tissues.[1,2]

Hypertension is one of the major risk factors that contributes to the development of cardiovascular diseases, and the initiation and progression of the disease are affected by inflammation and the host immune response.[3,4] Periodontitis is an inflammatory disease affecting both the hard and soft tissues leading to degeneration of the attachment apparatus caused by specific microorganisms in a susceptible host. Over the past few years, many studies have suggested periodontitis to be a risk factor for cardiovascular disease.

Magnesium is a biologically essential cation that acts as an important regulator of cell functions and its high normal serum magnesium concentrations are protective against various diseases. Recently, magnesium has received considerable attention in clinical medicine, especially with regard to the role of its depletion in cardiovascular pathophysiology.[5] Some data even support the role for magnesium in the pathophysiology of essential hypertension.[6]

Iron symbolizes a paradox for human health and serves as a metal cofactor for various enzymes (oxidases, peroxidases, catalases, etc.).[7,8] On the contrary, it plays a key role in the production of harmful oxygen radicals that eventually causes peroxidative damage to vital structures.[7,9] Thus, serum iron and total iron binding capacity and transferring saturation are considered as best indicators of nutritional deficiency arising from chronic infection, inflammation, or chronic neoplastic diseases.[10]

Very few studies have been documented suggesting a link between serum iron and magnesium levels in periodontitis and hypertension. So, in order to understand the role of these micronutrients in the pathogenesis of periodontitis and hypertension, the present study was conducted.

AIMS AND OBJECTIVES

The aim of the study was to estimate the levels of serum iron and magnesium in healthy, chronic periodontitis and chronic periodontitis with hypertension patients and also compare these levels with the clinical parameters.

MATERIALS AND METHODS

The present study is a randomized controlled double blind study where the patient and the pathologist who performed the blood analysis were blinded to the study. A total of 90 subjects of both sexes, with age group ranging between 25 and 65 years, were selected from the outpatient Department of Periodontics, P.M. Nadagouda Memorial Dental College and Hospital, Bagalkot, Karnataka, India. The study design was approved by the Ethical Committee of the same institute. All patients received verbal explanation of the nature of the study, and informed written consent was obtained from all patients prior to the study.

The inclusion criteria were as follows: (1) systemically and periodontally healthy subjects, (2) systemically healthy, but clinically and radiographically evident chronic periodontitis, (3) hypertensive patients having essential hypertension with systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg according to the US Joint National Committee (JNC) recommendation,[11] and (4) taking antihypertensive medications for at least 1 year and above were included in the study. The exclusion criteria were smokers, patients with recent trauma, a history of previous periodontal therapy within 6 months before the screening, presence of a periodontal abscess or a combined periodontal–endodontic lesion, general contraindications for periodontal surgery (e.g., psychiatric problems, pregnant or breast-feeding females) or presence of life-threatening conditions (e.g., malignant tumors or radiotherapy in the cervicofacial area, either current or within the previous 6 months), and use of antibiotics and analgesics within 6 months prior to the study.

Periodontal Examination and Study Groups

The following parameters were recorded for the whole mouth. Gingival index (GI), probing pocket depth (PPD), and clinical attachment loss (CAL) were measured by calibrated periodontal probe. The study subjects were categorized into three groups of 30 patients each. Group I (healthy subjects, n = 30) consisted of subjects with a GI score <1 and showing absence of clinical and radiographic features of periodontal disease. Group II (chronic periodontitis subjects, n = 30) consisted of subjects with a PPD ≥5 mm in at least 14 sites, CAL 3 to 6 mm, and GI ≥ 1. Group III (chronic periodontitis with hypertension) consisted of untreated chronic periodontitis patients with a PPD ≥5 mm in at least 14 sites, CAL 3 to 6 mm, and GI ≥1.

Sample Collection and Biochemical Analysis

About 5 mL of the venous blood sample was drawn from the subjects using a disposable syringe and transferred to tubes containing clot-activating factors. The collected blood samples were then sent to the Thyrocare laboratory, Bagalkot, India, for the estimation of serum magnesium levels, which was determined using the modified xylidyl blue reaction method and serum iron levels using the ferrozine method without deproteinization via photometry.

Statistical Analysis

The data obtained were compiled and analyzed using Statistical Package for the Social Sciences Inc., version 15.0 for Windows. Mean and standard deviations for all parameters were calculated. To compare periodontal parameters of the whole mouth and sampling sites, the Kruskal–Wallis analysis of variance (ANOVA) was used as appropriate. Pair-wise comparisons among the groups were done using Mann–Whitney *U* test. In order to compare the levels of iron and magnesium among the three groups, one-way ANOVA test was used. Since ANOVA test showed significant differences among the study groups ($p < 0.05$), Tukey's multiple *post hoc* test was performed to do pair-wise comparison among the groups. To analyze the correlation between periodontal data and the variables of the levels of iron (µg/dL) and magnesium (mg/dL), Spearman's rank correlation was used.

RESULTS

Periodontal parameters of the study groups were compared in Tables 1 to 3 and the GI, PPD, and CAL scores were found statistically significant ($p < 0.05$), between chronic periodontitis (group II) and chronic periodontitis with hypertension (group III) as compared with the healthy controls (group I). Table 4 demonstrates serum iron levels among the study groups and the results showed that subjects with chronic periodontitis had significantly lower serum iron levels than the healthy control subjects ($p < 0.05$). Significantly low serum magnesium levels were detected in the chronic periodontitis with hypertensive subjects as compared with healthy control subjects ($p < 0.05$, Table 5).

DISCUSSION

Periodontitis is a chronic inflammatory disease leading to elevation of cytokines. The proinflammatory cytokines thus released are thought to act as mediators in suppressing erythropoiesis from bone marrow, thus leading to anemia. The association of anemia and

Table 1: Comparison of three groups (healthy, chronic periodontitis, and chronic periodontitis with hypertension) with respect to GI scores by Kruskal–Wallis ANOVA

Group	*Mean*	*SD*	*Sum of ranks*
Healthy	0.79	0.08	525.00
Chronic periodontitis	1.83	0.53	1759.50
Chronic periodontitis with hypertension	1.90	0.55	1810.50
Total	1.51	0.67	
H-value	58.082		
p-value	0.00001*		
Pair-wise comparisons by Mann–Whitney U test			
Healthy *vs* chronic periodontitis			p = 0.00001*
Healthy *vs* chronic periodontitis with hypertension			p = 0.00001*
Chronic periodontitis *vs* chronic periodontitis with hypertension			p = 0.7062

*p < 0.05; SD: Standard deviation

Table 2: Comparison of three groups (healthy, chronic periodontitis, and chronic periodontitis with hypertension) with respect to PPD scores by Kruskal–Wallis ANOVA

Group	*Mean*	*SD*	*Sum of ranks*
Healthy	0.00	0.00	465.00
Chronic periodontitis	5.53	0.63	1766.00
Chronic periodontitis with hypertension	5.63	0.56	1864.00
Total	3.72	2.69	
H-value	66.2337		
p-value	0.00001*		
Pair-wise comparisons by Mann–Whitney U test			
Healthy *vs* chronic periodontitis			p = 0.00001*
Healthy *vs* chronic periodontitis with hypertension			p = 0.00001*
Chronic periodontitis *vs* chronic periodontitis with hypertension			p = 0.4688

*p < 0.05

Table 3: Comparison of three groups (healthy, chronic periodontitis, and chronic periodontitis with hypertension) with respect to CAL scores by Kruskal–Wallis ANOVA

Group	*Mean*	*SD*	*Sum of ranks*
Healthy	0.00	0.00	465.00
Chronic periodontitis	6.17	0.95	1788.00
Chronic periodontitis with hypertension	6.27	0.87	1842.00
Total	4.14	3.04	
H-value	63.5636		
p-value	0.00001*		
Pair-wise comparisons by Mann–Whitney U test			
Healthy *vs* chronic periodontitis			p = 0.00001*
Healthy *vs* chronic periodontitis with hypertension			p = 0.00001*
Chronic periodontitis *vs* chronic periodontitis with hypertension			p = 0.6897

*p < 0.05

Table 4: Comparison of three groups (healthy, chronic periodontitis, and chronic periodontitis with hypertension) with respect to iron (µg/dL) scores by one-way ANOVA

Group	*Mean*	*SD*
Healthy	76.90	27.03
Chronic periodontitis	59.17	25.64
Chronic periodontitis with hypertension	69.63	17.35
Total	68.57	24.57
F-value	4.2355	
p-value	0.0176*	
Pair-wise comparisons by Tukey's multiple post hoc procedures		
Healthy *vs* chronic periodontitis		p = 0.0133*
Healthy *vs* chronic periodontitis with hypertension		p = 0.4646
Chronic periodontitis *vs* chronic periodontitis with hypertension		p = 0.2078

*p < 0.05

Table 5: Comparison of three groups (healthy, chronic periodontitis, and chronic periodontitis with hypertension) with respect to magnesium (mg/dL) scores by one-way ANOVA

Group	*Mean*	*SD*
Healthy	2.10	0.14
Chronic periodontitis	2.07	0.10
Chronic periodontitis with hypertension	2.01	0.13
Total	2.06	0.13
F-value	3.8248	
p-value	0.0256*	
Pair-wise comparisons by Tukey's multiple post hoc procedures		
Healthy *vs* chronic periodontitis		p = 0.7252
Healthy *vs* chronic periodontitis with hypertension		p = 0.0235*
Chronic periodontitis *vs* chronic periodontitis with hypertension		p = 0.1395

*p < 0.05

periodontitis has been explored since the early 20th century.[12] Chawla et al[13] suggested that anemia is an important factor in the etiology or pathogenesis of periodontal disease. Siegel[14] reported a depression in the number of erythrocytes apparently secondary to the presence of periodontal disease. In the present study, when biochemical parameters were analyzed, the mean serum iron levels in chronic periodontitis (59.17) were found to be significantly reduced as compared with control group (76.90) and slightly increased in patients with chronic periodontitis with hypertension (69.63). This could be due to the increased release of proinflammatory cytokines that have led to an increased uptake of iron by activated macrophages and reticuloendothelial cells, thus causing retention of iron in macrophages by regulating the expression of ferritin, a transmembrane exporter of iron, thus blocking the release of iron from these cells.[14-23] Our results were similar to the study done

by Shetty et al,[24] wherein they proved a strong correlation of vitamin C and iron levels in predicting the development of periodontal disease. Contrasting results were obtained in a study done by Thomas et al[25] where there were significantly increased serum iron levels in chronic periodontitis patients.

Significantly low serum magnesium levels were detected in hypertensive subjects with chronic periodontitis (group III) and chronic periodontitis (group II) as compared with healthy controls. This could be due to periodontal inflammation causing the activation of neutrophils, which invades the periodontal tissues, thereby participating in periodontal destruction.[21] Similar results were reported by Van Laecke et al who reported that serum hypomagnesemia associated with hypertension, endothelial dysfunction, dyslipidemia, and inflammation may affect vascular stiffness in patients who underwent kidney transplantation, since the low serum magnesium was independently associated with pulse wave velocity assessed by SphygmoCor.[26]

An inverse relationship between magnesium and blood pressure is apparent according to various study results. Similar results were also reported in studies conducted by Paolisso et al[27] wherein they found that low serum magnesium levels were found in hypertensive subjects as compared with the normotensive control. The study indicated lowered level of plasma and erythrocytic magnesium in hypertensive than in normotensive subjects.

A nonsignificant increase in serum iron levels of hypertensive patients with chronic periodontitis (group III) as compared with chronic periodontitis (group II) was found. This could be attributed to the fact that high levels of serum iron and low levels of serum magnesium are considered to be major risk factors for hypertensives with periodontitis, leading to oxidative stress and increased cytokine production, thereby causing more destruction and disease progression.

When clinical parameters GI, PPD, and CAL were compared among the study groups, they were found to be significantly higher in study groups as compared with the control group. Further long-term and detailed investigations are necessary to gain insight into the nature of association of micronutrients and their role in the pathogenesis of periodontitis and hypertension.

CONCLUSION

Thus, reduced magnesium concentrations are associated with enhanced inflammatory response to bacterial challenge. Lower serum iron levels can thus reflect signs of anemia. Thus, iron and magnesium do have a link in the pathophysiology of periodontitis and were closely linked to hypertension.

CLINICAL SIGNIFICANCE

Therefore, health care professionals must not only identify and treat patients with chronic inflammatory diseases, but also promote a healthy lifestyle and preventive strategies to decrease the prevalence of such diseases in the general population.

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