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"Effect of Phase I Therapy on Systemic Inflammatory Markers inthe Peripheral Blood in Periodontitis Patients - A Clinico-Biochemical Study."

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Abstract:
AIM- *Effect of Phase I Therapy on Systemic Inflammatory Markers in the Peripheral Blood In Periodontitis Patients*
Materials and Methods:*Thirty subjects of periodontitis were selected from the outpatient department of Peridontics, Kothiwal Dental College & Research Centre.For all the thirty subjects involved, the blood sample was collected at baseline and sent for hematological examination. Clinical parameters were also recorded such as plaque index, gingival index and probing pocket depth. Then scaling and root planing was done. After three weeks, again blood was collected and sent for hematological examination along with clinical parameters were also recorded same as that of baseline. At this phase scaling and root planning was not performed. Then, patient was again recalled at six weeks and blood sample was taken and clinical parameters were recorded.*
Results: *Treatment Procedures resulted into statistically significant reduction into PI (P<0.001), GI (P<0.001), PPD (P<0.001), Serum Albumin (P<0.007), A:G ratio (P<0.001) from baseline. There was significant increase in Peripheral leukocyte numbers (P<0.015), Total Protein (P<0.001), Serum Globulin (P<0.001).*
Conclusions: *Peripheral leukocyte numbers and serum globulin level increases during periodontal inflammation and corresponds with GI and PI.Serum albumin level and albumin:globulin (A/G) ratios gets decreased during periodontal inflammation.There wasreduction in GI, PI and PPD following scaling and root planing causes reduction in peripheral leukocyte number & serum globulin level, while serum albumin level &abumin/globulin ratio gets increased. The periodontal treatment affects the level of peripheral leukocyte number, serum albumin & globulin level & albumin/globulin ratio.*
Keywords:*Periodontitis, Serum Albumin, Serum Globulin*

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I. Introduction

Periodontitis is defined as "an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession or both." It is also a bacterially induced, localized, chronic inflammatory disease, destroys connective tissue and bone that support the teeth. Predominantly anaerobic gram negative bacteria present on the tooth surface as microbial biofilms and other microbial substances gain access to the gingival tissue and initiate and perpetuate an inflammatory reaction, which leads to the destruction of the periodontal ligament and alveolar bone and, finally, to tooth loss.[1, 2]

Periodontitis has even higher prevalence in developing countries and considerable global variation although the prevalence of the severe generalized disease appears to be similar in most populations. Traditional periodontal diagnosis involves measures of probing depth, gingival recession, probing attachment level using graduated periodontal probe. These are indirect measures of bone loss. Unfortunately, the sensitivity of radiographs in detecting an early osseous lesion is poor. Biochemical markers can detect inflammatory changes in short period of time whereas longer period is required to detect measurable changes in bone density using

radiographs. A response of an organism to the periodontal infection includes production of several enzyme families and inflammation markers, which are released from stromal, epithelial, inflammatory or bacterial cells.[1,3]

Ogawa H *et al* carried out a study to identify risk factors for periodontal disease progression by individual characteristics at baseline among elderly people. The subjects above the age group of 70yrs. with good general health were selected. Thorough questionnaire regarding their drinking and smoking habits were obtained. The serum levels of the diseased markers were investigated and attachment levels were clinically recorded. There was a significant decrease in serum albumin level in periodontal disease patients. About 75% of the subjects exhibited additional attachment loss over the period of 2yrs. Serum albumin level increased after the treatment.[4,5,6]

II. Aim And Objective

To evaluate the effect of scaling and root planing on the level of systemic inflammatory markers in the peripheral blood comprising:-

1. Total and differential leukocyte count
2. Serum albumin(ALB), globulin(GLB) and A/G ratio

III. Material And Methods

Having discussed the review of literature and the aim and objective of the present study; the material and method adopted for the purpose of the study are as follows:-

Type of study: Aim of the study was to evaluate the effect of the phase I therapy on systemic inflammatory marker in the peripheral blood in periodontitis patient. Research protocol was submitted to and approved by ethical committee of Kothiwal Dental College and Research Centre (KDCRC), Moradabad, before conducting the study. The patients were selected from the OPD of Department of Periodontics, KDCRC.

Subjects: 30 subjects having periodontitis were selected on the diagnostic criteria of periodontal disease status will be according to the classification developed at the *international workshop for a classification of periodontal disease and conditions* in 1999.

The daily routine, attitude and responsiveness of the selected subjects were evaluated by asking routine questions. The aims and objectives of the study along with duration and method were explained thoroughly. After getting their acceptance to be a part of the study, the details of the consent form were given to read thoroughly. It was explained in Hindi or regional language to the illiterate persons, and their signature or thumb impression along with that of a witness were obtained.

PATIENT SELECTION

INCLUSION CRITERIA

1) Age group above 25 years.
2) Subjects with definite clinical evidence of periodontitis.
3) No periodontal therapy within the previous year.
4) No history of taking antibiotics since the last 3 months.
5) Subjects having a minimum of 20 natural teeth.

EXCLUSION CRITERIA

1) Medically compromised patients (uncontrolled diabetes, bleeding disorder etc.)
2) Mentally disabled and physically handicapped subjects.
3) Smoking.
4) Pregnant women or lactating mothers.
5) Disease severity requiring periodontal therapy other than scaling and root planing.

Clinical Parameters

Before and after the phase I therapy of the selected patients, following parameters were assessed at the interval of 3weeks and 6weeks.

A. Pre operative parameters

1) Plaque Index (Silness and Loe 1964)[7] -

2) Gingival Index (Loe and Silness 1963) [8]-

3) Probing Pocket Depth-

4. Blood Examination

B. Post operative parameters

All the parameters recorded pre-operatively were assessed at 3 weeks and 6 weeks post-operatively.After the collection of the pre and post-operative recordings, the data was subjected to statistical analysis.

Fig: 1 Clinical armamentarium for routine periodontal

Fig: 2 Materials used for hematological examination

Fig: 3 Collection of blood

Fig: 4 Syringe & Needle Destroyer

Fig: 5 Biochemistry analyzer

Periodontal Treatment-

A conventional non-surgical periodontal treatment protocol (scaling and root planing) was designed; oral hygiene instructions were properly explained to the patient.

Statistical Tools Employed-The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

IV. Results

The present study was carried out at Department of Periodontics, Kothiwal Dental College and Research Centre, Moradabad to evaluate the effect of phase Itherapy on systemic inflammatory markers in the peripheral blood in periodontitis patients. A total of thirty patients with definite clinical evidence of periodontitis were enrolled in the study and protocol followed involved baseline, 3 weeks and 6 weeks. The results of the study were statistically analyzed and compared and are presented here in a tabulated form.

Table 1: Demographic characteristic of the patients

Total number of subjects	Sex	Number of subjects	%	Mean Score	SD	p-value
30	M	22	73	40 25-55	9.786	0.65
	F	08	27	34 27-41	8.996	

The present study included thirty patients in which 22 males (73%) and 8 (27%)females, with 25 years being the minimum age of the selected subjects.

Table 2: Comparison of Hematological parameter (Hemoglobin) atBaseline, 3 weeks and 6 weeks

Hemoglobin	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	13.0	1.49	0.73	0.47
Baseline and 6 weeks	13.2	1.37	2.75	0.01*
3 weeks and 6 weeks	13.7	1.08	2.47	0.02*

***0.01 and *0.02-mild significant**

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.47 which was non-significant. But on comparing the parameter at baseline & 6 weeks 'p' value was 0.01 which was mild significant. Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.02 which was again mild significant.

Table 3: Comparison of Hematological parameter(Total Leukocyte Count) at Baseline, 3 weeks, and 6 weeks

Total Leukocyte Count	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	8340.00	1202.22	0.23	0.821
Baseline and 6 weeks	8390.00	1409.25	0.61	0.547
3 weeks and 6 weeks	8183.00	1285.44	0.88	0.386

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.821 which was non-significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.547 which was non-significant. Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.386 which was again non-significant.

Table 4: Comparison of Hematological parameter (Neutrophil) atBaseline, 3 weeks, and 6 weeks

Neutrophil	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	58.4	10.85	1.21	0.236
Baseline and 6 weeks	56.0	16.40	1.21	0.235
3 weeks and 6 weeks	54.8	10.45	0.65	0.523

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.236 which was non-significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.235 which was again non-significant Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.523 which was again non-significant.

Table 5: Comparison of Hematological parameter (Lymphocyte) at Baseline, 3 weeks, and 6 weeks

Lymphocyte	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	36.6	9.53	2.59	0.015*
Baseline and 6 weeks	32.1	14.56	0.77	0.45
3 weeks and 6 weeks	34.6	10.21	1.32	0.196

***0.015-mild significant**

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.015 which was mild significant. But on comparing the parameter at baseline & 6 weeks 'p' value was 0.45 which was non - significant. Again on comparing the parameters at 3 weeks & 6 weeks 'p' value was 0.196 which was again non - significant.

Table 6: Comparison of Hematological parameter (Total Protein) at Baseline, 3 weeks, and 6 weeks

Total Protein	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	7.6	0.76	7.29	<0.001***
Baseline and 6 weeks	6.6	0.62	7.99	<0.001***
3 weeks and 6 weeks	6.7	0.75	0.81	0.425

<0.001* and <0.001***-** Highly Significant

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.001 which was highly significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.001 which was again highly significant. But on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.425 which was non-significant.

Table 7: Comparison of Hematological parameter (Albumin) at Baseline, 3 weeks and 6 weeks

Albumin	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	3.7	0.70	0.58	0.569
Baseline and 6 weeks	3.8	0.76	2.89	0.007***
3 weeks and 6 weeks	4.1	0.51	3.55	0.001***

0.007* and 0.001*** - Highly Significant**

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.569 which was non-significant. But on comparing the parameter at baseline & 6 weeks 'p' value was 0.007 which was highly significant. Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.001 which was again highly significant.

Table 8: Comparison of Hematological parameter (Globulin) at Baseline, 3 weeks and 6 weeks

Globulin	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	3.9	0.96	6.03	<0.001***
Baseline and 6 weeks	2.8	0.67	10.39	<0.001***
3 weeks and 6 weeks	2.6	0.71	1.70	0.101

<0.001* and <0.001***- Highly Significant**

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.001 which was highly significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.001 which was again highly significant. But on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.101 which was non -significant.

Table 9: Comparison of Hematological parameter (A:G Ratio) at Baseline, 3 weeks and 6 weeks.

A:G Ratio	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	1.0	0.47	4.00	<0.001***
Baseline and 6 weeks	1.3	0.45	7.73	<0.001***
3 weeks and 6 weeks	1.6	0.49	3.22	0.003***

<0.001*, <0.001*** and 0.003***-** Highly Significant

On comparing the hematological parameter at baseline & 3 weeks, 'p' value was 0.001 which was highly significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.001 which was highly significant. Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.003 which was again highly significant.

Table 10: Comparison of Clinical parameter (Plaque Index) at Baseline, 3 weeks and 6 weeks

Plaque Index	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	2.2	0.37	17.88	<0.001***
Baseline and 6 weeks	1.0	0.30	31.20	<0.001***
3 weeks and 6 weeks	0.5	0.31	8.86	<0.001***

<0.001*-** Highly Significant

On comparing the clinical parameter at baseline & 3 weeks, 'p' value was 0.001 which was highly significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.001 which was highly significant. Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.001 which was again highly significant.

Table 11: Comparison of Clinical parameter (Gingival Index) atBaseline, 3 weeks and 6 weeks

Gingival Index	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	2.0	0.34	17.05	<0.001***
Baseline and 6 weeks	0.9	0.35	21.66	<0.001***
3 weeks and 6 weeks	0.5	0.31	5.85	<0.001***

<0.001*, <0.001*** and <0.001***-** Highly Significant

On comparing the clinical parameter at baseline & 3 weeks, 'p' value was 0.001 which was highly significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.001 which was highly significant. Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.001 which was again highly significant.

Table 12: Comparison of Clinical parameter (Probing Pocket Depth) at Baseline, 3 weeks and 6 weeks

Probing Pocket Depth	Mean	Std. Deviation	t-value	p-value
Baseline and 3 weeks	3.8	0.60	13.91	<0.001***
Baseline and 6 weeks	2.3	0.68	15.66	<0.001***
3 weeks and 6 weeks	1.8	0.62	3.78	0.001***

<0.001* -** Highly Significant

On comparing the clincal parameter at baseline & 3 weeks, 'p' value was 0.001 which was highly significant. Again on comparing the parameter at baseline & 6 weeks 'p' value was 0.001 which was highly significant. Again on comparing the parameters at 3 weeks & 6 weeks 'P' value was 0.001 which was again highly significant.

V. Discussion

Periodontitis is defined as "an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession or both."

The relationship between periodontal diseases and systemic health has been well recognized through epidemiologic studies. Several studies have shown the systemic effects of periodontal disease. Periodontal infection has been implicated as a risk factor for systemic disease such as coronary heart disease, diabetes etc. Traditionally, an elevation in the number of peripheral leukocytes and a variation in levels of serum proteins like albumin, globulin and other as acute-phase proteins are the characteristic feature of infectious conditions. Changes in blood components may also be detected in patients with periodontitis. Patients with periodontal disease have been found to be associated with increase in peripheral WBC count. Modulation of cellular and protein components may be the link between periodontitis and systemic conditions.[2]

Loos *et al* and others have investigated the blood cell components in patients with localized and generalized periodontitis and found that the number of peripheral WBCs increased with the increasing severity and extent of periodontitis. As expected, the number and percentages of neutrophils in patients with aggressive periodontitis were much higher than in healthy controls. Changes in blood cell variables may be a way that periodontitis affects systemic health.[9]

Hence, the present study was planned to compare and evaluate the effect of phase I therapy on systemic inflammatory marker in the peripheral blood in periodontitis patients. Thirty subjects were taken and blood sample was collected at baseline and sent for hematological examination. Clinical parameters were also recorded such as plaque index, gingival index and probing pocket depth. Then scaling and root planing was done. After three weeks, again blood was collected and sent for hematological examination along with clinical parameters was also recorded same as that of baseline. At this phase scaling and root planning was not performed. Then, patient was again recalled at six weeks and blood sample was taken and clinical parameters were recorded. No treatment was also given at this phase also. So, in this study we found that the peripheral leukocyte numbers and serum globulin level increases during periodontal inflammation and corresponds with GI and PI. Serum albumin level and albumin:globulin ratios gets decreased during periodontal inflammation. These changes might be associated with the severity of periodontal inflammation.Anemia of chronic disease (ACD) has been described in the literature, and seems to be one of the most common forms of anemia observed in clinical medicine. ACD is defined as the anemia occurring in chronic infections, chronic inflammatory processes or tumor formation that is not due to dysfunction of bone marrow cells or other diseases, and occurring despite the presence of adequate iron stores and vitamins.[9,10]

Various studies have tried to evaluate the relationship between periodontitis and hemoglobin. Hutter et al. and Thomas et al. found that periodontitis patients have lower hematocrit, lower numbers of erythrocytes, lower hemoglobin levels and higher erythrocyte sedimentation rates when compared to healthy controls. Rai and Kharb found increased in hemoglobin and RBC levels in patients with severe periodontitis after scaling and root planning. Also, Agarwal et al. demonstrated a significant improvement in hemoglobin value and erythrocyte count after periodontal treatment, including surgery in patient with generalized chronic periodontitis with anemia. On the other hands, Wakai et al. failed to show any association between hemoglobin levels and periodontal status. Furthermore, Havemose-Poulsen et al. failed to show any association between hemoglobin levels and periodontal status in patients with localized aggressive periodontitis, generalized aggressive periodontitis, juvenile idiopathic arthritis, and rheumatoid arthritis.[11,12,7]

In the present study there is no significant association of hemoglobin level at different intervels of time. The change in the hemoglobin and total leukocyte count in this study is not very much significant. The current study also showed a very slight significance($p=0.015$) in leucocyte count because of the inflammatory conditions of the patients at baseline. After giving phase I therapy to the periodontitis patients, it showed a marked decrease in leukocyte count at 3 weeks and 6 weeks. Previous studies suggested that numbers of peripheral WBCs increased with the increasing severity and extent of periodontitis. The leukocyte count has been demonstrated in several epidemiological studies to be an independant predictor of future coronary heart disease (Grimm et al. 1985, Zalokar et al. 1981). The majority of studies have shown a dose-response effect, in so far as increasing levels of leukocyte counts are associated with graded increases in cardiovascular risk (Grimm et al. 1985, Zalokar et al. 1981).

The difference between smoking periodontitis patients and smoking controls was not statistically significant. Wakai et al. (1999) reported an independent association between WBC count and periodontal disease severity defined by the CPITN (communityperiodontal index for treatment needs) after adjustment for smoking and other periodontal risk factors. The only intervention study was published by Christgau et al. (1998) who studied the effect of periodontal therapy in 20 diabetics and 20 non-diabetic controls with periodontal disease. They also reported leukocyte counts in the course of periodontal therapy. Although the differences between pre and post treatment values were not significant, leukocyte counts decreased in both groups after non-surgical periodontal therapy.

Corroborating all the above results, the study indicates that during inflammation of the peridontium there is significant increase in peripheral leukocyte count, serum globulin along with PI, GI and PPD. But, there is significant decrease in Serum albumin level and albumin/globulin ratios during active inflammatory process. After scaling and root planing, there is highly significant difference in both the hematological parameters and clinical parameters. These changes might be associated with the severity of periodontal destruction. So, it can be stated that Serum Albumin and serum Globulin is a marker of acute phase changes in periodontal status.

VI. Conclusion

From this study the following conclusions are drawn:-

1. Peripheral leukocyte numbers and serum globulin level increases during periodontal inflammation and corresponds with GI and PI.
2. Serum albumin level and albumin/globulin ratios gets decreased during periodontal inflammation. These changes might be associated with the severity of periodontal instructions.
3. Reduction in GI, PI and PPD following scaling and root planingcauses reduction in peripheral leukocyte number & serum globulin level, while serum albumin level &abumin/globulin ratio gets increased.

4. Periodontal treatment affects the level of peripheral leukocyte number, serum albumin & globulin level & albumin/globulin ratio.

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