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Comparative Evaluation of Levels of C-Reactive Protein in Patients with Chronic Obstructive Pulmonary Disease (COPD) and Chronic Periodontitis

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Abstract

Background: Periodontitis is a chronic inflammatory reaction to a specific group of bacteria that results in destruction of supporting connective tissue and bone of the dentition. An interrelationship between periodontal disease and systemic health has been suspected for centuries. Recent evidence suggests that periodontitis may significantly affect systemic health conditions such as cardiovascular disease, cerebrovascular disease, diabetes, respiratory diseases and adverse pregnancy outcomes. *Objective*: To find out the relation between chronic periodontitis and COPD using serum CRP as a potential marker. *Methods*: Thirty patients aged between 30–60 years were selected. Patients were divided into two groups, Group A comprised of 15 patients diagnosed as COPD with chronic periodontitis and Group B comprised of 15 patients diagnosed as chronic periodontitis only. *Results*: In this study C-reactive protein levels are significantly increased in both the groups. In group A, (patients with COPD with chronic periodontitis) the CRP levels were 4 times more than in group B (patients with Chronic periodontitis). The parameters evaluating gingival status revealed that GI, PBI and PI scores were highly significant in group B. *Conclusion*: Periodontitis may add to the inflammatory burden of the individual and could contribute at least in part to the increased risk for COPD associated with elevated CRP levels in these patients based on serum CRP levels.

Keywords: C-Reactive Protein; COPD; Chronic Periodontitis; Gingival Index; Papilla Bleeding Index; Periodontal Index.

Introduction

Periodontitis is a chronic inflammatory reaction to a specific group of bacteria that results in destruction of supporting connective tissue and bone of the dentition [1]. Bacterial plaque is the essential etiologic factor responsible for inducing host inflammatory response in periodontal disease. Thus patients suffering from severe periodontitis have increased local production of inflammatory cytokines (IL1b, TNF and IL6) and moderate systemic inflammatory response [2].

An interrelationship between periodontal disease and systemic health has been suspected for centuries. Recent evidence suggests that periodontitis may significantly affect systemic health conditions such as cardiovascular disease, cerebrovascular disease, diabetes, respiratory diseases and adverse pregnancy outcomes. Periodontal disease may be linked to systemic inflammation through two mechanisms. One pathway of model proposes that periodontal disease occurs as a joint response to local pathogens and to an underlying hyper-inflammatory trait which also causes elevation of systemic inflammatory mediators. However an additional synergistic mechanism is proposed in which local periodontal infection creates an elevated systemic inflammatory response [3].

Chronic obstructive periodontal disease (COPD), characterized by chronic blockage in airflow and breathing related problems includes two lung diseases, chronic bronchitis and emphysema [4]. It is possible that teeth and the surrounding tissues can serve as a reservoir for respiratory infection via dental plaque. Gingival crevicular fluid contains important bioactive molecules, such as enzymes and cytokines which may enter saliva and be aspirated, thus modulating the respiratory environment. Mojon suggests that periodontal disease and COPD may be

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related to inflammatory response to bacterial challenge [1].

In individuals with periodontitis, bacteria present in the gingival sulcus or the subsequently formed periodontal pockets, may have easy access to the blood vessels. The microorganisms may also enter the lungs by aspiration. Thus the oral microorganisms might infect the respiratory tract, causing COPD [5].

Localized infection resulting in increased inflammation and tissue loss in periodontium elicit systemic host changes manifested by increase in acute phase reactants. C-reactive protein is a strong, type-1 acute phase protein synthesized by hepatocytes which reflects a measure of acute phase response[4]. It shows the total systemic inflammation, Cardiovascular disorders, COPD, Acute myocardial infarction, Rheumatoid arthritis, Viral infections and Malignancies [5]. Chronic periodontitis has been shown to raise inflammatory markers such as CRP in blood which is also increased in patients with COPD [7].

Therefore, an attempt has been made to find out the relation between chronic periodontitis and COPD using serum CRP as a potential marker.

Materials and Methods

Patient Selection

Thirty patients aged between 30–60 years were selected on purposive selection criteria from the Outpatient Department of General Medicine, Basaveshwar general hospital Gulbarga. Patients were divided into two groups comprised of age- and gender-matched individuals. Group A comprised of 15 patients diagnosed as COPD with chronic periodontitis and Group B comprised of 15 patients diagnosed as chronic periodontitis only.

Group allocation

Group A: 15 patients diagnosed as COPD by the physician, dentate patients.

Group B: 15 patients with chronic periodontitis without respiratory diseases, dentate patients

Exclusion criteria

Group A: Edentulous patients, patients undergone periodontal therapy for last 3 months, Patients on medications (antibiotics) known to influence the periodontal tissues for last 6–8 weeks and patients with any other systemic diseases.

Group B: Edentulous patients, patients were undergone periodontal therapy for last 3 months, Patients on medications (antibiotics) known to influence the periodontal tissues for last 6–8 weeks.

Experimental Design

All 30 patients of groups A and B were examined for gingival and periodontal status by recording the following indices:

1. Gingival Index (GI) (Loe and sillness)
2. Papilla Bleeding Index (PBI) (Muhlemann's)
3. Periodontal Index (PI) (Russell's)

C-reactive protein

Sample collection: 5 ml of venous blood was collected and transferred to a sterilized test tube without anticoagulant. C-reactive protein is estimated using CRP test kit by slide agglutination method.

Procedure: Test serum has to be undiluted. Using the disposable plastic dropper, place one drop of test serum within circled area on the special slide provided in kit. Add one drop of Latex CRP reagent to above drop and mix well with applicator stick and spread out to edge of test area. Rock the slide to and fro for 2 minutes and examine for macroscopic agglutination under direct light source.

Statistical Analysis

To evaluate any differences between the Group A and Group B student's t test is done using STHS software. The values of different parameters collected are expressed as means + SD. *P* values ($p < 0.05$) were considered statistically significant.

Results

In this study C-reactive protein levels are significantly increased in both the groups. On comparison, Group A and Group B showed statistically significant difference in CRP values (p value 0.05). In group A, (patients with COPD with chronic periodontitis) the CRP levels were 4 times more than in group B (patients with Chronic periodontitis). All the clinical parameters such as GI, PBD and PD values were highly significant in Group A (patients with COPD with chronic periodontitis) when compared to Group B (patients with Chronic periodontitis) (Table II).Mean values of CRP in group A(34.00) in group B(8.33) mean

value of GI in group A (2.41) in group B(2.11), mean value of PBI in group A (2.80) in group B (2.40), and PI group A(2.71) and in group B (2.09) was found.(Table I, Figure.1).

Table 1: Means and Standard Devition (Sd) of C - Reactive Protein Level and Clinical Parameters Between Chronic Obstractive Pulmonary Disease and Chronic Periodonlitis

	Chronic Obstractive Pulmonary Disease				Chronic Periodonlitis			
	Crp	Gingival Index	Papillary Bleeding Index	Periodontal Index	Crp	Gingival Index	Papillary Bleeding Index	Periodontal Index
Mean	34.00	2.41	2.80	2.71	8.33	2.11	2.40	2.09
Sd	15.75	0.27	0.40	0.54	5.83	2.47	2.37	2.64

Table 2: Comparsion Between Chronic Obstractive Pulmonary Disease and Chronic Periodonlitis With Student 'S T Test

T Value	5.83	2.47	2.37	2.64

Conclusion: All T Values (> 2.048 For P=0.05) Shows Significate Difference Between Chronic Obstractive Pulmonary Disease and Chronic Periodonlitis

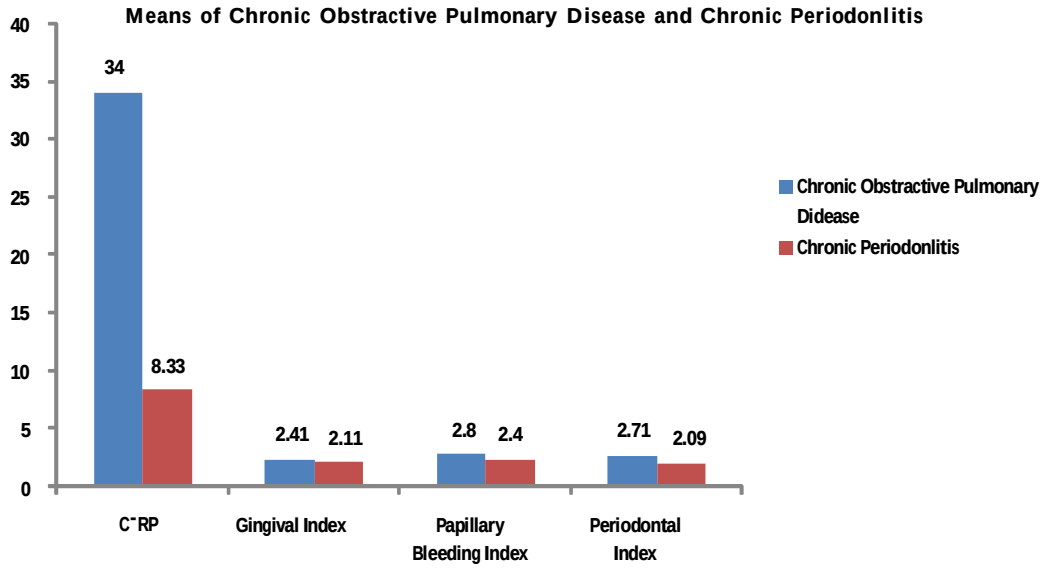

Fig. 1: Comparsion between Chronic Obstractive Pulmonary Disease and Chronic Periodonlitis

Discussion

Several possible mechanisms have been proposed to explain the potential link between periodontal disease and respiratory function. Periodontal disease is a chronic bacterial infection which may provide a direct source of aspirated bacterial organisms that may lead to progression and exacerbation of respiratory disease. These bacteria of oral origin may stimulate the respiratory tissues, resulting in inflammatory response associated with obstructive pulmonary disease [1].

COPD is characterized by chronic blockage in the airflow and difficulty in breathing and includes chronic bronchitis, emphysema and sometimes asthma [11]. The main etiological factor is tobacco smoking but bacteria may play a key role in the progression of the disease. Genetic factors have also been strongly implicated in the pathogenesis [12]. A possible association between COPD and periodontitis has been identified. Oral cavity being continuous with the trachea serves as a possible portal entry for the colonisation of respiratory pathogens in to the lower respiratory tract as a result of oropharyngeal aspiration [13].

Scannapeico in 1999 described four modes by which oral pathogens play a role in the pathogenesis of respiratory infections. Oral pathogens such as P ginivalis and Aggregaribacter actinomy cetemcomitans are aspirated into the lungs elevated levels of proteolytic bacteria such as P.gingivalis and

spirochetes, protease activity may alter the mucosal epithelium to increase the adhesion and colonisation of respiratory pathogens. Another mechanism is by the destruction of protective salivary pellicles by oral bacteria. Thus an increased microbial load may result in elevated levels of salivary hydrolytic enzymes , which in turn destroy protective barriers. This diminishes the non specific host defence against respiratory pathogens in high risk subjects. Lastly the epithelial cells are also known to alter the expression of various cell adhesion molecules on their surface in response to cytokine stimulation. Variation in expression of such adhesion molecules may alter the interaction of bacterial pathogens with the mucosal surface [13].

A variety of oral anaerobes and facultative species have been cultured from the infected lungs such as Pgingivalis, Fusobacterium nucleatum, Fusobacterium necrophorum, Bacteriodes oralis, Aggregatibacter actinomycetemcomitans [14, 15] that can cause both periodontal disease and respiratory infection [16]. A study done by Ana Pejcic et-al showed that periodontitis and subgingival periodontopathogens are associated with increased CRP levels [6]. Noack B. et al showed that periodontitis and subgingival periodontopathogens are associated with increased CRP levels, the presence of periodontal pathogens P.g., P.i., C.r., and B.f. in subgingival samples was positively associated with elevated CRP levels (P= 0.029) [8]. These findings suggest that periodontal infection may contribute to systemic inflammatory burden.

In this study C-reactive protein levels are significantly increased in both COPD patients and chronic periodontitis patients. In COPD patients with chronic periodontitis CRP levels were 4 times more than in chronic periodontitis patients. Evaluation of gingival status parameters revealed that GI, PBI and PI scores were highly significant in COPD patients with chronic periodontitis than in patients with chronic periodontitis without COPD. Periodontal disease may also lead to transient increase in circulating levels of IL-1, TNF-alpha and Prostaglandin E_2. This may be first step in contribution of periodontal diseases to systemic inflammation [3].

In our study the levels of CRP in group A (COPD patients with chronic periodontitis) were 4 times more than in group B (patients with Chronic periodontitis), which is similar to the study conducted by Pinto-Plata et al, which showed that there was significantly higher level of CRP in COPD patients (50.03+1.51mg/L) rather than smoking (2.02mg/L) and non-smoking (2.24mg/L) control group [9]. Scannapieco and Genco, in their study suggested that poor oral hygiene and periodontal attachment loss is an independent risk factor for COPD. These results also positively correlate with results obtained by Scannapieco and Ho and Xiaojing et al. Their study also proved that more severe the mean attachment loss, greater is association with COPD [10]. In this study evaluation of gingival status parameters revealed that GI, PBI and PI scores were highly significant in COPD patients with chronic periodontitis than in patients with chronic periodontitis [9].

Cardiovascular disease is one of most common cause of mortality in all stages of COPD patients. COPD patients without cardiovascular disease are at risk of future events and CRP may help predicting them. In this study mean CRP levels in COPD patients is 34mg/L. It has been understood that Poor oral health (periodontitis) alone is not responsible for COPD, Rather poor oral health may work as an adjunct with other factors (such as continued smoking, environmental pollutants, viral infections, allergies and/or genetic factors) to promote the progression and/or exacerbation of COPD [5]. However, yet there is no direct evidence for causal relationship between periodontal diseases and respiratory disease. In contrast, there is extensive evidence available indicating that a greater burden of oral infections in a particular susceptible host may increase the risk for nosocomial pneumonia and for exacerabation of COPD [4].

Thus it can be concluded that periodontitis may add to the inflammatory burden of the individual and could contribute at least in part to the increased risk for COPD associated with elevated CRP levels in these patients based on serum CRP levels.

Limitations

Lack of healthy control group and small sample size limited the statistical analysis of the study. Also, microbial assay was not performed; so the effect of bacterial endotoxins on cytokine mediated CRP production could not be assessed.

Conclusion

From the analysis of the results, and within the limitations of the study, it can be concluded that chronic periodontitis patients, both with and without COPD, showed significantly greater serum CRP levels. Chronic periodontitis group with COPD showed almost double fold increase in serum CRP

levels compared to chronic periodontitis group. Chronic periodontitis can be considered a significant risk factor for developing COPD. Further longitudinal and interventional molecular biologic studies are required to establish the role of chronic periodontitis in the causation and progression of COPD.

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