Comparative Analysis of Salivary Sialic Acid Levels in Patients with Chronic Obstructive Pulmonary Disease and Chronic Periodontitis Patients: A Biochemical Study

Abstract

Aim: Sialic acid plays a central role in the functioning of biological systems, in stabilizing the glycoproteins and cellular membranes, assisting in cell–cell recognition and interaction. The aim of this study is to evaluate and compare the periodontal health status and salivary Sialic acid levels in patients suffering from chronic obstructive pulmonary diseases (COPD) and chronic periodontitis patients. Materials and Methods: Ninety subjects were included in the study, which were divided into the following groups, 30 in each group. Group 1: patients suffering from COPD and chronic periodontitis, Group 2: periodontitis patients without any systemic diseases Group 3: healthy subjects. Unstimulated whole saliva samples were collected around 9–10 AM; 2 h after the subjects had breakfast. The sialic acid content was determined by a combined modification of the thiobarbituric acid method of Skoza and Mohos. Results: The mean salivary sialic acid levels were least in the healthy group followed by the periodontitis group, and it was highest in the COPD group. Conclusions: We can thus conclude that promotion of dental care knowledge is very much essential in the prevention and treatment of COPD. Thus, estimation of levels of salivary sialic acid can be used as an adjunct to diagnose the current periodontal disease status and to assess the treatment outcomes in subjects with COPD and chronic periodontitis.

Keywords: Chronic obstructive pulmonary disease, periodontitis, sialic acid

Introduction

A connection between the mouth and the rest of the body first appeared in the medical literature since more than a century. According to William Hunter, there was notion of oral sepsis then termed as the “focus of infection” was extensively debated among the dentist and the physician. Numerous diseases with unknown etiology were thought to be causally linked to common oral infection such as dental caries and pyorrhea (periodontal disease). Focal infection theory fell in disrepute as it was found that the extraction failed to eliminate or reduce the systemic disease to which the infected teeth were linked. However, recent evidence-based literature again strongly suggests that oral health is indicative of systemic health supporting the association between periodontal disease and systemic conditions.

A significant association between periodontal disease and chronic obstructive pulmonary disease (COPD), diabetes, preterm low birth weight and osteoporosis has been found, thus bridging the wide gap between medicine and dentistry. In the United States, COPD accounts for a morbidity of 4% and is listed as the fourth leading cause of death. Globally, COPD by 2020, is expected to rise to 3rd position as a cause of death and to 5th position as the cause of loss of disability-adjusted life years according to the baseline projections made in global burden of disease study.

In recent years, periodontal disease has been linked to a number of systemic health outcomes including chronic obstructive pulmonary disease. There are various hypotheses that have been formulated to test possible biological mechanisms linking disease and systemic health outcomes. Periodontitis is implicated as an important risk factor for development and progression of COPD. A number of recent microbiologic and epidemiologic studies have been suggested a relationship between the poor periodontal health and respiratory disease, especially in high-risk subjects.

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How to cite this article: Rathod S, Shori T, Sarda TS, Raj A, Jadhav P. Comparative analysis of salivary sialic acid levels in patients with chronic obstructive pulmonary disease and chronic periodontitis patients: A biochemical study. Indian J Dent Res 2018;29:22-5.
Authors have suggested an association between the poor oral health and COPD after adjusting other confounding variables such as smoking, gender, age, and sex.\[^4\]

In the literature, there is very little data regarding estimation and comparison of total sialic acid content in saliva of subjects with COPD and chronic periodontitis patients. Sialic acid is a biomarker for periodontal diseases. The present study was therefore undertaken to evaluate and compare the periodontal health status and salivary sialic acid levels in patients suffering from COPD and chronic periodontitis.

**Materials and Methods**

The study was approved by the Institution’s Ethical Committee, and a written informed consent was obtained from those who agreed to participate voluntarily.

**Patient selection**

A total of 90 subjects both smokers and nonsmokers in the age range 35–65 years were categorised into three groups with 30 subjects each.

- **Group 1:** Chronic periodontitis patients suffering from COPD
- **Group 2:** Chronic periodontitis patients without any systemic diseases
- **Group 3:** Healthy subjects.

Group 1 included 30 patients (15 males and 15 females; 15 smokers and 15 nonsmokers) previously diagnosed with COPD by chest physicians at NKP SIMS Hospital, Nagpur, followed by subsequent screening for chronic periodontitis at VSPM Dental College, Nagpur. Group 2 included systemically healthy subjects (15 males and 15 females; 13 smokers and 17 nonsmokers) suffering from chronic periodontitis with at least 20 teeth in the oral cavity having 6 sites with probing pocket depth (PPD) ≥5 mm. Group 3 included periodontally and systemically healthy subjects. (13 males and 17 females; 13 smokers and 17 nonsmokers).

**Exclusion criteria**

- Any other systemic diseases except COPD
- History of periodontal debridement or periodontal surgery in preceding 6 months
- Pregnant women and lactating mothers.

**Clinical parameters**

Clinical measurements such as PPD, clinical attachment level (CAL), gingival index (GI) (Loe and Silness, 1963), oral hygiene index-simplified (OHI-S) (John C Greene and Jack Vermillon, 1964) were recorded for all subjects. All clinical measurements were performed by a single examiner using William’s graduated periodontal probe.

**Sample collection and chemical analysis**

A volume of 3 ml of unstimulated whole saliva samples was collected by spitting method from all participants between 9 AM and 11 AM. The samples were then centrifuged for 10 min at 800 g to obtain a clear supernatant fluid, which was assayed immediately. The remaining sediment was washed with saline (0.9%, pH 5.5) and further centrifuged at 4°C, 11000 g for 3 min. The saline supernatant fraction was discarded, and the wash procedure was repeated. Sialic acid content was determined by a combined modification of the thiobarbituric acid method of Skoza and Mohos.

**Statistical analysis**

Statistical analysis was carried out using EPI info software. The analysis of variance test was applied to compare between the three groups. Values were expressed as mean along with the standard deviation. \(P < 0.001\) was considered as statistically significant.

**Results**

In Group 1 (mean age of 38.77 years) OHI-S was 2.84, GI was 2.63, PPD was 6.47 mm, and CAL was 7.12 mm and mean sialic acid levels were 2.41 μg. In Group 2 (mean age of 40.13 years) mean PPD was 5.57 mm, mean CAL was 6.07 mm, mean OHI-S was 2.05, mean GI was 2.03, and salivary sialic acid level was 1.70 μg. The healthy group (mean age of 33.07 years) mean PPD was 2.49 mm, mean OHI-S was 1.30, and mean sialic acid levels was 0.77 μg [Table 1]. CAL and sialic acid levels were compared in all the three groups [Graphs 1 and 2].

**Discussion**

These oral flora has been implicated in causing pulmonary diseases. These microflora release certain bacterial enzymes which are responsible for damaging the epithelial cell surfaces. This subsequently increases susceptibility to colonization by pathogenic bacteria. Certain protective proteins are released by the host cells that inhibit the adherence to other epithelial cells and promote their elimination from the host. Enzymes from oral bacteria can modify these protective proteins and prevent them from binding to invading pathogens.\[^5\]

**Table 1: Distribution of various demographic variables and levels of salivary sialic acid in the three groups**

| Age (years) | Sex (male; female) | Smoker | PPD (mm) | CAL (mm) | OHI-S | GI | Sialic acid levels |
|-------------|--------------------|--------|----------|----------|-------|----|------------------|
| Healthy     | 33.07  13; 17       | 13     | 2.49±0.72| 0        | 1.30±0.39 | 0  | 0.77±0.34        |
| Periodontitis| 40.13  15; 15       | 13     | 5.57±1.71| 6.07±2.14| 2.05±0.49 | 2.03±0.48 | 1.70±0.46        |
| COPD        | 38.77  15; 15       | 15     | 6.47±0.77| 7.12±0.56| 2.84±0.15 | 2.63±0.28 | 2.41±0.47        |

COPD=Chronic obstructive pulmonary diseases, PPD=Probing pocket depth, CAL=Clinical attachment level, OHI-S=Oral hygiene index-simplified, GI=Gingival index
Cytokines may contribute to colonization of the respiratory epithelium. Contamination of the respiratory epithelium by orally released cytokines, or release of cytokines by the respiratory epithelium itself in response to contact with oral bacteria, may promote respiratory infection. In the United States, COPD affects 14 million people, and in 1991, it was the fourth leading cause of death, a number that has been increasing over recent years. The main etiological factor is tobacco smoking, but bacteria (including oral bacteria) may play an important role in progression of the disease. Genuit et al. in a prospective study on 95 Intensive Care Unit patients, evaluated the role of CHX oral rinse along with ventricular weaning protocol on reduction and delay in occurrence of pneumonia.

Our study was conducted with an aim to evaluate and compare the periodontal health status and salivary sialic acid levels in patients suffering from COPD and chronic periodontitis. We found that patients with COPD had a mean probing depth of 6.47 mm and a mean clinical attachment level of 7.12 mm which was found to be in accordance with a similar study conducted by Scannapieco and Ho. Scannapieco et al. in his previous research had failed to draw any evidence to support an association between acute respiratory diseases and poor oral health in the adult U. S. population. In a recent analysis based on a more detailed survey, Scannapieco and Ho found a significant association between COPD and periodontal attachment loss. The likelihood of COPD increased with severity of attachment loss, and lung function appeared to diminish as the amount of attachment loss increased.

In a longitudinal study, alveolar bone loss was measured with periapical radiographs at baseline and up to 25 years later in 1,118 healthy men (about 45 years old). About a quarter of the subjects developed COPD over the subsequent 25 years, and these had greater bone loss at baseline.

Amina et al. compared the periodontal health status of healthy individuals with COPD patients and concluded that poor oral health may work in concert with other factors such as continued smoking, environmental pollutants, viral infections, and allergy, which are also thought to be responsible for COPD. Ide et al. found that scaling and root planing alone is insufficient to reduce the levels of circulating sialic acid. They further pointed out the need for more extensive periodontal therapeutic modalities.

In a study performed by Hasan et al., lipid-associated sialic acid (LASA) levels have been reported to be a useful in monitoring patients having inflammatory diseases. Jawazaly et al., in a study of monitoring periodontitis disease, found that LASA levels were also elevated as periodontitis advanced. In our study, we have evaluated the GI and also the sialic acid levels in periodontitis group and COPD group. The mean GI was 2.03 (standard deviation 0.48) and 2.63 (standard deviation 0.80). The mean salivary sialic acid level for periodontitis group was 1.70 (standard deviation 0.46) and 2.41 (standard deviation 0.47), and it was 0.77 (standard deviation 0.34) in the healthy group, showing an increase in the sialic acid levels in the periodontitis and COPD patients as compared to the healthy controls. There is an elevation in salivary LASA concentration of periodontitis compared with that of control so that it can be used as a useful parameter in distinguishing between healthy individuals and patients. Such elevation in LASA concentration can be explained to be due to the damage occurs in collagen contents.

Oktay et al. conducted a study to investigate the changes in serum total sialic acid (sTSA) and TSA levels in saliva in patients having both periodontitis and cardiovascular disease (CVD) versus periodontitis patients without diagnosed CVD. The study group consisted of 26 patients with proven periodontitis and 26 controls with no diagnosed systemic disease but periodontitis. sTSA and saliva TSA levels were determined by the thiobarbituric acid method, and C-reactive protein (CRP) was evaluated by the nephelometric method. The severity of periodontitis has been determined by the community periodontal index of treatment needs (CPITN). TSA in blood and saliva and CRP levels in blood were significantly increased in...
CVD patients compared with the control group. CPITN ranged from 2 to 4 in both groups. Significant and positive correlations were found between sTSA and saliva SA levels in patients and controls and between tooth loss and TSA both in blood and saliva. Therefore, TSA in saliva may be a useful marker similar to sTSA in CVD patients.\[11\]

Rathod et al. suggested that salivary and serum TSA levels can differentiate between periodontal disease and normal condition.\[12\]

**Conclusions**

After adjusting for confounding factors such as smoking, it can be concluded periodontal disease is a contributing factor for systemic disease. Thus, the relationship of COPD, as well as chronic periodontitis with sialic acid levels, has been well established. Further, there is a need for long-term evaluation which may be carried out including more subjects and parameters to further validate the results of the present study and confirm that periodontal disease is a true factor for systemic disease and that initiation or progression of these medical conditions can be reduced by periodontal treatment.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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