

Obstructive Sleep Apnea and Periodontal Disease: Review of Established Relationships and Systematic Review of the Literature

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Introduction

Periodontal diseases are caused by pathogenic bacteria locally colonized in the dental biofilm creating infection and subsequent inflammatory response in the supporting structures of the teeth and tissues at the gingiva. That bacterial proliferation leads to periodontal attachment loss, alveolar bone loss, and ultimately tooth loss [1]. Inflammatory and immune responses are key to the periodontal disease process; many studies have shown relationships between periodontal disease and systemic conditions like diabetes [2,3] or cardiovascular disease [4]. Established risk factors for periodontal disease include dental plaque, calculus, smoking, and some specific bacterial pathogens such as *Actinobacillusactinomycetemcomitans*, *P.gingivalis* and *B.forsythus*.

Obstructive sleep apnea is episodic collapse of the upper airway during sleep by cessation or reduction of airflow that causes intermittent hypoxia and fragmented sleep, and this itself can be a risk factor for many systemic diseases like stroke, coronary heart disease, and Type II diabetes. The causes for obstructive sleep apnea are not totally elucidated but one of the established contributory factors is obesity. Presence of obesity has been associated with obstructive sleep apnea in sixty to ninety percent of cases since the earliest investigations of the syndrome in the middle of the last century [5-7]. As rates of global obesity continue to consistently increase, the incidence of obstructive sleep apnea may likely rise also. The relationship between periodontal disease and systemic disease has been studied widely, and many studies have shown greater prevalence of periodontitis in patients with diabetes, cardiovascular disease, rheumatoid arthritis, and osteoporosis [2,3]. The relationship between periodontal disease and obstructive sleep apnea had gone uninvestigated until Gunaratnam et al. [8,9]. Evidence exists that systemic inflammation from sleep apnea might be one major mechanism (other than hypertension) which causes vascular morbidities associated with obstructive sleep apnea [8,10]. Research indicates that patients with sleep apnea have increased plasma markers of systemic inflammation and increased levels of circulating cytokines of the kind seen in obesity [8,11]. It is this inflammatory response which might potentiate disease in individuals who already have inflammatory disease. Gunaratnam and colleagues hypothesized that both periodontitis and obstructive sleep apnea are associated with systemic inflammation and cardiovascular disease, and found the prevalence of periodontal disease four times higher than national (Australian) averages among people with obstructive sleep apnea [8]. Gunaratnam and colleagues hypothesized that the presence of obstructive sleep apnea was linked to increased risk of periodontal disease because sleep apnea is associated with an elevated inflammatory response, and suggested but left unexplored the role of the mouth breathing that accompanies obstructive sleep apnea in elevating those levels of systemic inflammatory cytokines. Much research [10,11], including pharmaceutical research investigating medications that cause xerostomia [12,13], suggest that whether systemic or medication-induced, patients with xerostomia face increased risk of caries and tooth decay, and oral infections such as candidiasis or those that lead to periodontal disease and eventual tooth loss.

In this review we describe the common processes involved in periodontal disease and obstructive sleep apnea and investigate the literature correlating gingival and periodontal health, salivary flow, and the bacterial composition of saliva relating to the development of periodontal disease.

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Periodontal disease

Periodontal disease is multifactorial and at the same time one of the most common chronic adult diseases. Manifestations of periodontal disease range from gingivitis to chronic periodontal disease. Periodontal disease is characterized by chronic inflammation of the gingiva caused by bacteria and plaque formation. The disease state stems from infection and inflammation that is the result of the activity of pathogenic bacteria. Among these bacterial pathogens are *Actinobacillusactinomycetemcomitans*, a microaerophilic species, and *Porphyromonasgingivalis*, and *Bacteroidesforsythus*, two anaerobic species [14].

Periodontitis is caused by pathogenic bacteria that effect an inflammatory response on periodontal tissues. This inflammation can result in destruction of tooth-supporting tissues, loss of periodontal attachment, pocket formation, loss of alveolar bone and eventual tooth loss [15]. Prevalence of periodontal disease increases with age and is greater in males [16]. Also associations have been established between periodontal disease and obesity and ethnicity [16].

The relationship between periodontal disease and systemic disease has been investigated with conflicting results. Periodontal disease may be associated to diabetes, cardiovascular disease and osteoporosis. Periodontal disease may contribute to systemic inflammatory disease by increasing the production of inflammatory mediators [17]. Since obstructive sleep apnea and periodontal disease are common disorders and both are associated with systemic inflammation, we questioned whether they may be associated.

Saliva and pathogenic organisms

Saliva is an important regulator of oral microbial flora. Salivary flow changes with the time of day. The flow is greater during waking hours because of the stimulus of food. It appears that the saliva at night is different from day-time salivary flow [18].

Saliva acts as a culture medium for the oral micro-organisms and regulates the oral microbiota. Salivary minerals influence the microbiota through pH buffering capacity and as co-factors for enzymes. During the day saliva lubricates the oral tissues, helps swallowing and digestion and protects oral tissues and the dentition. During sleep, physiologic activities including saliva production decrease. Seventy-four percent of patients who snore or have obstructive sleep apnea (OSA) have reported dry mouth [19]. Persistent dry mouth has the potential to increase individual susceptibility to caries or periodontal disease. Usually obstructive sleep apnea and its associated snoring are treated with either continuous positive airway pressure (CPAP) devices or mandibular advancement splints or devices (MAD) which present roughly similar success in lowering blood pressure, decreasing daytime sleepiness, or improving general quality of life. One of the side-effects of the use of these devices is oral and nasal dryness [20,21].

Obstructive sleep apnea

Obstructive sleep apnea is a condition of repetitive episodes of partial or complete upper airway obstruction during sleep, resulting in apnea (complete cessation of breathing) or hypopnea

(partial airflow) leading to hypoxia. Symptoms of obstructive sleep apnea include morning headache, daytime sleepiness, snoring, and breathing pauses during sleep [22].

The Wisconsin Sleep Cohort Study is the first research to report the prevalence of obstructive sleep apnea [23]. Prevalence of obstructive sleep apnea (defined as Apnea-Hypopnea Index (AHI) ≥ 5) in that study was 24 percent in men and nine percent in women. Summarizing data in recent studies, prevalence of obstructive sleep apnea (AHI ≥ 5) ranged 17 to 27 percent in men and from three to twenty-eight percent in women. Varying estimates of prevalence could be due to differences in methodology or other factors like disparate populations, health status or age [23]. Generally obstructive sleep apnea is more prevalent among men than women [23].

Risk factors for obstructive sleep apnea include age, gender, obesity, genetics, ethnicity, nasal obstruction, craniofacial anatomy, increased alcohol consumption and possibly periodontal disease. Obstructive sleep apnea is highly prevalent among obese and overweight people. The Wisconsin Sleep Cohort Study showed a ten-percent weight gain in patients without obstructive sleep apnea was associated with a six-fold increase in the risk of developing moderate to severe obstructive sleep apnea (AHI ≥ 15). Ten-percent weight gain among individuals already diagnosed with obstructive sleep apnea resulted in 30 percent deteriorating of the condition; the reverse was true for ten-percent weight loss among sufferers [23].

Risk factors for obstructive sleep apnea are similar to the risk factors for periodontal disease. Obstructive sleep apnea like periodontitis is linked to systemic conditions such as metabolic syndrome including obesity and diabetes mellitus and cardiovascular complications including hypertension, congestive heart failure and stroke.

Obstructive Sleep Apnea and periodontal disease

Periodontal disease is a chronic inflammatory disease, its prevalence increasing with age. Risk factors for periodontal disease are age, smoking, obesity and socioeconomic factors. Recently periodontal disease has received increasing attention because it may have relationship to systemic disease like diabetes, coronary disease, osteoporosis, low birth weight deliveries, and other systemic diseases. Obstructive sleep apnea is another one of these conditions associated with an inflammatory response [24].

The presence of obstructive sleep apnea is determined by the Apnea-Hypopnea Index (AHI). An AHI ≥ 5 is indicative of the presence of obstructive sleep apnea. Obstructive sleep apnea is a common disorder in which recurrent collapse of the upper airway during sleep results in intermittent hypoxemia and sleep fragmentation. Additional symptoms of obstructive sleep apnea are chronic and loud snoring, mouth breathing and interrupted sleep. Some studies have shown that obstructive sleep apnea increased levels of systemic inflammation and could be associated with stroke, cardiovascular disease and diabetes [23].

Risk factors for periodontal disease [16] include age, smoking, drinking, obesity and diabetes, and both periodontal disease and obstructive sleep apnea are associated with systemic inflammation. The etiology of systemic inflammation and obstructive sleep apnea is not clear but may be related to inflammation in the oral cavity and periodontal disease.

Systematic review of the literature, periodontitis related to obstructive sleep apnea

OVID MEDLINE™ search of the literature on periodontal disease and obstructive sleep apnea [from 1946, conducted December 2013, only articles in English reviewed] yielded only fourteen articles regarding the subject.

In a research from the Korean Genome and Epidemiology Study (2009-2010), Seo et al. [25] conducted a cross-sectional study of 687 subjects (460 men/227 women, ages 47-77) defining periodontitis as clinical attachment loss (CAL) \geq 6 mm and probing pocket depths \geq 4 mm and obstructive sleep apnea using apnea-hypopnea index (AHI) \geq 5. They concluded that 17.5 percent of subjects had periodontitis, 46.6 percent had obstructive sleep apnea, and sixty percent of those diagnosed with periodontitis also had obstructive sleep apnea. Obstructive sleep apnea was positively associated with periodontal disease (OR=2.51).

Gunaratnam [8,9], in cross-sectional study of obstructive sleep apnea and periodontitis in Australia (n=66: 54 men/12 women), conducted periodontal examinations on subjects with obstructive sleep apnea (AHI \geq 5). Defining periodontal disease according to NSAOH and CDC/AAP, they concluded obstructive sleep apnea was associated with periodontitis.

In case-control research on obstructive sleep apnea in association with periodontitis, Ahmad et al. [26] identified two groups, fifty patients with moderate to severe periodontitis as cases and 104 patients with gingivitis or slight periodontitis as controls (61 males/93 females). Patients received full-mouth periodontal examinations from the investigators and risk for obstructive sleep apnea was decided by response to the four-item "STOP" obstructive sleep apnea screening questionnaire, assessing self-reported snoring, excessive daytime sleepiness, witnessed apnea during sleep, and history of hypertension. Patients with moderate to severe periodontitis were 4.1 times more likely to be at risk for obstructive sleep apnea than the control patients with gingivitis or slight periodontitis (p=0.007). The authors concluded significant association existed between moderate or severe periodontitis and risk for obstructive sleep apnea.

Keller et al. [27] looked at associations between obstructive sleep apnea and chronic periodontitis in a population-based case-control study. Using 7673 subjects with a history of obstructive sleep apnea as cases and 21,963 subjects without history of OSA as controls and following logistic regression analyses, the authors found significant difference in the prevalence of prior chronic periodontitis between cases and controls (33.8 per cent versus 22.6 per cent p<0.001). They concluded there is associated between OSA and periodontitis.

Publications by Donovan [28-30] also concluded there is association between periodontitis and obstructive sleep apnea. A single review article titled "Sleep disorders and the dental patient: an overview" [31] showed the role of the dentist in the management of some sleep-related disorders.

Conclusion

In conclusion, the role of dentists in the management of sleep-related disease is relevant. All these articles confirm that

association between obstructive sleep apnea and periodontal disease does exist, but further prospective study with large sample populations is necessary to validate the relationship.

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