



AN INEVITABLE LINK BETWEEN OBSTRUCTIVE SLEEP APNEA AND PERIODONTITIS

Dental Science

Dr. Rizleena Majeed	Assistant Professor, Department of Periodontology, Kannur Dental College, Anjarakandy, Kerala, India.
Dr. Reshma. T.S	Post Graduate Students, Department Of Periodontology, Kannur Dental College, Anjarakandy, Kerala, India.
Dr. Anwer Safeer	Post Graduate Students, Department Of Periodontology, Kannur Dental College, Anjarakandy, Kerala, India.
Dr. Sunith Sudhakaran	Associate Professor, Department of Periodontology, Kannur Dental College, Anjarakandy, Kerala, India
Dr. Shermil Sayd*	Assistant Professor, Department of Oral and Maxillofacial Surgery, Kannur Dental College, Anjarakandy, Kerala, India- 670612. *Corresponding Author

ABSTRACT

Periodontal diseases are related to diabetes, coronary disease, osteoporosis, low birth weight deliveries, and other systemic diseases. There is an inevitable link between periodontitis and Obstructive sleep apnea, and this review aims to evaluate the relation between the two conditions.

KEYWORDS

snoring; obstructive sleep apnea; OSA; periodontitis

INTRODUCTION

Periodontal disease is a chronic and infectious condition leading to the destruction of the tissues supporting the tooth due to the bacterial biofilm (Kornman et al., 1997). Immune responses and inflammatory responses of the host body are key to the periodontal disease process. Recognized risk factors for periodontal disease include dental plaque, calculus, smoking, and some specific bacterial pathogens such as *Actinobacillus actinomycetemcomitans*, *P.gingivalis*, and *B.forsythus*.

Obstructive sleep apnea (OSA) is defined as the collapse of the upper airway during the sleep cycles, which episodically leads to the reduction or cessation of airflow, causing intermittent hypoxia and fragmented sleep. The individual is susceptible to risk factors entailed with multiple systemic diseases. The pathophysiology for obstructive sleep apnea is not yet fully comprehended. Still, one of the established contributory factors is obesity (Grossi & Genco, 1998). The earliest investigations of the syndrome were reported in the middle of the last century and concluded that in about 90% of cases, obstructive sleep apnea's associated with obesity (Benumof, 2001; Tremblay et al., 2011). Due to their inter-relationship, OSA and periodontitis have been a topic of interest for the fraternity since (Gunaratnam et al., 2008, 2009). Obesity, nasal breathing difficulty, smoking, and drinking are positively associated with periodontitis (Chaffee & Weston, 2010; Mathur et al., 2011). The inflammatory mediators that play a role in the pathogenesis of both OSA and periodontitis, along with shared risk factors, are the basis of the entire premise of a potential association between the two (Al-Zahrani et al., 2003).

Obstructive sleep apnea

A characteristic feature of OSA is the recurrent events of upper airway obstruction, which happens during sleep. It is also associated with recurrent cycles of desaturation and re-oxygenation, sympathetic over-activity, and intra-thoracic pressure changes. These may lead to fragmented sleep and consequent daytime fatigue and sleepiness (McNicholas et al., 2007). An apnea-hypopnea index (AHI) helps in the regular assessment of sleep apnea. An AHI is the number of complete or incomplete obstructive events per hour of sleep (Young et al., 1993).

OSA's daytime sleepiness rate is approximately 3% to 7% in adult men and 2% to 5% in adult women (Kapur, 2010; Punjabi, 2008). One of the most potent recognized risk factors for OSA is Obesity (Peppard et al., 2000). When considering the individuals having a body mass index greater than 28, 41% exhibits OSA. The prevalence of OSA is as high as 78% in patients referred for bariatric surgery (Newman et al., 2005; Vgontzas et al., 1994). There is a reduction in lung volumes associated

with obesity, especially functional residual capacity, contributing to decreased tracheal tug and upper airway size and increased airflow resistance (Lopez et al., 2008; Steier et al., 2014).

The hormone produced by adipocytes is *leptin*. Leptin is well-balanced in its triglyceride content and is involved in suppressing appetite (Münzberg & Morrison, 2015). It acts on the central respiratory centers to arouse ventilation and leptin deficiency associated with hypoventilation (Atwood, 2005; Kalra, 2008). Central leptin resistance is used to measure obesity. A reduced hypercapnic response leads to a worsened state, impairing arousal from sleep during apneas (Malhotra et al., 2006). In adults, there is a rise in the prevalence of OSA with age. This increase is attributable to the soft palate's lengthening, parapharyngeal fat deposition, and changes in other parapharyngeal structures (Young et al., 2002). The Sleep Heart Health Study proved that the prevalence of OSA did not increase after the age of 60 years (DJ et al., 2010). The increased risk of all cardiovascular mortality associated with OSA is limited to middle-aged adults, especially men (Shahar et al., 2003).

There is a 2 to 3 fold higher prevalence of OSA in men (Punjabi, 2008). In the pathogenesis of OSA, sex-hormones play a significant role. Post-menopausal women present OSA more than pre-menopausal women, and the replacement of hormone in post-menopausal women may protect against the disorder (McNicholas et al., 2007; Westström et al., 2005). The independent role for OSA in promoting adverse cardiovascular outcomes is found in studies explaining its relationship with hypertension (Hedner et al., 2006). Multiple studies observed that snorers were more likely to have hypertension (Nieto et al., 2000). Numerous clinical and epidemiological studies recognized a dose-response relationship between OSA severity and the possibility of prevalent hypertension (Jin et al., 2007). It is independently associated with an increased prevalence of clinically overt heart failure (Bradley & Floras, 2009).

Patients with OSA are at increased risk of atrial fibrillation (A.F.) (Tremblay et al., 2011). The severity and presence of sleep-disordered breathing forecasts incident stroke. OSA causes tissue hypoxia, systemic inflammation, oxidative stress, and immune dysregulation, all associated with oncogenesis.

Periodontal disease

Periodontal disease is a multifactorial and common chronic disease in adults. Periodontal disease manifestations range from gingivitis to chronic periodontal disease. The gingiva's chronic inflammation is characterized by bacterial and plaque formation and an age-related increase in incidence with a male predilection. The association

between periodontal disease, obesity, and ethnicity has been well documented(Mathur et al., 2011)

Pathogenic bacteria, which cause periodontitis, elicit an inflammatory response on periodontal tissues. This inflammation-mediated destruction of the tooth-supporting tissues leads to loss of periodontal attachment, pocket formation, loss of alveolar bone, and ultimately, tooth loss. Periodontal disease contributes to systemic inflammatory diseases by increasing inflammatory mediators' production and has been proven to be associated with diabetes, cardiovascular diseases, and osteoporosis. Since OSA and periodontal disease are common disorders associated with systemic inflammation, their association should be studied.

Obstructive Sleep Apnea and periodontal disease

Recently periodontal disease has received increasing consideration because it relates to systemic diseases like diabetes, coronary disease, osteoporosis, low birth weight, and other systemic diseases. Obstructive sleep apnea is one of these conditions associated with an inflammatory response (Hedner et al., 2006).

Smoking, age, alcohol, diabetes, and obesity are major risk factors for periodontal diseases. Both periodontal disease and obstructive sleep apnea are associated with systemic inflammation. There is no evidence on the etiology of systemic inflammation and obstructive sleep apnea, but it can be related to inflammation in the oral cavity and periodontal diseases. A lot of pathological and physiological mechanisms may contribute to the relationship between sleep apnea and periodontitis. It is plausible that periodontitis is mediating the activation of inflammatory pathways in OSA. In both OSA and periodontitis, an elevation in C-reactive protein (CRP) levels is observed. However, a reduction in CRP level did not reduce the strength of association between OSA and periodontitis, suggesting that CRP is a doubtful mediator of this relationship. Other inflammatory proteins common to both of these conditions, like interleukin-6 and soluble intercellular adhesion molecule, should also be studied (Gunaratnam et al., 2009).

Irreversible and accumulative destruction of alveolar bone is a symbol of periodontitis. Chronic intermittent hypoxia may stimulate bone remodeling, preserving bone density in elderly adults. The same has been demonstrated in laboratory rats under experimental conditions. A protective effect of hypoxia against bone loss is one reason for the silent relationship between OSA and periodontitis among older adults. Drugs like NSAIDs, immunosuppressants diminish inflammatory reactions and protect against destructive loss of alveolar bone. It has been reported that intermittent hypoxia as a result of airway obstruction would not be responsible for systemic inflammation, which may support that increased systemic inflammation in OSA patients may be more closely associated with other factors (Jin et al., 2007).

Apart from obesity, snoring, prolonged mouth opening, and tobacco use also act as a risk factors for developing periodontal diseases in OSA patients. Studies also linked the strong association between snoring and periodontal diseases while excluding diabetes.

An additional mechanism for the relationship between OSA and periodontitis is the role of Neutrophil Elastase. Neutrophil Elastase plays a role in the degradation of non-collagenous protein-covering collagen fibrils in periodontal disease's early destructive phases. The increased levels of Neutrophil Elastase (N.E.) in GCF samples act as indicators for the periodontal condition's severity. OSAS activates the circulating neutrophils and increases plasma markers of systemic inflammation. It also affects the neutrophils by increasing neutrophil activation, production of reactive oxygen species, expression of adhesion molecules, and decreasing apoptosis rates.

Members of the MMP family, like MMP-2, -8, and -9, are involved in periodontal tissue destruction. Studies conducted by Ye et al. (Jin et al., 2007) demonstrated an increase in serum MMP-9 levels in patients with OSAS, but these studies do not involve a clinical periodontal examination. Salivary and serum concentrations of pro-MMP-2 and -9 levels correlated with each other. This association suggests that these biofluids are exposed to similar influences, and the salivary source of these zymogen MMPs could be related to the serum. Patients with a high risk of OSA were more likely to have periodontitis. Several studies have shown a statistically significant association between periodontal problems and OSA. OSA was not significantly associated

with the prevalence of moderate or severe periodontitis and the periodontal parameters.

Conspicuous changes in the oral environment induced by OSA could cause adverse periodontal conditions. In OSA patients, there is more expression of enzymes and cytokines. Studies show that increased IL-6 and IL-33 salivary concentrations in OSA patients simultaneously, IL-1 β , IL-21, and pentraxin-3, were not affected by OSA.

Multiple inflammatory conditions inherent in obese patients could mask the relationship between OSA risk and their periodontal conditions. Another elucidation is that the relationship between OSA and periodontal disease is dependent on other variables, which were not observed in multiple prior studies (Bradley & Floras, 2009).

Positive airway pressure

Positive airway pressure (PAP) is considered as the First-line treatment for OSA. PAP is very active in serving the patient to beat daytime sleepiness symptoms. This non-invasive treatment uses a mask to be worn over the nose at night, with the air supplied by a quiet blower. It acts as a pneumatic splint by slightly pressurizing the upper airway and preventing it from collapsing during sleep and is indicated when rapid control for OSA is required.

CONCLUSION

The occurrence of periodontitis with concomitant impaired breathing and the detrimental effects of subsequent periods of asphyxia on overall systemic health elicit the importance of incorporating recognition protocols for the same during initial and recurring evaluations of these patients' dentists. Dentistry in sleep medicine is emerging to include increased emphasis on screening and patient evaluation. It also incorporates blood pressure and weight monitoring to recognize the best time to changeover from an oral device to positive airway pressure therapy.

REFERENCES

1. Al-Zahrani, M. S., Bissada, N. F., & Borawski, E. A. (2003). Obesity and periodontal disease in young, middle-aged, and older adults. *Journal of Periodontology*, 74(5), 610-615.
2. Atwood, C. W. (2005). *Sleep-related hypoventilation: the evolving role of leptin*. Elsevier.
3. Benumof, J. L. (2001). Obstructive sleep apnea in the adult obese patient: implications for airway management. *Journal of Clinical Anesthesia*, 13(2), 144-156.
4. Bradley, T. D., & Floras, J. S. (2009). Obstructive sleep apnoea and its cardiovascular consequences. *The Lancet*, 373(9657), 82-93.
5. Chaffee, B. W., & Weston, S. J. (2010). Association between chronic periodontal disease and obesity: a systematic review and meta-analysis. *Journal of Periodontology*, 81(12), 1708-1724.
6. DJ, G., Yenokyan, G., AB, N., GT O, C., NM, P., & SF, Q. (2010). Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure. *Circulation*, 122, 352-360.
7. Grossi, S. G., & Genco, R. J. (1998). Periodontal disease and diabetes mellitus: a two-way relationship. *Annals of Periodontology*, 3(1), 51-61.
8. Gunaratnam, K., Taylor, B., Cistulli, P., Curtis, B., & others. (2008). Periodontitis and sleep apnoea. *Annals of the Royal Australasian College of Dental Surgeons*, 19, 48.
9. Gunaratnam, K., Taylor, B., Curtis, B., & Cistulli, P. (2009). Obstructive sleep apnoea and periodontitis: a novel association? *Sleep and Breathing*, 13(3), 233-239.
10. Hedner, J., Bengtsson-Bostrom, K., Peker, Y., Grote, L., Rastam, L., & Lindblad, U. (2006). Hypertension prevalence in obstructive sleep apnoea and sex: a population-based case-control study. *European Respiratory Journal*, 27(3), 564-570.
11. Jin, Y. E., Hui, L. I. U., Yuan, L. I., Xian, L. I. U., & Zhu, J. (2007). Increased serum levels of C-reactive protein and matrix metalloproteinase-9 in obstructive sleep apnea syndrome. *Chinese Medical Journal*, 120(17), 1482-1486.
12. Kalra, S. P. (2008). Central leptin insufficiency syndrome: an interactive etiology for obesity, metabolic and neural diseases and for designing new therapeutic interventions. *Peptides*, 29(1), 127-138.
13. Kapur, V. K. (2010). Obstructive sleep apnea: diagnosis, epidemiology, and economics. *Respiratory Care*, 55(9), 1155-1167.
14. Kornman, K. S., Page, R. C., & Tonetti, M. S. (1997). The host response to the microbial challenge in periodontitis: assembling the players. *Periodontology* 2000, 14(1), 33-53.
15. Lopez, P. P., Stefan, B., Schulman, C. I., & Byers, P. M. (2008). Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. *The American Surgeon*, 74(9), 834-838.
16. Malhotra, A., Huang, Y., Fogel, R., Lazic, S., Pillar, G., Jakab, M., Kikinis, R., & White, D. P. (2006). Aging influences on pharyngeal anatomy and physiology: the predisposition to pharyngeal collapse. *The American Journal of Medicine*, 119(1), 72-79.
17. Mathur, L. K., Manohar, B., Shankarapillai, R., & Pandya, D. (2011). Obesity and periodontitis: A clinical study. *Journal of Indian Society of Periodontology*, 15(3), 240.
18. McNicholas, W. T., Bonsignore, M. R., of EU Cost Action B26, M. C., & others. (2007). Sleep apnoea as an independent risk factor for cardiovascular disease: current evidence, basic mechanisms and research priorities. *European Respiratory Journal*, 29(1), 156-178.
19. Münzberg, H., & Morrison, C. D. (2015). Structure, production and signaling of leptin. *Metabolism*, 64(1), 13-23.
20. Newman, A. B., Foster, G., Givelber, R., Nieto, F. J., Redline, S., & Young, T. (2005). Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. *Archives of Internal Medicine*, 165(20), 2408-2413.
21. Nieto, F. J., Young, T. B., Lind, B. K., Shahar, E., Samet, J. M., Redline, S., D'agostino, R. B., Newman, A. B., Lebowitz, M. D., Pickering, T. G., & others. (2000). Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-

- based study. *Jama*, 283(14), 1829–1836.
22. Peppard, P. E., Young, T., Palta, M., Dempsey, J., & Skatrud, J. (2000). Longitudinal study of moderate weight change and sleep-disordered breathing. *Jama*, 284(23), 3015–3021.
 23. Punjabi, N. M. (2008). The epidemiology of adult obstructive sleep apnea. *Proceedings of the American Thoracic Society*, 5(2), 136–143.
 24. Shahar, E., Redline, S., Young, T., Boland, L. L., Baldwin, C. M., Nieto, F. J., O'Connor, G. T., Rapoport, D. M., & Robbins, J. A. (2003). Hormone replacement therapy and sleep-disordered breathing. *American Journal of Respiratory and Critical Care Medicine*, 167(9), 1186–1192.
 25. Steier, J., Lunt, A., Hart, N., Polkey, M. I., & Moxham, J. (2014). Observational study of the effect of obesity on lung volumes. *Thorax*, 69(8), 752–759.
 26. Tremblay, M., Gaudet, D., & Brisson, D. (2011). Metabolic syndrome and oral markers of cardiometabolic risk. *J Can Dent Assoc*, 77, b125.
 27. Vgontzas, A. N., Tan, T. L., Bixler, E. O., Martin, L. F., Shubert, D., & Kales, A. (1994). Sleep apnea and sleep disruption in obese patients. *Archives of Internal Medicine*, 154(15), 1705–1711.
 28. Wesström, J., Ulfberg, J., & Nilsson, S. (2005). Sleep apnea and hormone replacement therapy: a pilot study and a literature review. *Acta Obstetrica et Gynecologica Scandinavica*, 84(1), 54–57.
 29. Young, T., Palta, M., Dempsey, J., Skatrud, J., Weber, S., & Badr, S. (1993). The occurrence of sleep-disordered breathing among middle-aged adults. *New England Journal of Medicine*, 328(17), 1230–1235.
 30. Young, T., Peppard, P. E., & Gottlieb, D. J. (2002). Epidemiology of obstructive sleep apnea: a population health perspective. *American Journal of Respiratory and Critical Care Medicine*, 165(9), 1217–1239.