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EVALUATION OF A CORRELATION BETWEEN SLEEP HOURS, SLEEP QUALITY AND SALIVARY LEVELS OF 8-HYDROXY-2'-DEOXYGUANOSINE IN CHRONIC PERIODONTITIS PATIENTS- AN OBSERVATIONAL STUDY

Periodontology

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ABSTRACT

Aims: To determine if there was a correlation between sleep hours, sleep quality with the salivary levels of 8-hydroxy-2'-deoxyguanosine in chronic periodontitis patients, and to decide its relationship with the established clinical periodontal parameters.
Settings And Design: Observational analytical study with 100 patients based on the inclusion criteria, who visited the Department of Periodontology of a tertiary care setting.
Methods And Material: Bleeding on probing, pocket depth, clinical attachment loss, plaque index score were recorded. Sleep behaviour longer than a month time stretch was surveyed by Pittsburgh Sleep Quality Index, a validated questionnaire. 8-OHdG levels in un-stimulated saliva of all subjects were examined by ELISA.
Statistical Analysis Used: Sleep-hour correlations with sleep quality at salivary 8-OHdG levels as well as clinical periodontal parameters were assessed using the Pearson correlation coefficient. All statistical analysis was performed using SPSS software version 17.0.
Results: Salivary 8-OHdG levels and clinical parameters (PPD, CAL, PI) were significantly higher among sleep deprived individuals. On comparison, subjects with a poor quality of sleep (PSQI score>5) showed a significantly higher 8-OHdG levels.
Conclusions: Short sleep durations and poor sleep quality can instigate inflammation and oxidative stress and could be a risk factor for periodontitis.

KEYWORDS

Periodontitis; Sleep; Oxidative stress; 8-OHdG

INTRODUCTION

Reactive oxygen species (ROS) creation in polymorphonuclear leukocytes leads to oxidative stress and influences the periodontal tissues[1]-[8].Sleep deprivation increases free radical creation by hindering anti-oxidant defense mechanisms of the brain [9] producing oxidative stress [10],[11],[12] and disrupts hormonal profile and balance of host immune and inflammatory mechanisms with overproduction of cytokines causing periodontal destruction[13],[14]. Oxidative stress induced DNA damage releases 8-hydroxy-2'-deoxyguanosine [1],[15]-[18]. This study aimed to determine if there was a correlation between sleep hours, sleep quality with the salivary levels of an oxidative stress marker 8-hydroxy-2'-deoxyguanosine in chronic periodontitis patients and to decide its relationship with the established clinical periodontal parameters.

SUBJECTS AND METHODS

An observational analytical study to evaluate the correlation between sleep hours, sleep quality and salivary levels of 8-OHdG in chronic periodontitis patients was conducted with an aggregate of 100 patients who visited the Department of Periodontology of Sri Sankara dental college, Kerala and a signed informed consent was obtained from all members. Ethical clearance was obtained from the Institutional Review Board of Sri Sankara dental college (IEC/003/2017) and the study was conducted in accordance with the Declaration of Helsinki. The subjects inside age group of 35-50 years with generalized moderate chronic periodontitis according to AAP 1999 [19] classification were included in the study whereas subjects with known systemic diseases, pregnant or lactating, shift workers, smokers, obese, subjects who have received periodontal treatment and/ antibiotic therapy within the preceding 6 months, or under any anti-inflammatory, antimicrobial, psychotropic drugs, antidepressants and immunosuppressive therapies during previous 6 months were excluded from the study.

ASSESSMENT OF SLEEP BEHAVIOUR

Information was collected by personal interview on the profession, demographic characteristics and sleep hours. Clinical parameters were reported, including pocket depth (PD), probing bleeding (BOP), loss of clinical attachment (CAL), plaque index (PI)[20]. In patients with chronic periodontitis, salivary levels of the oxidative stress marker 8-OHdG were analysed using ELISA.

Sleep behavior was analyzed using the Pittsburgh Sleep Quality Index (PSQI) - a self-reported questionnaire that measures the quality of sleep and disruptions over a month. Seven "component" scores were generated by nineteen individual items: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleep medication use and daytime dysfunction. The sum of scores produced one global score for those seven components. The whole index required 5-10 min for completion, and 5 min for scoring. A global PSQI score < 5 shows good sleep; and score > 5 shows bad sleep [21],[22]. Upon collecting the data, the selected participants were classified as subjects with a)<5hours, b) 6-8hours and c)>8 hours based on previous research according to their self-reported responses of sleep hours[23],[24].

COLLECTION OF SALIVA

All the subjects were asked to refrain from eating, drinking, exercising and smoking for at least two hours before collecting the saliva. In the morning (10a.m-12 p.m.) non-stimulated whole saliva (2 ml) was collected from all subjects using Navazesh's adjustment method [25]-[28] into a graduated Eppendorf collection tube.

Collected saliva was placed in a nitrogen flask until transportation to the research laboratory where it was stored at -800°C. Samples were defrosted, centrifuged for 10 min at 12,000 rpm, and the supernatant was separated for analysis.

ELISA ASSAY PROCEDURE

The method used was Competitive-ELISA kit (ImmunoTag a Geno Technology Inc., USA). In this kit the microtiter plate was pre-coated with 8-OHdG. Spectrophotometrically, at a wavelength of 450 nm, the color transition was measured at the end of an enzyme-substrate reaction. The 8-OHdG concentration in the samples was then determined through comparison of the optical density of the samples to standard curve.

STATISTICALANALYSIS

The percentage, mean and standard deviation were used to describe patient characteristics and clinical parameters. Sleep-hour correlations with sleep quality at salivary 8-OHdG levels as well as clinical periodontal parameters (PPD, CAL, PI) were assessed using the Pearson correlation coefficient (r). All statistical analysis was performed using statistical software (SPSS software 17.0).

RESULTS

A total of 100 samples were included in the study based on inclusion and exclusion criteria with a confidence interval set at 95 per cent. Included in the study were 53 females and 47 males with general chronic periodontitis (AAP 1999) and 19 males aged 35-50 years. Of these, 44% were between 36-40 years of age, 40% were between 41-45 years of age, and 16% were between 46-50 years of age. The percentage distribution of the sample by sleep hours showed that 77% of the chronic periodontitis patients included were individuals with short sleep (< 5 hours), only 19% of those subjects with chronic periodontitis included in the analysis had regular sleep (6-8 hours) and only 4% had longer sleep durations. PSQI score percentage distribution of the sample suggested that 79 per cent of the chronic periodontitis patients included in the study were of poor sleep quality. A statistically significant negative correlation between sleep hours and salivary levels of 8-OHdG ($p<0.01$) was observed (Table 1). Nonetheless, a statistically significant positive correlation between PSQI score and salivary levels of 8-OHdG ($p<0.01$) (Table 1) was seen. In subjects with a short sleep period of < 5 hours relative to regular sleep (6-8 hours) or long sleeping persons (> 9 hours), there was a statistically significant rise in the salivary 8-OHdG rates.

Between sleep-hours and periodontal clinical parameters (mean PPD, CAL, PI) a statistically significant negative correlation ($P<0.01$) was determined (Table 2). In subjects with a short sleep span of < 5 hours relative to normal sleep (6-8 hours) or long sleep (> 9 hours), a statistically significant increase in the clinical periodontal parameters (mean PPD, CAL, PI) was observed (Graph 1). A statistically significant positive correlation between the PSQI score and the periodontal clinical parameters (mean PPD, CAL, PI) ($p<0.01$) was revealed (Table 3). A statistically significant increase in mean PPD, CAL, PI with salivary 8-OHdG levels was also noted (Graph 2)

Table 1: Correlation Between Sleep Hours, PSQI Score To Salivary 8-OHdG Levels In Chronic Periodontitis Patients

	r	P	Significant
Sleep hours	-0.796**	p<0.01	Sig
PSQI score	0.931**	p<0.01	Sig

(r: Pearson's correlation coefficient, P: probability value, sig: statistically significant) **:- Significant at 0.01 level

Table 2: Correlation Between Sleep Hours And Periodontal Parameters (Mean PPD, CAL, PI)

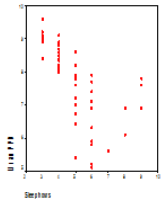
	r	P	Significant
Mean PPD	-0.718	p<0.01	Sig
Mean CAL	-0.679	p<0.01	Sig
PI	-0.678	p<0.01	Sig

(r: Pearson's correlation coefficient, P: probability value, PPD: probing pocket depth, CAL: clinical attachment loss, PI: plaque index score, sig: statistically significant) **:- Significant at 0.01 level

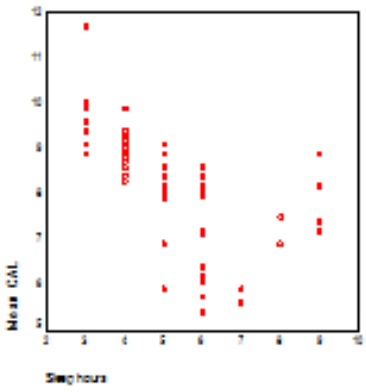
Table 3: Correlation Between PSQI Score And Periodontal Parameters (Mean PPD, CAL, PI)

	R	P	Significant
Mean PPD	0.813	p<0.01	Sig
Mean CAL	0.777	p<0.01	Sig
PI	0.827	p<0.01	Sig

(r: Pearson's correlation coefficient, P: probability value, PPD: probing pocket depth, CAL: clinical attachment loss, PI: plaque index score, sig: statistically significant)**:- Significant at 0.01 level



Mean PPD



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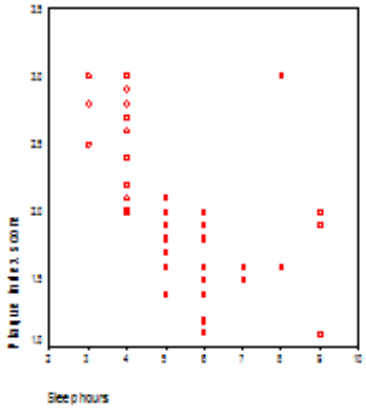
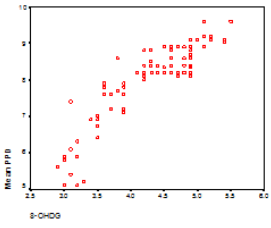


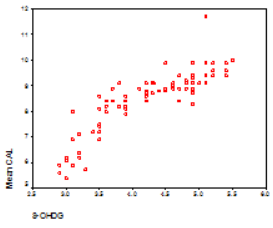
Plaque Index Score

Graph 1: Scatter diagram for sleep hours and periodontal parameters (mean PPD, CAL, PI)*(PPD: probing pocket depth, CAL: clinical attachment loss, PI: plaque index score)***:- Significant at 0.01 level**



8-OHdG levels

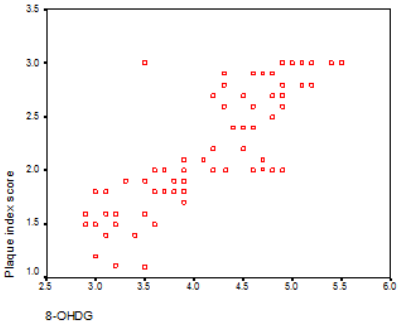
Mean PPD



8-OHdG levels

Mean CAL

Plaque index score



8-OHdG levels

Graph 2: Scatter diagram for severity of periodontitis and salivary 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels in chronic

periodontitis patients*(8-OHdG: 8-hydroxy-2'- deoxyguanosine, PPD: probing pocket depth, CAL: clinical attachment loss, PI: plaque index score)*

DISCUSSION

Periodontal disease is the result of complex inflammatory immune responses with multiple component causes, some of which are based on genetics, some of which are due to epigenetic influences, and some of which are modifiable because they relate to patient behaviours, medicines or environmental factors, all of which may cause and spread periodontitis lesions. Sleep is a process of oxidative stress recovery. The increased level of inflammatory, pro-inflammatory markers and increased oxidative stress in sleep deprived individuals point out that sleep deprivation could also be considered as a factor that could accelerate periodontal destruction. A vicious cycle between periodontitis stage and grade, sleep problems, and quality of life in which a pathological problem contributes to sustaining or deteriorating the other into a bidirectional relationship that can be difficult to break and resolve has been proposed.[7,8,9] The aim of this study was to determine whether there is any correlation between sleep time, sleep quality and salivary levels of the 8-hydroxy-2'-deoxyguanosine (8-OHdG) oxidative stress marker in chronic periodontitis patients.

Salivary 8-OHdG rates in sleep-deprived individuals (< 5 hours of sleep) were significantly higher than average (6-8 hours) or sustained (> 8 hours) individuals (Table 1). Clinical parameters such as probing pocket depth and clinical attachment loss among sleep deprived individuals were also statistically higher than those with normal sleep cycles or extended sleep patterns (Table 2, Graph 1). And there was a statistically significant increase in the periodontal parameters (PPD, CAL, PI) with elevated levels of the 8-OHdG salivary oxidative stress biomarker (Graph 2). In contrast, subjects with poor sleep quality (PSQI score>5) reported statistically higher values of 8-OHdG (Table 1) salivary levels as well as periodontal parameters as compared to subjects with good sleep quality (Table 3).

The present study observed a significant increase in periodontal parameters (PPD, CAL, PI) in persons deprived of sleep relative to normal or extended sleeping persons. The direct correlation suggesting a particular connection between periodontitis and short sleep time was consistent with the study of Grover V. et al.[29], which elucidated a positive correlation between PSQI score and gingival index (GI) and probing depth (PD) indicating that PSQI scores are commensurate with periodontal destruction.[29]And another cross-sectional study by Singla R. et al.[30], examined the effect of lifestyle on periodontal health, and lack of sleep was reported as a major lifestyle factor that played a role in periodontal disease progression.[30]

A U-shaped relation in regard with periodontal damage was identified between regular and extended sleeping individuals in a study done by Romandini M et al. [31], Han K et al. [23], Han K et al. [32] and the cause was proposed to be the elevated rates of Interleukin-1 and tumour necrosis factor in the latter. However, in sleep deficient individuals the level of damage was more dramatically higher compared to normal or extended sleeping individuals.

A significant positive correlation of PSQI score to the periodontal parameters (Table 3) in the study pointed out to an increased periodontal destruction in subjects with poor quality of sleep. Throughout the study, a strong positive correlation between the PSQI score and the periodontal parameters revealed increased periodontal degradation in subjects with low sleep quality. These findings of the present study elucidating an increased periodontal destruction in poor quality subjects were in accordance with the previous studies by Singh V et al .[33], Karaaslan F, Dikilitaş A.[34]

However, the results of the present analysis were in conflict with an analysis by Wiener R et al. [35] who in their study measured the level of sleep by a self-reported dichotomized response (less or more than 7) compared to the PSQI score in our research. Yet their research had failed in the adjusted analysis to hit the correlation at a significant level. [35]

According to various previous studies, sleep deprivation could induce oxidative stress [36-39] and activation of inflammatory pathways that explain the higher levels of the oxidative stress biomarker 8-OHdG among sleep deprived persons found in our study (Table 1). A statistically significant increase in periodontal parameters with salivary levels of 8-OHdG (Graph 2) reported in our study was in accordance with some previous studies [1-7] suggesting an increased oxidative stress in periodontitis that may accelerate tissue destruction.

In agreement with Takane M.et al. [1] a statistically significant positive correlation of salivary 8-OHdG levels with periodontal clinical parameters (PPD, CAL, PI) was determined in our study as well. But we used un-stimulated which is more reliable and easier to collect, compared to stimulated saliva which was used in the former.

Tissue damage mediated by excessive extracellular reactive oxygen species (ROS) produced predominantly from polymorphonuclear leukocytes during periodontopathic bacterial phagocytosis is considered to be one of the major factors in the pathogenesis of periodontal disease [8,40] and may occur through a number of mechanisms such as protein disruption,[41] lipid peroxidation,[42,43] proinflammatory cytokine induction [8] and DNA damage [44]. Excessive release of neutrophils and other phagocytes in association with poor sleep leads to production of O2- (superoxide) by a single-electron reduction in oxygen at the expense of NADPH (nicotinamide adenine dinucleotide phosphate). The majority of O2- reacts to form H2O2 (hydrogen peroxide) by itself. A great many highly reactive microbicidal oxidants are formed from these agents. These reactive oxidants are manufactured to kill invading microorganisms, but they also cause damage to nearby tissues and may result in a state of oxidative stress when these radicals are excessively produced. [15] All of these are thought to be pathogenic in many inflammatory diseases including periodontitis.

Thus it suggests that due to its potential to influence systemic inflammation and oxidative stress, which are included in the pathogenetic mechanisms of periodontal damage, short durations of sleep may affect periodontitis. [8, 45-47]

In the present study, the study sample was unstimulated saliva, which is more reliable and easy to collect. Moreover, in the present study, sleep duration was self-reported by the participants, which is considered to be more accurate in detecting chronic (long-term) sleep habits and use of a universally accepted Pittsburgh sleep quality index which assessed the sleep behavior over a month time interval, added the strength of the study.

However, an association with long sleep duration was reported in the study, which couldn't arrive at a statistically significant conclusion because of inadequate numbers of individuals reporting long sleep durations and that was a limitation of the present study.

The present study found a significant correlation of sleep hours in patients with chronic periodontitis along with sleep quality to salivary 8-OHdG levels. In sleep deprived individuals, the salivary 8-OHdG levels and clinical periodontal parameters (PPD, CAL, PI) were significantly higher. In comparison, subjects with poor sleep quality showed significantly higher levels of salivary 8-OHdG than subjects with good sleep quality. The study also showed a statistically significant increase of the salivary 8-OHdG levels with the periodontal parameters. In the study, an association between long sleep duration and periodontal destruction was reported but failed to reach a statistically significant level due to the inadequate number of persons reporting long sleep durations and this is considered as a limitation of the present study.

CONCLUSION

Within the limitations our study concluded that extreme sleep durations along with quality of sleep could be a risk factor for periodontitis. It was noted that in subjects with chronic periodontitis having short sleeping hours and poor sleep quality, the salivary 8-OHdG levels along with periodontal parameters were significantly higher. Changes in sleeping habits could be included in the preventive and therapeutic approaches to periodontitis and a good quality sleep of about 6-8 hours is recommended for good systemic and periodontal health. Further, determining the role of salivary 8-OHdG levels in the diagnosis of the severity of periodontal destruction as well as sleep deprivation is warranted. Studies are still needed to determine the impact of long sleep duration and factors affecting the quality of sleep on the prevalence and severity of periodontitis.

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