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Original Article

Evaluation of the association between stress, depression and periodontitis a clinicobiochemical study.

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ABSTRACT

ABSTRACT: Background: Stress and depression may affect the onset and progression of periodontal disease. Only few studies has been established whether the mechanisms by which stress and depression influence periodontal disease are physiologic, behavioral, or both. Objectives: This cross-sectional pilot study explored the associations between periodontal disease, psychologic factors, salivary markers of periodontal disease, psychoneuroimmunologic variables, and behavior. Methods: The study includes 12 control group (healthy individuals) and 13 recall periodontal patients aged 30-80 years visiting Out Patient Department of Periodontology, AECS Maaruti College of Dental Sciences and Research Centre, Bangalore. Psycho-neuro-immunologic variables like stress and depression assessed through Derogatis Stress Profile (DSP) and Center of Epidemiologic Studies Depression scale (CES-D). Stress marker (Chromogranin- A) have been measured from saliva. Evaluation of the presence of dental plaque on lingual and buccal surfaces, gingival index, and probing depth were assessed. Results: Stress and salivary stress marker chromogranin A was significantly correlated with clinical parameters of periodontal disease. Neglecting to brush teeth during stress was associated with missing teeth. After adjusting for stress variables, salivary chromogranin A was significantly associated with tooth loss and periodontal clinical parameters. Conclusions: This study suggests that stress might be associated with periodontal disease through physiologic and behavioral mechanisms. In making diagnoses of psychiatric patients, the association between salivary stress markers and periodontal disease needs to be included.

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1. Introduction

Periodontal disease is one of the most common causes of tooth loss. Stress, depression, and ineffective coping may contribute to the development of periodontitis¹. One model proposes that psychologic stress may result in immunologic and inflammatory responses that influence periodontal disease, whereas an alternative model hypothesizes that negative affective states may reduce compliance with preventive behaviors².

Stress and depression are indeed more common in subjects experiencing a high financial strain along with inadequate coping

strategies and more plaque accumulation². It has also been reported that reduced social isolation and anger expression might play an important role in maintaining oral health, general health and well-being³. Reduced cell-mediated immune function has been found in depressed patients and in distressed persons undergoing life-threatening events⁴.

Two primary neuroendocrine systems have been of specific interest in the study of human stress, the hypothalamus-pituitary-adrenocortical (HPA) system with the secretion of cortisol and the sympathetic adrenomedullary (SM) system with the secretion of catecholamine. In the HPA system, cortisol secretion is regulated by the adrenocorticotropic hormone from the pituitary gland. Salivary cortisol levels are closely correlated to blood cortisol levels and, therefore, reliably reflect HPA activity. It was reported that various kinds of

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psychologic stress activate the HPA system and consequently induce significant increases in salivary cortisol levels. In the SM system, direct measurements of salivary catecholamine do not reflect SM activity¹⁰.

Chromogranin A (CgA) is an acidic glycoprotein that is stored and coreleased by exocytosis with catecholamines from the adrenal medulla and sympathetic nerve endings, and thus, it is considered to be a sensitive and important index of SM. Salivary chromogranin A was shown to be produced by the human submandibular gland and secreted into saliva¹⁰.

Although research supports the associations among stress, depression, and periodontal disease, the mechanism could be psychologic, neurologic, immunologic, or behavioral or a combination of these mechanisms. The present cross-sectional study extends the research on chronic stress or depression and periodontal disease by measuring behaviors, psychologic variables, and salivary stress marker CgA, levels to explore the behavioral and immunologic correlates of periodontal parameters.

2. Materials and Methods

25 subjects (12 healthy individuals (M=8, F=4) and 13 recall periodontal patients (M=9, F=4) of age ranging between 30-80 yrs were recruited from Department of Periodontology, AECS Maaruti College of Dental science and Research Centre, Bangalore.

12 subjects are healthy individuals and 13 patients had a history of non-surgical periodontal therapy, in some cases augmented by surgical intervention, followed by continued enrollment in a maintenance regimen. The use of recall patients ensured that all patients were receiving regular periodontal monitoring and maintenance. Patients taking steroids (e.g., prednisone) and any other antibiotics in past 3 months. Other systemic diseases (e.g., cardiovascular disease) and Smoking & alcoholic were excluded from this study

Procedure

Patients completed a consent form and self-report measures assessing health and oral hygiene, chronic stress, depression, and coping. Participants provided a salivary sample prior to their dental examination. The gingival index⁶ and plaque index⁷ of subjects were calculated as the means of the sums of scores. Probing depths (PDs) and clinical attachment levels were measured with a using a Michigan probe. PD was measured at six sites per tooth, and facial REC was measured for each tooth. PD was averaged and combined with REC to calculate CAL per tooth. PD was coded <5, 5 to 7, and >7 mm. REC was coded <2, 2 to 4, and >4 mm. Dependent variables were the number of sites with PD 5 to 7 or >7 mm; number of teeth with REC 2 to 4 or >4 mm; and

number of teeth with CAL >5 to 7 or >7 mm. Relatively few patients had sites with PD >7 mm or teeth with REC >4 mm. As a result, regressions were run with missing teeth and number of teeth with CAL >5 mm as dependent variables

Measures

Health and oral hygiene survey.

The health and oral hygiene survey included questions about age, family history of periodontal disease, smoking, and frequency of brushing and flossing. Participants also indicated whether they neglected oral hygiene during periods of stress or depression.

Derogatis Stress Profile (DSP).

The DSP is a self-report measure designed to assess chronic stress. This 77-item inventory assesses 11 components of stress, including vocational environment, domestic environment, health environment, time pressure, driven behavior, attitude posture, relaxation potential, role definition, hostility, anxiety, and depression. Participants rated each statement from 0 (not at all true of me) to 4 (extremely true of me). The DSP contains items such as, "I take some time out almost every day just to relax", and "I am usually worried about something."

Center for Epidemiologic Studies Depression

Scale (CES-D). The CES-D is a 20-item self-report measure of depression. Participants were instructed to indicate how often they have felt or behaved in a certain way in the past week. Items include, "I was bothered by things that usually don't bother me", and "I felt hopeful about the future."

Chromogranin A sample.

Participants provided a sample of saliva prior to their maintenance visit to measure levels of Cg A. Saliva was collected by passive drool through a 1-inch straw into a vial. The samples were stored in a freezer and sent to a laboratory for Cg A assays. Salivary (free) Cg A levels were determined by Enzyme immunoassay method⁸. The minimum detection level was 0.9 pmol/mg protein. There were no significant differences in psychosocial or dental variables in those with adequate saliva compared to those without (P>0.05).

DATA ANALYSES.

Data were analyzed with a statistical program[¶]. Multiple regression analyses were used to examine the relationships between the measures of stress and depression and periodontal disease. The number of teeth with CAL >5 mm and the number of missing teeth were the dependent variables in multiple regression models.

3. Results

A description of the sample is included in Table 1. 42.3% of the participants reported a family history of periodontal disease. The majority of participants brushed their teeth twice per day (2 times/day), and 36.8% of participants reported flossing daily (1 time/day). There were no gender differences in behavioral variables, CgA, or measures of periodontal health.

Most of the participants brushed their teeth twice daily, and there were no sex differences in behavioral variables, salivary markers of stress, or measures of periodontal status (Tables 1 and 2). The gingival index and plaque index means (SD) were 1.52 and 1.24, respectively.

A positive relationship existed among depression scores, salivary CgA and the number of teeth lost (Table 3). DSP was significantly correlated with a clinical AL of 5 to 8 mm, missing teeth, and PD of 5 to 8 mm. There was a negative correlation among DSP and brushing frequency. Relatively few patients had sites with PD >8 mm or teeth with REC >3 mm. Hence, to capture the most extreme periodontal conditions, regressions were run with missing teeth and number of teeth with clinical AL >5 mm as dependent variables.

Multiple regressions were used to relate periodontal disease severity with depression, stress ratings, and salivary stress marker CgA, while controlling for other confounders (Tables 2 and 3). For tooth loss, depression was a significant ($P < 0.001$) predictor after controlling for sex and brushing frequency, but the model did not account for a significant proportion of the variance.

The regression model reported that salivary marker of stress was strongly associated with tooth-loss markers of periodontal disease. Also, analyses predicting the number of teeth with clinical AL >5 mm, CgA was significant predictors after adjusting for smoking history, history of alcohol intake, age, and brushing frequency.

Table 1: Descriptions of samples

Variable	Recall patients (n=13) (PD>3mm) Mean values	Control group (n=12) (PD≤3mm) Mean values
Tooth brushing (no of times)	1.3	2.4
CES-D score	10.1	5.2
DSP score	115	65
Teeth lost	1.8	-
Sites with PD ≤3 mm	1.9	6.2
Sites with PD >3 mm	4.52	-
Teeth with CAL ≤3 mm	2.02	-
Teeth with CAL >3 mm	4.03	-
Salivary CgA (pmol/mg protein)	3.62	1.63

Table 2 : Bivariate correlations between Psychosocial variables and Markers of periodontal disease.

Variable	Salivary CgA	DSP	CES-D
Brushing frequency	-0.30*	-0.43*	-0.23
Missing teeth	0.14	0.22	0.21*
Control group PD ≤3 mm	0.24	0.12	-0.11
PD >3mm	0.36*	0.51*	-0.10
CAL > 3 mm	0.29	0.49*	0.09

*denotes statistical significant

Table 3: Multiple linear regression analysis relating stress, depression and stress marker with number of teeth with CAL >3mm

Variable	β weight	tStatistic	p value
No of teeth with CAL >3mm	0.011	0.048	0.52
DSP	0.38	3.2	<0.04
CES-D	0.52	4.2	<0.01
Salivary CgA	0.28	2.1	<0.05

Total R² = 0.48. R², Multiple regressions are used to relate periodontal disease, depression, stress rating and salivary stress marker (Chromogranin A (CgA)).

4. Discussion

The results of the present study are consistent with previous reports suggesting that stress and depression symptoms are associated with periodontal disease. The correlations between depression scores and number of missing teeth; stress and CAL; and stress and PD confirm the hypothesized association between psychosocial variables and periodontal disease.

In terms of behavior, patients affirmed through self-report that stress interfered with oral hygiene (brushing and flossing); in turn, these reports were associated with tooth loss. This is consistent with previous research on stress and oral hygiene. In contrast, toothbrushing frequency was not associated with PD, REC, CAL, or tooth loss, despite the negative correlation between stress and brushing frequency. The effect of oral hygiene may not be apparent because of patients' adherence to a periodontal maintenance program. In contrast, the development of periodontal disease might also be related to conditions that alter the host's resistance to periodontopathic bacteria. A positive relationship exists among depression scores, salivary CgA and the number of teeth lost. This is likely because of factors such as altered immune responses that facilitate increased colonization by pathogenic bacteria and the breakdown of the periodontal attachment.

The immune response plays an important protective and destructive role. If the immune system cannot protect the body

against infection, the body has to rid itself of the bacteria by exfoliating the teeth to which the bacteria are attached. The immune response does not operate autonomously but in close cooperation with the neuroendocrine systems. When the body is in stress, there is an increase of stress markers and immune cells in the plasma mobilized from lymphoid organs⁹. Furthermore, in the present study, salivary CgA levels have a positive relation with periodontal disease; this might be due to the release of hormone in saliva by sympathetic nerve endings.

A positive relationship exists between depression scores, salivary CgA, and periodontitis. This is likely due to factors such as altered immune responses that facilitate increased colonization by pathogenic bacteria and the breakdown of the periodontal attachment

A recent systematic review of case-control, cross-sectional studies examining psychologic factors and periodontal disease indicated that 57.1% of the studies reported a positive correlation between stress or other psychologic factors and periodontal disease, and 14.2% did not. Therefore, the weight of the evidence seems to suggest an association between psychologic distress and periodontal health⁹

The study was conducted to explore the association between psychologic factors, markers of periodontal disease like salivary cortisol level, psycho-neuro-immunologic variables and behavior. In this study, 45 periodontal patients were referred by dentists. Participants completed composite health, chronic stress, depression and demographic questions and salivary cortisol was measured. In conclusion, stress and depression may be associated with periodontal destruction through behavioral and physiologic mechanisms¹¹.

The study has attempted to link periodontitis with stress and planned to explore association between periodontal disease, psychological factors and salivary markers of stress like chromogranin-A, cortisol, alpha-amylase and beta-endorphin. Stress and salivary stress markers were significantly correlated with clinical parameters of periodontal disease. After adjusting for stress variables, cortisol, and beta-endorphin were significantly associated with tooth loss and with clinical parameters of periodontal disease¹⁰

4. Conclusion

The results of this study indicated that stress and salivary stress marker is important correlates of periodontal disease, independent of dental hygiene. Therefore, it is likely that periodontitis is related to immunologic and behavioral changes related to psychologic states. Further, stress marker seems to have different associations with periodontal outcomes in models involving stress compared to models involving depression. The

cross-sectional design of the study does not allowed us to draw causal conclusions about whether psychosocial variables affect periodontal outcomes. It could also be possible that periodontal inflammation affects immune response and salivary stress marker level, rather than the reverse, or that tooth loss results in psychological depression.

FOOTNOTES

¶Statistical software (SPSS version 11.5; SPSS, Chicago, IL, USA)

§YKO70 Human CgA EIA kit, Yanaihara Institute, Shizuoka, Japan

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The authors report no conflicts of interest related to this study.

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