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Original Article

Periodontitis and Serum Interleukin-6 Levels in the Elderly

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SUMMARY: The elderly lose teeth as a result of dental caries and periodontitis caused by pathogenic oral bacteria. Periodontitis produces inflammatory cytokines due to the presence of lipopolysaccharides from oral gram-negative bacteria. Although the number of circulating inflammatory cytokines is related to the severity of the periodontitis, it is unclear whether the concentrations also correlate with periodontitis in the elderly. We investigated the relationship between periodontitis status and the concentrations of serum interleukin-6 (IL-6) in the serum from 276 subjects of 70- and 80-year-olds. Of the 276 subjects, 227 (82%) were dentate, 149 (54%) were found to be positive for serum IL-6, and 29 (13%) of the dentate subjects had severe periodontitis. However, there were no significant differences between the severity of periodontitis or the number of teeth and the mean serum IL-6 concentrations. These results provided no evidence to support an association between circulating IL-6 and periodontitis in the elderly.

INTRODUCTION

Periodontitis is a major oral disease caused by gram-negative bacteria in dentate people. Gram-negative bacteria that cause periodontitis affect systemic health, sometimes leading to severe sepsis (1). Major clinical manifestations of sepsis have been caused by proinflammatory cytokines such as interleukin-6 (IL-6) that are produced by lipopolysaccharide (LPS) derived from gram negative bacteria (2,3). As the concentrations of serum inflammatory cytokines are related to the severity and the outcome of sepsis (4,5), inflammatory cytokines can be used as possible predictors of disease (6-9). Detection of the proinflammatory cytokine IL-6 stimulated by bacterial LPS and the role of this cytokine in destroying periodontal tissue have been extensively studied both in sites of localized periodontitis (10) and in vitro (11,12). However, the relationship between periodontitis and the concentrations of circulating inflammatory IL-6 has not been investigated with regard to the decreasing resistance of the elderly to bacteria due to aging and accumulating bacteria in the oral cavity.

In this study, we assessed the relationship between periodontitis and the serum concentrations of IL-6 in elderly people.

MATERIALS AND METHODS

Study population: We chose a study sample of 276 subjects, composed of 207 (112 males and 95 females) 70-year-olds and 69 (30 males and 39 females) 80-year-olds. None of the subjects was hospitalized or institutionalized, and each came to the examination center either alone or accompanied by their family. They were in good general health and did not require special care for their day-to-day activities. Informed consent was obtained from all subjects prior to the study, allowing us to ascertain their oral health status and serum IL-6 concentrations.

Oral examinations: Four trained and experienced dentists assessed the oral health of the subjects under sufficient illumination provided by artificial light. The condition of subjects' teeth, including any decayed and missing teeth, was assessed in accordance with World Health Organization (WHO) criteria (13), using dental mirrors and WHO ball-pointed periodontal probes (Vivadent, Schaan, Liechtenstein), without hurting the periodontal tissue. The periodontal conditions for all teeth, including bleeding upon probing, periodontal probing depths, and loss of attachment in millimeters were recorded. The four examiners were calibrated on volunteer patients at the University Hospital before and during the survey. Kappa values between each pair of examiners were in the range of 0.81 to 0.63 for assessing periodontal conditions.

Measurement of serum IL-6: Blood samples were collected in order to determine cytokine concentrations. Clotted blood samples were centrifuged immediately at 3,000 rpm for 10 min, and the serum was stored at −80°C. The levels of serum IL-6 were analyzed using commercially available ELISA kits (Endgen, Inc., Woburn, Mass., USA) and following the manufacturer's instructions. The manufacturer reported the sensitivity thresholds as 1 pg/ml for IL-6. To avoid interobserver variation, all measurements were performed by a single trained individual. All samples were assayed in duplicate.

Statistical analysis: Before examining the study data, all cut-off points for categories of variables were determined. The number of teeth present was categorized into four groups based on our knowledge of the distribution of the number of teeth present in subjects admitted to the study wards: edentulous, 1 to 9 teeth, 10 to 19 teeth, and 20 teeth or more. The severity of periodontal disease was dichotomized as moderate or severe based on the presence of both periodontal pockets more than 6 mm in depth and bleeding upon probing at the same periodontal pocket in dentate subjects. Statistical analysis of the data was based on the Student's *t*-test to

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compare age and gender differences with the mean concentrations of IL-6. One-factor analysis of variance (ANOVA) was used to determine the association between serum IL-6 levels and the number of teeth present. All analyses were performed using the statistical program STATVIEW Version 4.5 (Abacus Conceptus, Inc., Berkeley, Calif., USA).

RESULTS

Of the total sample, 227 subjects (82%) were dentate and 149 (54%) were found to be positive for serum IL-6. These dentate subjects were categorized into three groups according to the number of teeth present. We found that serum IL-6 concentrations did not differ significantly across these three groups (Table 1).

Twenty-nine of the dentate subjects (13%) had severe periodontal disease. There were no significant differences between the mean serum IL-6 concentrations and the severity of periodontitis (Table 2). Furthermore, there were no significant differences between the mean serum IL-6 concentrations of males and those of females, or between the mean serum IL-6 concentrations of 70- and 80-year-olds (data not shown).

Table 1. Mean concentrations of IL-6 in relation to the number of teeth present in the total subjects

	No. of subjects (%)	Mean±SD[1] (pg/ml)	*P* value[2]
Edentulous	49 (17.8)	3.1±3.9	
1-9	57 (20.6)	2.9±5.2	
10-19	69 (25.0)	3.5±7.6	
20 or more	101 (36.6)	3.8±8.3	0.8781

[1] Less than 1 pg/ml was considered as 0.5 pg/ml.
[2] *P* values were determined by ANOVA.

Table 2. Mean concentrations of IL-6 in relation to the severity of periodontitis in the dentate subjects

	Concentration of IL-6		
	No. of subjects (%)	Mean±SD[1] (pg/ml)	*P* value[2]
Periodontitis			
Moderate	198 (87.0)	3.4±7.4	
Severe	29 (13.0)	4.0±7.8	0.651

[1] Less than 1 pg/ml was not detected in the ELISA and, therefore, calculated as 0.5 pg/ml for convenience in the statistical analysis.
[2] *P* values were determined by the Student's *t*-test.

DISCUSSION

Periodontal diseases give rise to gingival inflammation as well as to the destruction of periodontal tissues, and in severe cases can be accompanied by the loss of alveolar bone with eventual tooth loss. Both of these conditions are infectious diseases caused by microorganisms in dental plaque.

Numerous studies have reported that these oral bacteria can also affect systemic health (1,14-18). Indeed, several epidemiological studies have shown a correlation between oral hygiene status and respiratory infectious diseases (13), periodontal diseases and coronary heart disease (19), periodontal disease and cerebral vascular accident (20), and periodontitis and pregnancy complications (21). All of the dentate subjects in the present study had one or more clinical features of periodontal diseases such as redness and swelling. According to WHO criteria (13), complex professional treatment is indicated for periodontitis associated with a periodontal pocket 6 mm or more in depth. However such deeper periodontal pockets do not always present inflammation but may suggest an experience of past severe inflammatory disease or a current stable inflammatory condition. Accordingly, we dichotomized the severity of periodontal disease as "moderate" or "severe" based on the presence of both periodontal pockets more than 6 mm in depth and bleeding upon probing at the same periodontal pocket. We considered the presence of such signs to be an indication of severe periodontitis in the active phase. Of the 227 dentate subjects, 29 (13%) were found to have such severe stages of periodontal disease. There is at least a possibility that temporary bacteremia could occur in these subjects through subgingival dental plaque. We also recorded the number of teeth present, as elderly people have a tendency to accumulate inflammatory periodontal sites when more teeth are present.

The release of proinflammatory cytokines, including tumor necrosis factor, IL-1, IL-6, and IL-8, from activated monocytes, macrophages, and other cells stimulated by LPS, is an important component of the host immune response (22,23). Septic shock has also been shown to be associated with elevated levels of these molecules (4,5). In particular, IL-6 is believed to be a good indicator of an exaggerated proinflammatory response, and the concentrations of circulating IL-6 correlate with the severity and outcome of sepsis (24). Many bacteria related to periodontitis are gram-negative anaerobic bacteria. The detection of proinflammatory cytokine IL-6 stimulated by bacterial LPS and the role of this cytokine in the destruction of periodontal tissue have been reported in sites with localized periodontitis (10) and in vitro (11,12). In this context, we assessed the relationships between periodontitis and the concentrations of circulating proinflammatory cytokine IL-6. However, we could not find any evidence to support a correlation between oral health and serum IL-6 concentrations. This lack of correlation may reflect a decreased ability to control infection and/or a disregulation of the production of cytokines in the elderly. The circulating proinflammatory cytokine thus may not be of importance as an indicator for an increased incidence of periodontitis with increasing age.

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