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Gingivitis Susceptibility and its Relation to Periodontitis in Men

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Abstract

The objective of this cross-sectional study was to evaluate whether gingivitis susceptibility is associated with periodontitis. We analyzed data of 462 men in the VA Dental Longitudinal Study aged 47 to 92 years who had never smoked or had quit smoking 5+ years previously. Multiple logistic regression models, with tooth-level bleeding on probing at sites with attachment loss ≤ 2 mm as the dependent variable, were derived with adjustment for plaque, calculus, crown coverage, age, income, education, marital status, body mass index, diabetes, and vitamin C intake, and stratification by age (< 65 , $65+$ years). Periodontitis and mean attachment loss were positively associated with bleeding on probing, with stronger associations among men < 65 years old (for periodontitis, OR 2.1; 95% CI 1.5, 3.1) than men $65+$ years of age (OR 1.2; 95% CI 0.9, 1.6). Our results suggest that among never and former smokers, gingivitis susceptibility is higher among men with periodontitis compared with that in men without periodontitis.

Keywords

gingivitis; pathogenesis; periodontitis; susceptibility

INTRODUCTION

The classic experimental gingivitis study (Löe *et al.*, 1965) established the causal relationship between the quantity of bacterial plaque and the degree of gingivitis. In contrast, the role of gingivitis in the pathogenesis of periodontitis remains controversial. For many years, gingivitis and periodontitis have been regarded by many as a continuum, where longstanding gingivitis eventually progresses to periodontitis over time. However, epidemiologic studies have clearly demonstrated that not all gingivitis progresses to periodontitis. Furthermore, advances in the understanding of the pathogenesis of periodontitis have identified various host factors that determine susceptibility to periodontitis. Consequently, plaque-induced gingivitis is considered a necessary, but insufficient, cause of periodontitis. In turn, whether susceptibility to gingivitis is related to periodontitis susceptibility is unknown. The subject has recently been thoroughly reviewed (Tatakis and Trombelli, 2004; Trombelli, 2004).

In experimental gingivitis experiments, virtually every participant developed some degree of gingival inflammation in response to plaque accumulation. However, gingivitis susceptibility (as measured by the degree of gingival inflammation that develops in response to a given quantity of plaque) varied considerably between participants (Trombelli *et al.*, 2004).

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The purpose of the present study was, using clinical periodontal data from the VA Dental Longitudinal Study (DLS), to evaluate the hypothesis that susceptibility to gingivitis is higher among participants with greater susceptibility to periodontitis.

MATERIALS & METHODS

Study Participants

The VA Dental Longitudinal Study (DLS) is a closed-panel prospective cohort study of oral health and aging in men (Kapur *et al.*, 1972), ongoing since 1968. The DLS initially enrolled 1231 medically healthy men, ages 21 to 84 yrs, who also were participants in the Normative Aging Study (NAS) (Bell *et al.*, 1966). The men were not patients of the VA healthcare system. Rather, they received dental and medical care from the private sector. Participants returned to the study site approximately every 3 yrs to receive clinical dental examinations and radiographs, and to answer questions about dental care, nutrition, and lifestyle. The study was reviewed and approved by the Department of Veterans Affairs Subcommittee on Human Studies and the Boston University Medical Center Institutional Review Board. All participants gave written informed consent.

At each examination, the number of teeth remaining was counted, and each tooth was evaluated for restorations, plaque, and calculus. Plaque ('none', 'inter-proximal only', 'interproximal with continuation on buccal or lingual', 'all surfaces with 2/3 of tooth') and calculus ('none', 'discontinuous flecks', 'noncontinuous band on parts of tooth', 'continuous band around tooth') were recorded as ordinal scores *per* tooth. Beginning in examination cycle 7 (1987), the periodontal examination recorded probing pocket depths and attachment levels in mm, as well as bleeding on probing (BoP) at multiple sites *per* tooth. In all teeth, the direct mesiobuccal, midbuccal, distolingual, and lingual sites were probed. In addition, the buccal site of the mesial root was probed in molars. Since examination cycle 5, all dental examinations have been conducted by the same sole clinical examiner, a trained and calibrated periodontist (RIG).

Participants' education, marital status (married, other), income at baseline, and smoking history were obtained by interviewer-administered questionnaires. Information on smoking intensity (number of cigarettes *per* day) and years since last smoked, if applicable, was updated at each examination. Height and weight were measured at each examination, and body mass index (BMI) was calculated. For inclusion in the NAS cohort, all participants had to be systemically healthy. At follow-up examinations, participants were classified as diabetic if their fasting blood glucose was greater than 140 mg/dL, their two-hour post-prandial blood glucose was greater than 200 mg/dL, or if they were documented as having a clinical diagnosis of diabetes in their medical record, or if they were taking insulin or oral hypoglycemic drugs.

Vitamin C intake level was derived from self-administered semi-quantitative food frequency questionnaires that were introduced with DLS cycle 7 (Willett *et al.*, 1985). Participants reported how often they consumed standardized portions of 146 food items in the preceding year, and current and past use of vitamin/mineral supplements. Mean daily vitamin C intakes (diet plus supplements) were computed from this information.

Statistical Analysis

For the present analysis, data of completed DLS examination cycles 7 through 9, with comprehensive periodontal examinations, were used (1987–1998). We conducted a cross-sectional analysis of gingivitis susceptibility in participants with or without periodontitis. The analysis was restricted to never-smokers and former smokers who had quit at least 5 yrs prior to the examination.

Participants were classified as having periodontitis if they had at least 1 interproximal site with periodontal attachment loss and probing depth of 5+ mm (modified after Tomar and Asma (2000)) (excluding 3rd molars). Furthermore, mean interproximal attachment loss was calculated for each participant.

We conducted a tooth-level analysis restricted to teeth not affected by periodontitis, *i.e.*, interproximal sites not exceeding 2 mm of attachment loss. A tooth was considered positive for bleeding on probing if either the mesial or distal interproximal site showed bleeding. Susceptibility to gingivitis can be defined as the degree of gingival inflammation, given a certain amount of plaque and calculus (Trombelli *et al.*, 2004). Hence, multiple logistic regression models were fit with BoP as the dependent variable, and calculus score, plaque score, and full crown coverage (yes/no) as independent variables. Periodontitis status (as defined above, based on all present teeth) was entered as a dichotomous variable. In separate models, mean attachment loss was entered as both a categorical and a continuous variable. The models were stratified by age (< 65, 65+ yrs), and full models were adjusted for age (continuous), education (up to high school/more than high school), income at DLS baseline (3 categories), marital status (married/other), BMI (continuous), diabetes (yes/no) (Hugoson *et al.*, 1989; Cutler *et al.*, 1999), and vitamin C intake (continuous) (Leggott *et al.*, 1991).

The data were analyzed by logistic regression analysis, with the tooth as the unit of analysis. To compensate for the correlated nature of data obtained from the same individual, we used generalized estimating equations (GEE) (Liang and Zeger, 1993) with exchangeable correlation (STATA 7.0, College Station, TX, USA).

RESULTS

In total, we examined 579 men, each with at least 10 remaining teeth, in cycles 7 through 9. Of these, 483 were never-smokers or had quit smoking at least 5 yrs prior to the examination. Twenty-one participants had no teeth with interproximal attachment loss ≤ 2 mm remaining, and were excluded. The final analytic sample consisted of 462 men with a mean age of 68 yrs (range, 47–92 yrs). In this sample, sociodemographic characteristics were similar for participants with and those without periodontitis; however, the participants who had periodontitis were more likely to have diabetes, had lower vitamin C intakes, higher levels of bleeding, plaque, calculus, crown coverage, attachment loss, and fewer crowns (Table 1).

There were positive associations between periodontitis and gingival bleeding independent of plaque, calculus, and crown coverage. Additional adjustment for other predictors of gingivitis yielded similar estimates (Table 2). Compared with men < 65 yrs without periodontitis, sites in men < 65 yrs with periodontitis had approximately twice the odds of bleeding (OR: 2.1, 95% CI 1.5, 3.1). The association was considerably weaker in older men (65+ yrs), and did not reach statistical significance (OR: 1.2, 95% CI 0.9–1.6). Similarly, compared with men with mean interproximal attachment loss of less than 1.5 mm, sites in younger and older men with mean attachment loss of at least 2.5 mm had 50% (OR: 1.5, 95% CI 1.1, 2.0) and 40% (OR: 1.4, 95% CI 1.1, 1.7) increased odds of bleeding on probing, respectively.

DISCUSSION

In the present study, we found that men with periodontitis had more gingival bleeding at gingival sites without attachment loss than did men without periodontitis, independent of plaque, calculus, crown coverage, and other determinants of gingivitis and gingivitis susceptibility. The association appeared to be stronger among younger men and was not statistically significant among older men.

The analysis of gingivitis susceptibility in natural gingivitis and its relationship to susceptibility to periodontitis is not straightforward. Both susceptibility to gingivitis and susceptibility to periodontitis represent subject-level phenomena. This is an important difference compared with studies that aim to determine whether gingivitis precedes periodontitis in the pathogenesis of periodontal disease, where the local, site-level relationship between the two conditions is of primary interest (Albandar *et al.*, 1998; Schatzle *et al.*, 2003). However, the assessment of gingivitis susceptibility has to account for tooth-specific determinants of gingivitis, *e.g.*, plaque and calculus. This is particularly important in natural gingivitis as opposed to experimental gingivitis (Trombelli *et al.*, 2004), because the former exhibits a higher degree of intra-individual (*i.e.*, inter-site) variability than the latter. We therefore conducted tooth-specific analyses, adjusting for tooth-specific determinants of gingivitis.

The situation is further complicated by the fact that gingival bleeding on probing is a symptom of both gingivitis and periodontitis. Hence, once periodontitis is established, gingival bleeding due to gingivitis is impossible to distinguish from that due to periodontitis. Sites affected by periodontitis have showed more gingival bleeding, even if bleeding on probing was assessed at the marginal gingiva (Dietrich *et al.*, 2004). In the present analyses, the assessment of gingivitis susceptibility was therefore restricted to sites without attachment loss. Furthermore, the analysis was restricted to never-smokers and ex-smokers who had quit at least 5 yrs previously, because of the strong suppressive effect of smoking on gingival bleeding (Bergström and Preber, 1986; Dietrich *et al.*, 2004). Adjustment for smoking status (never vs. former) yielded identical results (data not shown).

The relation between gingivitis susceptibility and periodontitis was first evaluated by a group of investigators about 20 years ago (van der Velden *et al.*, 1985a,b; Abbas *et al.*, 1986; Winkel *et al.*, 1987). These studies provided indirect evidence for an association between gingivitis susceptibility and periodontitis, although they were limited mainly by the small number of participants. In an experimental gingivitis model in a total of 13 individuals with successfully treated periodontitis (*i.e.*, a reduced but healthy periodontium), van der Velden *et al.* found that younger individuals (25–39 yrs, *n* = 7) developed higher levels of gingival bleeding compared with older individuals (45–54 yrs, *n* = 6) (van der Velden *et al.*, 1985a). In further experimental gingivitis studies, this group found that gingivitis susceptibility was unrelated to age (Winkel *et al.*, 1987), and the former results were thus interpreted as supporting a positive association between susceptibilities to gingivitis and periodontitis (van der Velden *et al.*, 1985a). Furthermore, in a small cross-sectional study of seven individuals with untreated juvenile periodontitis and seven individuals aged 52 yrs and older, apparently not susceptible to periodontitis, the same authors found significantly higher bleeding/plaque ratios among the susceptible individuals (with juvenile periodontitis), and hence proposed this ratio as a possible prognostic indicator for periodontal breakdown (van der Velden *et al.*, 1985b). However, the results of the latter study may be partially explained by the increased bleeding in the presence of attachment loss in the periodontitis group. Furthermore, the use of a bleeding/plaque ratio did not account for other determinants of gingivitis.

Notwithstanding these limitations, these results are consistent with our findings in the present study. More recently, Trombelli *et al.* 2006 conducted an experimental gingivitis study in 13 individuals with treated aggressive periodontitis. The degree of gingivitis that developed in response to *de novo* plaque formation in these individuals was compared with that in historical controls from a similar experimental gingivitis study (Trombelli *et al.*, 2004). Individuals with aggressive periodontitis had significantly higher volumes of gingival crevicular fluid than did periodontally healthy participants; however, no differences were found for clinical gingivitis indices (Trombelli *et al.*, 2006).

In the present study, the association between gingivitis susceptibility and periodontitis appeared to be stronger among younger men. This is consistent with our hypothesis, since younger individuals with levels of periodontal breakdown similar to that in older individuals may be considered to be more susceptible to periodontitis (van der Velden *et al.*, 1985a).

Recently, our understanding of the pathogenesis of both gingivitis and periodontitis has changed with the realization that inflammatory tissue changes in both diseases are mediated, for the most part, by the host. While the etiology of both diseases is clearly the bacterial biofilm, the pathogenesis is that of an inflammatory disease. Hence, the relationship between gingivitis and periodontitis, when considered in the context of the degree of inflammation, or the magnitude of the inflammatory response, is biologically plausible. This concept is supported by several levels of evidence. In addition to the data presented here, there are several reports of genetic polymorphisms related to inflammatory response that demonstrated an association between high inflammatory response and susceptibility to disease (Kornman *et al.*, 1997; Kornman and di Giovine, 1998; Scapoli *et al.*, 2005). Further, analysis of more recent data suggests that failure of endogenous pathways that regulate resolution of inflammation is a characteristic of periodontitis that points to the importance of regulation of inflammation (or lack of it) as a determinant of susceptibility to gingivitis and periodontitis (Serhan *et al.*, 2003; Van Dyke and Serhan, 2003).

This study had limitations. First, it was cross-sectional, and there is a possibility that prevalent periodontal disease affected gingivitis susceptibility. Second, statistical adjustment for major gingivitis determinants may not have been complete, resulting in residual confounding by plaque, calculus, or other determinants of gingivitis susceptibility. Similarly, we could adjust for plaque only as quantified by a standard clinical index, and had no information on plaque quality. However, older men had higher amounts of plaque and calculus than younger men, which would not be consistent with a stronger association among younger men if due to residual confounding. Third, even when performed by a single examiner, clinical gingivitis measures have notoriously high variability (Newbrun, 1996; Van der Weijden *et al.*, 1994). We would expect such measurement error to be non-differential and introduce bias toward the null, underestimating the true association between gingivitis susceptibility and periodontitis. Finally, the present cohort was restricted to white non-Hispanic men, and results may not be generalizable to women or other racial/ethnic groups. However, in a similar analysis using NHANES III data, we found similar results and no differences between genders and racial/ethnic groups (unpublished observations).

In conclusion, the results of the present study suggest that susceptibility to gingivitis may be associated with susceptibility to periodontitis among men.

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Table 1
Distribution of Participant Characteristics by Periodontal Status

	Periodontitis [Mean $\pm$ SD and n (%)]	
	Yes (n = 86)	No (n = 376)
Age (yrs)	68.7 $\pm$ 7.5	67.9 $\pm$ 7.2
Income at DLS baseline (1968–1973)		
$\leq$ \$14,999	29 (34)	139 (37)
\$15,000–24,999	42 (49)	176 (47)
$\geq$ \$25,000	15 (17)	61 (16)
Married	68 (79)	297 (79)
Education > high school	53 (62)	239 (64)
Body Mass Index (kg/m ²)	27.8 $\pm$ 3.6	27.3 $\pm$ 3.8
Diabetes	10 (12)	21 (6)
Vitamin C intake (mg)	120 $\pm$ 202	197 $\pm$ 267
%Bleeding ^a	0.37 $\pm$ 0.32	0.28 $\pm$ 0.24
Mean plaque score ^a	0.78 $\pm$ 0.46	0.68 $\pm$ 0.39
Mean calculus score ^a	0.63 $\pm$ 0.53	0.51 $\pm$ 0.37
%Crown ^a	0.10 $\pm$ 0.22	0.16 $\pm$ 0.22
Mean attachment loss ^a (mm)	3.0 $\pm$ 0.8	2.2 $\pm$ 0.8
Never-smokers	29 (34)	168 (45)
Time since smoking cessation ^b (yrs)	26 $\pm$ 12	26 $\pm$ 12

^aProportion or means for all available teeth.

^bFormer smokers only.

Table 2
Association between Periodontitis/Attachment Loss and Bleeding on Probing by Age Groups

	< 65 yrs			65+ yrs		
	OR	Basic Model 95% CI	Full Model 95% CI	OR	Basic Model 95% CI	Full Model 95% CI
Periodontitis yes/no	2.1 ^a	1.4, 3.0	1.5, 3.1	1.2	0.9, 1.6	0.9, 1.6
Mean attachment loss						
< 1.5 mm	1.0	Reference	Reference	1.0	Reference	Reference
1.5–2.5 mm	1.1	0.9, 1.4	0.9, 1.4	1.0	0.8, 1.2	0.8, 1.2
≥2.5 mm	1.5 ^a	1.1, 2.0	1.1, 2.0	1.4 ^a	1.2, 1.8	1.1, 1.7
Trend (<i>per</i> mm)	1.2 ^a	1.0, 1.4	1.0, 1.4	1.1	1.0, 1.3	1.0, 1.2

^aOR = Odds Ratio, statistically significant at 5% level.

95% CI = 95% confidence interval.

Dependent variable: bleeding on probing.

Basic model - adjusted for plaque, calculus, and crown coverage.

Full model - adjusted for plaque, calculus, crown coverage, age, education, income at baseline, marital status, body mass index, diabetes, and vitamin C intake.