Periodontal Medicine: A New Paradigm

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Abstract

Recent evidence indicates that we need to change how we think about the etiology and pathogenesis of periodontal disease. Although bacteria are a necessary factor in the equation, the reaction of the host's immuno-inflammatory system is responsible for most of the destruction found in periodontal disease. Thus, it makes sense that a number of environmental and acquired factors may modify a patient's risk of developing periodontal disease. This paper reviews the scientific evidence for a number of these risk factors including age, genetics, smoking, diabetes mellitus, stress and osteoporosis.

MeSH Key Words: *periodontal diseases; risk factors*

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Before the 1980s, periodontitis was thought to be universally prevalent in humans by middle age and all preventative measures were directed at controlling the bacterial challenge. In 1986, Löe and others[1] published a landmark paper that challenged this paradigm. Over a period of 15 years, he examined a group of male tea workers in Sri Lanka. These men did not use any oral hygiene methods and had no access to dental care, allowing the study of the natural progression of untreated periodontal disease. The results showed that all individuals were not equally affected. The vast majority (81%) of the men showed moderate progression in attachment loss, 11% did not progress beyond gingivitis and the remaining group (8%) exhibited rapid loss of attachment, losing between 10 and 32 teeth over 15 years.

These findings bring up a number of interesting points, which have shifted the focus of periodontal research over the last few decades. First, although gingivitis may represent an early stage in the natural history of periodontitis, it may also be a separate disease entity, which in some patients will not progress. Second, it appears that the prevalence of periodontal disease severe enough to cause tooth loss is lower than originally believed. Finally, the findings suggest that periodontitis is not a single disease entity, but rather a family of closely related diseases that vary in etiology, natural history and response to therapy. All of these theories have been substantiated by other researchers,[2-4] indicating that although bacteria are essential for periodontal disease to occur, other factors may play a significant role.

Environmental and acquired risk factors affect the onset, rate of progression and severity of periodontal disease as well as the response to therapy. Risk factors are defined as "an aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic, which on the basis of epidemiologic evidence is known to be associated with a health-related condition."[5] Although the risk factor may not be a proven cause of a particular disease, its presence implies a direct increase in the probability of the disease occurring.

Proving the link between cause and effect of chronic diseases, such as periodontal disease, is not an easy task. In acute conditions, an immediate reaction (e.g., mandibular fracture) follows exposure to the suspected cause (e.g., blow to the chin). As periodontal disease is generally slowly progressing, people studied over a long period may be exposed to a multitude of potential causes making determination of a cause–effect link more difficult. However, there are some rules we can apply when evaluating the literature; we must be sure that the association is consistent, strong and makes some biologic sense.

The repeated demonstration, by different investigators in different settings, of an association between exposure to a putative cause (e.g., smoking) and the outcome of interest (e.g., periodontal attachment loss) constitutes consistency. The strength of the evidence is determined by the type of study. Although the best evidence is derived from a randomized clinical trial, it is neither practical nor ethical to produce periodontal disease in some patients and ensure that others do not get the disease. Thus, a prospective cohort study, in which we follow a group of people with and without exposure to a suspected cause over time (e.g. a particular genetic defect) to see who develops the disease of interest (e.g. aggressive periodontal disease) is the best level of evidence. Unfortunately, cohort studies are expensive and time consuming. A case-

control study examines people with the disease in question (e.g. periodontal disease) and matches them with "controls" who are disease free to determine differences between the 2 groups in the rate of exposure to a potential cause (e.g. comparing the 2 groups for rates of the genetic defect). Although results from this type of study are associated with a greater potential for bias than those from a cohort study or randomized trial, they are often the only evidence available. The final criterion is that there should be some reasonable biologic explanation for the putative cause to play a role in the outcome.

The relation between periodontal disease and its potential risk factors can be expressed in terms of the probability that a person exposed to the factor will develop periodontal disease. For a randomized controlled trial or cohort study, this is calculated as relative risk (RR). In a case-control study, it is calculated as the odds ratio (OR). An RR or OR of 1.0 means that there is no increased likelihood of developing the disease as a result of exposure to the factor. The greater the ratio over 1.0, the greater the likelihood.

A recent review[6] surmised that, based on good quality clinical research, age, genetics, smoking and diabetes mellitus are likely risk factors for periodontal disease. Based on less rigorous research, psychosocial stress and osteoporosis are less likely, but still potential risk factors. The evidence for each of these risk factors is outlined below.

Age

The prevalence of periodontal disease increases with age.[7,8] However, it is unclear whether becoming older is related to increasing attachment loss (by virtue of having teeth for a longer period of time) or if the worsening periodontal status is related to the consequences of aging. Although aging is associated with metabolic changes, it has not been directly linked with periodontal attachment loss. While the rate of periodontal destruction increases after the age of 70 years, up to that age, the rate of attachment loss is the same.[9]

Genetics

There is evidence from multiple sources that genetics play a significant role in certain periodontal diseases. Early-onset periodontal diseases (prepubertal, juvenile and rapidly progressive periodontal diseases), for example, have a strong genetic component.[10] Recently, it has been shown that a combination of 2 polymorphisms in the interleukin-1 (IL-1) gene is associated with a severe form of adult periodontitis.[11] In the populations tested to date, a genotype-positive patient is up to 20 times more likely to develop advanced adult periodontitis beyond 40 years of age than a genotype-negative patient.[12]

Smoking

A wealth of data show that smoking is strongly associated with periodontitis. The majority of tooth loss in adults aged 19-40 is associated with smoking more than 15 cigarettes a day.[13] A linear dose–response relation between smoking and bone loss has also been shown. In a study of over 1,400 people, Grossi and others[14] found that, compared with a nonsmoker, a light smoker (<10 cigarettes a day) was 2.0 times more likely to have alveolar bone loss. In a heavy smoker (>10 cigarettes a day), the odds were 7.3.

The biologic basis for smoking as a risk factor for periodontal disease is clear. Smoking inhibits neutrophil function in saliva as well as in connective tissues.[15] It suppresses immunoglobulin G2 antibody response and enhances the release of interleukin-1 beta (IL-1β), affecting osteoblast function.[16] In addition, it constricts the gingival blood vessels, which accounts, in part, for the lack of bleeding on probing found in most smokers. Periodontal therapy, both surgical and nonsurgical, is less likely to be effective in smokers and disease is more likely to recur than in non-smokers.[17,18]

Diabetes

People with diabetes mellitus are 15 times more likely to be edentulous than people without the disease. Both type 1 (insulin controlled) and type 2 (noninsulin controlled) diabetes have the same effect. The likelihood of periodontal disease increases when diabetes is poorly controlled.[19] People with well-controlled diabetes, with good oral hygiene and on a regular maintenance schedule have the same chance of developing severe periodontitis as people without diabetes. The mechanism is multifactorial. The small blood vessels of people with diabetes have thickened basement membranes, leading to a reduction in transport across the vessel walls. There is a reduction in collagen production by gingival and periodontal fibroblasts. In addition, high levels of pro-inflammatory mediators responding to endotoxin from gram-negative bacteria lead to an increase in collagen breakdown.

Potential Risk Factors

Several case studies and case-control studies have linked generalized osteopenia (a decrease in the amount of normal mineralized bone found in patients with osteoporosis) with alveolar bone loss. In addition, Jeffcoat and Chesnut[20] have shown that the use of bisphosphonates, a class of drug used to treat postmenopausal osteoporosis, slowed the rate of alveolar bone loss in postmenopausal women with periodontitis. Unfortunately, the interaction of several known risk factors, including smoking, clouds the results of these studies.

There is a strong association between psychosocial stress and acute necrotizing ulcerative gingivitis (ANUG).[21] ANUG patients under stress have reduced neutrophil chemotaxis and phagocytosis, leading to a diminished host response to bacterial challenge. However, the link between stress and periodontal diseases on the whole has not been adequately evaluated.

Periodontal Disease as a Risk Factor

Examining some of this evidence from another angle, it may be reasonable to assume that periodontal infections could influence overall health and the course of some systemic diseases. In fact there is accumulating evidence that this may be the case.

One example is the effect periodontal disease may have on adverse pregnancy outcomes. Preterm, low birth weight (PLBW)

infants represent a significant cause of perinatal morbidity and mortality. Identified risk factors include maternal age (<17 years or >34 years), socioeconomic status, inadequate prenatal care, hypertension, substance or tobacco abuse, genitourinary tract infections, diabetes and African-American ancestry. Efforts to control these risk factors have not resulted in a significant reduction in the number of PLBW births.[22] Thus, there may be other, unrecognized factors contributing to this phenomenon.

A number of biologically active mediators such as prostoglandin E_2 (PGE_2) and tumour necrosis factor alpha (TNFα) are also involved in normal parturition. These mediators are raised to artificially high levels during infections and thus may foster premature labour.[23] Lipopolysaccharides from gram-negative anerobes found in periodontal pockets trigger release of PGE_2 and TNFα, which may, in turn, affect the course of pregnancy. Evidence to support this hypothesis has been obtained in rodent models. In addition, a recent study of mothers of PLBW infants,[24] with otherwise low risk, had significantly more periodontal disease than a similar group of women with normal weight infants at birth.

Cardiovascular diseases (CVDs), including myocardial infarction and stroke are the major causes of death in North America. The classic risk factors — age, hypertension, hypercholesterolenemia and cigarette smoking — can only account for 2/3 of the variation in the incidence of CVD cases. Again, unrecognized risk factors may contribute to the pathogenesis of CVD. Recent studies have found that patients with periodontal disease have a 1.5- to 2.0-fold greater risk of incurring fatal CVD than patients without periodontal disease.[25,26] In fact, oral infections seem to increase the risk of coronary artery disease to a degree similar to the classic risk factors.

The association between periodontitis and diabetes mellitus is outlined above. It has been assumed that the association is due to the fact that people with diabetes have a compromised ability to fight infections such as periodontal disease. However, this relation is currently being challenged. It may be that periodontal disease predisposes or exacerbates the diabetic condition. A recent survey[27] has shown that the concentration of glycated hemoglobin (a measure of diabetic control) is elevated in people with type 2 diabetes and severe periodontal disease. In another study of people with type 2 diabetes, severe periodontitis was strongly associated with an increased risk of poor glycemic control.[28]

Implications for Clinical Practice

What does all of this mean to the practising clinician? We know that although plaque is still the primary etiology of gingival and periodontal diseases, the host response is probably the most important link in the causal chain. Unfortunately, there is no way to reliably (and cost-effectively) predict whether the patient with gingivitis sitting in our chair will develop attachment loss slowly, quickly or not at all. However, knowing some of the risk factors can assist with these predictions.

Although we are not able to change our age, our gender or, to date at least, our genetic composition, there is a genetics test that will identify people with the IL-1 phenotype (PST, Interleukin Genetics, San Antonio, TX [approximately $120 US]). By identifying people who are at greater risk of developing severe adult periodontitis, we may be able to carry out earlier or more aggressive intervention for these patients.

Due to the strong association of smoking with periodontal disease, it would be prudent to advise our patients that compared to nonsmokers and former smokers they are at greater risk of developing periodontal disease; less likely to respond well to periodontal therapy; and more likely to suffer postsurgical complications. Patients requiring dental surgery might be referred for smoking cessation counselling or treated by more conservative means.

In people with unexpected attachment loss, we should be suspicious of systemic problems, particularly diabetes mellitus. For people with diagnosed diabetes who have difficulty maintaining their blood sugar at a constant level, we should be monitoring their periodontal situation closely.

Currently, the rationale for treating periodontal diseases is to preserve the structure, function and esthetics of the dentition. In fact, such treatment may be just as important in terms of preventing untoward effects on a patient's overall health. ◆

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