Literature Review

MedInform

DOI: 10.18044/MEDINFORM.202292.1511

ISSUE 2, 2022

The significance of stress for the development of periodontal disease

Antoaneta Mlachkova, Velitchka Dosseva-Panova

Faculty of Dental Medicine, Department of Periodontology, Medical University, Sofia, Bulgaria

Abstract

The term "stress" is derived from the Latin word "stringere" which means "strained". Today, stress is classified as a "risk factor" for the development of periodontitis. Stress is seen as a cognitive perception of uncontrollability and/or unpredictability, i.e. expressed in physiological and behavioral response. Therefore, stress can be seen as a process with psychological and physiological components. Already in 1976, Selye defined stress as a state of the body's reaction to physical and mental forces beyond adaptive capacity, which leads to adaptation diseases and ultimately to exhaustion and death. It recognizes stress factors that act and cause positive changes in the body (e.g. pleasant and positive emotions) leading to a state of response that is defined as "eustress", or stressors that can be negative and cause sensations, which threaten homeostasis by triggering pain, discomfort and physiological pathology. The author defined the state of negative response as "distress".

It is known that stress is a response to the action of constant adverse stimuli. At one point or another, every individual can suffer from stress. Stress is compatible with health because it is necessary to cope with the challenges of everyday life. Problems for the individual begin when the stress response is inappropriate to the intensity of the stressor present. Psychological stress can regulate the cellular immune response. Communication between the central nervous system and the immune system occurs through a complex network of two-way signals linking the nervous, endocrine, and immune systems. Stress disrupts the homeostasis of this network, which in turn alters the immune system's response. The direct link between periodontal disease and stress remains to be proven, partly due to the lack of animal models and the difficulty in quantifying the strength and duration of stress, as well as the presence of many factors influencing the severity of periodontal disease. According to Breivik et al, stress is not what happens to an individual, but how that individual responds to what happens. They define stress as a psychophysiological response of the body to the threat caused by stressors.

Keywords: *stress, risk factor, periodontopathogens, cortisol, necrotic-ulcerative gingivitis.*

Introduction

Today, periodontitis is known to be a chronic inflammatory disease characterized by gingival bleeding, presence of periodontal pockets, destruction of connective tissue supracrestal attachment and loss of alveolar bone (1, 2). Abnormal responses of the body, such as an increase in pro-inflammatory cytokines from the presence of pathogenic bacteria in the dental biofilm, play a crucial role in the progression of periodontitis. The etiopathogenesis of periodontal disease indicates that periodontitis is a multifactorial disease caused by periodontopathogens in which host and environmental factors play an important role (2). Microorganisms play an essential role as primary etiologic agents, but alone appear to be insufficient to explain the onset or progression of disease. The onset and progression of periodontal disease are influenced by a variety of systemic diseases, environmental factors, and psychological stressors that have the potential to alter periodontal tissues and the body's immune response, leading to more severe periodontal destruction (3, 4). There is evidence that stress can negatively affect the outcome of adequately administered periodontal treatment (3). As with many other chronic infections, the onset and progression of periodontal disease is largely programmed by the influence of certain systemic risk factors such as: diabetes, smoking and genetic predisposition, for example interleukin-1 polymorphism (a specific genetic marker that identifies patients with increased risk of developing severe periodontal disease) (2, 4). But studies are still needed to support stress as a true risk factor in the etiology of periodontal disease.

Types of psychological stress factors

A stressor is any stimulus, situation, or circumstance with the potential to trigger a stress response. The effects of the stress response include anxiety, depression, impaired cognition, and altered self-esteem (3). Although much more is known about the role of disease processes, such as infection and cancer, as stressors capable of triggering widespread and prolonged inflammatory and classical stress syndromes, it is now believed likely that emotional, behavioral, and psychosocial stressors also are able to activate the stress system, along with its associated effects on the immune system.
Psychosocial stressors are generally classified as:

✓ Major stressful life events

✓ Minor daily stressors or "problems"

✓ Other psychosocial stressors are the well-known behavioral and emotional responses to the common consequences of periodontal disease, which include pain conditions, bleeding, unpleasant tastes and odors from the oral cavity, and unaesthetic appearance of the teeth and adjacent soft supporting structures (5).

Other signs and symptoms, such as abscesses and intense pain, loose teeth, and the ever-present threat of tooth loss at an early or adult age, are also often factors that serve as potentially powerful negative emotional stressors. In addition, the treatment of periodontitis is associated with pain and discomfort, takes time and resources. All of these disease-related perceptions, concerns, and emotions can themselves constitute and act as an important set of stressors that can trigger stress system responses that are further detrimental to periodontal health (2, 4, 5).

Effects of stress on periodontal diseases

A number of mechanisms have been proposed that could account for the hypothesized relationship between psychosocial conditions and inflammatory periodontal disease.

ENDOCRINE CHANGES

Periodontal status has been suggested to be related to changes in adrenal corticoid concentration. Psychosocial stressors may play a role in initiating a cascade of events in the corticotropin-releasing hormone/hypothalamic-pituitary-adrenal (HPA) axis, the autonomic nervous system, and the central nervous system, the physiological consequences of which are immunosuppression, increasing the likelihood of infection and especially periodontitis. Recent studies confirm the fact that the concentrations of cytokines [interleukin (IL)-6, IL-1β, etc.] and cortisol in the gingival crevicular fluid (GCF) are higher in people showing signs of depression (2, 4, 5). High levels of cortisol can have a particularly negative impact on periodontal tissues, due to the extremely rapid exchange of some components of inflammation. Elevated glucocorticoid levels can reduce the amount of fibroblasts and collagen production. These changes may be sufficient to cause an imbalance in the synthesis and degradation of periodontal tissues, especially if preexisting inflammation is present.

In summary, it can be said that stress provokes the secretion of corticosteroids from the adrenal cortex with corresponding effects on the immune system - an inhibitory effect on the function of monocytes, polymorphonuclear cells, eosinophils, mast cells, and also inhibition of the synthesis of certain cytokines - IL-1, IL -2, IL-3, IL-6, TNFα, INF-γ, PGE2, leukotrienes, etc (2, 4-6).

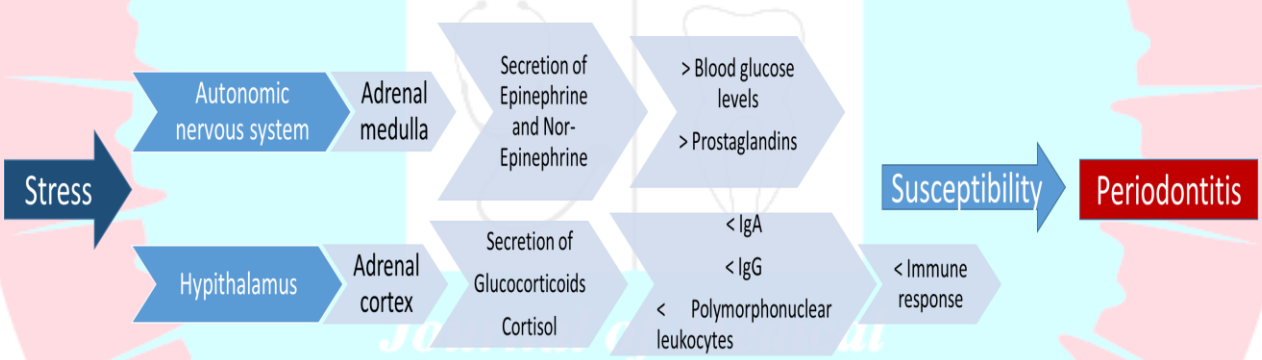

Figure 1. Relation "stress-immune response-periodontal disease".

CHANGE IN THE QUANTITY AND QUALITY OF SALIVA

It has been hypothesized that both increases and decreases in salivation induced by emotional disturbance may adversely affect the periodontium. Emotional distress can also lead to changes in salivary pH and chemical composition such as immunoglobulin (IgA) secretion. These interrelationships between salivary physiology and psychological status do not necessarily indicate periodontal disease causation, but they do indicate a pathway by which periodontal health is affected by changes occurring in saliva (7).

REDUCED BODY RESISTANCE

Periodontal diseases are inflammatory diseases associated with local and systemic elevations of pro-inflammatory cytokines, such as TNF-α, IL-6 and prostaglandins, and lead to tissue destruction induced by matrix metalloproteinases (4, 7, 8). Stress damages the balance between pro-inflammatory and anti-inflammatory responses. The relationship between stress and periodontal diseases may be mediated by changes in the levels of GCF, IL-1, IL-6 and a decrease in chemotaxis and phagocytosis of polymorphonuclear leukocytes and decreased lymphocyte proliferation. Psychosocial stress stimulates the brain, and its stimulation or inhibition depends on the individual's adaptive and maladaptive coping, respectively. When stimulated, the autonomic nervous system leads to the secretion of prostaglandins and proteases, leading to the progression of periodontal disease. HPA leads to the production of glucocorticoids (cortisol), which suppress the immune system by reducing the secretion of IgA and IgG, thus enhancing the progression of periodontal disease and poor response to treatment. Subsequently, this process can increase the vulnerability of periodontal tissues to pathogenic microorganisms by activating cellular responses leading to local tissue disruption (1, 2, 6, 8).

Studies have shown that periodontal pathogens are influenced by stress hormones. For example, it has been found that catecholamines can affect bacterial motility, growth and virulence, as well as 'quorum sensing'. Nor-Epinephrine has been found to suppress the growth of P. gingivalis and A. actinomycetemcomitans. Cortisol can suppress the metabolic activity of F. nucleatum, P. intermedia, E. corrodens and T. forsythia (1, 9).

The study by Dubar et al. showed a statistically significant correlation between some periodontal pathogens and stress, most notably P. gingivalis and T. forsythia, which belong to the red Sokransky complex (9). Results indicated a significant relationship between cortisol levels and the presence of T. forsythia, cortisol concentration and P. micra (4). Dubar et al. found higher levels of T. forsythia and C. rectus in stressed subjects compared to non-stressed subjects (9). Other studies have shown similar results, suggesting a close link between stress and the immune system, and increased levels of salivary cortisol (1, 5). The relationship between gingival inflammation, periodontal pocket depth, financial status of the study population and stress was also demonstrated. The issue of stress and periodontal disease is discussed by McGlynn et al. 1990, who investigated the processes of metabolizing stress hormones by subgingival pathogenic bacteria (10).

STRESS AND DEVELOPMENT OF NECROTIC-ULCERATIVE GINGIVITIS

The relationship of stress with some pathological conditions of the oral mucosa - for example, canker sores - has been documented in the literature (2, 4). Also, necrotizing ulcerative gingivitis (NUG) is the most studied periodontal disease in relation to psychosocial stressors (4, 5, 11). NUG has been suggested to have a psychogenic origin (1, 2, 4, 5, 8). Psychogenic factors probably predispose to the disease by favoring bacterial overgrowth and/or weakening the body's resistance.

The body's tissue resistance can be altered by mechanisms acting through the autonomic nervous system and endocrine glands, resulting in increased levels of corticosteroids and catecholamines. It can reduce the gingival microcirculation and salivation and improve the nutrition of Prevotella intermedia and at the same time suppress the functions of neutrophils and lymphocytes, which facilitates bacterial invasion and damage. Patients with NUG have been reported to experience:

- Suppressed chemotaxis and phagocytosis of polymorphonuclear leukocytes;
- Decreased proliferation of lymphocytes upon stimulation by a non-specific mitogen (5, 11).

STRESS AND BEHAVIORAL CHANGES

Stress affects the consequences of behavioral patterns ranging from neglected oral hygiene to inadequate diet, poor sleep, use of tobacco products, alcohol consumption, contributing to the "vicious cycle" of increasingly severe forms of advanced periodontal inflammation and disease (2-6). It has been shown that proper oral hygiene depends in part on the mental health of the patient (2, 4). It has been reported that psychological disturbances may cause patients to neglect oral hygiene and that the resulting plaque accumulation is harmful to the adjacent periodontal tissues (2, 4, 7, 11). Academic stress has been reported as a risk factor for gingivitis. It is believed that emotional states can alter an individual's diet, thereby indirectly affecting periodontal status. Psychological factors influence food choices, consistency and amounts of food eaten (5). This may include, for example, the consumption of excessive amounts of refined carbohydrates and diets that require less intense chewing and therefore predispose to plaque build-up in risk areas. It is hypothesized that stress leads to other behavioral changes, such as overeating, especially on a high-fat diet, which can then lead to immunosuppression through increased cortisol production (5).

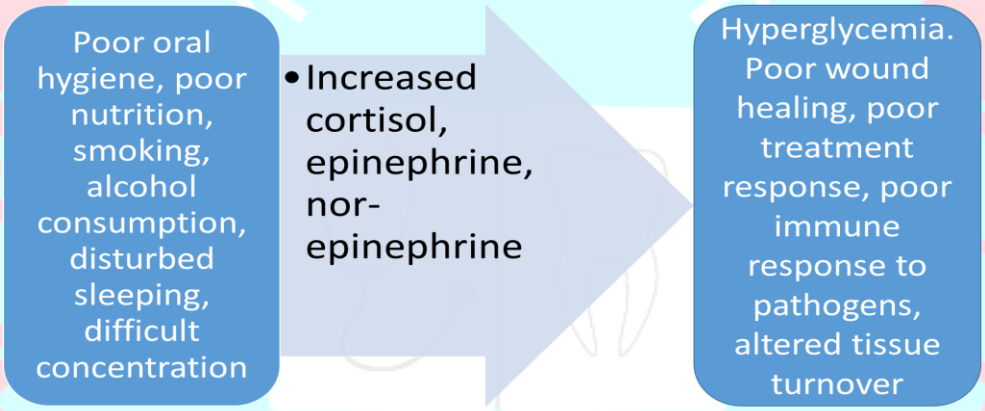

Figure 2. Stressors and their effects.

ROLE OF OXIDATIVE STRESS IN PERIODONTITIS

Oxidative stress is defined as an imbalance between oxidants and antioxidants in favor of oxidants, leading to disruption of redox signaling and control and/or molecular damage. Oxidative stress is a key driver of chronic inflammation and, as a result, has an important role in the pathogenesis of a wide range of chronic inflammatory diseases (eg, type 2 diabetes, cardiovascular disease, and metabolic syndrome). Oxidative stress has actually been proposed as a link between periodontitis and systemic disease (1, 2, 4). In health, there is a delicate balance between oxidants on the one hand and antioxidants found in all tissues of the body on the other hand. If this fine balance is disturbed by excessive production of oxidants and/or depletion of local antioxidants, the resulting excess of oxidants causes oxidative stress and is associated with local tissue damage seen in periodontitis.

Oxidative stress has recently been defined as “an imbalance between oxidants and antioxidants in favor of oxidants leading to disruption of redox signaling and control and/or molecular damage” (3). It can cause direct tissue damage by altering molecules, such as proteins, lipids, and DNA, thereby damaging cells

directly, or by activating redox-sensitive transcription factors in the cell, leading to changes in downstream gene expression and production of pro-inflammatory molecules. These cytokines or chemical signalers can further amplify and propagate the inflammatory response, increasing levels of oxidative stress. In susceptible patients, where the body's mechanisms to resolve inflammation do not work effectively, a cycle is established and leads to a transition from acute to chronic inflammatory lesions, as occurs in periodontitis (2).

Increased levels of oxidative stress can result from cellular metabolism mainly due to electron leakage from mitochondria or through the body's response to a range of stressful stimuli, e.g. periodontopathogens such as Porphyromonas gingivalis, one of the MOs strongly associated with periodontitis (3, 9).

Table 1. Provocation of stress and anxiety.

Medical issues	Severe general illnesses Ulcers Skin diseases Alcoholism Smoking Depressions Parafunctions
Family issues	Separation/divorce Widowhood Drugs Illness in the family
Professional issues	Unemployment Misunderstanding/conflict Risky occupations Exhaustion

STRESS AND MICROORGANISMS

Deinzer R (2004) postulates that microorganisms have the ability to recognize hormones in the body and use them to adapt to their environment (8). This supports the suggestion that psychological stress may favor the development of many bacterial infections. In vitro studies were conducted to determine whether norepinephrine and adrenaline (epinephrine), which are released during human stress responses, act as

environmental signals to alter the growth of 43 microorganisms found in subgingival microbial complexes. Twenty types of MO found in the subgingival biofilm significantly increased after inoculation with norepinephrine, and 27 types of MO increased after administration of adrenaline. Difference in growth response within bacterial species and within and between microbial complexes was also found. It is concluded that this variation may affect the in vivo composition of the subgingival biofilm in response to stress-induced changes in local catecholamine levels, and this fact has implications for the etiology and pathogenesis of periodontal diseases (8). The ramifications of these findings are of great importance because P. gingivalis is the most frequently cited periodontal pathogen implicated in the relationship between periodontal disease and cardiovascular disease (2).

MANAGEMENT AND CONTROL OF STRESS

Coping with stress is the effort and attempt to reduce, control or tolerate the state of stress. Adjustment and coping strategies are required (3). These coping strategies can be used in generalized stressful situations. Individuals use coping measures to reduce its intensity or overcome stress altogether. Successful coping is when the subject feels able to face the stressor and is able to control the situation. Failed coping is when the subject is consumed by stressors and is in a state of stress.

ATTENTION TO STRESS IN PATIENTS

The results of the studies suggest that the importance of stress (data from medical history, personality) in relation to reduced immune response and periodontal problem should not be ignored (1, 3, 5, 11). On this basis, some authors talk about patients with increased risk and those with low risk (3, 8). Various events from everyday life (personal, health, economic) could lead to a stressful situation and lowering of the immune defense. In clinical practice, attention should be paid to the conditions associated with parafunctions (e.g. bruxism, abrasive facets, hypertrophy of the masticatory muscles), which points to the presence of hyperfunction and stress, which must be controlled.

Conclusion

There is evidence in the literature that psychological stress can lower the cellular immune response. Communication between the central nervous system and the immune system occurs through a complex network of two-way signals linking the nervous, endocrine, and immune systems. Stress disrupts homeostasis, which in turn alters immune function. The direct relationship between periodontal disease and stress remains to be proven, partly due to the lack of adequate animal models and the difficulty in quantifying the strength and duration of stress. In addition, multiple variables influence the severity of periodontal disease and there is uncertainty about the individual onset of periodontal disease.

Furthermore, it is not possible to separate the effects of physical stress from emotional stress in these animal studies. It is also likely that systemic diseases associated with periodontitis such as diabetes, cardiovascular disease, etc. share psychosocial stress as a common risk factor.

Thus, the available scientific evidence does not conclusively support a casual association between psychosocial factors and inflammatory periodontal disease. The information reviewed above nevertheless indicates the possible influence of psychosocial factors in the etiology of inflammatory periodontal diseases, although currently the more suggestive evidence concerns NUG. Studies have shown that psychosocial stress is a risk indicator for periodontitis. Therefore, it is worth noting that it is important for the dental practitioner to be aware of this factor and to have foreseen the consequences for the patient. The clinical

management of inflammatory periodontal diseases may benefit from investigating these relationships, particularly when the severity of the disease cannot be explained by established etiological factors and when there is no response to periodontal treatment or when there is a sudden, marked and explainable increase in the rate of periodontal disease destruction.

References

1. Charon J, Mouton C. Parodontie medicale. Éditions Cahiers de prothèses groupe liaisons, Paris; 2003; 434, ISBN: 978-2843610578 .
2. Newman M, Takei H, Klokkevold P, Carranza F. Carranza's clinical periodontology. Ed. Saunders Elsevier Inc.; 2006, tenth edition, 1286, ISBN 13 978-1-4160-2400-2.
3. Bhagat M, Tapashetti R, Fatima G, Bhutani N. Effects of stress over periodontium. Galore International Journal of Health Sciences and Research 2020; 5(1):46-57. P-ISSN: 2456-9321.
4. Genco J, Ho W, Kopman J, Grossi G et al. Models to evaluate the role of stress in periodontal disease. Annals of Periodontology 1998; 3: 288-302.
5. Wasu S, Wasu P, Thakare S, Umale B. Stress and Periodontal Disease. Int J Oral Care Res 2017; 5(3):233-237.
6. Spector M, Postolache T, Akram F. Scott A et al. Psychological stress: a predisposing and exacerbating factor in periodontitis. Current Oral Health Reports 2020; 7:208–215.
7. Reners M, Brecks M. Stress and periodontal disease. Int J Dent Hyg. 2007; 5(4):199-204. doi: 10.1111/j.1601-5037.2007.00267.
8. Dubar M, Clerc-Urmès I, Baumann C et al. Relations of psychosocial factors and cortisol with periodontal and bacterial parameters: a prospective clinical Study in 30 patients with periodontitis before and after non-surgical treatment. Int. J. Environ. Res. Public Health 2020; 17 (20):7651. doi:10.3390/ijerph 17207651.
9. McGlynn D, Gale N, Glaros G, LeResche L et al. Biobehavioral research in dentistry: Some directions for the 1990s. Annals of Behavioral Medicine 1990; 12(4): 133–140.
10. Gunepin M, Derache F, Trousselard M et al. Impact of chronic stress on periodontal health. J Oral Med Oral Surg 2018; 24 (1) 44-50.doi.org/10.1051/ mbcb/2017028.
11. Deinzer R, Kottman W, Forster P, Herforth A et al. After-effects of stress on crevicular interleukin-1beta. J Clin Periodontol 2000: 27: 74–77.

Corresponding author:

Antoaneta Mlachkova
Medical University – Sofia, Faculty of Dental Medicine
Department of Periodontology,
1 St. George Sofiyski Str., 1431 Sofia.
e-mail: dr_mlachkova@abv.bg