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Psychosomatic disorders and periodontal pathogens virulence relationship

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Abstract

AIM. The relationship between psychosomatic diseases and inflammatory diseases of periodontal tissues, depending on the constant action of stressors on the human body, and the increased virulence of periodontopathogenic organisms in patients with psychiatric disorders.

MATERIALS AND METHODS. Current information in the electronic databases Google Scholar and PubMed was examined through a systematic literature review. Articles with content related to the influence of psychosomatic diseases and constant stress on the increase in virulence of periodontopathogenic microorganisms were selected and included.

RESULTS. A total of 271 publications were reviewed. After analyzing the literature according to the inclusion criteria, the final number was 58.

CONCLUSIONS. Based on the analyzed data, in patients with psychosomatic diseases and chronic stress, the oral microflora becomes favorable for the active growth of periodontopathogenic microorganisms. In response to the introduction of these bacteria and their virulence factors, chronic inflammation is observed in periodontal tissues, cells secrete IL-1α, IL-1β, IL-6, IL-17, IL-10, TNF-α, which decrease the body's resistance to periodontopathogens. This group of patients has an increased amount of catecholamines in the blood, which increase the virulence of bacteria such as P. Gingivalis, which are the main ones in the pathogenesis of inflammatory diseases of periodontal tissues. High concentration of cortisol reduces the activity of immune cells, changing the balance of T-helper and T-suppressors and making the body more susceptible to various infections.

Keywords: periodontitis, psychosomatic diseases, stress, periodontopathogens, virulence, cytokines, catecholamines, cortisol, neuropeptides

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Психосоматические расстройства и вирулентность пародонтопатогенов

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Резюме

ЦЕЛЬ. Исследование взаимосвязи между психосоматическими заболеваниями и воспалительными заболеваниями пародонта, в зависимости от постоянного действия стрессоров на организм человека, а также повышенной вирулентности пародонтопатогенных микроорганизмов у пациентов с психическими расстройствами.

МАТЕРИАЛЫ И МЕТОДЫ. Путем систематического обзора литературы были изучены данные из электронных баз Google Scholar и PubMed. Были отобраны статьи, содержащие информацию о влиянии психосоматических расстройств и хронического стресса на повышение вирулентности пародонтопатогенных микроорганизмов.

РЕЗУЛЬТАТЫ. Всего было проанализировано 271 публикация. После применения критериев включения в итоговый анализ вошли 58 публикаций.

ВЫВОДЫ. На основании анализа данных у пациентов с психосоматическими расстройствами и хроническим стрессом микрофлора полости рта становится благоприятной для активного роста паро-

донтопатогенных микроорганизмов. В ответ на внедрение бактерий и их вирулентных факторов в тканях пародонта наблюдается хроническое воспаление, клетки секретируют IL-1α, IL-1β, IL-6, IL-17, IL-10, TNF-α, что снижает сопротивляемость организма к пародонтопатогенам. У этой группы пациентов в крови наблюдается повышенное содержание катехоламинов, усиливающих вирулентность таких бактерий, как *P. Gingivalis*, которые играют ключевую роль в патогенезе воспалительных заболеваний пародонта. Высокие концентрации кортизола подавляют активность иммунных клеток, нарушая баланс Т-хелперов и Т-супрессоров и делая организм более восприимчивым к инфекциям.

Ключевые слова: пародонтит, психосоматические заболевания, стресс, пародонтопатогены, вирулентность, цитокины, катехоламины, кортизол, нейропептиды

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INTRODUCTION

The gingival sulcus microflora is a highly sensitive indicator system, disturbance of its composition creates dysbiosis either as a result of overgrowth of specific or non-specific microorganisms or as a result of changes in local host response, where periodontopathogenic bacteria can maintain a disease state [1]. Dysbiosis provides a link between the patient's systemic diseases and members of the oral microflora and can lead to periodontal tissue destruction [2].

Periodontitis is an inflammatory-dystrophic process in the periodontium, arising under the influence of nonspecific and specific factors [3]. In the pathogenesis of this disease, special attention should be paid to the relationship between conditionally pathogenic microorganisms of dental plaque and the patient's organism [4]. Including the realisation of pathogenic action of microorganisms depends on their number and virulence, resistance factors of the organism and its immune status [5]. Periodontopathogenic microorganisms act as mediators that initiate the inflammatory reaction in periodontal tissues, whose cells secrete proinflammatory mediators. This interaction, in general, reflects the overall condition of the host organism – the patient with periodontitis. These relationships are particularly strongly influenced by generalised diseases, the patient's socioeconomic status, bad habits such as smoking, and psychological stress [6].

Despite the fact that periodontitis is commonly considered a disease of aging [7], at the moment the most common psychosomatic diseases among the population are psychosomatic diseases, such as: gastric and duodenal ulcers, essential arterial hypertension, coronary heart disease, rheumatoid arthritis, bronchial asthma, autonomic disorders, etc. [8; 9]. The main factor in the occurrence and progression of this group of diseases is emotional tension, i.e. stress, which make the human body more susceptible to many diseases, including those affecting periodontal tissues [10]. Many studies and clinical data have already been collected on the relationship between the psychological status of the patient and periodontal disease, which will be discussed in this article [11; 12].

AIM

To analyse the relationship between psychosomatic diseases and inflammatory diseases of periodontal tissues, depending on the constant action of stressor factors on the human body, as well as the increased virulence of periodontopathogenic organisms in patients with psychiatric disorders.

MATERIALS AND METHODS

PISO question: What mechanisms in patients with psychosomatic disorders/chronic stress complicate the course of periodontitis?

- *Population*: Periodontitis in people with psychosomatic disorders/chronic stress.
- *Comparison*: Immune defence disorders in patients with psychosomatic disorders.
- *Correlation*: Effect of stress hormones on the activity of periodontopathogens.
- *Results*: Increased virulence of periodontopathogens against the background of immune system imbalance and increased levels of stress-related hormones.

Examination of publications obtained by searching the electronic databases Endodontics Today, Google Scholar, PubMed, and prearticle reference lists was done through a systematic literature review.

Inclusion criteria: Inclusion Articles published in the English / Russian language or those having a summary in English; case series; randomized controlled trials; randomized experimental trials.

The articles are based on the following:

1. Influence of acute emotional-pain stress on the state of periodontal tissues.
2. Peculiarities of oral microbiome in various psychosomatic diseases.
3. Specific periodontopathogenic microorganisms.
4. Increase in blood catecholamines and their effect on anaerobic bacteria.
5. The effect of stress hormones on the growth of selected bacterial species.
6. Evaluation of the association between potential stress markers and periodontal tissue health.

RESULTS

A total of 271 publications were reviewed (203 – PubMed, 53 – Google Scholar, 15 – Endodontics Today). After analysing the papers for inclusion criteria, the final number of articles was 58. The studies discussed provide evidence for the influence of psychosomatic diseases and constant stress on the increased virulence of periodontopathogenic microorganisms.

Flow diagram: 31 articles were selected after the selection process for final qualitative and quantitative analysis which has been described in the following flow diagram (Fig. 1).

DISCUSSION

According to statistics, people with chronic high levels of stress are more prone to periodontal diseases [13–15]. Stress is a confirmed and important factor in the etiology and development of many inflammatory and chronic diseases such as: rheumatoid arthritis, diabetes mellitus, cardiovascular diseases or periodontal diseases [16]. Patients with psychosomatic diseases have been shown to be more prone to the development of periodontal diseases, alveolar bone loss and increased prevalence of generalised periodontitis.

The role of stressors in the pathogenesis of periodontitis and its treatment has been proved in the course of ongoing studies in patients with different psychological statuses, a decrease in antimicrobial defence in the oral cavity has been noted, which in turn increases the virulence of microorganisms [17]. Many experiments on animals have been performed, which prove that constant stress serves as a trigger mechanism for inflammation of periodontal tissues, manifested by radiological "eaten" bone, a decrease in the number of osteoblasts and the development of osteoporosis [18]. There was also an increase in the concentration of proinflammatory and proresorptive factors, such as interleukin 1β (IL-1β), interferon gamma, osteoprotegerin [19].

Stress leads to a slowdown in connective and bone tissue regeneration, apical migration of multilayer epithelium and periodontal pocket formation [20]. This occurs under the influence of changes in the body's defences, which acquire an immunosuppressive effect, increasing the propensity to develop diseases.

Oral microflora reacts with quantitative and qualitative disturbances in its composition under the influence of various risk factors, such as stress and psychoemotional disorders [2; 9]. During the action of stressors, there is an imbalance between the representatives of resident microflora of the gingival groove biofilm with increased multiplication of specific facultative species of microorganisms. In addition, a stimulating effect of stress hormones on the synthesis of adhesive parodontopathogens has been established, which accelerates the formation of dental biofilm.

The most common periodontopathogenic microorganisms are Porphyromonas gingivalis (P. gingivalis), Tanerella forsythia (T. forsythia), Prevotella intermedia (P. intermedia), Aggregatibacter actinomycetemcomitans (A. actinomycetemcomitans) [21–24]. In response to the introduction of these bacteria, the following are secreted: prostaglandin E (PGEi), interleukin L, IL-6; matrix metalloproteinases (MMP), etc. Also, these pathogens induce the release of cytokines, which in combination with their virulence factors cause chronic systemic inflammation and subsequently affect neural function and alter the permeability of the blood-brain barrier [25]. In addition, the complement system will be activated, which leads to bacterial opsonisation.

Cytokines and other inflammatory mediators act as strong activators of the central stress response. Under their influence, glucocorticoids are released, which can regulate the recruitment of immune cells to inflamed tissues to help the body cope with psychological stress. There is an increase in pro-inflammatory cytokines, IL-1α, IL-1β, IL-6, IL-17, IL-10, tumour necrosis factor (TNF)-α and decreased expression of regenerative factors including basic fibroblast growth factor in serum and gingival sulcus [26–28]. There is an imbalance of cytokine such as IL-1β, which deregulates host response as well as resistance to pathogens, exacerbating the damage in chronic periodontal tissue lesions [29; 30].

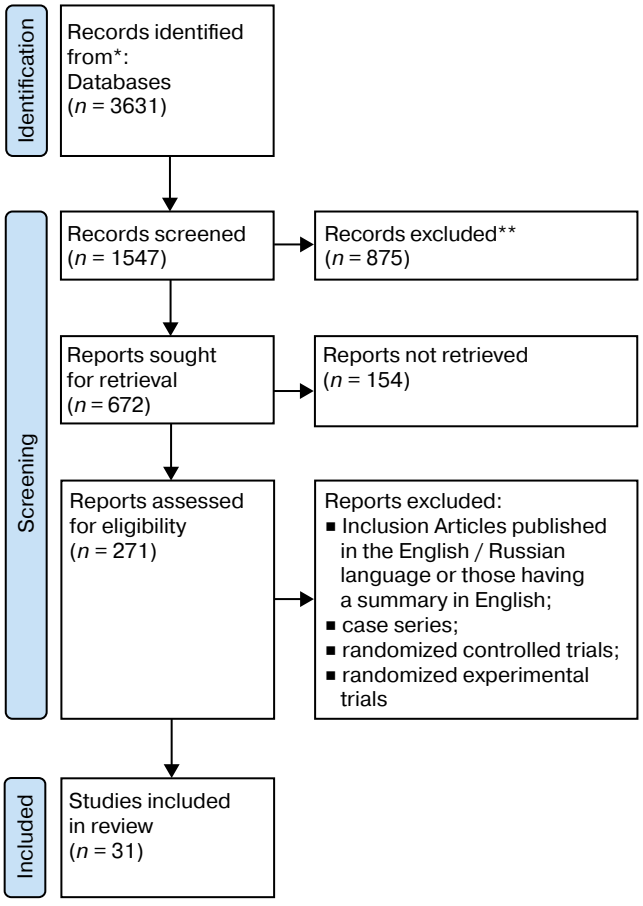

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flow diagram

Рис. 1. Диаграмма потока предпочтительных элементов отчетности для систематических обзоров и метаанализов

Also in patients with psychosomatic diseases there is stimulation of the hypothalamic-pituitary adrenal adrenal system by cytokines [31; 32]. There have been studies that have shown that in the gingival sulcus of patients with psychological illnesses there are changes in the growth of 43 microorganisms, especially the localised immune response is directed towards P. Gingivalis. Microorganisms have the ability to recognise hormones within the host and use them to adapt to their environment [33]. Psychological stress is known to increase circulating levels of the hormones catecholamines, noradrenaline and adrenaline, which have been shown to be able to act as environmental signals to alter the growth of individual organisms in subgingival biofilms such as Fusobacterium nucleatum, Prevotella spp, Porhyromonas spp., Tanerella forsythia and Propionibacterium acnes, and can increase the expression of virulence genes such as Clostridium perfringens, Porphyromonas gingivalis and Brachyspira pilosicoli [34; 35].

These hormones can exert their effects on subgingival organisms by initiating the production of autoinducers or simply by acting siderophore, scavenging bound iron from the local environment, thereby increasing the virulence of microorganisms. For example, P. gingivalis has been observed to express genes related to iron acquisition (hmuR), oxidative stress (tpx, oxyR, dps, sodB and aphC) and pathogenesis (hem, hagA and ragA) upon exposure to adrenaline and noradrenaline [36]. For example, the Dps protein contains a ferroxidase centre and protects bacteria from damage by reactive oxygen species [37]. In many bacteria, OxyR acts as a transcriptional regulator that facilitates infection by degrading hydrogen peroxide (H_2O_2) generated by the host defence response [38; 39]. This gene increases the resistance of cells to reactive oxygen species (ROS) by increasing their perception of their environment and maintaining their oxidative phosphorylation at a reasonable level to avoid overproduction of endogenous ROS [40]. RagB has been linked to the virulence of P. gingivalis, promoting efficient growth, development of subcutaneous lesions and invasion of epithelial cells [41].

Possible that autoinducer mechanisms may play an important role in the response of oral microorganisms to stress hormones, thereby contributing to the clinical course of stress-associated periodontal diseases [42]. A study was conducted and observed a positive effect of catecholamine growth in Actinomyces naeslundii (+49.4%), Actinomyces gerenscseriae (+57.2%), Eikenella corrodens (+143.3%) and Campylobacter gracilis (+79.9%). Inhibitory effects were also observed for Porphyromonas gingivalis (–11.9%) and Bacteroides forsythus (–22.2%) [43].

Patients with psychosomatic diseases, first of all, have reduced salivary secretion, which accelerates the formation of dental plaque, as well as neurotransmitters and neuropeptides, neuroendocrine substances that can simulate the immune response to bacteria. Changes in saliva pH and secretory IgA release occur, IL-1 levels increase and oral hygiene quality decreases [44].

An experiment was conducted in which an increase in saliva cortisol levels, which is responsible for maintaining the homeostasis of the organism, was also proved [28; 45–47]. One experiment revealed that prolonged high levels of cortisol can reduce the activity of immune cells by altering the balance of T-helper and T-suppressor lymphocytes and changing the functioning of Natural Killer cells [48]. In addition, increased cortisol may possibly favour surface translocation of P. gingivalis [49; 50].

Consequently, chronic psychosomatic illnesses may indirectly contribute to the onset and worsening of microbial infection and may increase pro-inflammatory cytokines, in turn causing mild chronic inflammation [51; 52]. It is also possible to detect other stress markers in saliva: chromogranin A, α-amylase and β-endorphin [53–55]. It is important to highlight that patients with psychiatric disorders have been found to have increased amounts of neuropeptides such as: neuropeptide Y (NPY), substance P, intestinal vasoactive polypeptide (VIP), calcitonin gene-related peptide (CGPR), insulin-like growth factor-2 (IGF-2) [56]. Many studies have shown a positive relationship between clinical measurements of SP and NKA, demonstrating their influence on the severity of periodontal disease. However, anti-inflammatory neuropeptides such as NPY play an important role in maintaining periodontal health. VIP is a macrophage deactivating factor that prevents the overproduction of pro-inflammatory factors and inhibits lipopolysaccharide (LPS)-induced TNF-α, IL-6 and IL-12 production in activated macrophages [57]. This shows that SP and VIP play an antagonistic role in periodontal inflammation, but in patients with psychosomatic diseases, the balance between pro- and anti-inflammatory neuropeptides is disturbed, leading to the progression of periodontal inflammation.

CONCLUSION

In this article, various studies have been cited and analysed on the effect of psychosomatic diseases and constant stress on increasing the virulence of periodontopathogenic microorganisms. Most studies show that periodontitis is associated with neurogenic inflammation.

After studies, it was found out that psychosomatic diseases, for example, gastrointestinal disorders, can cause inflammatory periodontal diseases [58]. Under the influence of stress factors, proinflammatory cytokines are released, which disturb the balance of gingival sulcus microflora, which, in turn, creates a favourable environment for the growth of many types of periodontopathogenic microorganisms.

Also, patients with psychosomatic disorders have increased blood levels of catecholamines. Individual organisms from different microbial complexes differ in their in vitro growth responses to noradrenaline and adrenaline. In addition, catecholamines can increase the virulence of bacteria such as P. Gingivalis, which play a leading role in the pathogenesis of periodontitis. Such variations may affect the composition of the subgingival biofilm in vivo in response to stress-induced changes in local catecholamine levels and play a significant role in the etiology and pathogenesis of periodontal disease [43].

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