EXPERIMENTAL SUBSTANTIATION OF THE ANTIDISBIOTIC ACTION OF DRUG COMPOSITION FOR THE TREATMENT OF PATIENTS WITH GENERALIZED PERIODONTITIS AND PSYCHOSOMATIC STRESS

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Abstract

Introduction. Psychological stress is an important factor in the pathogenesis of the periodontal disease. It is therefore essential to determine the relationship between psychosomatic stress and periodontal disease. For the treatment of stress in patients with generalized periodontitis, a medicinal composition is proposed, for determining its antidisbiotic effect in the experimental substantiation of its periodontio-protective action. **Aim.** to determine the psychosomatic state of subjects, the influence of psychological stress on the periodontal tissue and the experimental substantiation of the antidisbiotic effect of drug composition for stress neutralization. **Materials and methods.** To study the subjective human responses to the effect of various environmental factors, a specially designed questionnaire is advisable to be used. Diagnosis of the anxiety level was made by a self-determination test including reactive and personal anxiety according to Spielberger. Adrenaline stress was followed on rats, by oral application of a gel with adrenalin in a 0.36 mg/kg dose, for 10 days. Lincomycin was introduced with drinking water in a dose of 60 mg/kg. The gel of adrenoblockers (zocson + nicergolin and sibason) was applied in a 0.6 mg/kg does. The activity of urease, lysozyme, elastase was determined in serum, and the degree of disbiosis was calculated according to Levitsky. **Results and disscusions.** The Spielberger test showed a moderate level of reactive anxiety among respondents - 34.72±2.45, and a high level of personal anxiety - 50.64±3.58. In patients with a high level of personal anxiety, a significantly higher prevalence of periodontal disease, especially generalized periodontitis, has been detected. Experimental studies have shown that gel adrenoblockers decrease urease activity, increase lysozyme levels, which leads to a significant reduction of disbiosis. **Conclusions.** A high level of personal anxiety - 50.64±3.58 - leads to a significant increase in the prevalence of periodontal diseases – 95.09±6.7%, especially generalized periodontitis – 88.72±6.5%. Oral application of a gel containing adrenoblockers had an antidisbiotic effect after modeling of the adrenaline stress by administration of adrenalin and lincomycin to animals.

Keywords: *reactive and personal anxiety of residents, periodontal diseases, adrenaline stress, adrenoblocker, antidisbiotic action.*

1. INTRODUCTION

To date, the most urgent problem of dentistry is represented by periodontal diseases, especially generalized periodontitis. Among people aged 35-44 and older [1,2], its prevalence reaches 92-98%, increasing among young people (19-24 years) to 30%, and among those of 25-30 years to more than 60% [3-6].

To date, the main etiological factor of periodontal diseases is considered the periodontopathogenic microflora [7-9]. The modern principles of the local therapy of periodontal diseases refer to its influence on the main pathogenesis, with inhibition of the periodontopathogenic microflora and pharmacological correction of the inflammatory process [8-13]. Therefore, in the complex treatment of periodontal lesions, it is advisable to use drugs with combined effect. The results of numerous investigations evidenced the high effectiveness of drugs with antimicrobial effect in the treatment of patients with generalized periodontitis [3,7,14-19].

Among the main general etiological factors of the periodontal diseases, psychological stress also plays an important role. Clinical investigations have shown that people under psychological stress revealed a higher prevalence of generalized periodontitis [20-26]. Researchers referred to a possible negative impact of psychological stress on the state of periodontal tissues of young people [27,28].

Taking into account the above observations, it was important to identify the level of anxiety among the surveyed inhabitants of Ukrainian cities and to provide an experimental

substantiation of a complex of drugs that could neutralize the possible influence of psychological stress upon the organism of patients with a periodontal disease [29]. Considering the etiological role of microflora, an experimental substantiation of the antidisbiotic effect of the proposed drug composition was important.

Aim. To determine the psychosomatic state of patients, the influence of psychological stress on the periodontal tissue and the experimental substantiation of the antidisbiotic effect of drug composition for stress neutralization.

2. MATERIALS AND METHODS

To determine the level of (reactive and personal) anxiety, the Spielberger-Khanin anxiety test [30-32] was used as a questionnaire filled in by patients. 350 young inhabitants from different regions of the cities of Kiev, Vinnytsia and Dnepr were questioned and examined.

Subsequently, assessment of the condition of periodontal tissues was performed. The presence, localization and intensity of the inflammatory process of gingiva were determined using the Schiller-Pisarev test [12,33]. Biofilms and dental plaques were detected using diagnostic dyes. Diagnosis of periodontal tissue lesions was determined by the classification of periodontal diseases made by M.F. Danilevsky (1994) [12]. The hygienic state of the oral cavity was determined using the hygienic index of Green-Vermillion (1964) [12], and the level of gingival inflammation was determined using the PMA index [12,33,34].

In the presence of anxiety state (psychoemotional stress) in patients, for its neutralization, a medicinal composition that included zoxone (0.002 g 1 time per day), nicergoline (0.005 g 3 times a day), sibazon (0.005 g 1 time a day) was proposed, to be taken 1-2 hours before each session of the treatment of periodontal diseases.

To substantiate the periodontoprotective (membrane-stabilizing) effect of this drug composition, experimental studies were performed on rats in which the adrenalin stress was modeled [35], being induced through inoculation of adrenaline and lincomycin. These substances produce, in the experimental animals, the inflammatory process in the periodontium against the background of violations of lipid peroxidation processes.

For experimental studies, white rats of the Vistar line were selected: 21 female, 12-13 month-old animals with live weight 290-330 g. Adrenalin stress was modeled with daily additions of gel with adrenaline (0.36 mg / kg of animal weight) and inoculation of lincomycin (added into the drinking water) for 10 days. The experimental animals were divided into three groups of 7 rats each. The first group consisted of animals that modeled adrenalin stress, but did not carry out drug treatment (control group). The second (main) group included animals that modeled adrenalin stress, receiving adrenaline stress through daily gel application of the proposed drug composition with adrenergic blockers (zoxone, nicergoline, sibazon). The third group (comparison) was formed of animals that received daily quartulin gel application under conditions of adrenaline stress. The experiment lasted for 10 days. Euthanasia of rats was performed on day 11, under thiopental anesthesia (20 mg / kg) by total blood flow from the heart.

To assess the presence of inflammatory process in the periodontium of experimental animals in serum, the activity of catalase was determined. The activity of urease, lysozyme, elastase and catalase was determined for establishing the effect of the proposed drug composition upon the processes of disbiosis in serum. According to the ratio of relative activity of urease and lysozyme, the degree of disbiosis according to Levitsky was calculated. The results were processed using standard statistical methods.

3. RESULTS AND DISCUSSION

The level of morbidity of the surveyed subjects was evaluated subjectively on the basis of questionnaires. Health deterioration was assessed by one or more indicators (morbidity, adaptation, physical condition, psycho-emotional status). The presence of various systemic diseases was detected in 301 (86.0%) respondents. Among them, 126 (36.0%) had different chronic diseases (digestive tract, cardiovascular system, diabetes,

etc.). Thus, the survey showed that 204 (58.29%) of the 350 respondents considered their health insufficient, and 146 (41.71%) of them considered their health satisfactory.

Based on Spielberger test data, a high level of personal anxiety was detected - 50.64 + 3.58, while the level of reactive anxiety was moderate - 34.72 + 2.45.

It was important to elucidate the relationship between the presence of chronic systemic diseases and the level of anxiety. A similar analysis showed that in 204 (58.29%) of respondents who assessed their health as having an unsatisfactory level of reactive anxiety the value recorded was 58.22+4.1,1 whereas personal anxiety was 68.14+4.81. In 146 (41.71%) respondents who believed that their state of health was satisfactory, the reactive anesthesia level was 49.73+3.51, and personal anxiety - 49.13+3.47. Thus, it was established that the presence of diseases increases the level of reactive and personal anxiety of respondents. In 32 (22.76%) of respondents who noticed no clinical manifestations of the disease, the level of personal anxiety registered a low range - 28.33.

The presence of periodontal diseases in people who assessed their health as satisfactory was observed in 119 (81.51±7.6%) persons. Among them, generalized periodontitis was detected in 108 surveyed patients – 73.97±6.9% of persons. In the group of respondents who evaluated their health as unsatisfactory, periodontal diseases were found in 194 (95.09±6.7%) persons. Generalized periodontitis was detected in 181 (88.72±6.5%) patients. Thus, a certain relationship was established between the level of morbidity, the degree of reactive and personal anxiety and the prevalence and structure of periodontal diseases. The presence of such a state of psychosomatic stress should be taken into account in the case of complex treatments of the periodontal diseases, in particular generalized periodontitis.

To reduce the negative influence of psycho-emotional stress on patient's organism, several types of drugs were proposed: zoxone (0.002 g 1 time per day), nicergoline (0.005 g 3 times a day), sibazon (0.005 g 1 time per day). This complex of medicinal preparations was recommended to be applied prior to each session of dental treatment.

In patients with generalized periodontitis, the main etiological factor is considered periodontopathogenic microflora. It was interesting to find out the presence of an antidisbiotic action in the proposed complex of drugs.

For experimental researches, the model of adrenalin stress was selected. Evaluation showed that introduction of adrenaline and lincomycin in the serum of blood reduces the activity of catalase and the content of total cholesterol, which increases adrenalin stress. Introduction of lincomycin against the background of adrenalin stress causes a decrease in the activity of lysozyme, and an increase in the degree of disbiosis as well as in the activity of the marker of inflammation of elastase.

In rats with adrenaline stress in blood serum, glucose levels (up to 7.46±0.3 mmol / l), triglycerides (up to 1.42±0.1 mmol / L) and cholesterol (to 1.56±0.08 mmol / l) were determined. The indices characterizing the level of antibacterial defense get worse, namely: an increase in the marker of microbial contamination of urease (to 1.40±0.14 mmol / l), a decrease in the level of protection - lysozyme (up to 63±3 units / l) and an increase in the level of disbiosis to 1.81±0.22 units. Development of adrenaline stress in animals causes changes of inflammation (elastase) and peroxidation (malonic dialdehyde - MDA). In particular, the level of elastase increases to 138±10.4 mmol / liter, and the content of MDA increases to 1.06±0.06 mmol / liter. At the same time, development of adrenalin stress decreases the activity of catalase to 0.22±0.02 mmol / l and of the antioxidant-prooxidant index (API) to 2.07±0.17 units.

Thus, reproduction of this model in the organism of animals marked significant changes, which in some way correlate with similar changes in the organism of patients with generalized periodontitis.

Determination of the influence of gel applications with proposed adrenoblockers has shown that they lead to a significant decrease in these indices. In rats with adrenaline stress, an increase in the marker of microbial contamination of urease (to 1.40±0.14 mmol / l), a decrease in the level of protection - lysozyme (up to 63±3 units / l) and an increase in the level of disbiosis to 1.81±0.22 units Gel applications with blockers reduce the urease activity to 0.66±0.21 mmol / l and increase lysozyme levels to 73±6 units / l.

This leads to a significant reduction of the degree of disbiosis - to 0.74±0.20 units. A similar improvement in these parameters was observed in the control group: decrease of urease activity to 1.47±0.43 mmol / l and increase of lysozyme level to 73±5 units / l. The degree of disbiosis decreased to 1.63±0.18 units. Thus, application of gel with adrenoblockers is significantly better ($p < 0.05$), improving the biochemical parameters of disbiosis.

The obtained results indicate that gels with adrenoblockers have anti-inflammatory effects at the level of quartulin and greatly improve the biochemical parameters of disbiosis.

This situation testifies to the ability of the investigational drugs proposed to positively affect the disturbed psychosomatic state of the organism, which is promising in the case of their clinical application in the complex treatment of patients with generalized periodontitis in the presence of psychosomatic stress.

4. CONCLUSIONS

The investigations have evidenced the relationship between the prevalence of systemic diseases, the level of anxiety (reactive and personality) and the prevalence and structure of periodontal diseases. The higher level of personal anxiety surveyed positively correlates with the widespread occurrence of generalized periodontitis in subjects. Experimental studies have shown that the drug composition of adrenergic blockers produces anti-inflammatory and antidisbiotic effects (more pronounced than applications for the preparation, for comparative purposes of quartulin). This indicates the positive effect of the proposed drug combination on the distrophic-inflammatory process in periodontal tissues.

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