

CORRECTION OF NITRIC OXIDE METABOLISM IN THE COMPLEX THERAPY OF PATIENTS WITH GENERALIZED PERIODONTITIS

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Abstract

Urgency. Periodontal disease is the most common human disease, so that a rational treatment of generalized periodontitis is especially relevant. Traditionally, the complex treatment of generalized periodontitis makes use of different groups of drugs, among which nitric oxide plays a special part in the development of various pathologic processes. Important aspects of generalized periodontitis include: oxidative stress, disturbed metabolism of nitric oxide and haemomicrocirculation, which requires correction of the pathogenesis mechanisms of generalized periodontitis through complex treatments. To this end, a medicinal composition of arginine - L-arginine, is recommended as a source of nitric oxide.

Aim. Experimental substantiation and clinical investigation on the clinical efficacy of the proposed pharmaceutical composition containing arginine in the treatment of patients with generalized periodontitis.

Materials and method. Clinical studies performed on a group of 20 patients with generalized periodontitis, subjected to a complex examination of the periodontal tissue both before and after the treatment. Evaluation of the clinical efficacy of the treatment was made with the Schiller-Pisarev test (1962), the index of PMA of C.Parma (1961), the hygienic index of Volodkina-Fedorov (1978), the vacuum test of Kulazhenko (1961).

Results. The investigation revealed that inclusion of the proposed pharmaceutical composition in the complex therapy of patients with generalized periodontitis allows a more effective suppression of the dystrophic-inflammatory process in periodontal tissues. This confirms the decline of the PMA index, increase of the time of hematoma formation during the vacuum tests of Kulazhenko, and an improved oral hygiene.

Conclusions. Application of the proposed pharmaceutical composition increases the effectiveness of treatment in patients with generalized periodontitis.

Keywords: *generalized periodontitis, nitric oxide, pharmaceutical composition, arginine.*

1. INTRODUCTION

Periodontal disease is the most common human disease, the affected periodontal tissues having an

adverse effect on the body, possibly contributing to the installation of a chronic septic state. Therefore, the problem of a rational treatment of periodontal diseases and especially generalized periodontitis is a most actual one [1-4].

In the complex treatment of patients with generalized periodontitis, different groups of drugs are traditionally used: antibiotics (antiseptics, antibiotics, antifungal and antiprotozoal drugs), proteolytic enzymes and inhibitors of proteolysis, nonsteroidal anti-inflammatory drugs (NSAD), immunomodulators, calcium supplements, etc. [1,4, 5-9]. An important aspect of the treatment refers to drugs that improve the metabolic processes in periodontal tissues, due to their membrane-stabilizing effect and, consequently, to the protective effect upon alveolar bone loss.

Nowadays, the role of nitric oxide in the development of various pathologic processes attracts a special interest [10-13], due to its involvement in many biological processes: blood circulation and normalizing blood pressure, activity of the central and autonomous nervous system, metabolism, immune system activation, etc. [14-16]. It was shown that one of the major elements of intimate development of periodontal diseases refers to the NO-dependent endothelial dysfunction [16,17]. Against the background of the activation of free radical oxidation, depletion of the protective antioxidant system revealed significant morphological changes in the structure of the endothelium in the gingival microvascular system, accompanied by inhibition in the activity of endothelial NO-synthetase [18-21]. Thus, it was shown that an important role in the pathogenesis of generalized periodontitis is played by the

metabolic disorder of nitric oxide and blood microcirculation, which calls for the correction of these mechanisms of pathogenesis of generalized periodontitis through a complex treatment.

To this end, an arginine preparation with L-arginine as a source of nitric oxide has been proposed. For clinical use, it has been recommended a pharmaceutical composition comprising cardioarginin (syrup), «Holisal» dental gel and essential oil of peppermint (Ukrainian utility model patent number 97 987/04.10.2015).

The aim of this work was the experimental substantiation and clinical investigation of the clinical efficacy of the proposed pharmaceutical composition with arginine for the treatment of patients with generalized periodontitis.

2. MATERIALS AND METHOD

Experimental studies were conducted on 24 Wistar white female rats (8 month- old, average weight: 200 ± 10 g), divided into 3 equal groups: the first - control (standard), the second and the third - experimental, individuals with periodontitis, caused by a combination of input lincomycin with drinking water (60 mg/kg daily, for 5 days) and a highly fat diet administered to rats for 21 days [22-24]. The rats from the third group received, as early as the first day of the experiment, applications with the oral mucosa gel «Arginine», in a dose of 0.3 ml per rat, corresponding to 200 mg/kg «Cardioarginin» syrup.

The animals were taken out of the experiment after 22 days under tiopentalum anesthesia (20 mg/kg), by total blood letting from the heart. In homogenates of gingiva there was determined the activity of urease [25], lysozyme [26], elastase [27], catalase [27], content of malondialdehyde (MDA) [27], degree of dysbiosis by A.P.Levytsky [26,28], and antioxidant-prooxidant index (API) by A.P.Levytsky [28].

20 patients (8 men and 12 women) with chronic generalized (mild-moderate) periodontitis have been examined and treated. Average age of patients: 38 ± 3 years. For the complex treatment of generalized periodontitis in the patients of this group, the proposed pharmaceutical composition

was used. The control group included 10 patients of the same age, with the same degree and course of generalized periodontitis. Treatment of patients with generalized periodontitis was carried out by a traditional standard technique using mefenaminum acid sodium salt [1,29].

Patients were subjected to a thorough examination of the periodontal tissue, both before and after the treatment. After removal of all irritating factors, the proposed pharmaceutical composition and antibacterial drugs were administered.

Methods of local treatment. The proposed method of treatment was performed as follows. After the removal of the whole dental plaque and of other irritants of the periodontal tissue, an efficient oral hygiene, a professional dental prophylaxis cleaning was performed by a ultrafine ultrasonic method, with an «AirFlow» system, after which the proposed pharmaceutical composition was applied onto the same area of the periodontal tissue, as a suspension, for 10-20 min. The drug composition was introduced into the periodontal pockets in a similar manner.

Patients were asked to perform at home the following procedure: after brushing with «Parodontax» toothpaste, to apply a pharmaceutical composition on the gingiva, followed by rinsing with a «Parodontax» conditioner. The procedure was carried out 2 times a day, in the morning and in the evening. The treatment lasted for 14 days.

In the control group of patients, the treatment was similar, however the proposed pharmaceutical composition was replaced by mefenaminum acid sodium salt.

The clinical efficiency of the treatment was appreciated with the Schiller-Pisarev test [1,30], the PMA index of C. Parma [31], the hygienic index of Fedorov-Volodkina [32], and vacuum test of Kulazhenko [7]. Statistical processing of the results was carried out [33].

3. RESULTS AND DISCUSSION

Experimental research showed that the presence of dysbiosis against the background of experimental periodontitis in the gingiva of rats significantly increased urease activity, which indicates an increase of microbial contamination of gingiva, and

a dramatic (3.75 times) reduction of lysozyme activity, a sign of a significant weakening of nonspecific immunity. As a result, the degree of dysbiosis in the gingiva records a 5.4 times increase.

Application of the «Arginine» gel practically normalizes the high activity of urease, increases (2.5 times) the activity of lysozyme and reduces (3.55 times – up to almost normal values) the degree of dysbiosis in the gingiva.

Examination of patients with generalized mild-moderate periodontitis showed a dystrophic-inflammatory process in the periodontal tissues. The hygienic index of Fedorov-Volodkina was high – around 3.2 ± 0.3 , and the Schiller-Pisarev test was positive in all patients. The PMA index in patients with generalized mild-moderate periodontitis was high – around $62.2 \pm 0.58\%$. Gingival vessels resistance was reduced, and vacuum hematoma appeared within 13.2 ± 1.1 seconds.

After the treatment by conventional methods, the anti-inflammatory effect was recorded in the patients of the control group. The hygienic index of Fedorov-Volodkina was reduced up to 1.9 ± 0.3 , on the average, and the Schiller-Pisarev test was weakly positive in 4 (40.0%) patients. The PMA index in patients with generalized mild-moderate periodontitis was reduced up to a mean value of $33.5 \pm 0.5\%$. Gingival vessels resistance was elevated, vacuum hematoma being formed after about 19.5 ± 1.7 seconds.

After application of the proposed pharmaceutical composition, a significant inhibition of the inflammatory and degenerative processes in the periodontium was observed. The hygienic index of Fedorov-Volodkina was reduced up to a mean value of 1.3 ± 0.2 , and the Schiller-Pisarev test was weakly positive in 1 (5%) patients. The PMA index in patients with mild-moderate generalized periodontitis was reduced up to a mean value of $24.5 \pm 0.55\%$. Gingival vessels resistance has been greatly enhanced, vacuum hematoma being formed after about 28.5 ± 1.7 seconds.

Reduction of inflammation in the periodontal tissues after administration of the proposed pharmaceutical composition also improves the oral hygiene of patients, as determined by the hygienic index Fedorov-Volodkina. Before the treatment, the hygienic level of patients was assessed as poor. In patients with generalized mild-moderate

periodontitis, it was of 3.2 ± 0.3 . The hygienic index in patients with generalized mild-moderate periodontitis was 1.9 ± 0.3 . More significantly, the level of oral hygiene increased in patients with generalized periodontitis subjected to the treatment with the proposed pharmaceutical composition. Generally, it has been evaluated as satisfactory, being equal to 1.3 ± 0.2 .

Reduction of the dystrophic-inflammatory process in periodontal tissues under the influence of the proposed pharmaceutical composition is also evidenced by the longer time of hematoma formation, as evidenced by the Kulazhenko test. The results of the study showed that a hematoma in the area of teeth 31, 32, 41, 42, in patients with generalized mild-moderate periodontitis appeared, before the treatment, within 13.2 ± 1.1 seconds, after the treatment by traditional methods it occurred after 19.5 ± 1.7 seconds while, after the treatment with the proposed pharmaceutical composition – within 28.5 ± 1.7 seconds.

The positive results of the treatment were confirmed by a significant decrease of patients subjective feelings: pain and reducing swelling of the gingiva. In patients of the control group, after the conventional treatment, the subjective feelings were reduced on the fifth day in 40.0% of patients, completely stopped on the eighth day in 60.0% of patients and, on the tenth day – in 70.0% of them. After the treatment with the proposed pharmaceutical composition, the sensation of pain, itching, burning and swelling in the gingiva significantly decreased on the third day in 13 (65.0%) patients, completely stopped on the fifth day in 17 (85.0%) patients and on the 8th day – in 19 (95.0%) patients. Thus, application of a complex therapy based on the proposed pharmaceutical composition in patients with generalized periodontitis significantly reduces the time of treatment.

4. CONCLUSIONS

The results of the study show that introduction of the proposed pharmaceutical composition in the complex treatment of patients with generalized periodontitis allows a more efficient suppression of the dystrophic-inflammatory

processes in periodontal tissues, as confirmed by the decline of the PMA index, increase of gingival vessel resistance, and improvement of patients' oral hygiene.

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