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Prevention Of Chronic Generalized Periodontitis In Patients With Pulmonary Infiltrative Tuberculosis.

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ABSTRACT

The study is concerned with the urgent issue of dentistry - chronic generalized periodontitis in patients with infiltrative pulmonary tuberculosis. The efficiency of alpha lipoic acid in the prevention and treatment of periodontitis in patients with pulmonary tuberculosis has been analyzed. Current methods of periodontal screening are described. The main dental indices, cytological examination of the gingival fluid and gingival capillary blood prior to the treatment and in dynamics have been assessed. The standard method of combined etiopathogenetic treatment of periodontitis is presented. The antioxidant preparation with alpha lipoic acid has proven its efficacy in prevention and therapy of inflammatory periodontal disease due to its anti-inflammatory effect and the ability to improve cellular metabolism.

Keywords: chronic generalized periodontitis, infiltrative pulmonary tuberculosis, prevention, alpha lipoic acid (ALA).

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INTRODUCTION

In 1948 the scientist Irwin C. Gunsalus in the study of aerobic bacteria found a decrease, and then the cessation of their growth in the absence of one compound. It was first called oxidant factor pyruvate. In 1951, this compound was isolated in crystalline form from beef liver extract by the American biochemist Lester Reed, and its structure was established as α -lipoic or thioctic acid [14].

The main function of α -lipoic acid is a direct part in carbohydrate metabolism. Lipoic acid performs an important role in lipid metabolism. The acid has a positive lipotropic effect, facilitating the transfer of acetate and fatty acids from the cytosol to the mitochondrial matrix for subsequent oxidation by increasing the production of co-enzyme A. ALA shifts the spectrum of blood lipids towards unsaturated fatty acids, lowers cholesterol and saturated fatty acids in the blood, preventing the development of atherosclerosis. Lipoic acid can exist in the oxidized (-S-S-) and recovered (SH-) forms, allowing implemented it co-enzyme and antioxidant function. The reduced form, dihydrolipoic acid serves as an electron donor for the recovery of other antioxidants (vitamin C, vitamin E and glutathione), and under conditions of massive membrane oxidation it carries out the recycling of vitamin E when it is depleted [7].

In the pathogenesis of chronic generalized periodontitis of great importance is the strengthening of free radical processes of lipid peroxidation, which determines one of the leading areas of pharmacological influence in this disease [8, 9]. A study was conducted on the role of antioxidant component in the treatment of chronic generalized periodontitis, and the following conclusions: using traditional therapy of chronic generalized periodontitis, local changes in the mucous membrane of the gums and homeostasis disorders at the organizational level are corrected slowly and incompletely, which causes frequent relapses of the disease. Inclusion in the basic therapy of the disease of the drug with an antioxidant action type allows to increase the effectiveness of treatment, which is manifested by accelerated positive clinical and laboratory dynamics and reduction of treatment time of patients [10, 12].

Periodontitis is currently an urgent issue of dentistry [4]. One of the most severe and prevalent periodontal diseases is chronic generalized periodontitis resulting in the defective dental and alveolar apparatus, tooth loss and homeostatic disorders [3]. The pathology of the periodontal disease is rarely isolated; usually it is associated with comorbid diseases [2,4]. In infiltrative pulmonary tuberculosis, chronic generalized periodontitis develops with prolonged and frequent relapses, which is caused by a decrease in the antioxidant system activity and an imbalance in lipid peroxidation. Modern dentistry considers antioxidant therapy in the treatment of periodontal diseases aimed at mitigating tissue damage caused by excess free radicals and accelerating the recovery process [1].

Purpose of the study was to evaluate the efficiency of alpha-lipoic acid (ALA) in the prevention and treatment of chronic generalized periodontitis in patients with infiltrative pulmonary tuberculosis.

MATERIALS AND METHODS

The research represents a clinical investigation involving 50 patients with mild chronic generalized periodontitis combined with infiltrative pulmonary tuberculosis. Patients were randomized 1: 1 and divided into two groups, comparable in age, sex and severity of the disease. Patients were divided into two groups with similar severity of the disease. 33 (66%) men aged 30 to 40 years and 17 (34%) women 20 to 40 years old were under observation. The first group (cases, n=25) was given combined treatment with "Octolipen" (alpha-lipoic acid drug) taken orally at a daily dose of 600 mg for three months. The second group (controls, n=25) received standard combined anti-inflammatory therapy. In both groups, complex therapy included professional oral hygiene, toothbrush training, treating periodontal pockets with 0,06-0,2 % chlorhexidine solution, use of medicinal bandages with 1 % metronidazole gel, general anti-inflammatory treatment administered in the form of vitamin therapy (Vit. And 8-10 drops 2-3 times daily for 3 weeks; ascorutin 2-3 tablets 3-4 times a day), desensitizing agents (calcium gluconate 1 tablet 3 times a day) and nonsteroidal anti-inflammatory drugs (ointment "holisal" in the form of applications) during the present study included exacerbation. During the recovery phase, the main group continued to receive alpha lipoic acid.

The efficiency of prevention and treatment of periodontitis in patients with infiltrative pulmonary tuberculosis was assessed in the case group and in the control group according to their clinical and laboratory

data prior to treatment and in dynamics after 3 months of therapy. All patients underwent dental and general clinical examination, cytological examination of gingival capillary blood and gingival fluid.

To study the area and the severity of affection of periodontal tissues, various indices were used. The hygiene index (Hygiene index, HI) is estimated by determining the presence or absence of plaque on four surfaces of the teeth (oral, vestibular, distal and mesial). The data obtained are calculated by the formula [10]:

$$HI = \frac{\text{number of coated surfaces}}{\text{number of all examined surfaces}}$$

Papillary marginal alveolar index (PMA) is used for studying initial changes in the periodontal tissue [10]. Inflammation of the papilla (P) – 1, gingival margin (M) – 2, alveolar gum (A) – 3. The sum of the values for the condition of the marginal periodontium of all teeth is calculated. $PMA = \frac{\text{the sum} \times 100}{3 \times \text{number of teeth}} \%$

Sulcus bleeding index (Muhleman H., Son S.) is determined using a periodontal probe [10]. Index value $= \frac{\text{the sum of all the teeth}}{\text{number of teeth}}$

Using the plaque index (PI) by Russel A., the depth of the periodontal pocket, gingival inflammation and tooth mobility were assessed with a scale from 0 to 8, where 0 – the inflammation is absent, 1 - the inflammation is present, but it does not cover the entire tooth, 2 - the inflammation surrounds the entire tooth, but there is no damage to epithelial attachment, 4 - initial degree of resorption of the peaks of interdental septa (evaluation is given only radiologically), 6 - epithelial attachment is damaged, pathological dentogingival pocket is present, tooth is not damaged, 8 - severe destruction of bone tissue of the tooth, loss of chewing function, tooth is displaced [10]. Evaluation of results: 0.1-1.5 points-initial and stage I disease; 1.5-4.0 points-stage II; 4.0 – 8.0 – III stage. $PI = \frac{\text{Sum of scores for all teeth}}{\text{number of teeth present}}$

Cytological examination of gingival capillary blood was carried out according to the follows: periodontal pockets and surrounding tissues were pre-washed with isotonic sodium chloride solution, the biological material was sampled and transferred onto the slide with a sterile probe and a rubber bulb-type pipette. Specimens were fixed and stained with Romanovsky – Giemsa solution. The gingival fluid was taken with cotton threads, the threads were soaked with the fluid for 5 minutes and were placed onto the slide. Smears were stained by Romanovsky – Giemsa technique. The data obtained in the course of the study were processed by variational statistical methods. To compare the results obtained before and after the treatment, the Wilcoxon test was used.

RESULTS

Upon examination, it was determined that after three months of treatment the number of patient’s gingival bleedings was significantly reduced, and a bad breath disappeared. Objectively there were reduced signs of inflammation: hyperemia and swelling of the gums disappeared, periodontal pockets decreased, and oral hygiene improved.

Studies have shown that the use of the alpha-lipoic acid (ALA) in the standard combined therapy of chronic generalized periodontitis in patients with infiltrative pulmonary tuberculosis resulted in a significant improvement in all index figures (Table 1).

Table 1: Dynamics of index figures for the state of periodontal tissues in patients suffering from chronic generalized period on tit is with infiltrative pulmonary tuberculosis (M±m).

Indices	Casegroup (n=25)		Controlgroup (n=25)	
	Beforetreatment	In 3 months	Beforetreatment	In 3 months
Hygieneindex	43.7±0.5 [#]	74.1±0.5	42.9±1.1 [#]	68.8±0.8
Papillarymarginalalveolar index	26.4±0.5 [#]	12.8±0.5	26.1±1.1 [#]	15.4±1.31
Sulcusbleedingindex	1.77±0.12 [#]	0.22±0.15	1.73±0.05 [#]	0.5±0.08
Plaqueindex	0.79±0.06 [#]	0.11±0.08	0.75±0.04 [#]	0.48±0.04

Note: # - differences are statistically significant before treatment and in 3 months of it (p< 0.05).

According to Table 1, in three months of treatment with the implementation of ALA in the combined therapy of chronic generalized periodontitis in patients with pulmonary infiltrative tuberculosis, the hygiene index increased by 1.7 times ($p < 0.05$). When comparing the hygiene indices with the values of the comparison group, the increase in this figure was 1.08 times ($p < 0.05$).

In the case group, PMA index decreased by more than 2 times compared to the initial value, and in the reference group - by 1.7 times ($p < 0.05$). Such dynamics of figures of PMA index was noticed on the basis of objective and subjective clinical criteria, meaning that the use of ALA preparation in addition to the combined therapy arrests the inflammatory process more readily.

When using the ALA preparation in patients of the study group, the bleeding index and the plaque index also changed. The bleeding index decreased by 8 times, and the plaque index – by 7 times ($p < 0.05$).

Improvement of all index figures and data of general clinical examination against the background of taking the ALA preparation in the combined therapy in patients suffering from chronic generalized periodontitis in combination with infiltrative pulmonary tuberculosis suggests a more rapid arrest of the inflammatory process in the periodontal tissues. According to our observation, 64% of patients with periodontitis and pulmonary tuberculosis who received standard therapy were registered for 1 to 2 exacerbations of periodontitis within 3 months. Against the background of complex treatment with the preparation of α -lipoic acid, the exacerbation of periodontitis was stopped within 2 weeks and was not observed later.

Figure 1 shows the results of investigating the gingival capillary blood demonstrating the efficiency of the use of the ALA preparations in the combined therapy of mild chronic generalized periodontitis. After three months of treatment in the case group, a statistically significant decrease was observed in the number of neutrophils – by 1.2 times, monocytes – by 1.8 times ($p < 0.05$) (Fig. 1). In the reference group, positive dynamics was also observed: the number of neutrophils decreased by 1.1 times, monocytes – by 1.6 times ($p < 0.05$).

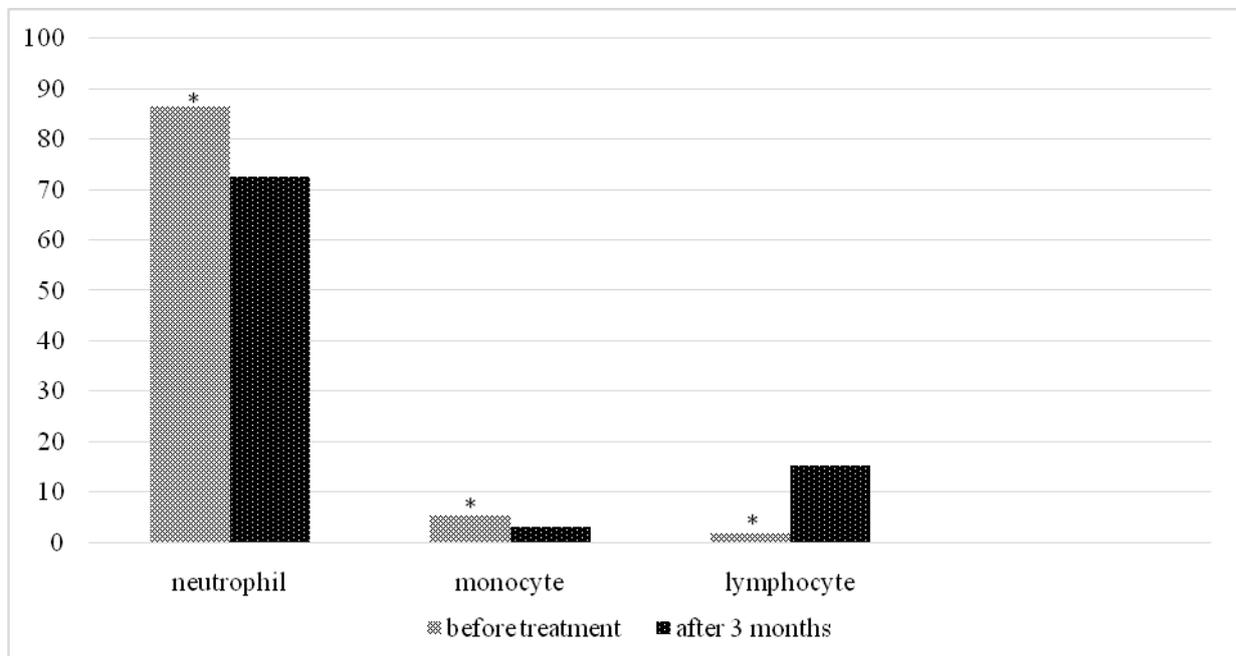


Figure 1: Dynamics of cytochrome for gingival capillary blood in patients suffering chronic generalized periodontitis combined with infiltrative pulmonary tuberculosis the background of taking the ALA preparation.

Note: * - differences are statistically significant before treatment and in 3 months of it ($p < 0.05$).

Table 2 demonstrates that the use of ALA preparation for the treatment of chronic generalized periodontitis in patients with infiltrative pulmonary tuberculosis facilitated bringing the content of gingival fluid to normal.

Table 2: Dynamics of cytogram for gingival fluid in chronic generalized periodontitis against the background of infiltrative pulmonary tuberculosis.

Content of gingival fluid	Case group (n=25)		Control group (n=25)	
	Before treatment	In 3 months	Before treatment	In 3 months
Epithelial cells	64.0±0.2 [#]	43.7±0.5 ^{*#}	63.9±0.3 [#]	51.5±0.3 ^{*#}
Candida albicans	More than 10 colonies in the field of vision [#]	From 2 to 7 colonies in the field of vision [#]	More than 10 colonies in the field of vision [#]	From 2 to 7 colonies in the field of vision [#]
Macrophages	4.1±0.2 [#]	2.4±0.2 ^{*#}	4.0±0.3 [#]	3.1±0.2 ^{*#}

Notes: * - differences are statistically significant between the case group and the control group (p < 0.05); # - differences are statistically significant before treatment and in 3 months of it (p < 0.05).

DISCUSSIONS

The main anti-tuberculosis drug is isoniazid, the side effect of which is the neurotoxic effect. The side effect of rifampicin is hepatotoxicity. Prevention of toxic adverse reactions in a patient with tuberculosis begins with the appointment of a complex of vitamins and detoxification therapy. The appointment of antihypoxants, antioxidants and angioprotectors not only prevents the development of toxic reactions from various organs, but also positively influences the pathogenesis of the tuberculosis process [11, 13]. To date, a requirement has been formulated for an ideal neuroprotective agent - a tool that improves the energy metabolism of neurons and adapts local hemodynamic processes to the level of neuronal activity that reduces oxidative stress. One such medication is alpha-lipoic acid, the cytoprotective effect of which is directly related to its antioxidant properties [5].

Thioctic acid is a strong lipophilic antioxidant and is rightfully considered the "gold standard" of the pathogenetic treatment of diabetic polyneuropathy. A number of studies have shown that the use of alpha-lipoic acid at a dose of 600 mg / day intravenously or orally for 3 weeks up to 6 months reduces in clinically significant degree the main symptoms of polyneuropathy, including pain, paresthesia and numbness [2, 7].

The course use of alpha-lipoic acid in children with mild mental retardation during a month at a daily dose of 75 mg contributes to an increase in volume and improved concentration of attention, improving short-term memory by numbers and images, and increasing mental stability [6].

The use of the ALA preparation in the combined therapy of mild chronic generalized periodontitis in patients with infiltrative pulmonary tuberculosis has shown its rather high efficiency in the prevention of periodontal pathology. Use of "Octolipen" is accompanied with a significant decrease in the number of disease relapses and an earlier remission. Also, the use of the alpha-lipoic acid as a prophylactic preparation prevents the development of the inflammatory process in the periodontium, which is confirmed by clinical and laboratory investigations: number of patients' complaints decreased, signs of inflammation were practically absent, the basic dental indices and the figures of gingival capillary blood improved, the content of gingival fluid was back to normal.

In further studies, we plan to study various doses of alpha-lipoic acid in the treatment and prevention of chronic generalized periodontitis.

CONCLUSION

- The implementation of the alpha-lipoic acid preparation in the combined therapy of chronic generalized periodontitis in patients with infiltrative pulmonary tuberculosis normalizes the state of protective mechanisms eliminating the effects of impaired metabolism in periodontal tissues.

- Due to its powerful antioxidant properties, the alpha-lipoic acid preparation should be used for preventive purposes, as it creates the immunity of periodontal tissues to damaging agents, which makes it difficult to develop relapses of the disease.

REFERENCES

- [1] Ivanov P.V. Antioxidant therapy in the combined treatment of periodontitis. *Fundamental Researches*.2008;11:33-8. (In Russ.)
- [2] Gorodetsky V.V. Treatment of diabetic polyneuropathy and other degenerative and inflammatory diseases of the peripheral nervous system by metabolic drugs: method. Recommendations. Moscow. 2004.30 p. (In Russ.)
- [3] Lunina N.A., Velikaya O.V., Kunin V.A. Effect of oral prophylaxis on the quality of life for patients with pulmonary tuberculosis.*System analysis and management in biomedical systems*. 2013;12.4:1035-8. (In Russ.)
- [4] Lunina N.A., Kunin V.A., Velikaya O.V. Clinical-laboratory characteristics of chronic generalized periodontitis in patients with infiltrative pulmonary tuberculosis (tb) with various drug susceptibility. *Research journal of pharmaceutical, biological and chemical sciences*. 2017;8.4:422-6. (In Russ.)
- [5] Poleshchuk A.V. Morphochemical substantiation of the use of alpha-lipoic acid in severe craniocerebral trauma: author's abstract. Cand. Med. Sciences. Vladivostok medical university. Vladivostok. 2011.23 p. (In Russ.)
- [6] R. Fardieva. Study of the influence of thioctic acid on the intellectual and mnesic functions of the brain in children with mild mental retardation: dis.cand.med.sciences. Kazan medical University. 2013.22 p. (In Russ.)
- [7] Shavlovskaya OA Thioctic acid: antioxidant therapy of neurological diseases. *Endocrinology*. 2014;13:15-19. (In Russ.)
- [8] Wolf G.F. Periodontics. Herbert F. Wolf, Edith M.Ratejtshak, Klaus Rateytshak. In G.M. Barer editor.MEDPressinform. Moscow. 2008.548 p.
- [9] Birsan I. Polymerase chain reaction as a prospect for the early diagnosis and prediction of periodotal disease in adolescents. *Eur Arch Paediatr Dent*.2015;16(1):9-12.
- [10] Doseva-Panova V.T. Subgingival microbial profile and production of proinflammatory cytokines in chronic periodontitis. *Folia Med. (Plovdiv)*. 2014;56(3):152-160. (In Russ.)
- [11] Ertapenem in the treatment of multidrug-resistant tuberculosis: first clinical experience.*EurRespir Journal*.2015; 47(1): 333-336.
- [12] Heasman P.A. Drugs, medications and periodontal disease. *Br. Dent Journal*. 2014;217(8):411-419.
- [13] Pharmacokinetics of ertapenem in patients with multidrug-resistant tuberculosis. *EurRespir Journal*.2016;47(4):1229-1234.
- [14] Molchanova O.V. Pharmacological effects of alpha-lipoic (thioctic) acid. *Scientific bulletins*. 2012;22 (141): 24-29 (In Russ.)