THE EFFECT OF LOW INTENSITY LASER RADIATION ON SPECIFIC INFLAMMATION ACTIVITY IN TUBERCULOSIS PATIENTS AND THE SHORT- AND LONG-TERM RESULTS OF THEIR TREATMEN

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The aim of the investigation was to study the changes in tuberculous process activity by morphological data, and assess the short- and long-term results of the treatment of patients exposed to low intensity laser radiation.

Materials and Methods. We studied the short- and long-term results of treatment and the tuberculous process activity by morphological data in 60 patients with infiltrative pulmonary tuberculosis: the main group consisted of 30 patients exposed to low intensity laser radiation, and the control group included 30 patients with no radiation therapy used. In all patients the provided treatment resulted in the transformation of infiltrative tuberculosis into tuberculoma or cavern, followed by conservative lung reductions with postoperative histological examination. We compared the degree of specific process activity with the short- and long-term results of treatment. Inflammation activity was determined by B.M. Ariel classification (1998). According to the classification there are 5 inflammation degrees: from the minimal degree 1 (inactive tuberculosis), to degree 5, maximum (acutely progressive tuberculosis).

Results. The application of laser therapy was found to promote the reduction of inflammatory process activity in pulmonary tuberculosis and improve the short- and long-term results of treatment. The average morphological activity degree of tuberculous process in the treatment group was 2.8±0.1 (the control group — 3.2±0.1) permitting to perform operative therapy at early stage of chemotherapy (an average preoperative stage in the patients of the treatment group — 5.2±0.2 months, in the control patients — 6.5±0.3 months) and reduce hospitalization period. In the follow up period the number of clinically cured tuberculous patients in this group increases.

Key words: low intensity laser radiation; infiltrative pulmonary tuberculosis; degrees of tuberculous process activity.

The main method of the pulmonary tuberculosis treatment is chemotherapy, but in recent years its effectiveness decreases significantly due to the increasing prevalence of destructive forms of tuberculosis and increasing drug resistance of the agent [1]. The necessity of the long-term use of antituberculous drugs leads to the appearance of side effects resulting in the development of toxic and allergic reactions. All this causes the search and use of non-medical pathogenetically grounded methods that can improve the effectiveness of chemotherapy. One of them is a low-intensity laser radiation (LILR), which has anti-inflammatory, immunomodulatory, anti-oxidant action, stimulates regeneration and improves microcirculation in the tissues [2, 3]. Usage of the chemo-laser therapy in the pulmonary tuberculosis enables to achieve resorption of infiltrative changes, closure of disintegration cavities and abacillation of sputum in the earlier periods and in a greater number of cases [4, 5], to accelerate the preoperative preparation of patients [6]. However, the effect of the LILR on the long-term results of treatment of patients with the pulmonary tuberculosis has been studied poorly. Some authors [6] during the treatment of tuberculosis using the LILR note the rapid clearing of caverns from caseous necrotic masses and their subsequent healing in some cases, more favorable productive inflammatory reaction with the formation of small granulomas along the lymph paths, active macroorganism's immunological response in the form of proliferation of lymphoid elements in the lung and well-marked signs of healing. But the reports on the effect of LILR on the change in the degree of activity of tuberculosis (according to morphological studies) are practically absent in available sources of information.

The aim of the investigation was to study the changes in tuberculous process activity by morphological data, and

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assess the short- and long-term results of the treatment of patients exposed to low intensity laser radiation.

Materials and Methods. 60 patients treated in the Nizhny Novgorod Regional Clinical Tuberculosis Dispensary were examined on the subject of newly diagnosed infiltrative pulmonary tuberculosis. The main group consisted of included 30 patients exposed to low intensity laser radiation, and the control group included 30 patients with no LILR applied. The ratio of men and women in the groups were similar: 24 men (80%) and 6 women (20%) in each group. Age of the treatment group patients ranged from 19 to 62 years and averaged 32.7±2.1 years, in the control group — from 18 to 53 years and the average age was 37.8±1.8 years. In the treatment group there were 21 working people (70%) including 8 officers and 13 workers. In the control group there were 17 working people (56.7%) including 2 officers and 15 workers.

All patients received the antituberculous treatment with the primary and the secondary agents in accordance with the accepted standards. The treatment group patients also received 1–2 courses (depending on results) of the low-intensity infrared laser therapy. The first course of the laser therapy was administered from the end of the second week of the treatment, the second course — 2 weeks after the first course, i.e. about 1.5 months after beginning of the therapy. The infrared exposure course consisted of 15 daily procedures (with a two-day break on Saturday and Sunday) and was carried out using devices “Mustang” and “Mustang-2000” (Russia). The impact of the LILR was in accordance with the projection of changes in the lungs to the chest percutaneously from 2–4 points, with the frequency of 50–150 Hz, the power 5–10 W, the total exposure time was 6–9 minutes.

The patients in both groups against the background of the provided treatment achieved a partial resorption of infiltration, foci, reduction or closure of disintegration cavities, and infiltrative form of tuberculosis transformed into tuberculoma or cavern, on the subject of which all patients underwent lung sparing resections (up to 3 segments).

The histological material was studied postoperatively. The activity of specific changes in in tuberculosis was assessed according to the ratio of caseous-necrotic and fibrotic changes, and the predominance of a particular cell type according to the classification of B.M. Ariel (1998). We distinguished 5 degrees of the tuberculosis activity: 1 — the subsiding inflammatory process, 2 — limited active tuberculosis, 3 — stable inflammatory changes, 4 — inflammatory changes with the progression starting, 5 — acute progressive tuberculosis. [7] The study was carried out in collaboration with B.M. Ariel, Doctor of Medicine, and O.M. Ostashko, Candidate of Medical Science (St. Petersburg).

The long-term results of the treatment were studied in 21 cases of the treatment group and 27 cases of the control group (for a five-year follow up period on outpatient medical records and extracts from medical records).

Results and Discussion. The diagnosis of infiltrative pulmonary tuberculosis was based on clinical and radiological data and results of laboratory instrumental and microbiological examinations. The tuberculous process was identified by the clinical method, more often in the treatment group than in the control. 17 patients (56.7%) of the treatment group and 19 patients (63.3%) of the control group had concomitant diseases. 5 patients (16.7%) of the treatment group and 2 patients (6.6%) of the control group had complications of tuberculosis (hemoptysis, bronchial tuberculosis). The average volume of interstitial lung disease in both groups was 3 segments including lesions of bronchogenic seeding. All patients were bacteriologically proven and had destructive changes in the lungs.

Resistance graph data were obtained from 27 patients of the treatment group and 22 patients of the control group. 23 cases (85.2%) in the treatment group and 17 cases (77.3%) in the control group had drug-sensitive causative agent strains. Monoresistance of tuberculosis mycobacteria was detected in 3 patients in the treatment group and in 2 patients of the control group. Multiresistance of the causative agent was identified in 3 cases in the control group, and multiresistance as multi-drug resistance — in 1 case of the treatment group. Thus, the characteristics of the tuberculous process in patients of the treatment group and the control group were comparable.

Conservative closure of disintegration cavities was observed in 6 cases (20%) in the treatment group and in 5 cases (16.7%) in the control group.

When studying the post-operative histological material there were determined degrees 2, 3 and 4 of the tuberculous process activity (see Table). As an illustration there are the fragments of histotopographic sections: Fig. 1, 2 — the resection material of the treatment group patients, Fig. 3–5 — resection material of the control group patients.

The proportion of patients with the limited active tuberculosis (degree 2 of the tuberculous process activity) in the treatment group was twice more than in the control group. The proportion of patients with the degree 4 of the tuberculous process activity (inflammatory changes with starting progression) was approximately two times more in the control group than in the treatment group. On average, in the treatment group the degree of the morphological activity of the tuberculous process was 2.8±0.1, significantly different from the control group — 3.2±0.1 (p=0.006). Thus, the morphological data strongly suggest that the use of the LILR results in the inflammatory activity reduction that corresponds to the reports of other authors [6]. Reduction in the activity of a specific process under the influence of the LILR enables to improve the short-term results of the treatment: the average term of closure of disintegration cavities in the treatment group was about 4.9±0.1 months,

Morphological activity of tuberculosis process in patients of the treatment group and the control group, absolute number/%

The degree of morphological activity of tuberculous inflammation	Treatment group	Control group
1	—	—
2	10/33.3	5/16.7
3	15/50	13/43.3
4	5/16.7	12/40
5	—	—

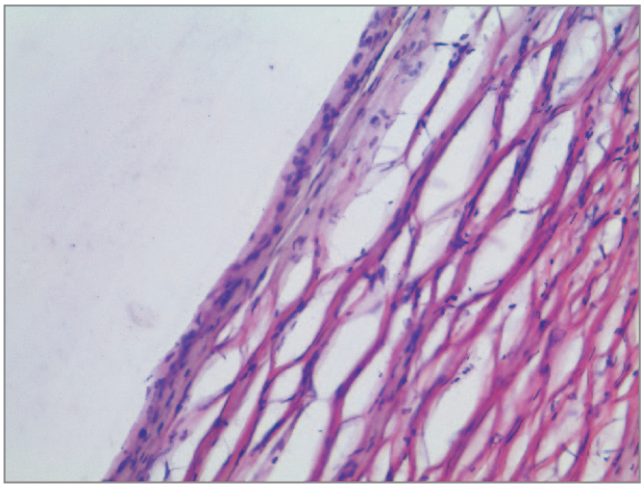

Fig. 1. Resection material of Patient A. The cavern wall represents fibrous tissue without necrotic masses (activity degree 2). Hematoxylin-eosin staining; ×250

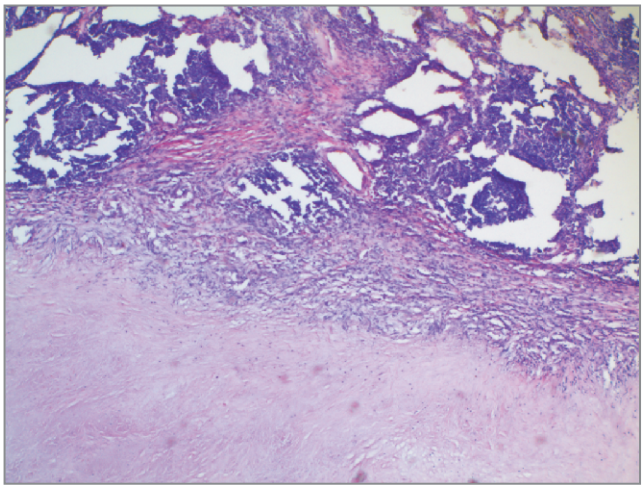

Fig. 2. Resection material of Patient Sh. Tuberculoma capsule consists of fibrous tissue with moderate diffuse round cell infiltration (activity degree 2). Hematoxylin-eosin staining; ×250

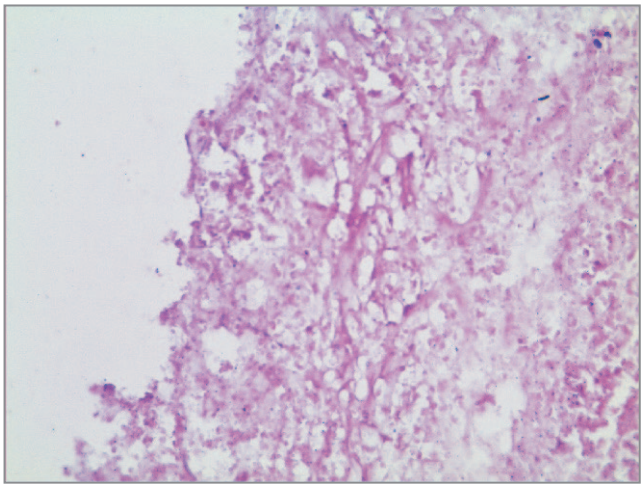

Fig. 3. Cavern wall. Resection material of Patient K. Cavern wall with excessive necrotic masses (activity degree 4). Hematoxylin-eosin staining; ×250

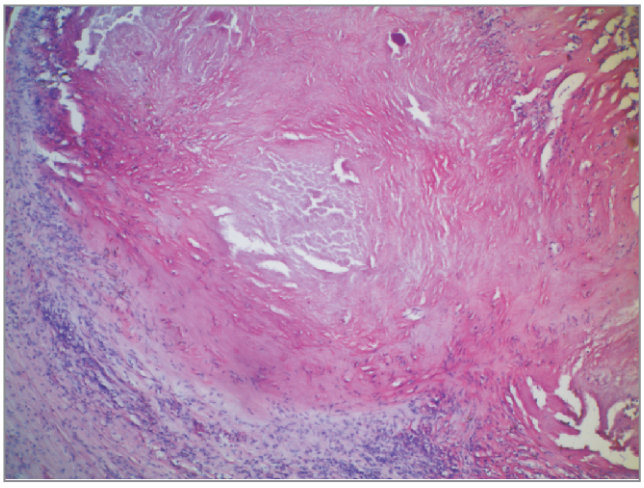

Fig. 4. Resection material of Patient K. Culling near the cavern. In the pulmonary tissue surrounding the cavern there are numerous epithelioid cell granulomas with the presence of giant Pirogov–Langhans cells and caseous-like necrosis in the central zone (activity degree 4). Hematoxylin-eosin staining; ×250

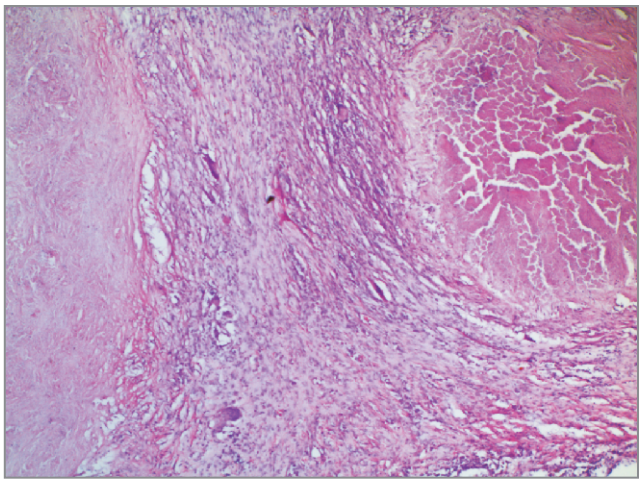

Fig. 5. Tuberculoma. Resection material of Patient S. Tuberculoma capsule with a great number of epithelioid and giant cells of the Pirogov–Langhans cell type (activity degree 4). Hematoxylin-eosin staining; ×250

in the control group — 6.1±0.3 months, which is statistically significantly higher (p=0.0001). Preoperative period, on average, in the treatment group was 5.2±0.2 months, in the control group — 6.5±0.3 months (p=0.0001).

During a five-year follow up 2 patients (9.5%) of the treatment group and 1 patient (3.7%) of the control group changed their place of residence. 1 patient (4.8%) of the treatment group and 4 patients (14.8%) of the control group died of other diseases. 2 patients (7.4%) of the control group died of tuberculosis progression, in the treatment group there were no deaths from tuberculosis. Clinical cure was achieved in 16 cases (76.1%) in the treatment group and in 17 (62.9%) in the control group. Thus, 61.9% of patients in the treatment group and only 40.8% of control patients were deregistered in the dispensary with a clinical cure. Minor residual changes were detected in patients in the treatment group (87.5%) more frequently than in the control group (64.7%). Considerable changes, by contrast, were more frequent in the control group (35.3%) than in the treatment group (12.5). 2 patients (9.5%) of the treatment group and 5 control patients (18.5%) had adverse outcome (progression, exacerbation, recurrent tuberculosis).

It should be noted that in the first follow up year the progression of the process was observed in 1 case (with the process activity degree 4) in the control group; in the third follow up the control patients had 2 tuberculosis relapses (with degrees 3 and 4 of the process activity) and 1 exacerbation process (with degree 2 of the process activity); by the 5th year of the follow up period there were 3 recurrences (with the process activity degree 3): 2 — in the treatment group and 1 — in the control group. Therefore, in the early follow up period there was only 1 case of progression in a patient with degree 4 of the inflammatory activity (starting progression of the process), in long-term follow up periods the recurrences and exacerbations of the process were observed in patients with degrees both 4 and 2, 3 of the inflammation activity.

Conclusion. The use of the low intensity laser radiation in the treatment of patients with pulmonary tuberculosis reduces the degree of the inflammatory activity, which allows to carry out surgical treatment in the earlier period from the chemotherapy start, and thereby to reduce the hospital stay. In long-term follow up periods the proportion of patients with clinical cure of tuberculosis increases, the number of patients with treatment failure decreases.

References

1. Shilova M.V. Epidemiologicheskaya obstanovka po tuberkulezu v Rossiyskoy Federatsii k nachalu 2009 g [Epidemiologic situation on tuberculosis in the Russian Federation by the beginning of 2009]. *Tuberkulez i bolezni legkikh — Tuberculosis and lung diseases* 2010; 5: 14–21.

2. Kozlov V.I. Mekhanizmy fotobiostimulyatsii [Photobiostimulation mechanisms]. *Lazernaya meditsina — Laser Medicine* 2010; 14(4): 4–13.

3. Ulashchik V.S. Lazernaya terapiya. V kn.: *Fizioterapiya i kurortologiya*. Kniga 1 [Laser therapy. In: Physiotherapy and balneology. Volume 1]. Pod red. Bogolyubova V.M. [Bogolyubov V.M. (editor)]. Moscow: BINOM; 2012; p. 330–343.

4. Dityatkov A.E. Ispol'zovanie lazerov v kompleksnom lechenii tuberkuleza [The use of lasers in tuberculosis combination therapy]. *Lazernaya meditsina — Laser Medicine* 2003; 7(1): 21–22.

5. Levkina M.V. *Lazeroterapiya v kompleksnom lechenii infil'trativnogo tuberkuleza legkikh*. Dis. … kand. med. nauk [Laser therapy in combination therapy of infiltrative pulmonary tuberculosis. Abstract for Dissertation for the degree of Candidate of Medical Science]. Saint Petersburg; 2007.

6. Dobkin V.G., Bagirov M.A., Fayzullin D.R., Kuz'min D.P. Endokavitarnoe obluchenie ul'trafioletovym lazerom v predoperatsionnoy podgotovke bol'nykh progressiruyushchim fibrozno-kavernoznym tuberkulezom [Endocavitary ultraviolet laser radiation in preoperative preparation of patients with progressive fibrous cavitary tuberculosi]. *Problemy tuberkuleza — Tuberculosis Issues* 2006; 2: 25–28.

7. Ariel' B.M., Bellendir E.N. Patologicheskaya anatomiya i patogenez tuberkuleza. V kn.: Rukovodstvo *po legochnomu i vnelegochnomu tuberkulezu* [Pathological anatomy and pathogenesis of tuberculosis. In: Pulmonary and extrapulmonary tuberculosis manual]. Pod red. Levashev Yu.N., Repin Yu.M. [Levashev Yu.N., Repin Yu.M. (editors)]. Saint Petersburg: ELBI-SPb; 2006; p. 67–94.