

## OPTIMIZATION OF PREOPERATIVE PREPARATION OF PATIENTS WITH BILATERAL PULMONARY TUBERCULOSIS

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To develop a preoperative preparation method of patients with bilateral pulmonary tuberculosis and to prove its advantages in comparison with the standard procedure. The study included 44 patients with bilateral fibrous-cavernous pulmonary tuberculosis. The patients were divided into two groups. The treatment group included 20 patients in the preoperative preparation of which the retrosternal lymphotropic antibacterial therapy developed by us was additionally included. In 24 patients, the preoperative preparation, including its antibacterial part, was carried out according to the standard procedure. The complex clinical observation of patients with bilateral cavernous tuberculosis showed that the use of the retrosternal administration route of chemotherapeutic agents for  $28.6 \pm 1.2$  days allowed to achieve a significant effect in 39.8% ( $p = 0.014$ ), and partial effect in 51.1% of patients. The medicinal effect was not observed in 9.1% of patients ( $p = 0.008$ ). When using the conventional method of preoperative preparation for  $56.5 \pm 1.3$  days, which included oral administration of Isoniazid, the obtained results were significantly worse, as follows: significant clinical effect was 11.7%, partial clinical effect was 40.5%, and no effect was 47.8%. The use of retrosternal administration route of chemotherapeutic agents in patients with bilateral fibrous-cavernous pulmonary tuberculosis as a part of preoperative preparation allows to achieve a significant clinical effect in almost 40% of patients, which is 3.4 times more often than in the control group; herewith, preparation time for surgery decreases by a factor of 1.8. The high confidence of the results obtained ( $p < 0.05$ ) confirms the need for more effective chemotherapy in the preoperative period and, at the same time, the insufficiency of the conventional methods of antibacterial treatment in the preoperative stage in patients with bilateral destructive pulmonary tuberculosis.

**Keywords:** tuberculosis, preoperative preparation, lymphotropic therapy, bilateral pulmonary tuberculosis

Surgical treatment of patients with bilateral pulmonary tuberculosis caused by specific fibrous and destructive changes in the lungs, MBT drug resistance and reduced functional respiratory reserves requires special preoperative preparation [1]. Maximum suppression of the *Mycobacterium tuberculosis* population and a decrease in the activity of specific inflammation are the main goals [2]. The key to successful surgical treatment of patients with bilateral cavernous lung disease is the stabilization of the tuberculous process before the operation. The severity of a specific inflammatory process affects not only the surgical tactics, but also the prognosis of surgical treatment [3, 4].

Most foreign surgeons recommend the implementation of early surgical interventions because long periods of preoperative preparation against the background of ongoing bacterial excretion, the formation of irreversible destructive changes significantly increase the risk of unsuccessful results of surgical treatment [5–7]: in 10-month preoperative preparation, 8% were unsatisfactory the results of [8, 9], with a 14-month – 26.6% [10].

As a rule, standard chemotherapy is carried out by taking 4 to 5 anti-tuberculosis drugs within patients with bilateral pulmonary tuberculosis during preoperative preparation, the expected effect is the clinical stabilization of the tuberculosis process. The reasons that counteract the achievement of the result is the low efficiency and the long duration of this

method of preoperative preparation involving the administration of tablets. The reasons that counteract the result achievement is the low efficiency and the long duration of this method of preoperative preparation involving the tablets intake. Furthermore, there is a low bactericidal concentration in case of peroral intake (due to the loss of their activity under the influence of the gastrointestinal tract and inactivation in the liver). Thus, the creation of high concentrations of drugs in the patient's blood is impossible due to their rapid inactivation, they do not create a depot in the lymph nodes of the lung root and mediastinum. Moreover, the oral route of drug intake involves long-term chemotherapy (60 – 90 days), which is not consistent with the goal of reducing the period of preoperative preparation [11].

The method of preoperative preparation of patients with bilateral pulmonary tuberculosis is used, the introduction of water-soluble forms of anti-tuberculosis drugs is performed retrosternally by puncture of the retrosternal space from the jugular fossa, which allows to create a depot in the retrosternal tissue. The method has several disadvantages, the main of which is the fact that the needle is inserted into the retrosternal space blindly, which significantly increases the risk of injury to the mediastinal pleura, the development of pneumothorax, and damage to the v. brachiocephalica sinistra. Puncture of the retrosternal space from the jugular fossa does not achieve lung root level and doesn't create a depot of drugs in this particular

area, which, in fact, is the goal of lymphotropic therapy. In addition, the implementation of this technique requires systematic puncture of the retrosternal space every day, which significantly increases the risks described above with the duration of preoperative preparation up to 45 days. In view of this we have developed a new method of preoperative preparation – retrosternal lymphotropic therapy.

### Materials and methods of research

The study included 44 patients with bilateral fibro-cavernous pulmonary tuberculosis. Patients were divided into 2 clinical groups. The first main group included 20 people, in the preoperative preparation of which the retrosternal lymphotropic antibacterial therapy developed by us was additionally included. Preoperative preparation, including its antibacterial part, was carried out according to standard methods within 24 patients. Selected clinical groups differed insignificantly ( $p > 0.05$ ) by sex, age, number of comorbidities and nature of comorbidities.



Retrosternal lymphotropic therapy for the preoperative preparation of patients with bilateral pulmonary tuberculosis. The introduction of drugs through a retrosternal catheter

We developed a method of preoperative preparation of patients with bilateral pulmonary tuberculosis that is outlined as follows: in the position when patient is on the back, surface anesthesia of the xiphoid process zone of the sternum is performed with 6 ml of 1% lidocaine solution. A needle from the set for the central vein catheterization is injected retrosternally, it is held behind the sternum in the direction of the II<sup>nd</sup> rib behind the sternum. At the same time, hydraulic tissue preparation is constantly performed, pre-supplying a solution of 1% lidocaine as the needle is being held. When the end of the needle reaches the level of attachment of the II<sup>nd</sup> rib to the sternum, a

guide is inserted through the needle, and the needle is removed. When the conductor is installed this way, a catheter is inserted into the retrosternal space from the kit and guided to the level of the II<sup>nd</sup> rib, and then conductor is removed. The installed catheter is fixed to the skin with a separate suture (figure). Every day, 10 ml of a 5% solution of isoniazid, 1.0 amikacin or kanamycin, 5000 IU of heparin, 4 ml of a 0.5% solution of novocaine, 2 ml of a 2% solution of hydrocortisone with a total volume of 18 ml are injected through the catheter. The course of preoperative retrosternal lymphotropic therapy consists of 20 injections.

As criteria for the effectiveness of preoperative preparation, the reduction or elimination of symptoms of tuberculous intoxication, cessation of bacteria excretion, resorption of infiltrative foci, closure of decay cavities were taken into account. The introduction of microcatheters from the retroxifoidal region allows to avoid injuring v. brachiocephalica sinistra, which significantly reduces the invasiveness of the intervention, and the implementation of the technique of Seldinger helps to avoid injury to the pleura. The location of microcatheters at the level of the II<sup>nd</sup> rib with the introduction of anti-tuberculosis drugs allows to create their depot in the lymphatic system of the roots of the lungs, ensures the penetration of drugs into the lung tissue to the visceral pleura. The use of catheterization of the retrosternal space allows to create a high concentration of anti-tuberculosis drugs directly in the lymphatic system of the mediastinum and to obtain a bactericidal effect by daily administration of drugs, thereby reducing the time of preoperative preparation. In addition, the introduction of anti-tuberculosis drugs directly into the mediastinal tissue leads to the resorption of infiltrative changes and fresh foci in both lungs, greatly improving the condition of patients with bilateral lung lesions.

### Results of research and their discussion

We studied the concentration of GINK in the blood by the method of T. V. Satirova (2010) [13] with a single oral intake of isoniazid at a dose of 10 mg / kg body weight and retrosternal administration of 10 ml of a 5% isoniazid solution within 20 patients with bilateral cavernous lung disease. After oral intake of isoniazid 600 mg 1 time per day, the concentration of the drug after 4 hours was  $3.2 \pm 0.3$   $\mu\text{g} / \text{ml}$ , after 8 and 12 hours – respectively  $1.5 \pm 0.2$  and  $0.17 \pm 0.12$   $\mu\text{g} / \text{ml}$ . After 8 hours the concentration of the drug was close to the minimum bacteriostatic. With the retrosternal administration of isoniazid, after 4 hours, the

concentration was  $6.1 \pm 0.56 \mu\text{g} / \text{ml}$ , after 8 and 12 hours, respectively, it decreased to  $2.6 \pm 0.27$  and  $0.29 \pm 0.1 \mu\text{g} / \text{ml}$ . Thus, with retrosternal administration, the rate of decrease in concentration (half-life) remained the same, however, the concentration of the drug was 1.7 times higher than when administered orally. During the retrosternal lymphotropic method of administration the depot GINK was created, its concentration was higher and maintained for a longer time. In addition, retrosternal administration of GINK did not require the use of high doses of pyridoxine to prevent the neurotoxic effect of the drug.

The analysis conducted during the study showed that the results of preoperative preparation depended not only on the duration of the disease and the clinical form of tuberculosis but also on the effectiveness of chemotherapy. In this regard, we isolated various degrees of the effectiveness of chemotherapy for preoperative preparation, depending on the clinical, radiological, laboratory and bacteriological picture of the disease before and after the treatment.

**The pronounced effect** of chemotherapy was noted with:

- absence of complaints and clinical manifestations of intoxication;
- stable normalization of body temperature and hemogram;
- reduction of the size of cavities or their transformation into thin-walled cavities according to x-ray data;
- closing of cavities of disintegration or the formation of caseous-necrotic foci in both lungs;
- abacillation.

**The partial effect** of preoperative preparation was characterized by:

- lack of complaints and intoxication;
- persistent normalization of body temperature;

- radiographic disappearance of infiltrative perifocal changes, partial resorption of dissemination foci, reduction of cavities and cavities of decay;

- abacillation or oligobacillus.

We regarded the similar result of specific chemotherapy as a partial effect of treatment, which allows to perform surgical intervention.

**The lack of treatment effect** consisted in improving the patient's overall well-being while maintaining individual symptoms of intoxication, radiologically stable picture with the presence of lung tissue destruction zones on both sides, as well as infiltrative changes and foci of dissemination; preservation of bacteria.

We considered the described condition as the absence of the treatment effect and the presence of an active, unstable destructive tuberculous process. Considering further treatment to be unpromising, an operation was suggested.

Comprehensive clinical observation of patients with bilateral cavernous lesion of the lungs showed that using the retrosternal method of administering chemotherapy for  $28.6 \pm 1.2$  days made it possible to achieve a significantly pronounced effect in 39.8% ( $p = 0.014$ ), a partial effect in 51.1% of patients. The treatment effect was significantly less common in 9.1% of patients ( $p = 0.008$ ). When applying the generally accepted method of preoperative preparation, which includes inter alia, oral administration of isoniazid, significantly worse results were obtained for  $56.5 \pm 1.3$  days: a pronounced effect – 11.7%, a partial effect – 40.5%, no effect – 47.8% (table 4.1).

Thus, the use of more intensive chemotherapy with the proposed method led to a reduction in the length of patients staying in the hospital before surgery by 1.8 times ( $p < 0.001$ ) and to a significant improvement in the results of preoperative preparation (table).

The results of preoperative preparation of patients with bilateral cavernous pulmonary tuberculosis, depending on the method of chemotherapy

Chemotherapy method before surgery	Number of patients	The duration of preoperative preparation (days), $M \pm m$	The result of preoperative preparation ( $P \pm mp\%$ )		
			Pronounced effect	Partial effect	Lack of effect
Standard oral chemotherapy	24	$56,5 \pm 1,3$	$11,7 \pm 1,1$	$40,5 \pm 2,7$	$47,8 \pm 2,3$
Retrosternal chemotherapy + standard chemotherapy	20	$28,6 \pm 1,8$	$39,8 \pm 1,2$	$51,1 \pm 2,4$	$9,1 \pm 1,3$
$p$		$p < 0,001^{2)}$	$p = 0,014^{1)}$	$p = 0,199^{1)}$	$p = 0,008^{1)}$

The level of differences significance between chemotherapy methods before surgery:

1) by criterion 2 – Pearson;

2) by one-way analysis ANOVA

For effective preoperative preparation it is necessary to conduct pathogenetic and symptomatic therapy aimed at correcting the main parameters of the body's vital activity and eliminating functional disorders of all organs and systems in addition to conducting specific anti-tuberculosis therapy in accordance with accepted standards. The main directions of such treatment were:

- correction of the acid-base state;
- correction of water and electrolyte balance;
- correction of protein and carbohydrate metabolism;
- correction of anemia;
- correction of hemostasis;
- detoxification therapy;
- elimination or reduction of signs of pulmonary and heart failure;
- correction of intestinal dysbiosis;
- hepatotropic therapy;
- vitamin therapy with the use of multivitamin preparations and complexes with a high content of vitamins;
- carrying out rehabilitation PBS in the presence of endobronchitis;
- treatment of comorbidities.

### Conclusion

As a result of the conducted research, it was established that the use of the retrosternal method of chemotherapy in patients with bilateral fibrous-cavernous tuberculosis allows to achieve a pronounced effect of preoperative preparation in almost 40% of patients, which is 3.4 times more often than in the comparison group; at the same time, preparation time for the operation is reduced by 1.8 times. The high reliability of the results obtained ( $p < 0.05$ ) indicates the need for more effective chemotherapy in the preoperative period and at the same time the insufficiency of the standard methods of antibacterial treatment in the preoperative period in patients with bilateral destructive pulmonary tuberculosis.

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