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Research Article

Characteristics of Oxygen-Dependent Processes in Pulmonary Tuberculosis and Their Dynamics in the Course of Complex Treatment

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Abstract

In conditions of tuberculous inflammation, decompensation occurs in the system of peroxidation – antioxidant protection, in which the mechanisms of oxygen transport by blood play an important role. Many pathogenetic links in the development of Tuberculosis (TB) lungs insufficiently studied, in particular, of blood Oxygen Carrying (OC) of blood.

Purpose of the work

To determine the nature of changes in the oxygen-binding properties of blood and the main parameters of the pro-oxidant-antioxidant balance in pulmonary tuberculosis and in the conditions of complex treatment of destructive forms of pulmonary tuberculosis.

Material and methods

120 patients with different types of pulmonary tuberculosis were examined. In the first 10 days after the patient's admission to the hospital, 10 ml of blood was taken from the ulnar vein against the background of restored outflow. OC was evaluated within one hour after venous blood sampling. The remaining part of the blood was separated by centrifugation into plasma and red blood cell mass, which were stored at a temperature of-80° C, followed by measurement of the pro-oxidant-antioxidant state for one month.

Then, 26 patients with various forms of destructive pulmonary tuberculosis were examined, in the treatment of which, along with standard chemotherapy, an artificial pneumothorax was used.

Results

It was found that the deterioration of blood oxygen transport function indicators occurs depending on the prevalence of the tuberculosis process and the severity of the patient's condition. High values of nitrate/nitrite concentrations are observed: in disseminated forms, they increase by 45.7% ($p<0,05$), while in small forms - by 18.6% ($p< 0,05$). The development of tuberculosis causes the development of oxidative stress. The highest activity of free radical processes is observed in disseminated, and less pronounced in small forms of pulmonary tuberculosis. the analysis of the oxygen transport function of blood and the pro-oxidant-antioxidant state in different types of tuberculosis process was carried out. Changes in the oxygen transport function of the blood, the activity of free radical oxidation in pulmonary tuberculosis depends on the prevalence of the tuberculosis process, the presence of destruction in the lung tissue, bacterial excretion, and especially multidrug resistance. The main parameters of blood oxygen transport function and pro-oxidant-antioxidant balance were studied in patients with destructive pulmonary tuberculosis under the conditions of complex treatment (a combination of chemotherapy and artificial pneumothorax)

Conclusions

These results indicate an important role of oxygen-dependent processes in the pathogenesis of pulmonary tuberculosis, which should be taken in to account when it comes to complex therapy of this disease. It was found that the positive effect of collapse therapy is realized through the influence of the oxygen transport function of blood and the NO gas transmitter, which is manifested in a decrease in the pro-oxidant-antioxidant imbalance.

Relevance:

Many pathogenetic links in the development of Tuberculosis (TB) lungs insufficiently studied, in particular, of blood Oxygen Carrying (**OC**). Blood hemoglobin affinity in the body (SGC) it largely determines the diffusion of oxygen from the alveolar air into the blood, and then, at the level of the capillaries of the large circulatory circle, into the tissue [10]. Due to the S-shaped configuration of the oxyhemoglobin dissociation curve, blood oxygenation in the lungs remains at a high level even with a relatively low alveolar pressure. pO_2, and its deoxygenation significantly changes even with a small change in the capillary-tissue gradient pO_2 [9, 11]. TB is a chronic specific infectious disease that develops in response to the introduction into the body and intracellular reproduction of Mycobacterium Tuberculosis (MBT) in the cells of the mononuclear phagocyte system, and all human body systems can be affected, but the respiratory organs are

most often affected [2]. Respiratory diseases, including TB, are considered a priority by WHO, along with circulatory diseases and cancer. All over the world, the pathology of the bronchopulmonary system still remains a serious public health problem, since it is of great social importance, due to the temporary or permanent disability of the population and, as a result, a decrease in the quality of life [27]. In conditions of tuberculous inflammation, decompensation occurs in the Lapid Peroxidation – Antioxidant Protection (LPO-AOP) system. The severity of shifts directly depends on the severity of the specific process, the presence of bacterial release and decay cavities in the lung tissue, and the course options [26]. Blood OC mechanisms play an important role in maintaining dynamic equilibrium in the LPO-AOS system. Nitrogen Monoxide (NO), which belongs to the class of gas transmitters, is involved in the formation of the oxygen regime and blood OC. This factor plays an important role in a complex set of interrelated processes that determine the delivery of oxygen, its extraction and utilization in various tissues of the body. However, under conditions of excessive NO production, it can initiate an imbalance in the functioning of many body systems [39], determine the availability or deficiency of oxygen delivery to tissues [16]. To increase the effectiveness of Chemotherapy (CT) for TB, collapse-forming techniques are successfully used (Artificial Pneumothorax (AP), local artificial lung collapse with endobronchial valve insertion, and then extrapleural pneumolysis with silicone filling) [19]. Currently, hypotensive pneumothorax is widely used, the mechanism of action of which is explained by mechanobiological theory, but many aspects of its effects have no been studied [4]. In this regard, it is advisable to assess the effect of hypotensive AP on oxygen-dependent processes.

Purpose of the work:

To determine the nature of changes in the oxygen-binding properties of blood and the main parameters of the pro-oxidant-antioxidant balance in pulmonary tuberculosis and in the conditions of complex treatment of destructive forms of pulmonary tuberculosis.

Material and methods:

To assess the features of oxygen-dependent processes (blood OC, prooxidant-antioxidant balance, and L-arginine NO system activity) in lung TB, two groups were formed: the main group and the control group. a randomized, controlled prospective study. Main group (the first group consisted of 120 patients with various clinical forms of lung TB, the second group consisted of 23 practically healthy individuals aged 20–30 years old. Characteristics of patients in the main group: 97 (80.8%) men and 23 (19.2%) women. In 75 (62.5%) patients, lung TB was diagnosed for the first time, and in 45 (37.5%) – repeatedly. During the examination, a number of patients were found to have risk factors for developing TB: contact with a TB patient in 32 (26.7%), income from prison – 17 (14.2%), Alcohol Dependence Syndrome (ADS) – 40 (33.3%), Diseases of The10 Gastrointestinal Tract (DGT)-19 (15.8%), the presence of several factors simultaneously– in 33 patients (27.5%). Upon admission to the hospital, the following clinical forms of pulmonary TB were diagnosed: cavernous – in 11 (9.2%) patients, infiltrative – in 55 (45.8%), focal – in 21 (17.5%), tuberculosis – in 18 (15%), disseminated – in 15 (12.5%). Due to the absence of differences in the clinical picture, in the nature of the course of the process, in the prevalence and the absence of significant differences between each other – tuberculosis, focal, bronchobular and rounded infiltrate were grouped into the "small forms" group (n=49). The control group consisted of almost healthy individuals (23 people) aged 20-30 years. In the next series of studies, to study the patterns of changes in blood OC, pro-oxidant-antioxidant balance, and L-arginine-NO system activity during the application of AP, a group of 26 people was formed, in which these parameters were evaluated before the application of AP and after 2 months of its application. The clinical characteristics of this group of patients are presented in (Table 1). In this group, infiltrative pulmonary tuberculosis in the decay phase is also the most common, with Multidrug-Resistant TB (MDR-TB) predominating in 73.8% of cases.

Table 1: Characteristics of patients (n=26) who underwent an assessment of the, of blood oxygen carrying and the pro-oxidant-antioxidant state during the use of AP

Indicator	n	%
Paul		
male	19	73,08
female	7	26,92
Age		
20-29 years old	10	38,5
30-39 years old	6	23,1
40-49 years old	7	26,9
50 years and older	3	11,5
Clinical form of TB		
focal point	1	3,7
infiltrative	15	57,7
disseminated	2	7,8
cavernous	8	30,8
Prevalence of the process		
limited	10	38,5
widespread	16	61,5
Bacterial release		
MBT +	23	88,5
MBT- -	3	11,5
Drugs resistance		
without MDR	7	26,92
MDR	19	73,08
Destruction	26	100
Number of decay cavities		
1 cavity	20	76,9
2 cavities or more	6	23,1
Size of decay cavities		
up to 2 cm	8	30,8
2-4 cm	14	53,8
more than 4 cm	4	15,4
Identification		
newly identified patients	12	46,2
re-treated patients	14	53,8
Aggravating factors		
contact information		
arrived from places of deprivation of liberty	12	46,2
ADS	4	15,4
diseases of the gastrointestinal tract	12	46,2
	4	15,4

CT was performed according to the current clinical protocols, taking in to account the sensitivity of the Office to anti-TB drugs, and consisted of two phases: the intensive phase and the continuation phase [21]. the effectiveness of treatment at the inpatient stage was evaluated according to generally accepted phthisiatric standards: the time of abacillation and the time of closing the decay cavities.

Blood OC was evaluated using a micro-gas analyzer Synthesis-15 "of the company" Instrumentation Laboratory "(USA) with the definition of the following parameters: pO_2, pCO_2, pH, blood Oxygen Saturation (SO_2), Blood Oxygen Capacity (OCB) at a temperature of 37° C. The affinity of hemoglobin to oxygen was evaluated by the p50 index (pO_2, corresponding to 50% oxygen saturation

of hemoglobin), determined by spectrophotometric method at a temperature of 37° C, pH=7.4 pCO_2=40 mmHg ($p50_{std}$Then, the p50 was calculated at real pH values, pCO_2 and temperature ($p50_{real}$ money) according to the formulas of J. W. Severinghaus [37]. Based on the obtained data, the position of the Oxyhemoglobin Dissociation Curve (ODC) was determined using the Hill equation. The acid-base state of the blood was determined on the basis of Siggard-Andersen nomograms According To The Following Indicators: True Excess Of Buffer Bases (ABE), Standard Excess Of Buffer Bases (SBE), Total Carbon Dioxide (TCO) concentration2), the Concentration Of Standard Bicarbonate (SBC), Bicarbonate Concentration (HCO_3-).The content of Diene Conjugates (DC) was determined by the intensity of UV absorption characteristic of conjugated diene structures of hydroperoxides in the region of 232–234 nm on a spectrophotometer "Solar» PV1251C [14]. Level Malonic Dialdehyde (MDA) was evaluated spectrophotometrically according to the color intensity of the pink complex formed in the reaction with 2' - thiobarbituric acid,"Solar» PV1251C at a wavelength of 535 nm [14]. Catalase activity was recorded by the amount of colored product in reaction H2About2 with ammonium molybdate having the maximum light absorption at a wavelength of 410 nm, on a spectrophotometer "Solar» PV1251C [31]. The content of reduced glutathione was studied by the modified method of J. Sedlak and R. Lindsay [35]. The ceruloplasmin level was determined by the Ravin method [20]. The concentration of alpha-tocopherol and retinol in plasma was evaluated by the method of S. T. Taylor [36].NO production was evaluated by the total nitrate/nitrite content (NO_3-/NO_2-) in blood plasma by a spectrophotometric method based on color reactions c using a Griess reagent at a wavelength of 540 nm [14]. Statistical processing of the obtained results was carried out using the data processing package Statistica for Windows, version 10.0 and the Excel office app. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine the correspondence of the obtained values to the law of normal distribution. For comparison of quantitative indicators, the median (Me) and 25-75% quartiles were calculated if the normal distribution did not match. To analyze the significance of differences in the quantitative characteristics of two related populations, the Wilcoxon test was used. The Kraskall - Wallis test was used to assess the differences between three or more samples simultaneously.

Results and discussion

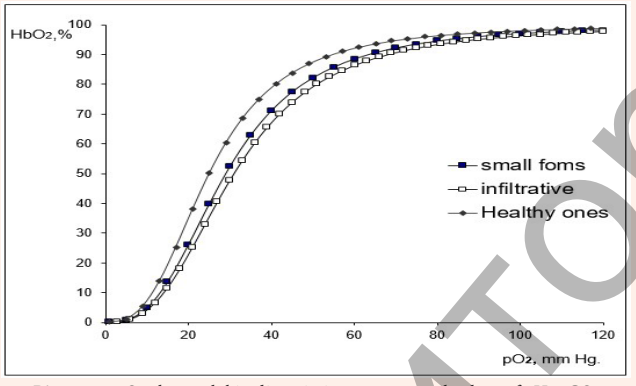
(Table 2) shows changes in the main parameters of blood OC

Table 2: Oxygen carrying of venous blood in different clinical forms of pulmonary tuberculosis, Me (25%, 75%

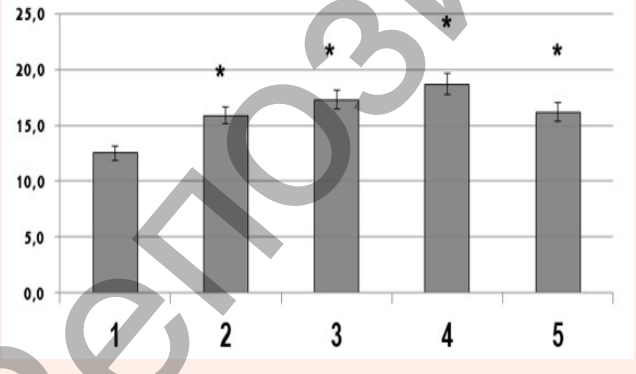
Indicator	Healthy ones	Clinical forms tuberculosis of the lungs			
		small forms	infiltrative	disseminated	cavernousone
n	23	49	45	15	11
Hb (g / l)	145,0 (138,5-153)	131,0 * (122-137)	114,0* (104-124)	119,0* (114,5-122,5)	131,0* (113,5-135,5)
OCB (v%)	20,6 (19,9-21,85)	17,9* (16,5-18,8)	15,3* (13,6-17,1)	16,3* (14,9-16,9)	17,3* (15,5-18,1)
SO_2 (%)	39,2 (36,15-42,3)	36,2 (32,4-38,8)	32,3* (27,4-35)	26,8* (25,4-33,8)	33,2* (29,1-34,4)
pO_2 (mmHg)	24,0 (23,0-25,0)	23,0 (21,0-25,0)	23,0 (20,0-24,0)	21,0* (20,0-22,0)	24,0 (20,5-25,0)
pH (units)	7,384 (7,375-7,403)	7,368 (7,336-7,368)	7,353* (7,325-7,372)	7,342* (7,324-7,362)	7,386 (7,356-7,407)
pCO_2 (mmHg)	53,2 (51,2-54,8)	49,1* (46,1-51,4)	48,4* (46,1-51,8)	46,9* (44,8-49,2)	48,2 (47,5-48,9)
$p50_{real}$ (mmHg)	26,8 (25,5-28,3)	28,0 (22-28,8)	29,8* (28,9-30,9)	32,7* (31,2-33,7)	28,1 (27,9-28,3)
$p50_{std}$ (mmHg)	27,1 (25,6-28,6)	26,8 (25,6 -28,0)	28,7* (27,4-30,5)	30,4* (28,9-32,8)	28,3 (27,4-28,9)

Note - * - significant differences in relation to the group of healthy people (p<0,05), Kruskal-Wallis test

As we can see from the presented table, the deterioration of indicators occurs depending on the prevalence of the tuberculosis process and the severity of the patient's condition in clinical terms. The lowest hemoglobin concentration is observed in infiltrative (decrease by 21.4%, p<0,05) and disseminated (by 17.9%, p<0,05) lung TB; in small forms and cavernous lung TB, the decrease (compared to healthy individuals) is 9.7% (p<0,05). Decline OCB is noted in small forms of lung TB by 13.1% (p<0,05), with infiltrative – by 27.7% (p<0,05), with disseminated – by 20.9% (p<0,05). Reducing SO_2 It is most pronounced in disseminated, infiltrative, and cavernous pulmonary TB: a decrease of 31.6% (p<0,05), 17.6% (p<0,05), and 15.3% (p< 0,05), respectively. pO value$_2$ it is most reduced in disseminated TB – by 12.5% (p< 0,05). Indicators of the acid-base state of the blood changed, but remained within the normal range. An increase in $p50_{real}$ was detected in disseminated lung TB – by 22.01% (p<0,05), in infiltrative TB-by 11.2% (p < 0,05). The most pronounced changes in $p50_{std.}$ They are observed in disseminated TB – an increase of 12.1% (p<0,05) and infiltrative TB-an increase of 5.9% (p < 0,05). changes slightly. Increasing the indicator $p50_{real}$ reflects the ODC shift to the right under real circulation conditions (Picture 1) and this is a typical reaction to hypoxia in the tissues, which occurred due to insufficient function of external respiration [38]. the nitrate/nitrite concentration varies with the prevalence and severity of tuberculosis inflammation (Picture 2). Thus, in disseminated lung TB, this indicator increases by 49.6% (p<0,05), while in small forms – by 27.2% (p < 0,05). Long-term exposure to toxins in the body in TB causes the expression of an inducible isoform of nitric oxide synthase and the formation of large amounts NO. This is a non-specific reaction to the action of an infectious factor [32]. At the same time, the active nitrogen radical and peroxynitrite, which are characterized by pronounced cytotoxic activity, can oxidize .and proteins of the cell surface membrane [34]. In this case, the endothelium can partic in the formation of violations of blood OC, since only the endothelium synthesized by it in an adequate amount can be used. NO supports normal blood flow and oxygen transport to the tissues.



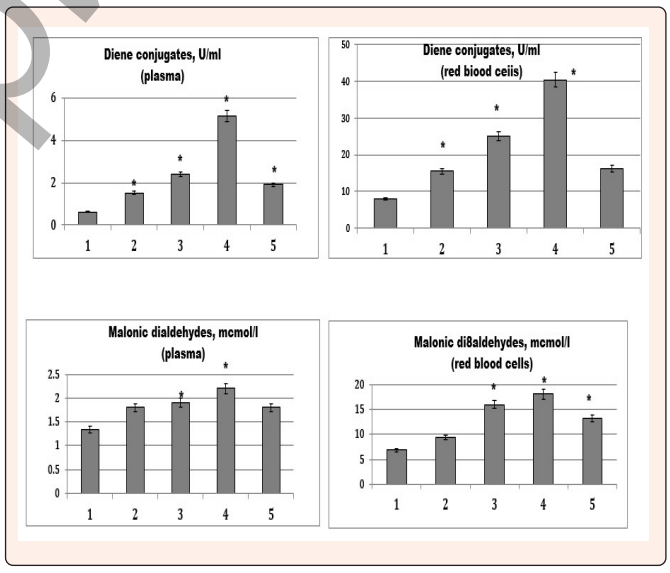
Picture 1: - Oxyhemoglobin dissociation curve at real values of pH, pCO_2



Picture 2: Concentration of nitrate/nitrites(mmol/l) in blood plasma in different clinical forms of pulmonary tuberculosis (1–healthy individuals,2–small forms,3–infiltrative, 4–disseminated,5-cavernous)

Note - * - significant differences in relation to the group of healthy people (p<0,05), the Kruskal-Wallis test

Oxygen-binding properties of blood affect the condition L- arginine-NO a system that determines the functional properties of hemoglobin by modifying its affinity for oxygen through intra-erythrocyte regulation mechanisms, the oxygen-dependent nature of its formation NO, regulation of vascular tone, action of peroxynitrite [5]. Increased gas transmission output NO, judging by the increase in the level of nitrates/nitrites, through the formation of various compounds with hemoglobin (methemoglobin, nitrosylhemoglobin, nitrosohemoglobin), peroxynitrite can change the hemoglobin affinity, which is important for the processes of gas exchange and the implementation of blood OC [7, 8]. Lung TB causes an increase in the activity of LPO processes. The highest activity of free radical processes is observed in disseminated lung TB, and less pronounced in small forms of lung TB. In comparison with the group of healthy individuals, the concentration of DC in plasma increases with a widespread tuberculosis process and, accordingly, the greatest increase is noted in disseminated-8.4 times (p<0,05), in infiltrative-3.9 times (p<0,05), less pronounced changes in cavernous-3.1 times (p<0,05) and small forms-2.4 times (p < 0,05). Growth DC in the erythrocyte mass is noted in small forms - by 93.8% (p<0,05), in cavernous-by 102.5% (p<0,05), but an even more significant increase ocurs in infiltrative pulmonary TB-by 212.5% (p<0,05) and in disseminated TB-by 405.0% (p The most significant increase in MDA in plasma is observed in disseminated–by 69.2% (p<0,05),the minimum-in small forms-by 38.5% (p<0,05).Significant increase in MDA In red blood cell mass occurs in patients with disseminated 2.7times (p<0,05) and in infiltrative2.4 (p<0,05) times, less pronounced change in the cavernous pulmonary TB-increase by 1.9 times (p<0,05) and the small forms of TB in the lungs-1.4 times (p>0,05) (Picture 3).As the tuberculosis process progresses in the lungs, there is a decrease in the indicators of antioxidant protection (Table3).The decrease in catalase activity in comparison with the group of healthy individuals is most significant in disseminated TB-by 18.1% (p<0,05), to a lesser extent in small forms-by 13.5% (p<0,05), cavernous TB-by 13.1% (p<0,05) and infiltrative TB-by 12.4% (p Reduced glutathione levels decreased by 23.2% in disseminated and 21.6% (p<0,05) in infiltrative lung TB, less pronounced in cavernous lung TB –b17.1%(p<0,05) and minor forms of lung TB-BY14.35%(P<0,05).



Note - * - significant differences in relation to the group of healthy people (**p<0,05), the Kruskal-Wallis test** (Figure 3) -Changes in peroxidation indicators in different clinical forms of pulmonary tuberculosis(1–healthy individuals, 2–small forms,3-infiltrative, 4–disseminated, 5cavernou**Table 3:** Changes in the blood antioxidant system in different clinical forms of pulmonary tuberculosis, Me (25%, 75%) (25%, 75%)

Table 3: Changes in the blood antioxidant system in different clinical forms of pulmonary tuberculosis, Me (25%, 75%) (25%, 75%)

Indicator	Healthy ones	Clinical form of pulmonary tuberculosis			
		small forms	infiltrative	disseminated	cavernous
n	23	49	45	15	11
Catalase, (mmol N_2About$_2$/min / gNv)	28,2 (27,2-29,1)	24,4* (21,7-26,3)	24,7* (22,7-26,6)	23,1* (21,8-23,9)	24,5* (22,8-26,5)
Ceruloplasmin, (mg / l)	237 (218,5-260,5)	301,0* (269,0-332,0)	308,0* (278,0-375)	346,0* (329,0-374,0)	295,0* (282,0-324,0)
Reduced Glutathione, (mmol / gNv)	31,5 (29,4-33,6)	27,0* (24,6-29,2)	24,7* (19,9-28,8)	24,2* (23,1-25,0)	26,1* (25,6-27,0)
alpha-tocopherol, (mmol / l)	24,6 (23,0- 27,3)	8,9* (8,2-10,5)	8,0* (6,5-8,8)	6,3* (4,6-8,1)	8,0* (6,9-8,1)

Note - * - significant differences in relation to the group of healthy people (p<0,05), Kruskal-Wallis test

Marked changes in the concentration of ceruplasmin are observed in disseminated and infiltrative TB – an increase in 1.5 times (p<0,05) and 1.3 times (p<0,05), respectively, compared with the group of healthy individuals, a less significant increase in small forms of TB – by 1.3 times (p<0,05), in cavernous TB – by 1.2 times (p < 0,05). The most significant decrease in the concentration of alpha-tocopherol occurs in disseminated forms – by 74.4% (p<0,05), less pronounced – in small forms of lung TB – by 63.8% (p < 0,05). The development of oxidative stress in this pathology indicates a decrease in the efficiency of oxygen use. When the balance between the antioxidant system and the generation of reactive oxygen species is disturbed, the latter exhibit excessive aggressiveness, which leads to oxidative modification of cellular structures, proteins, carbohydrates, and nucleic acids [25]. Strengthening of free radical reactions is a fast-acting mechanism that underlies the restructuring of energy metabolism at the level of the body and is a trigger that determines the direction of adaptation [1]. Oxygen homeostasis reflects the maintenance of optimal oxygen tension in all cells that carry out oxybiotic processes, which provides physiological conditions for the functioning of oxidative enzymes and forms the energy basis for optimizing the vital processes of the entire organism [15]. The process of adaptation to hypoxia, aimed at maintaining the oxygen homeostasis of the body, is realized through a complex system of intercellular signal interactions, which are consistently involved at different stages [17]. Of great importance are data on the study of the features of blood OC and pro-oxidant-antioxidant balance, depending on the nature of the tuberculosis process, which is understood as a number of indicators that characterize clinical and morphological manifestations (prevalence, presence of destruction, primary detection or repeated treatment, presence or absence of bacterial excretion, MDR-MBT). These indicators have an impact on the course and outcomes of the disease, the effectiveness of therapy. In comparison with the group of healthy individuals with TB, there is a decrease in hemoglobin concentration by 16.0% (p This is more pronounced with a widespread process (by 20.7%, p<0,05) than with a limited one (by 11.0%, p <0,05). In the presence of a decay cavity – destruction in the lung tissue – the hemoglobin concentration decreases by 19.0% (p<0,05), while without it-by 12.8% (p < 0,05).

There is a decrease in OCB in lung TB compared to healthy people by 18.4% (p with a widespread process, this indicator decreases by 25.2% (p<0,05), compared with a limited process, it is lower by 9.4% (p < 0,05). In the presence of destruction in the lung tissue, the decrease in OCB is more pronounced (by 24.3%, p<0,05) than without destruction – by 16.5% (p the decrease in OCB was more pronounced in re – treated patients – by 21.4% (p<0,05) than in newly diagNOsed patients-by 18.0% (p < 0,05). A more pronounced decrease in OCB in the presence of bacterial excretion – by 20.4% (p<0,05) than in patients with MBT minus-by 13.1% (p>0,05), respectively, with MDR of MBT-by 21.4% (p < 0,05), and in its absence-by 17.0% (p<0,05.SO value$_2$ Patients with advanced lung TB were 23.2% (p<0,05) less than in healthy subjects, and those with limited TB were 10.7% (p>0,05) less. According to this criterion, the difference between a common and limited process is significant. In the presence of destruction in the lungs, a decrease in SO occurs2 by 16.1% (p<0,05), and in its absence – by 12.0% (p < 0,05).2 in newly diagnosed patients, it decreases by 14.3% (p<0,05), in re – treated patients-by 14.0% (p < 0,05). SO Changes2 in bacterial excretors (decrease by 15.82%, p<0,05) and, accordingly, in the presence of MDR, MBT (decrease by 16.3%, p<0,05) are more pronounced than in patients with MBT minus (decrease by 5.4%, p>0,05) and in the absence of MDR, MBT (decrease by 13.8%, p<0,05) are more pronounced than in patients with MBT minus (decrease by 5.4%, p>0,05). In the tuberculosis process in the lungs pO_2 it decreases by 5.0% (p>0,05) and is more pronounced with a widespread process – by 8.3% (p<0,05), but there were no significant differences between the widespread and limite process in this indicator. In pulmonary TB, there is an increase in $p50_{real}$ by 7.8% (p>0,05)/ With limited TB, it increases by 4.9% (p>0,05), with widespread TB-by 14.6% (p>0,05)/ In the presence of a decay cavity in the lungs, an increase in $p50_{real}$ it occurs by 13.1% (p<0,05), and in its absence – by 6.0% (p>0,05). There are significant differences in this indicator between patients with and without destruction. With bacterial excretion and MDR MBT, an increase in $p50_{real}$ it is 10.5% (p<0,05) and 9.9% (p With MBT minus and no MDR MBT increase in $p50_{real}$ it is 6.3% (p>0,05) and 7.1% (p> In re-treated patients, an increase in $p50_{real}$ it is Noted by 11.2% (p<0,05), in newly diagnosed patients – by 6.7% (p < 0,05).There is a shift of ODC to the right with a different nature of the tuberculosis process, which contributes to the extraction of oxygen from the blood into the tissue [3]. The most pronounced changes in $p50_{std}$ in comparison with healthy patients, there is an increase of 9.6% (p<0,05) in the widespread tuberculosis process and exceeds the changes in the limited one by 8.8% (p<0,05). increase in $p50_{std}$ when destruction occurs in the lung tissue by 6.6% (p<0,05) and compared with the process without destruction is higher by 6.6% (p < 0,05). In the presence and absence of bacterial excretion, as well as the nature of drug sensitivity, there were no significant differences in this indicator.

Lung TB causes an increase in the activity of LPO processes. There is a significant increase in all the SEX indicators analyzed by us in relation to the group of healthy individuals. The concentration of DC in plasma increases 4.0-fold in pulmonary TB (p<0,05). The greatest increase in this indicator is observed in the extended process – 5.4 times (p<0,05), while in the limited process-3.2 times (p<0,05), the increase in the extended process in relation to the limited process is higher – 1.7 times (p < 0,05). In the process with the presence of bacterial excretion, an increase in DC in plasma was Noted by 4.2 times (p<0,05), while in MBT minus-by 2.9 times (p<0,05), the difference between bacterial excretors and patients with MBT minus is 31.4% (p<0,05)/. The increase in the level of DC in the erythrocyte mass in pulmonary TB is 3.4 times (p<0,05), but with a widespread process – 4.2 times (p<0,05), and with a limited process-2.7 times (p<0,05), the increase in a widespread process is about 1.6 times greater than with a limited process (p<0,05). A more pronounced increase in this parameter was observed at bacteriovision - by 3.9 times (p<0,05), while in the absence of MBT – by 2.5 times (p>0,05). The increase in DC in the erythrocyte mass during bacterial excretion is 1.5 times higher (p<0,05). In pulmonary TB, there is an increase in plasma MDA levels by 98.9% ((p<0,05). A significant increase in MDA in the erythrocyte mass occurs with a widespread tuberculosis process – by 185.7% (p<0,05), while with limited lung TB, this indicator increases by 82.9% (p>0,05).In the presence of destruction, the growth of MDA in the erythrocyte mass is 164.5% (p<0,05), in its absence-96.2% (p<0,05), the increase in destruction in relation to its absence is 34.8% (p A significant increase in MDA in the red blood cell mass occurs in the presence of MBT plus – by 146.9% (p<0,05), while in the presence of MBT minus - by 56.5% (p>0,05), the difference between these indicators is 58.2% (p<0,05), while in the presence of MBT minus - by 56.5% (p<0,05). In the presence of MDR-MBT, this parameter increases by 151.3% (p<0,05), in its absence-by 91.8% (p<0,05), while the increase in MDR-MBT in relation to its absence is 31.0% (p<0,05). As the tuberculosis process progresses in the lungs, there is a change in the indicators of

antioxidant protection. Catalase activity decreased by 14.5% (p<0,05) in comparison with the group of healthy patients with lung TB, while the most pronounced decrease in this antioxidant is observed in the widespread process – by 16.1% (p < 0,05). we noted a decrease in the concentration of reduced glutathione by 21.3% (p<0,05) in the extended process, and by 13.2% in the limited process (p< 0,05). In lung TB, this antioxidant is reduced by 18.7% ((p< 0,05). During the destructive process, its decrease is more significant than without destruction, and amounts to 19.1% (p<0,05) and 18.1% (p< 0,05), respectively. A significant decrease in reduced glutathione is observed in the presence of bacterial excretion and MDR of MBT–by 20.6% (p<0,05) and 21.3% (p<0,05). – by 13.8% (p>0,05) and by13.3% (p> 0,05). The newly identified patients have a more pronounced decrease in the concentration of reduced glutathione – by 19.4% (p<0,05) than in the newly treated patients – by 17.5% (p < 0,05).

The most pronounced change in the concentration of ceruloplasmin in a widespread tuberculosis process-an increase in comparison with the group of healthy individuals by 1.4 times (p<0,05), a less significant increase in a limited process-by 1.3 times (p<0,05), in general, in TB, an increase in the concentration of ceruloplasmin-by 1.3 times (p<0,05). When decomposing in the lung tissue, the level of ceruloplasmin increases by 1.4 times (p<0,05), and in the absence-by 1.3 times (p<0,05); in the presence of MBT and MDR-MBT, the increase in this parameter is 1.3 times(p<0,05) and 1.3 times(p<0,05),respectively,and with MBT minus and no MDR,MBT increased by1.37 times(p<0,05)and 1.38 times(p<0,05).In newly diagnosed patients,the level of ceruloplasmin increased by 1.4 times(p<0,05),in re-treated patients-by 1.3 times(p<0,05).In this pathology, there is a significant decrease in the concentration of alpha-tocopherol in comparison with the group of healthy individuals-by 3.0 times (p<0,05), but the most significant decrease in its concentration is observed in the widespread tuberculosis process – by 3.4 times (p<0,05), less pronounced – in the limited one-by 2.9 times (p<0,05). With a widespread process, the reduction in relation to a limited one is 15.1% (p<0,05). With destruction in the lung tissue, the concentration of α-tocopherol decreases to a greater extent (3.2 times p<0,05) than in its absence (2.9 times p < 0,05). In re-treated patients, a decrease in the concentration of alpha-tocopherol is observed – by 3.1 times (p<0,05), in newly diagnosed patients – by 2.9 times (p < 0,05). In the presence of MBT and MDR of MBT, changes in the concentration of alpha-tocopherol are more pronounced (decrease) – 3.15 times (p<0,05) and 3.19 times (p<0,05), respectively, than in MBT minus and in the absence of MDR of MBT-2.7 times (p<0,05) and 2.8 times (p<0,05). According to the obtained data, in lung TB, ODC is shifted to the right, which is accompanied by a shift in the pro-oxidant-antioxidant balance towards LPO activation and a decrease in the reserve of the antioxidant system. the edox state of cells, in particular, a violation of the balance between GSH and GSSG, can regulate the rate of no intake from extracellular S-nitrosothiols, which affects the functional state of the L-arginine-NO system and, subsequently, the implementation of blood OC [6]. Increased generation of free radicals and damage to the main mechanisms of antioxidant protection are defined as oxidative stress [13]. Changes in blood OC and the activity of free radical oxidation processes depend on the nature of this pathology. Na more significant increase $p50_{real}$ it is observed in the presence of a widespread tuberculosis process (by 13.1%, p<0,05), in the presence of destruction in the lung tissue (by 14.6%, p<0,05), in the presence of bacterial excretion (by 9.3%, p<0,05) and MDR-MBT (by 9.33%, p<0,05. This is accompanied by a more pronounced activation of LPO and a decrease in the reserve of antioxidant protection. NO plays an important role in the pathogenesis of TB and in the regulation of blood OC. During the inflammatory process, an expression of the inducible isoform of NO synthase is observed in the body, which leads to an increase in the NO concentration as a manifestation of non-specific resistance of the body [28].

In the case of pulmonary TB (in comparison with the group of healthy individuals), an increase in the concentration of nitrate/nitrites was found by 32.7% (p<0,05), but in the case of widespread tuberculosis inflammation, this parameter increased by 44.0% (p<0,05), and in the case of limited inflammation – by 28.7% (p < 0,05), the ratio of the process to the limited one is 11.9% p<0,05. When analyzing changes in the nitrate/nitrite concentration depending on other characteristics of the tuberculosis process, an increase in this parameter was found in comparison with the group of healthy individuals, but when comparing this parameter within the analyzed signs, no differences were found. Evaluating the literature data and indicators obtained in the course of our study, it should be noted that the level of nitrate/nitrite in lung TB depends on the biological material (plasma, leukocyte mass, alveolar macrophages, etc.) in which this parameter is determined, on the immunological characteristics of the macro organism, virulence and pathogenicity of the microorganism [33]. M. E. Dyakova and co-authors indicate that the NO concentration correlates with classical markers of systemic inflammatory response [18], R. Yu. Abdulaev et al. note that changes in the plasma NO level in TB patients characterize the course of a specific process [24]. The imbalance that occurs in the metabolic links that are very important for the Normal functioning of the body undoubtedly has an adverse effect on the course of the tuberculosis process, the effectiveness of therapy, and requires correction. The identified features justify the appointment medicines that enhance the body's antioxidant potential and improve oxygen utilization.

Due to the lack of dynamics of destructive changes in the lungs on the background of standard CT, the treatment was supplemented with AP. 26 patients with various forms of destructive pulmonary TB were examined. The study group of patients was dominated by males (73.1%), young and able-bodied people. Among the clinical forms, infiltrative pulmonary TB prevails (57.7%), MDR-MBT is observed in 73.1% of cases, and there is a high proportion of TB risk factors. The duration of CT before the use of AP was: up to 3 months-8 patients (30.8%); up to 6 months-18 (69.2%). In the course of complex therapy, a decrease in the severity of inflammatory processes was noted, and clinical improvement was observed. Application AP in terms of up to 6 months allowed to achieve abacillation in 92.3% (24 people) of cases and closure of decay cavities – in 88.5% (23 people). Under the conditions of AP application, an increase in hemoglobin concentration by 5.8% (p<0,05) is noted , more pronounced in infiltrative TB – by 5.9% (p < 0,05). At the same time growth is observed kek. Its growth is 4.7% (p<0,05), a more pronounced increase in this indicator is observed in infiltrative TB – by 15.9% (p < 0,05). SO $value_2$ at the same time, it increases by 12.5% (p<0,05), with cavernous TB – by 20.4% (p<0,05), with infiltrative TB-by 6.3% (p<0,05).There is an increase in pO_2 with AP by 15.2% (p<0,05), and if with cavernous pulmonary TB – by 2.0% (p>0,05), then with infiltrative TB-by 26.1% (p<0,05), and if with cavernous pulmonary TB-by 2.0% (p> 0,05). Indicators of the acid-base state of the blood under these conditions did not significantly change and remained within the Normal range. When using this method in the treatment of destructive forms of lung TB, a decrease in p50rea was detected by 7.7% (p<0,05). oxyhemoglobin to the left. Reducing $p50_{std}$ is 6.2% (p<0,05). There were no significant differences in the shift of this parameter between the studied forms of lung TB on the background of AP. And it is known that NO in the lungs at physiological concentrations inhibits cyclooxygenase, inhibiting the release of thromboxane A2, and when the inducible isophome of NO synthase is stimulated, NO overproduction occurs, exerting a proinflammatory effect [22]. In our study, the use of AP is accompanied by a decrease in the NO concentration by 36.8%. The observed change in the activity of the L-arginine-NO system may affect the SGC. It is assumed that the NO gas transmitter is involved in the formation of the functional properties of hemoglobin by modifying its affinity for oxygen through systemic and regional, intra-erythrocyte regulatory mechanisms, which is important in the pathogenesis of hypoxic states, oxidative stress of the body, and especially for their correction [5]. NO is involved in the regulation of oxygen-binding properties of blood in the vascular compartment, as a result of interaction with hemoglobin, its various forms are formed, which play the role of a kind of allosteric regulator of the functional activity of this protein at the level of its individual tetramers, which may be important for the formation of functional properties of hemoglobin and the formation of O flow2 in the tissue and maintaining the pro-oxidant-antioxidant balance in the body [12]. Against the background of complex therapy with the use of AP, there is a decrease in all the indicators of the activity of LPO processes analyzed by us. The DC concentration in plasma decreases by 34.0% (p<0,05). A more significant decrease in this parameter is observed in infiltrative pulmonary TB – by 44.26% (p<0,05), while in cavernous TB – by 33.3% (p < 0,05). A decrease in the level of DC in the erythrocyte mass is Noted by 39.7% (p<0,05), with cavernous, this indicator decreases by 42.2% (p< 0,05). there is also a decrease in the level of MDA in plasma by 38.8%(p<0,05), in the erythrocyte mass – by 22.1% (p<0,05). in the course of complex treatment with the use of AP, the degree of antioxidant protection improves. Catalase activity increases by 27.4% (p<0,05) in comparison with the initial data: in infiltrative – by 17.9% (p<0,05), in cavernous – by 28.9% (p< 0,05). An increase in the level of reduced glutathione on the background of AP is observed by 17.4% (p<0,05), but it is more pronounced in cavernous pulmonary TB – by 18.2% (p< 0,05). When using AP, there is a decrease in the concentration of ceruloplasmin by 25.4% (p<0,05) compared to the initial data, with cavernous-by 16.8% (p<0,05), with infiltrative Lung TB – by 22.3% (p<0,05).

Nagainst the background of complex treatment, an increase in the concentration of α-tocopherol by 2.1 times was found (p<0,05). The level of this antioxidant increases to a greater extent against the background of AP with infiltrative (2.2 times, (p<0,05). Changes in pro-oxidant-antioxidant balance and concentration parameters NO in the blood of the studied contingent indicates a decrease in the severity of oxidative stress. In AP, the lung collapses and, as a consequence, the volume of the pulmonary field decreases, which reduces the vital capacity of the lungs, while the function of external respiration is disrupted [29]. According to literature data, AP leads to a decrease in ventilation by 10-15% and oxygen consumption by 5-14% from the initial function of the collapsed lung [4]. The use of collapse-forming techniques in the treatment of destructive forms of lung TB requires studying the functional aspects of these

methods [30]. Use of antihypertensive pneumothorax in a shortened procedure (for 4-6 months) minimizes the likelihood of developing a rigid lung, which was observed with prolonged (3-5 years) use of AP [4]. Revealed stimulating effect ep regional blood flow, which is increased in the affected area [23]. Improvement of microcirculation, increased arterialization of blood, occurring due to the shift of ODC to the left, it reduces the activity of peroxidation processes, increases the potential of antioxidant protection. The shift of ODC to the left can be regarded as an attempt by the body to compensate for oxygen deficiency in conditions where the function of external respiration is impaired, and this can also have a favorable value due to the antioxidant effect in conditions of impaired oxygen utilization by tissues.

Conclusions

1. Detected content in different clinical forms of pulmonary tuberculosis, changes in the indicators of oxygen transport function, the activity of free radical processes, and a decrease in blood antioxidant protection are significant significance in the pathogenesis of this disease. The most significant decrease in the affinity of hemoglobin for oxygen, namely, an increase in $p50_{real}$, it is observed with a widespread tuberculosis process (by 14.6%, $p<0,05$), in the presence of destruction in the lung tissue (by 13.1%, $p<0,05$), in the presence of bacterial excretion (by 10.5%, $p<0,05$) and MDR of M. tuberculosis (by 9.9%, ($p<0,05$). Pulmonary tuberculosis is characterized by the development of oxidative stress, the degree of which increases depending on the prevalence of the tuberculosis process and the severity of the patient's condition. In this pathology, an increase in the concentration of nitrate/nitrites in plasma was detected-by 32.7% ($p<0,05$), with widespread tuberculosis inflammation, an increase in this parameter is observed by 44% ($p<0,05$), and with limited-by 28.7% ($p<0,05$).

2. In the complex treatment of destructive forms of pulmonary tuberculosis with the proposed use of collapse therapy, a decrease in $p50_{real}$ by 7.7% ($p<0,05$). NO – by 36.8% ($p<0,05$), as well as a decrease in the activity of peroxidation processes: diene conjugates in plasma – by 34.0% ($p<0,05$), in erythrocyte mass – by 39.7% ($p<0,05$), malondialdehyde in plasma - by 38.8% ($p<0,05$), in erythrocyte mass-by 22.1% ($p<0,05$). When using this method, the degree of antioxidant protection improves: catalase activity increases by 27.4% ($p<0,05$),α-tocopherol - by 119.2% ($p<0,05$), the level of reduced glutathione - by 17.4% ($p<0,05$) and the concentration of ceruloplasmin decreases by 25.4% (p ($p<0,05$).

3. The positive effect of therapy of this pathology with the use of pneumothorax is realized through the correction of pathogenetically significant oxygen-dependent mechanisms, namely, through the contribution of the oxygen transport function of the blood and the gas transmitter NO reducing the pro-oxidant-antioxidant imbalance.

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