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Research Article

Analysis of the Activity of Oxygen-Dependent Processes in Rifamycin-Resistant Pulmonary Tuberculosis

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Abstract

Rifampicin-resistant tuberculosis (RR-TB) is a pressing public health problem in the World Health Organization (WHO) European Region. The region has achieved the highest rates of decline in tuberculosis (TB) incidence and mortality worldwide, but remains the world's highest level of RR-TB [1].

To evaluate the characteristics of oxygen-dependent processes (blood oxygen saturation, prooxidant-antioxidant balance, and L-arginine NO system activity) in pulmonary TB, three groups were formed: a study group of 78 patients with RR-TB, a comparison group of 42 individuals with drug-sensitive tuberculosis (DTB), and a control group of 23 apparently healthy individuals aged 20–30 years. A randomized, controlled, prospective study was conducted. A total of 120 patients with various clinical forms of pulmonary TB were examined. In all patients, the diagnosis of TB was confirmed by various laboratory methods.

In RR-TB, the increase in p50real is 10.5% ($p < 0.05$) and 9.9% ($p < 0.05$), respectively, in DS-TB.

A shift in the oxyhemoglobin dissociation curve (ODC) to the right is observed with different nature of the tuberculosis process, which promotes the extraction of oxygen from the blood into the tissue.

Pulmonary TB is associated with increased lipid peroxidation (LPO) activity. A significant increase in all LPO parameters analyzed was observed compared to healthy controls.

As the tuberculosis process progresses in the lungs, antioxidant protection indicators change.

Patients with pulmonary TB experience a rightward shift the oxyhemoglobin dissociation curve, which improves tissue oxygenation. The most significant change in hemoglobin affinity (HBV), namely an increase in p50real, is observed in RR-TB, which is accompanied by more pronounced activation of lipid peroxidation processes and a decrease in antioxidant defense capacity.

The nature of changes in the blood hemoglobin affinity and prooxidant-antioxidant balance in pulmonary TB is influenced by the activity of the L -arginine- NO system.

Keywords: tuberculosis; rifampicin-resistant tuberculosis; oxygen transport function of blood; prooxidant-antioxidant balance

Introduction

Rifampicin-resistant tuberculosis (RR-TB) is a case of TB with confirmed presence of Mycobacteria tuberculosis and established drug resistance of clinical isolates using phenotypic or genotypic methods, including the following patterns of resistance to rivompicin (R): monoresistance to R, polyresistance to R, multidrug resistance, extensive drug resistance [3].

Rifampicin-resistant tuberculosis (RR-TB) is a pressing public health problem in the European Region of the World Health Organization (WHO). The region has achieved the highest rates of decline in tuberculosis (TB) incidence and mortality worldwide, but remains the world's highest level of RR-TB [15].

The WHO European Region has developed the TB Action Plan for 2023–2030, which sets targets to be achieved by 2025 (compared to 2015 levels): a 75% reduction in TB mortality, a 50% reduction in TB incidence, and an increase in the treatment success rate in the cohort of patients with MDR/RR-TB to 80% [15].

RU-TB of the lungs is a severe pathology characterized by clinical activity of the disease, frequent progression, a tendency to reactivation, and a high frequency of bacterial excretion [9].

TB is interleukin-dependent Immunodeficiency infectious diseases that are accompanied by an inflammatory reaction with severe endogenous intoxication. Massive formation and subsequent resorption of tissue breakdown products of bronchopulmonary tissue during the formation of cavities, cytotoxic hypoxia, disruption of intracellular homeostasis, immunocytokine and hormonal imbalance are the main factors in the formation of endogenous intoxication in TB [2].

In TB, in parallel with structural changes, shifts occur in the functional status of the cellular elements of the vascular walls (especially endothelial cells), which have the ability to synthesize and secrete their own complex of biologically active compounds. These compounds have a decisive influence on the tone and permeability of blood vessels, rheological properties of blood, and processes [9].

Transport of respiratory gases by the respiratory and circulatory systems is one of the fundamental processes that ensures the body's vital functions. Significant or prolonged deviations from normal oxygen and carbon dioxide levels in the blood can lead to significant pathological changes, including hypoxia and ischemic events, changes in the blood's acid-base balance (acidosis or alkalosis), and others [4].

Oxygen transport and utilization processes are closely linked to mechanisms maintaining prooxidant-antioxidant balance. It is necessary to consider the functional oxygen transport system not only in terms of meeting tissue oxygen needs but also as a possible mechanism for physiological antioxidant protection [16, 17].

The blood oxygen carrying (BOC) should be considered in terms of the functional relationships between the oxygen transport system and the L-arginine-NO system. The oxygen-binding properties of blood influence the state of the L-arginine-NO system, but it can also determine the hemoglobin affinity for oxygen (HOA) through intraerythrocyte regulatory mechanisms, the oxygen-dependent nature of NO formation, the regulation of vascular tone, and the action of peroxynitrite [5, 17].

An analysis of literary data shows that the issues of respiratory dysfunction in TB have been covered in sufficient detail, but the problems of the blood oxygen carrying in TB have not been studied.

Material and methods

To evaluate the characteristics of oxygen-dependent processes (blood oxygen carrying , prooxidant-antioxidant balance, and L-arginine NO system activity) in pulmonary TB, three groups were formed: the main group consisted of 78 patients with RR-TB, the comparison group consisted of 42 people with drug-sensitive tuberculosis e tuberculosis (DS-TB), and the control group consisted of 23 practically healthy individuals aged 20–30 years. A randomized, controlled prospective study was conducted. A total of 120 patients with various clinical forms of pulmonary TB were examined. In all patients, the diagnosis of TB was confirmed by radiography and various laboratory methods.

In the RR-TB group, males predominated (84.6%), and young working-age individuals (under 40 years) accounted for 64.2%. Infiltrative pulmonary TB was observed in 72.8% of cases; 43 patients (55.1%) had disseminated tuberculosis (involving more than two segments); and 60.3% of cases had lung tissue destruction.

In the group of patients with DS-TB, 66.7% were male, and 52.4% were aged 30-39 years. In most cases, these were newly diagnosed patients (73.8%) with a limited tuberculosis process (66.7%) and a minor percentage of lung tissue destruction (16.7%).

During the first 10 days after the patient's admission to the hospital, 10 ml of blood was collected from the cubital vein with restored blood flow using a pre-cooled and heparinized syringe. Anaerobic conditions were maintained to prevent the blood from coming into contact with air. The blood oxygen carrying was then assessed. A portion of the blood was separated by centrifugation into plasma and red blood cell mass, which were stored at -20 °C, followed by measurement of prooxidant-antioxidant status.

The blood oxygen carrying was assessed using the Synthesis-15 microgas analyzer from Instrumentation. Laboratory» (USA) with determination of the following parameters: pO2, pCO2, pH, blood oxygen saturation (SO2), blood oxygen capacity (BOC) at a temperature of 37ºC. Hemoglobin affinity for oxygen was estimated by the p50 index (pO2, corresponding to 50% saturation of hemoglobin with oxygen), determined spectrophotometrically at a temperature of 37ºC, pH = 7.4 pCO2 = 40 mm Hg (p50standard) [13]. Then p50 was calculated at real values of pH, pCO2 and temperature (p50real) using the formulas of JW Severinghaus [8]. Based on the obtained data, the position of the oxyhemoglobin dissociation curve (ODC) was determined using the Hill equation.

The content of diene conjugates (DC) was determined by the intensity of UL absorption, characteristic of conjugated diene structures of lipid hydroperoxides, in the region of 232–234 nm using a Solar PV1251C spectrophotometer. The level of malonic dialdehyde (MDA) was assessed spectrophotometrically by the intensity of the pink complex formed in the reaction with 2'-thiobarbituric acid on a Solar PV1251C at a wavelength of 535 nm [16]. Catalase activity was recorded by the amount of colored product in the reaction of H2O2 with ammonium molybdate which has a maximum light absorption at a wavelength of 410 nm, on a Solar PV1251C spectrophotometer [10]. The content of reduced Glutathione levels were studied using a modified method of J. Sedlak and R. Lindsay [7]. Ceruloplasmin levels were determined using the Ravin method [6]. The concentration of α-tocopherol and retinol in plasma was estimated using the ST Taylor method [11, 12].

NO production was assessed by the total nitrate/nitrite content (NO3-/NO2-) in blood plasma using a spectrophotometric method based on a color reaction using the Griess reagent at a wavelength of 540 nm [17].

Statistical processing of the obtained results was carried out using the Statistica data processing package for Windows, version 10.0 and the Excel office application. To determine whether the obtained values correspond to the normal distribution law, the Kolmogorov-Smirnov and Shapiro-Wilk tests were used. For a normal distribution of values, the arithmetic mean (M) and standard deviation (δ) were calculated. To compare quantitative indicators that obey the normal distribution, Student's t-test was used. In case of non-compliance with the normal distribution, the median (Me) and 25–75% quartiles were calculated. To analyze the significance of differences in quantitative characteristics of two related populations, the Wilcoxon test was used. To evaluate the differences simultaneously between three or more samples, the Kruskal - Walli's test was used.

Hypotheses regarding the presence or absence of relationships between qualitative characteristics in groups were tested using Fisher's exact test, $\chi 2$, at low frequencies with Yates' correction. Differences were considered statistically significant at $p < 0.05$.

Results

Compared to the group of healthy individuals, patients with RR-TB showed a decrease in hemoglobin concentration by 17.9 ($p < 0.05$), in general, in patients with TB there was a decrease in this parameter by 15.6%, and in the group with DS-TB - by 12.4%. A decrease in oxygen capacity of blood in pulmonary TB in relation to healthy people by

21.43% (p <0.05) was observed, respectively, in RR TB - by 22.86% (p <0.05), and in DS-TB - by 19.05% (p <0.05).

Changes in SO2 in the presence of RR-TB (a decrease of 16.3%, p <0.05) are more pronounced than in patients with DS-TB (a decrease of 13.8%, p >0.05).

In the case of a tuberculous process in the lungs, pO2 decreases by 5.0%

(p >0.05), and in the case of RR TB by 8.4% (p >0.05).

In RR-TB, the increase in p50real is 10.5% (p < 0.05) and 9.9% (p < 0.05), respectively, in DS-TB.

A rightward shift in oxyhemoglobin dissociation curve is observed with different types of tuberculosis, which promotes oxygen extraction from the blood into tissue. Changes in p50std compared to healthy individuals with RR-TB are insignificant, with an increase of 3.3% (p > 0.05).

Pulmonary TB is associated with increased activity of lipid peroxidation processes. A significant increase in all analyzed lipid peroxidation parameters was observed compared to the healthy control group. Plasma DC concentrations increased 4.0-fold in pulmonary TB. In RR-TB, plasma DC increased 4.2-fold (p < 0.05), while in DS-TB, it increased 3.6-fold (p < 0.05). The difference between RR-TB and DS-TB patients was 14.3% (p > 0.05).

The increase in the level of DC in the erythrocyte mass in pulmonary TB is 3.4 times (p <0.05). In the presence of RR-TB, an increase in this parameter is observed by 151.3% (p <0.05), in DS-TB - by 91.8% (p <0.05).

In pulmonary TB, an increase in the MDA level in plasma by 46.15% is observed (p <0.05). In the presence of RR-TB, an increase in this parameter by 122.73% (p <0.05) is observed, and in the presence of DS-TB, by 74.24% (p <0.05), while the increase in RU TB in relation to DS TB is 27.83% (p <0.05). antioxidant defense parameters change. The decrease in catalase activity compared to the healthy control group with pulmonary TB was 14.5% (p < 0.05). No differences in changes in catalase activity were found between RR-TB and DS-TB.

In pulmonary TB, a decrease in the concentration of reduced glutathione by 18.7% (p < 0.05) is observed. A significant decrease in reduced glutathione is observed in RR-TB by 21.3% (p < 0.05), and to a lesser extent in DS-TB - 13.3% (p < 0.05).

An increase in the concentration of ceruloplasmin in RR-TB is observed - 1.3 times (p <0.05), and 1.38 times (p <0.05).

In this pathology, there is a significant decrease in the concentration of α-tocopherol compared to the group of healthy individuals - by 3.0 times (p < 0.05), but the most significant decrease in its concentration is observed in RR-TB - by 3.2 times (p < 0.05), changes in DS-TB - a decrease of 2.8 times (p < 0.05).

According to the data obtained, in pulmonary TB, a shift in the oxyhemoglobin dissociation curve to the right is observed, which is accompanied by a shift in the prooxidant-antioxidant balance toward lipid peroxidation activation and a decrease in the antioxidant system reserve. The redox state of cells, in particular the imbalance between GSH and GSSG, can regulate the rate of NO influx from extracellular S-nitrosothiols, which affects the functional state of the L-arginine-NO system and subsequently the implementation of BOC [14]. NO plays an important role in the pathogenesis of TB and in the regulation of blood BOC. During the inflammatory process, the expression of inducible isoforms NO synthase, which leads to an increase in NO concentration as a manifestation of non-specific resistance of the body [1, 17].

In this study, in pulmonary TB (compared to a group of healthy individuals), an increase in the concentration of nitrates/nitrites by 32.7% (p <0.05) was found. When analyzing changes in nitrate/nitrite concentrations depending on the type of drug resistance, no differences were found.

Thus, under the conditions of the tuberculosis process, the nature of the change in the blood hemoglobin affinity, on the one hand, is important for tissue oxygenation, the formation of an optimal oxygen flow, and on the other hand, for the creation of a certain prooxidant - antioxidant balance in the body.

Conclusions

Patients with pulmonary TB show a rightward shift in oxyhemoglobin dissociation curve, aimed at improving tissue oxygenation. The most significant change in blood hemoglobin affinity, namely an increase in p50real, is observed in RR-TB, which is accompanied by more pronounced activation of lipid peroxidation processes and a decrease in antioxidant defense capacity.

The nature of changes in the blood hemoglobin affinity and prooxidant-antioxidant balance in pulmonary TB is influenced by the activity of the L -arginine- NO system.

The imbalance that occurs in metabolic pathways crucial for normal functioning undoubtedly has an adverse effect on the course of tuberculosis and the effectiveness of therapy and requires correction. The identified characteristics justify the use of antioxidant therapy and medications that improve tissue oxygenation. Changes in nitrate/nitrite levels in the blood plasma of patients with pulmonary TB are important for the formation of blood BOC and the activity of free radical processes in the studied forms of TB, which must also be taken into account when conducting pathogenetic therapy.

References

1. Chinta KC. (2016). Emerging role of fasotransmitters in the pathogenesis of tuberculosis. Ntric oxide, 59:28-41.
2. Dynamics of indicators of endogenous intoxication in multiresistant pulmonary tuberculosis with destructive changes / LD Todoriko [et al.] // Actual Infectology, 2014:4:54-58.
3. Eliseev PI, Bayrakova AL, Ganjalyan TA, Zorina VV, Balantsev GA, Maryandyshev A.O. (2025). Monitoring of Mutations Associated with Drug Resistance of Mycobacterium tuberculosis // Tuberculosis and Lung Diseases, 103 (1):45-53.
4. Nasyrdzhanova, Kh. R. (2017). Active forms of oxygen and their role in lung diseases / Kh. R. Nasyrdzhanova , A. M. Saburova, Kh. Y. Sharipova // Health, Demography, and Ecology of the Finno-Ugric Peoples, 3:49-52.
5. Oxygen tension, H2S, and NO bioavailability: is there an interaction? / G. K Kolluru[et al.] // J. Appl. Physiol, 2016: 2:120:263-270.
6. Ragino Yu.I. (2005). Application of new biochemical methods for evaluating the oxidation-antioxidant potential of low-density lipoprotein. Klin. lab. diagnosis, 4:11-15.
7. Sedlak J., Lindsay RN. (1968). Estimation of total, protein-bound, and protein sulfhydryl groups in combination with Ellman's reagent. Anal. Biochem, 25:1:192-205.
8. Severinghaus. (1966). JW Blood gas calculator. Journal of Applied Physiology, 21:5:1108-1116.
9. Signs of diffuse alveolar damage with high rates of systemic inflammatory response syndrome in patients with drug-resistant pulmonary tuberculosis / LN Lepekha [et al.] // Tuberc . and social. significant diseases, 2013:2:20-24.

10. Aruoma OI, Cuppett, SL. (1997). Antioxidant Methodology: in vivo and in vitro Concepts. New York, AOCSPress, 256.
11. Taylor SL, Lamden MP, Tappel AL. (1976). Sensitive fluorometric method for tissue tocopherol analysis. Lipids, 11:7:530-538.
12. Tregubova IA, Kosolapov VA, Spasov AA. (2012). Antioxidants: current status and prospects. Uspekhi fiziol . nauk, 43 (1):75-94.
13. Wagner PD, Wagner HE, Groves BM et al. (2007). Hemoglobin P50 during a simulated ascent of Mt. Everest, Operation Everest II. High. Alt. Med. Biol, 8: 1:32-42.
14. Wang, R. (2015). The role of H2S bioavailability in endothelial dysfunction.Trends. Pharmacol . Sci, 36:9: 568-578.
15. World Health Organization. Regional Office for Europe. Tuberculosis Action Plan for the WHO European Region 2023-2030.
16. Zinchuk, VV. (2016). Contribution of oxygen-binding properties of blood and gas transmitters to the development of oxygen deficiency conditions / VV Zinchuk // Ulyanovsk Medical and Biological Journal, 4:34-35.
17. Zinchuk, VV. (2016). NO-dependent mechanisms of intraerythrocytic regulation of hemoglobin affinity to oxygen: monograph / VV Zinchuk, TL Stepuro – Grodno: GrSMU, 176.

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