Biochemical Value Dynamics in Patients with Multidrug-Resistant Tuberculosis/HIV with CD4+ Lymphocyte Cells below 50 Cells/μCL and its Variability in the Application of Adjuvant Immunoglobulin Therapy

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Abstract

Context: Treatment of the patients with multidrug-resistant tuberculosis (MDR-TB)/HIV coinfection in a state of severely suppressed immune system remains under efficient. **Aims:** The aim of this study was to assess the effectiveness of adjuvant immunoglobulin therapy in TB/HIV patients. **Settings and Design:** The relationship between biochemical indexes in the patients with MDR-TB/HIV co-infection and adjuvant immunoglobulin therapy. **Materials and Methods:** The study involved 52 HIV-positive patients with MDR-TB and CD4+ lymphocyte cells below 50 cells/μCL. Patients in control group (Group 1) and in basic group (Group 2) received standard treatment with second-line antituberculosis agents and antiretroviral agents. In addition patients in basic group were treated by immunoglobulin G intravenously. The evaluation of biochemical parameters such as bilirubin level, thymol test, the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyltransferase (GGT) was carried out on automatic analyzer HumaStar 300 at the beginning and after 0.5–8 months of treatment. Statistical analysis was performed using the Statistica 10.0 software (Stat. Soft Inc., USA). Kruskal–Wallis, ANOVA, and Chi-square tests were used in this study. **Results:** After 8 months of treatment, studied biochemical indexes were lower in Group 2 than in patients from Group 1. For example, the number of patients in Group 2 with increased bilirubin level was 1.7 times more than in Group 1 ($P < 0.05$), with increased ALT, AST, or GGT activity in 2.5 times ($P < 0.01$), 2.7 times ($P < 0.01$), or 2.4 times ($P < 0.05$) correspondingly, comparatively with Group 1. **Conclusion:** The usage of immunoglobulins intravenously in the group of patients with MDR-TB associated with HIV infection, with CD4+ level <50 cells/μCL, is appropriate and essential because it improves treatment outcome.

Keywords: Biochemical indexes, drug resistance, HIV, tuberculosis

INTRODUCTION

Tuberculosis (TB) with multidrug resistance (MDR) remains a crucial issue in public health. According to the World Health Organization global report on tuberculosis for 2018, Ukraine is classified as a country where the number of MDR-TB patients is one of the highest in the world.[1] According to received data in Ukraine, one can see further increasing of spreading of Beijing family strains that are characterized by unfavorable course of TB and high drug resistance.[2,3] Today, TB remains the leading cause of death among HIV-positive people.[1]

The TB course against the background of progressive immunodeficiency often becomes aggressive with the accompanied generalization of infection.[4,5] This, in turn, leads to the development of a septic state assessed as a dynamic process initiated by bacterial antigens (*Mycobacterium*

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tuberculosis and activation of opportunistic pathogenic microflora), fungal infection, viral attack (HIV and opportunistic virus infections), and lowering of T-cell immune function and consists of the interaction of many pro- and anti-inflammatory mediators modulating the state of the endothelial tissues.[6-8] The general reaction to inflammation leads to the disturbance of microcirculation and creates the basis for the formation of Systemic Inflammatory Response Syndrome (SIRS) and later to multiple organ failure.[9,10]

According to modern concepts, the massive tuberculosis infection in combination with "compromised" immune system in HIV-positive patients leads to the (SIRS) that occurs as the immune system response, which exceeds biological expediency, being excessive in strength and modality, to generalized infection.[11,12]

In addition to SIRS the immune distress syndrome also includes a mixed antagonist response syndrome and compensatory anti-inflammatory response syndrome, which causes multiple organ dysfunction syndrome.[13,14] Therefore, during the study of biochemical homeostasis in patients with MDR-TB/HIV, there is an increase of liver and kidney function tests, which leads to the basis formation for the development of adverse drug response to the second-line antituberculosis agents and threatens the possibility of early administration of antiretroviral (ARV) treatment directly affecting the survival of patients with combined pathology of MDR-TB/HIV.[15-17] As a result, the impact of both infections on biochemical disorders in MDR-TB/HIV patients requires further study and coverage.[18]

The above-mentioned data indicate an urgent need to involve an adjuvant immunotropic therapy to the treatment complex as a mean of pathogenetic influence on the homeostasis of the patients' organism exhausted with comorbidity of MDR-TB/HIV in a state of severely suppressed immune system.

The aim of the research includes the study of biochemical indexes' changes in the patients with MDR-TB/HIV coinfection at the level of CD4+ lymphocytes below 50 cells/µCL and the effectiveness evaluation of immunoglobulin therapy.

MATERIALS AND METHODS

The study involved 52 patients aged 20–55 years; the average age was 37.2 ± 7.8 years. All patients were HIV-positive with laboratory-confirmed (cultural method or Gene Xpert method) MDR-TB with different types of *M. tuberculosis* resistance to first- and second-line agents (isoniazid- and rifampicin-resistant obligatory). Patients with MDR-TB/HIV were divided as follows:
- Group 1 (control) – 26 MDR-TB/HIV patients with CD4+ lymphocytes below 50 cells/µCL, who received standard treatment with second-line antituberculosis agents and ARV
- Group 2 (basic) – 26 patients with MDR-TB/HIV with CD4+ cells below 50 cells/µCL, who also received the standard treatment by antituberculosis second-line agents with ARV treatment with the addition of intravenous

immunoglobulin G (IgG) (solution 5% intravenous drip injection of 50 ml, Biopharma, Ukraine), which is a highly purified multivalent human immunoglobulin that matches to the fractional distribution of the IgG subclasses in the human blood. It has a wide range of opsonizing and neutralizing antibodies against bacteria, viruses, and other pathogens. Today, the medical agent as IgG is recommended for the treatment of primary and acquired immunodeficiency during various viral diseases.[19]

IgG was prescribed according to the following scheme: on the 1st day before the beginning of anti-tuberculosis treatment (ATT) IgG was administered at the rate of 4 ml/kg intravenously; on the 2nd day, the second-line antituberculosis agents were added, according to *M. tuberculosis* susceptibility; and finally, after 2 weeks, the ARV treatment was added. The following IgG injections were performed every 4 weeks for 3 months, followed by the 5th and 8th months of the intensive MDR-TB/HIV treatment phase.

Inclusion criteria
- Patients' consent to participate in the study
- Firstly diagnosed with MDR-TB in the background of HIV infection
- Age of patients from 20 to 55 years
- Patients with MDR-TB/HIV who have not previously been treated with antituberculosis second-line agents and ARV.

Exclusion criteria
- Patients' refusal
- Recurrent cases of MDR-TB with HIV infection
- Patients previously treated with second-line agents
- Patients who interrupted treatment and were transferred to palliative treatment
- Patients who were in the terminal phase of MDR-TB and HIV infection
- The presence of acute renal or hepatic failure
- Mental disorders.

Biochemical studies were conducted at the clinical diagnostic laboratory of the third-level accreditation of the Odessa Regional TB Hospital. The evaluation of biochemical parameters such as bilirubin level, thymol tests, the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), creatinine, and urea levels was carried out on the automatic analyzer HumaStar 300 ("Human GmbH," Germany). For the accuracy studies, the daily quality control Serodos was preformed, as well as the monthly international control Prevecal. Annual verification of the measuring device was held in the state organization "Odessa Regional Center for Standardization, Metrology, and Certification."

Statistical analysis was performed using the Statistica 10.0 software (Dell Software, Austin, TX, USA). It was determined whether there is a significant difference concerning frequency of studied criteria between the two studied groups. Quantitative indicators in the text and tables are presented in the form

M ± m (M – arithmetic average and m – standard deviation); quality indicators are presented in the form Q ± m_q (Q is the frequency of occurrence of the trait and m_q is the standard deviation). Statistical significance was assumed at the $P < 0.05$.

Ethical issued and date of approval for project

The project was approved by the Ethics Committee of Odessa National Medical University, Ukraine (protocol N84, June 16, 2015). It was conducted according to the Declaration of Helsinki standards.

All of the patients gave written informed consent and explicitly provided permission for treatment and blood analyses, as well as for the collection of relevant clinical data.

RESULTS

For more patients' informational value of the first and second groups, they were divided into two subgroups – with a normal level and an increased level of the studied biochemical index. The initial level of biochemical indexes in MDR-TB/HIV patients with CD4+ lymphocytes below 50 cells/μCL was increased in most cases, even before the beginning of highly toxic antituberculosis and ARV treatment, namely hyperbilirubinemia was registered in patients of both the groups – in 22 patients of Group 1 (84.6%) and 21 of Group 2 (80.8%). The average level of total bilirubin was 25.9 ± 4.8 μmol/l and 28.3 ± 3.9 μmol/l in Groups 1 and 2, respectively [Table 1 and Figure 1].

The increase in thymol tests was recorded in 100% of patients in both the groups, with an average of 9.1 ± 2.5 units (U) (Group 1) and 12.1 ± 2.3 U (Group 2) [Figure 1 and Table 2]. The ALT activity was increased in almost half of patients in both the groups – in 12 cases (46.2%) of Group 1 and in 13 (50%) of Group 2, with a level of 40.8 ± 4.9 U/l and 42.4 ± 6 U/l, respectively, to groups [Figure 2 and Table 1]. The activity of the AST enzyme was high in the majority of patients (21 and 20 cases of the control and basic groups), averaged 43.9 ± 6.5 and 43.2 ± 6.7 U/l, respectively, indicating the presence of toxic syndrome [Table 1].[20] The activity of GGT enzyme was higher than normal in almost all patients of both the groups (92.3% and 96.2% of Groups 1 and 2), and the average level reached 69.3 ± 14.6 U/l and 71.2 ± 13.6 U/l, respectively [Table 1].

The average creatinine level reached 123.0 ± 11.7 μmol/l in Group 1 and 129.8 ± 9.7 μmol/l in Group 2; in addition, it was increased in 20 patients in Group 1 and in 21 patients in Group 2 [Figure 3 and Table 2]. The urea serum level was higher than normal in 19 patients of Group 1 (73.1%) and 20 individuals from Group 2 (76.9%) and reached the level of 9.3 ± 0.7 mmol/l and 9.8 ± 1.3 mmol/l, respectively.

Table 1: Changes of biochemical indexes in the patients with multidrug-resistant tuberculosis/HIV with CD4+ lymphocytes count below 50 per mcl and IgG usage (0-8 months) (M±m)#

Patients' group	Index (month)							
	0	0.5	1	2-3	4	5	6-7	8
Increasing of bilirubin level								
Group 1	25.9±4.8	29.1±5.9	31.8±6.9	36.6±10.4	33.4±10.3	29±4.8	26±3.9	23.2±2.3
Group 2	28.3±3.9	26.4±3.8	26.1±3.4	25.3±3.5	24.7±2.2	24.3±2.1	23.4±1.3	22±1.3
Normal bilirubin level								
Group 1	15.0±3.9	20.0±2.8	19.0	0±0	0±0	16.8±2.9	15.5±2.9	12.6±3.7
Group 2	17.8±1.9	15.4±2.4	15.0±3.6	13.5±4	12.8±3.2	13.1±3.4	12.4±3.2	11.4±3
Increasing of ALT activity								
Group 1	40.8±4.9	55.1±22.1	57.9±20.8	63.4±20.2	53.7±13.4	51.0±12.6	47.6±11.9	35.8±2.9
Group 2	42.4±6	39.6±2.9	38.1±2.7	38.0±2.9	35±2.0	34.7±2.5	33.7±1.5	33±1.4
Normal ALT activity								
Group 1	14.5±4.8	18.2±4.6	20.8±4.5	23.6±4.4	20.5±5.0	18.4±5.6	16.1±6.2	12±6.5
Group 2	18.5±5.8	17.2±5.6	16.5±5.8	16.5±5.7	15.7±5.6	15.0±4.6	13.6±4.9	9.8±4.5
Increasing of AST activity								
Group 1	43.9±6.5	58.3±19.2	65.3±20.1	74.3±20.5	64.4±17.7	58.6±14.8	52.5±11.2	41.6±4.9
Group 2	43.2±6.7	42.2±4.4	39.9±5.1	38±3.4	37.7±3.9	36.3±3.1	35.4±2.9	34.7±1.6
Normal AST activity								
Group 1	19.3±4.2	19.8±4.8	23.7±5.0	26.7±3.5	0±0	15.6±3.6	14±2.8	9.3±3.4
Group 2	17.4±4.6	17.0±5.9	16.7±5.6	15.1±4.8	14.7±4.2	14.6±4.0	14.4±5.1	11.8±4.3
Increasing of GGT activity								
Group 1	69.3±14.6	72.5±14.3	76.2±14.3	80.6±14.8	74.6±14.4	70.7±13.3	67.8±13.2	60.3±12.3
Group 2	71.2±13.6	67.0±12.0	62.5±11.8	60.5±11.5	56.9±12.7	57.7±12.8	57.6±12.7	51.9±13.5
Normal GGT activity								
Group 1	23.0±2.8	24±0	0±0	0±0	0±0	22±8.5	22.8±6.7	19.9±5.6
Group 2	28.0	31±5.7	26±6.6	25.5±6.2	25.7±4.3	21.6±4.5	21.9±4.6	22.1±6.2

GGT: Gamma-glutamyltransferase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, #M: arithmetic mean and m – standard deviation

Table 2: Changes of biochemical indexes in the patients with multidrug-resistant tuberculosis/HIV with CD4+ lymphocytes count below 50 per mcl and IgG usage (0-8 months) M ± m[#]

Patients' group	Index (month)							
	0	0.5	1	2-3	4	5	6-7	8
Increasing of thymol test								
Group 1	9.1±2.5	10.9±2.1	11.6±2.2	12.9±2.1	11.8±3.0	10.7±2.8	10.0±2.6	8.2±2.1
Group 2	12.1±2.3	10.6±2.5	10.4±2.6	9.7±2.5	8.0±2.0	7.4±1.8	7.0±1.5	6.3±1.4
Increasing of creatinine level								
Group 1	123.0±11.7	135.6±17.7	146.6±25.4	150.9±36.6	141.7±24.8	141.0±27.3	135.0±22.5	124.9±21.2
Group 2	129.8±9.7	124.2±9.7	124.2±9.3	124.1±10.2	124±7.9	123.7±4.5	123.4±3.9	122.3±6.0
Normal creatinine level								
Group 1	98.2±9.8	98.3±3.1	100±2.8	105±0	0±0	104.2±3.7	104.8±3.2	100.9±8.3
Group 2	106.4±4.5	99.6±5.9	98.6±3.5	97.3±3.3	97.8±6.3	97.6±5.7	97.6±6.9	95.8±6.6
Increasing of urea level								
Group 1	9.3±0.7	9.5±0.7	9.6±0.7	9.8±0.8	9.4±0.8	9.3±0.8	9.0±0.6	8.9±0.6
Group 2	9.8±1.3	9.3±0.8	9.3±0.7	9.2±0.6	8.9±0.5	9.1±0.4	8.9±0.4	8.8±0.4
Normal urea level								
Group 1	7.3±0.9	7.3±0.9	7.4±1.1	7.5±1.1	7.6±0.6	7.5±0.8	7.5±0.8	7.4±0.6
Group 2	7.4±0.8	7.6±0.8	7.6±0.8	7.5±0.7	7.6±0.7	7.4±0.8	7.2±0.8	7.1±0.7

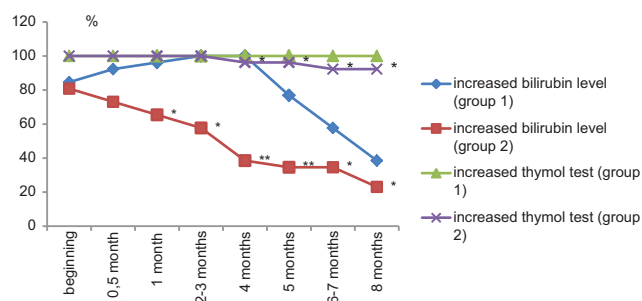[#]M: arithmetic mean and m – standard deviation

Figure 1: Number of patients with increased bilirubin level or thymol test according to the treatment strategy. *: The difference is significant between Group 1 and Group 2 ($P < 0.05$), **: The difference is significant between Group 1 and Group 2 ($P < 0.01$), ***: The difference is significant between Group 1 and Group 2 ($P < 0.001$)

Figure 2: Number of patients with increased alanine aminotransferase or aspartate aminotransferase activity according to the treatment strategy. *: The difference is significant between Group 1 and Group 2 ($P < 0.05$), **: The difference is significant between Group 1 and Group 2 ($P < 0.01$), ***: The difference is significant between Group 1 and Group 2 ($P < 0.001$)

The above-mentioned biochemical characteristics revealed that patients with MDR-TB/HIV with CD4+ lymphocytes below 50 cells/μCL, even before the beginning of anti-tuberculosis and ARV treatment, were in the state of chronic sepsis. According to the studies,[7,21] the tuberculosis locus of infectious inflammation in all patients with exhausted immunity quickly becomes a source of the pathogen hematogenic spreading, which leads to the development of a septicemic condition. That explained why even at the initial examination in the studied patients, the presence of sepsis markers (clinical, laboratory markers) was determined.

After the beginning of ATT, even during the first 2 weeks, patients of Group 1 had an increase of intoxication symptoms and adverse effects of antituberculosis agents. These clinical signs were displayed in the laboratory in the form of biochemical research indicator growth.

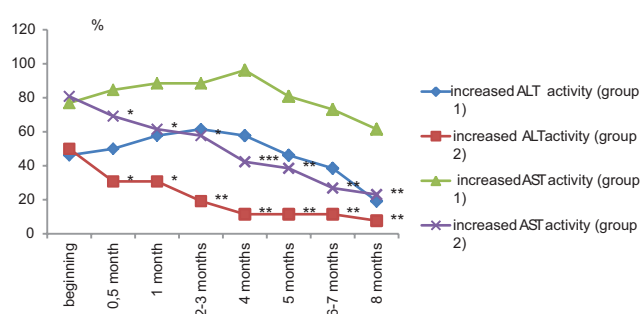The bilirubin rise was recorded in 1.3 times more often in patients of Group 1 than in Group 2 (92.3% vs. 73.1%); the

average level of total bilirubin was also lower in Group 2 and reached 26.4 ± 3.8 μmol/L. In Group 1, hyperbilirubinemia steadily increased monthly and was observed in 96.2% of the individuals after a month of treatment and in 100% after 4 months. Starting from the 5th month, the number of cases with increased bilirubin level gradually decreased by 1.3 times and reached 76.9%. At the 8th month of treatment, ten patients (38.5%) had an increase of total bilirubin level. In Group 2, on the contrary, the number of cases with hyperbilirubinemia decreased with each subsequent month of treatment, so that only 34.6% of patients ($P < 0.01$) were registered at the 5th month and in 23.1% of patients at the 8th month ($P < 0.05$) [Figure 1].

Thymol test after 2 weeks of treatment was increased in both the groups equally (100% of cases), but the increase of the average level was observed only in Group 1 where its maximal level reached 10.9 ± 2.1 U, while in Group 2, on the contrary, it had a decrease to 10.6 ± 2.5 U compared to the initial indexes.

Further on, 100% of patients in Group 1 during all 8 months had an increase in the thymol test. The individuals from Group 2 showed the index recovery in a single patient (3.8%) at the 3rd month of treatment and in 2 patients (7.7%) from the 5th to the 8th month inclusively [Figure 1 and Table 2].

The increase in the ALT and AST enzyme activities was observed only in patients of Group 1, whereas in patients of Group 2, on the contrary, one could see declining of the enzyme activities. During the first 2 weeks, the number of patients in Group 1 with elevated ALT level was 1.6 times higher than in Group 2 - 50.0% and 30.8%, respectively ($P < 0.05$); on the 3rd month it was 4 times more in patients of Group 1 than in Group 2 (61.5% vs. 15.4%, $P < 0.01$). Starting with the 5th month, an increased ALT activity was at 46.2% in patients of Group 1 and in 11.5% of Group 2 that proved a gradual recovery of ALT level in both the groups. However, on the 8th month, ALT increase was 2.5 times more frequent in patients of Group 1 (19.2%) against Group 2 (7.7%) ($P < 0.01$).

The increase in the AST activity was even more significant, but during the first 2 weeks in patients of Group 2, its increased level was 1.2 times less frequent than in Group 1 (69.2% vs. 84.6%) ($P < 0.05$). Moreover, the number of individuals with increased AST activity in Group 1 raised each month and at the 4th month of treatment was registered in 96.2% of patients. In Group 2, that index was 2.3 times less than in Group 1 and was 42.3% ($P < 0.05$) [Table 1 and Figure 2]. After the 5–8th months of treatment, increased ALT was observed less frequently in both the groups but was higher in the first group (61.5%) compared to the second group (23.1%).

Before treatment, most patients of both the groups had an increase of GGT activity, which reflected the presence and severity of intrahepatic cholestasis and intoxication. In the first 2 weeks, Group 1 had an increase of GGT average activity up to 72.5 ± 14.3 U/l, whereas Group 2, opposite, had a decrease of GGT activity up to 67 ± 12 U/l, but still, these two figures exceeded normal level. In addition, GGT activity from the 1st month to the 4th month inclusively was increased in 100% of the Group 1 patients. At the 5th month, the GGT

level gradually decreased in Group 1 but remained above the norm in 24 individuals (92.3%) and at the end of the 8th month in 19 patients (73%) [Table 1 and Figure 4]. Group 2 had a sustainable decrease in the GGT activity monthly, whereas on the 3rd month, the increased GGT activity was recorded in 21 patients (80.8%), on the 5th month in 15 patients (57.7%), and on the 8th month in 8 cases (30.8%).

The creatinine level had a rise in 23 patients (88.5%) of Group 1 with an average of 135.6 ± 17.7 µmol/l compared with 19 patients (73.1%) of Group 2 with an average of 124.2 ± 9.7 µmol/l. Two weeks of the treatment in patients of Group 1, this index increased and exceeded normal in 100% of cases at the 3rd month of treatment (159.3 ± 38.1 µmol/l). However, at the 5th month, the creatinine content gradually declined but still was increased in 80.8% of patients and at the 8th month of treatment in 53.8%, with an average level of 124.9 ± 21.2 µmol/l. At the same time, after 1 month of treatment, the frequency of patients in Group 2 with creatinine increased level subsided from 80.8% to 73.1%, after 5 months up to 38.5%, and from the 8th month to 23.1% ($P < 0.01$).

In the same time, the frequency of increased serum urea level among patients of Group 1 since the 2nd week of treatment was much higher than in Group 1 (80.8% vs. 69.2%) and remained at a high level (92.3%) until the 4th month of treatment inclusively. The patients' studies of Group 1, conducted after the 5th- and 8th-month treatment, showed a decline in the frequency of increased serum urea level from 80.8% to 38.5%, respectively. However, a more significant index of decline was observed in patients of Group 2 by 1.8 times (50%) on the 4th month, 2.1 times on the 5th month (38.5%), and 1.7 times (23.1%) on the 8th month ($P < 0.05$) [Table 2 and Figure 3]. It is interesting that among the patients whose studied biochemical indexes have not exceeded the limits, had a similar dynamics – a gradual increase in the average level of the studied values in the first group with a maximum of 2–3 months of the study. At the same time, biochemical indexes were gradually reduced in the second group since the beginning of the treatment.
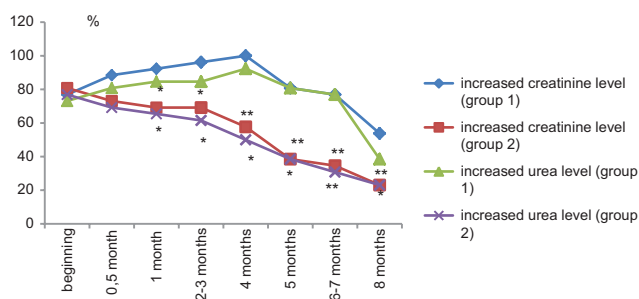

Figure 3: Number of patients with increased creatinine or urea level according to the treatment strategy. *: The difference is significant between Group 1 and Group 2 ($P < 0.05$), **: The difference is significant between Group 1 and Group 2 ($P < 0.01$), ***: The difference is significant between Group 1 and Group 2 ($P < 0.001$)

Figure 4: Number of patients with increased gamma-glutamyltransferase activity according to the treatment strategy. *: The difference is significant between Group 1 and Group 2 ($P < 0.05$), **: The difference is significant between Group 1 and Group 2 ($P < 0.01$), ***: The difference is significant between Group 1 and Group 2 ($P < 0.001$)
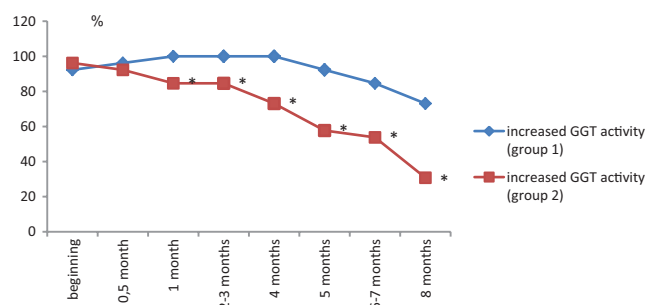
Discussion

The above-mentioned biochemical changes indicated that the patients of the control group, even after 2 weeks of ATT, exhibited symptoms of raising intoxication associated in parallel with worsening of hepatic and renal test results. In our opinion, this was because the appointment of the antituberculosis second-line agents to HIV-positive patients causes the *M. tuberculosis* destruction, as well as destruction of other Gram-negative bacteria sensitive to this medication, resulting in the bacteremia that is accompanied by viremia and fungemia. All these factors serve as a trigger for the further rapid development of SIRS due to decreasing number of circulated alive bacteria as well as structural elements of cell wall (endotoxins) and metabolites of bacterial origin. Through subsequent immune disturbance, the activation of bacterial-viral infections occurs, which increases intoxication syndrome. The raising intoxication, in turn, leads to further liver dysfunction with hyperbilirubinemia, alteration of aminotransferase activity, and development of renal failure with azotemia and oliguria.

All these hinder the use of ARV treatment in the early stages and delay the time of its prescription. In patients of the basic group, who in addition to standard therapy received intravenously IgG, the treatment outcome was more favorable than in the control group, so these patients after 2 weeks of taking of antituberculosis agents received additional ARV that, in turn, significantly increased their chances of survival during the treatment of such severe comorbid pathology as DR-TB/HIV with deep immune deficiency state.[22]

According to the presented clinical observation, the following features were determined: the basic group of the patients, who received immunoglobulin intravenously in addition to standard antituberculosis therapy, comparatively more easily carried out a period of bacteremia and endogenous intoxication; the clinical condition of patients improved even after the first use of immunoglobulin due to the action of specific antibodies against various bacteria, toxins, and viruses, which, when bind with antigen, provided an opsonizing effect and modulate the complement system, neutralized the action of toxins and viruses, suppressed the production of pro-inflammatory cytokines, and directly acted on the cell walls of pathogenic microorganisms.

The improvement of biochemical indexes can be explained as the result of neutralization of viruses and bacteria, reducing the intoxication burden on the hematopoietic system, hepatobiliary system, and urinary system. In patients of Group 2, even the number of adverse effects from antituberculosis agents was less than in patients of the control group.

Thanks to the immunologic support of the patients from the basic group, ARV treatment was successfully prescribed after 2 weeks of antituberculosis therapy, whereas the patients of the control group started ARV therapy at least a month, and some even 2–3 months of TB treatment, which was caused by the development of severe disturbances of biochemical indexes and manifestation of numerous adverse reactions.

In patients of the basic group after the ARV appointment, there was no manifestation of SIRS symptoms. In the same time, in patients without additional immunoglobulin therapy (control group), the rapid SIRS development was observed, which led to the formation of multiorgan disturbance in the early stages, and in some cases, and in later periods of MDR-TB/HIV treatment.

Conclusion

The usage of immunoglobulins intravenously in the group of patients with MDR-TB associated with HIV infection, with CD4+ level <50 cells/µCL, is appropriate and essential that was proved by more rapid normalization of the functional state of the liver and kidneys comparatively to standard antituberculosis treatment and ART. The obtained data proved the effectiveness of IgG application.

Conflicts of interest

There are no conflicts of interest.

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