ENTEROSORPTION IN EMERGENCE LUNG TUBERCULOSIS

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In a controlled open single center trials the results of chemotherapy newly diagnosed patients with pulmonary tuberculosis in combination with enterosorption one of three drugs: Enterosgel (polymethylsiloxane polyhydrate), aerosil or carbon sorbent. The effect on the performance of enterosorption intoxication and liver function during chemotherapy. As a result, due to hepatoprotective and detoxification effect enterosorption, managed to avoid the interruption of chemotherapy.

Key words: *pulmonary tuberculosis, chemotherapy, enterosorption, polymethylsiloxane polyhydrate, charcoal sorption preparation, colloidal silicon dioxide.*

Enterosorption (ES) is a treatment method of parenteral administration of sorption drugs currently accepted as one of the methods of "efferent medicine ", which includes such methods as hemosorption, plasmapheresis etc., and is widely used in various clinical areas [1-3]. As a non-invasive and having almost no contraindications or side effects, ES provides multiple positive changes recorded both clinically (elimination or reduction of severity of symptoms, intoxication, asthma attacks or angina pain, fever, gastro-intestinal disorders etc.), and with biochemical, functional, immunological methods. Various therapeutic effects were seen: primarily detoxification, then immune-modulating, antiatherogenic and normalizing effect on hemocoagulation, stabilizing cell membrane, activating synthesis ability of hepatocytes etc. [1, 4-6]. These positive effects are based on the following mechanisms: cleansing of gastrointestinal juice, which is in constant-intestinal visceral recycling, stimulation, normalizing modification of lipid and amino acid spectrum of blood etc. [1, 2]. Thanks to convincing arguments that have appeared only in the recent years, ES can be regarded as a method of general clinical (medical) lymphology and endoecological rehabilitation [7,8]. This is because enterosorbent administered in the intestinal lumen effectively detoxifies intestinal juice, which is in constant viscero-intestinal circulation. The latter is produced in body in an amount of 6-9 liters per day, it is in many ways close to the central lymph (thoracic duct) and in terms of pathology contains significant amounts of toxic substances [1, 2]. Exclusion of toxic metabolites from viscero-intestinal recycling significantly stimulates detoxification systems in maintaining body homeostasis.

As a mass-exchanger, enterosorbent manifests itself as a stimulator of lymphatic drainage of GIT tissues. [7] The latest data show that the sorbent particles administered in in the body cavities become kind of matrix for immune component cells, the result of the formation and structure, and function resembles lymph node [7]. With "artificial" lymphatic node regional lymph experiences lower load, functions more effectively and undergoes less structural changes, i.e. not only lymph-correcting, but also lymph-protective effect is achieved [7]. Authors regard this phenomenon as "synergy of lymphatic drainage apparatus, and sorbent '[7]. The above arguments enable to rank ES to lymphology methods.

The study was conducted due to the need of new effective opportunities of homeostasis correction in patients with tuberculosis and nonspecific lung diseases by non-invasive therapies. Among the disorders, some of the most important are caused by liver function deficiency and specific toxicity syndrome. [9] These and other disorders complicate

Table 1. Dynamics of intoxication indexes and transaminase in the groups before and after ES

Group	Intoxication indexes						Transaminases			
	LII_K		LII_O		$GISP_b$		ALT		AST	
Main group (M±m)	2,42±0,2	0,85±0,1	3,34±0,4	1,98±0,13	6,1±0,8	1,4±0,46	1,62±0,14	0,68±0,14	0,86±0,05	0,33±0,05
Experimental group (M±m)	1,68±0,28	1,51±0,27	2,72±0,26	2,45±0,18	4,3±0,4	3,3±0,	1,38±0,17	1,86±0,19	0,59±0,07	0,83±0,08
P1	-	<0,001	-	<0,001	-	<0,001	-	<0,001	-	<0,001
P2	-	#	-	#	-	<0,2	-	<0,1	-	<0,5
P3	-	<0, 05	-	<0, 05	-	<0, 05	-	<0,1	-	#
P4	-	<0,05	-	<0,02	-	<0,02	-	<0,001	-	<0,001

Notes. A - before treatment; B - after treatment; p – Student's test; p1- difference of the values before and after treatment in the main group; p2 difference of the values before and after treatment in the experimental group; p3 - difference between the two groups before treatment; p4- difference between the two groups after treatment; # - no significant difference - p> 0.1. LII_K - leukocyte index of intoxication by Kalf-Caliph; LIIo - leukocyte index of intoxication by Ostrovsky; GISP - haematological toxicity index.

clinical performance not only in phthisiology or therapy, but also in surgery, as they represent an important factor of operational risk, negatively affecting the prospective surgical procedures. [10]

A comparative controlled single- center open study has been conducted to examine the clinical effectiveness of ES as a method of non-invasive detoxification with sorption drugs: silicon-organic – polymethylsiloxane polyhydrate (Enterosgel), granulated coal (abbreviation SU) and colloid silicon dioxide (Aerosil, abbreviation of A-PS), in the treatment of adult patients with emergence lung TB.

Materials and Methods

The main group (MG) included 73 patients (49 males), the control group (CG) - 47 patients (32 males). Considering the main clinical, biological, and anamnestic social characteristics, as well as frequency of comorbidities in group, destructive pulmonary tuberculosis and its complications were more frequent in the main group.

Clinical, rentgenological and laboratory surveillance was conducted, leukocyte intoxication index was measured [11-13].

The effectiveness of detoxification and correction of some indicators of liver function with study sorbents the example of the dynamics of the indices of intoxication and serum transaminases (alanine aminotransferase - ALT and aspartate aminotransferase - AST) is shown in Table. 1. As a result, most of the initial values in the main group is very different from those in the experimental group, i.e. pathological abnormalities were more pronounced mi (p3 <0.001). Thus, intoxication values in the study group exceeded the norm by 3.5-7.0 times, and transaminases - more than 2-fold.

Study results

Despite this, intoxication values by the end of the ES course significantly decreased and reached almost normal values. Concentration of transaminases normalized in all patients of the main group (p1 <0.001). Although intoxication indexes in the experimental group decreased, it was not statistically significant and they were significantly greater than the reference values. Transaminase blood activity in the control group significantly increased (p2 <0.1 and 0.05). As a result, by the end of ES course the values oft he main group became substantially better than in the experiment group, and this conclusion was statistically significant (p4 <0.001-0.02-0.05).

The concentration of bilirubin in the blood of OG patients before treatment increased in 16 (21.9%) patients. After the treatment their number decreased to 4 (5.5%), the level of bilirubin in the blood significantly decreased (p <0,05). In the control group concentration of bilirubin before treatment increased in 7 (14.9%) patients, after treatment matched by term and duration with the treatment in the main group, it increased in 8 (17%) patients. The difference in blood concentrations of bilirubin between the two groups before treatment, was statistically insignificant, after treatment it was poorly reliable, and this comparison was in favor of the main group. It should be noted that statistical analysis included only observations with initially increased level.

The above data regarded generally the main group, i.e. it is still unclear whether all used drugs have

Table 2. Dynamics of average values of intoxication indexes and transaminase levels before and after treatment depending on enterosorbent used

Group	Intoxication indexes						Transaminases			
	LII_K		LII_O		$GISP_b$		ALT		AST	
Enteros gel (M±m)	2,25±0,4	0,67±0,2	3,16±0,5	2,0±0,2	,26,3±1,9	1,2±0,4	1,4±0,4	0,6±0,1	0,6±0,1	0,3±0,02
SU (M±m)	1,68±0,28	1,51±0,27	2,72±0,26	2,45±0,18	4,3±0,4	3,3±0,	1,38±0,17	1,86±0,19	0,59±0,07	0,83±0,08
A-PS (M±m)	-	<0,001	-	<0,001	-	<0,001	-	<0,001	-	<0,001
p_1	-	#	-	#	-	<0,2	-	<0,1	-	<0,5
P_2	-	<0, 05	-	<0, 05	-	<0, 05	-	<0,1	-	#
P_3	-	<0,05	-	<0,02	-	<0,02	-	<0,001	-	<0,001

Notes. A - before treatment; B - after treatment; p – Student's test; p1- difference of the values before and after treatment in the main group; p2 difference of the values before and after treatment in the experimental group; p3 - difference between the two groups before treatment; p4- difference between the two groups after treatment; # - no significant difference - p> 0.1.

Table 3. Dynamics of average intoxication indexes and transaminases before and after treatment of TV patients with concomitant chronic hepatitis

Sorbent	**Intoxication indexes**						**Transaminases**			
	LII_K		LII_O		$GISP_b$		ALT		AST	
	A	B	A	B	A	B	A	B	A	B
Enteros	2,03±1	0,44±0	2,75±1	1,44±0	3,05±1	0,72±0	1,93±0	0,79±0	0,79±0	0,40±0

gel (M±m)	,04	,32	,1	,18	,6	,42	,49	,24	,34	,03
SU (M±m)	3,5±0,75	0,82±0,22	2,85±0,49	1,79±0,15	4,92±0,94	0,93±0,23	2,72±0,44	1,6±0,52	0,99±0,1	0,61±0,19
A-PS (M±m)	0,74±0,12	1,12±0,29	1,53±0,48	2,2±0,55	1,1±0,54	1,2±0,34	1,43±0,62	0,94±0,38	0,83±0,29	0,48±0,14
p_1		#		#		#		<0.1		<0.05
P_2		<0.01		<0.05		<0.001		#		<0.1
P_3		#		#		#		#		#

Notes. A - before treatment; B - after treatment; p – Student's test; p1- difference of the values before and after treatment in the main group; p2 difference of the values before and after treatment in the experimental group; p3 - difference between the two groups before treatment; p4- difference between the two groups after treatment; # - no significant difference - p> 0.1.

positive detoxifying and normalizing effect on transaminases. In order to clarify this question, a special data analysis was performed (Table. 2).

It has been found that all the sorbents have such properties and can be successfully applied in phthisiology practice for these purposes. Each sorbent has shown the above properties, but there were some special features. Statistical significance of normalizing action of SU was the highest. A-PS reduced toxicity significantly less actively, but exceeded SU in correction of transaminases. The same was true for polymethylsiloxane polyhydrate (Enterosgel). Interestingly, polymethylsiloxane polyhydrate reduces even lower levels of transaminases in those cases where they are low, but (2) exceed the norm. Using SU, this situation was more difficult to correct. In general, all the sorbents were effective, and comparative statistical analysis of their clinical influence only confirms what has been said.

We can only add that Enterosgel was slightly more efficient in general detoxification than A-SS, but correction of transaminase levels was higher with the latter.

The findings have induced clarification of sorption efficiency of the studied sorbents in various clinical situations relevant to TB: chronic hepatitis concomitant to tuberculosis; toxic (medical) hepatitis; TB (specific) intoxication.

Thus, in chronic hepatitis the main effect of Enterosgel is normalization of transaminases in the blood, confirmed statistically at various stages of treatment (Table. 3).

SU shows more pronounced general detoxification effect than Enterosgel and A-PS, effectively normalizing bilirubin levels in the blood, but has little effect on the elevated transaminases. Despite the use of A-PS in patients with tuberculosis and chronic hepatitis, statistically insignificant increase of general intoxication and the similar decrease in transaminase levels was noted. The conclusion on the statistical unreliability of the effects of sorbents includes differences of averages (for Applications, Student's t test) and can be reviewed with more observations in the groups. Regarding trends, i.e. reliability of direction changes, the decrease of AE metabolites in the concentration of in all cases was statistically significant.

In case of toxic hepatitis all the studied sorbents normalized transaminase concentrations and bilirubin. Moreover, SU also manifested itself as a high-efficiency detoxifier of common action (Tab. 4).

It should be emphasized that treatment of this subgroup chemotherapy was not interrupted, and only in rare cases the most hepatotoxic sorbent was abolished for a period of no more than 5-10 days.

In the presence of only TB intoxication (i.e., in absence of liver disease), all the sorbents quickly reduce the syndrome, both in its clinical manifestations and in dynamics of computing hematological indexes

(Tab. 5). In this clinical situation, SU exceeds the properties of A-PS in severe intoxication or concomitant chronic diseases.

Table 4. Dynamics of average intoxication indexes and transaminases before and after treatment of TB patients with toxic hepatitis

Sorbent	**Intoxication indexes**						**Transaminases**			
	LII_K		LII_O		$GISP_b$		ALT		AST	
	A	B	A	B	A	B	A	B	A	B
Enterosgel (M±m)	1,31±1,08	0,67±0,32	2,98±0,4	2,43±0,99	2,49±2,31	1,54±1,22	2,57±0,12	0,55±0,21	86±0,28	0,24±0,16
SU (M±m)	1,9±0,39	0,62±0,14	2,88±0,38	1,77±0,17	3,75±1,52	0,67±0,15	1,97±0,23	0,54±0,08	0,63±0,09	10,26±0,07
A-PS (M±m)	1,19±0,45	1,05±0,34	2,64±0,55	2,14±0,43	2,8±1,14	1,4±0,49	2,87±0,81	0,63±0,29	1,13±0,29	0,26±0,05
p_1		#		#		#		<0.1		<0.05
P_2		<0.01		<0.05		<0.1		<0.001		<0.01
P_3		#		#		#		<0.05		<0.02

Notes. A - before treatment; B - after treatment; p – Student's test; p1- difference of the values before and after treatment in the main group; p2 difference of the values before and after treatment in the experimental group; p3 - difference between the two groups before treatment;; # - no significant difference - p> 0.1.

Table 5. Dynamics of the average value of intoxication index before and after treatment of patients with tuberculous intoxication (patients without liver disease)

Sorbent	**Intoxication indexes**					
	LII_K		LII_O		$GISP_b$	
	A	B	A	B	A	B
Enterosgel (M±m)	2,62±0,85	0,82±0,32	3,60±0,57	2,17±0,43	7,59±2,79	1,52±0,63
SU (M±m)	2,50±1,07	0,60±0,19	5,13±2,54	1,58±0,42	6,27±2,12	0,81±0,21
A-PS (M±m)	3,67±0,50	1,12±0,16	4,78±0,60	2,20±0,26	10,9±1,63	2,80±0,62
p_1		<0.1		<0.1		<0.1
P_2		<0.2		#		<0.1
P_3		<0.001		<0.001		<0.001
p_4		<0.1				<0.1

Notes. A - before treatment; B - after treatment; p – Student's test; p1- difference of the values before and after treatment in the main group; p2 difference of the values before and after treatment in the experimental group; p3 - difference between the two groups before treatment; p4- difference between the two groups after treatment; # - no significant difference - p> 0.1.

Analysis of the use of these drugs in the above pathologies reveals their effectiveness and some action features of each of them, which makes possible a more rational choice of sorbents for a variety of clinical situations. Since the effectiveness of anti-TB treatment is not reduced, it can be assumed that umnder condition of rational and proper application ES: a) does not negatively effect concentrations of antibacterial drugs in the patient's body; b) due to recovery of the intestinal biocenosis, desensitization and immune modulation has been increases probability of treatment of lung TB.

Conclusions

Thus, the following conclusions are true:

1. Application of enterosorption in the treatment of lung TB is both helpful and necessary because It provides a decrease of intoxication indexes, eliminates clinical symptoms and laboratory abnormalities.

2. All the studied sorption preparations have a positive impact on the overall state of the patient and significantly normalizes the performance of homeostasis.

3. Enterosorption with Enterosgel and other sorbents is feasible during chemotherapy of patients with pulmonary tuberculosis, as it provides a distinct, statistically valid detoxification effect and protects liver function non- invasively, preventing the forced breaks in chemotherapy courses of patients with concomitant liver pathology.

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