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APPLICATION OF THIOTRIAZOLINE IN COMBINATION WITH EXTRACORPORAL HEMOCORRECTION IN PATIENTS WITH ACUTE PULMONARY SUPPRESSIONS IN LATE PERIOD OF TRAUMATIC DISEASE

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ЗАСТОСУВАННЯ ТІОТРИАЗОЛІНУ В ПОЄДНАННІ З ЕКСТРАКОРПОРАЛЬНОЮ ГЕМОКОРЕКЦІЄЮ У ХВОРИХ З ГОСТРОЮ ІНФЕКЦІЙНОЮ ДЕСТРУКЦІЄЮ ЛЕГЕНЬ У ПІЗНІЙ ПЕРІОД ТРАВМАТИЧНОЇ ХВОРОБИ

Крутько Є.М.

Проведено порівняльний аналіз результатів комплексного обстеження та лікування 28 хворих з важкими формами гострої інфекційної деструкції легень в пізньому періоді (ТХ). 62,5% пацієнтів склали від 20 до 50 років. В основному це були чоловіки – 80,5%. Крім дренування, санації гнійних порожнин і традиційної консервативної терапії, у цих пацієнтів були використані методи екстракорпоральної гемокорекції для купірування прогресуючого ендотоксикозу. У пацієнтів, які отримували тіотриазолін (в складі передперфузійної підготовки і в складі інтенсивної терапії в постперфузійному періоді), відзначався більш сприятливий перебіг захворювання (швидка позитивна динаміка показників системної запальної відповіді, показників токсемії і кисневого гомеостазу, в порівнянні з пацієнтами, які отримують традиційну терапію), що сприяло скороченню термінів і підвищенню якості лікування пацієнтів.

Виявлені зміни вказують на доцільність застосування тіотріазоліну в складі передперфузійної підготовки та базової програми комплексного лікування хворих з гострою інфекційної деструкцією легень в пізньому періоді ТХ.

Ключові слова: травматична хвороба, тіотриазолін, легеневе нагноєння.

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APPLICATION OF THIOTRIAZOLINE IN COMBINATION WITH EXTRACORPORAL HEMOCORRECTION IN PATIENTS WITH ACUTE PULMONARY SUPPRESSIONS IN LATE PERIOD OF TRAUMATIC DISEASE

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A comparative analysis of the results of a comprehensive examination and treatment of 28 patients with severe forms of acute infectious destruction of the lungs in the late period (TB) was carried out. 62.5% of patients were people of the most working age – from 20 to 50 years. They were mostly men – 80.5%. In addition to drainage, sanitation of purulent cavities and traditional conservative therapy, these patients used extracorporeal hemocorrection methods to relieve progressive

endotoxicosis. In patients receiving thiotriazoline (in pre-perfusion preparation and as part of intensive treatment of the post-perfusion period), a more favorable course of the disease was noted (rapid positive dynamics of indicators of systemic inflammatory response, toxemia and oxygen homeostasis indicators, compared with patients receiving traditional therapy), which contributed to reduction of terms and improvement of the quality of treatment of patients.

The revealed changes indicate the advisability of using thiotriavzoline as part of pre-perfusion preparation and the basic program of complex treatment in patients with acute infectious lung destruction in the late period of TD.

Key words: traumatic disease, thiotriazoline, pulmonary suppuration.

Introduction. In patients with acute infectious lung destruction (AIDL) in the late period of traumatic disease (TD), the phase of acute suppuration is characterized by a pronounced systemic inflammatory response, significant toxemia, mixed hypoxia, severe disorders of the pro- and antioxidant systems [1].

Under such conditions, a universal reaction of activation of non-enzymatic limited proteolysis develops, when not complete degradation of the protein molecule occurs, but often only its biochemical modification. As a result, there is an increased formation of products of incomplete and perverted metabolism, pathological activation of free radical oxidation processes [2]. It has been established that the functions of identified endogenous toxic substances (ETS) can be performed by more than 40 different substances isolated from biological fluids of patients with symptoms of endogenous intoxication [3, 4].

Many researchers associate the formation of secondary toxemia as one of the main manifestations of endotoxicosis with an increased intake of such toxic substances into the transport media (lymph and blood) [5].

Often, perfect surgical technique, new antimicrobial agents and traditional approaches to intensive care do not allow stopping the development of endotoxicosis [6, 7]. Under these conditions, to stop the manifestations of endogenous intoxication, it may be necessary to use therapeutic measures aimed at extracorporeal blood cleansing [8].

Extracorporeal hemocorrection (EHC) contributes to a significant decrease in the level of endotoxemia, a decrease in intrapulmonary shunting of blood, and normalizes the parameters of external respiration and central hemodynamics [9, 10].

However, some authors highlight the unfavorable effects of efferent methods in the form of a decrease in the oxygen transport function of the blood, a decrease in the total amount of protein, and the destruction of blood corpuscles during this operation [11]. It was found that after plasmapheresis and plasmasorption sessions, along with the elimination of toxins, natural antioxidants such as catalase, peroxidase, superoxide dismutase are destroyed and removed [12].

A progressive decrease in oxygen tension in the blood and tissues leads to a sharp restriction of the transport of electrons along the respiratory chain of the cell and a decrease in the associated ATP resynthesis. Along with this, the content of ADP, AMP and inorganic phosphate increases, which naturally increases the phosphorylation potential. These disorders of energy metabolism activate anaerobic glycolysis. A rapid increase in the content of lactate in tissues is noted due to an increase in the rate of glycolysis and an increase in glycogenolysis due to the activation of phosphorylase under conditions of hypoxia. Mitochondrial dysfunction is the molecular mechanism that

determines energy disturbances under conditions of limited oxygen delivery to the cell [13]. Under these conditions, the expediency of using drugs with antihypoxic and antioxidant action is obvious.

The aim of the study was to increase the effectiveness of treatment of patients with acute pulmonary suppuration in the late period (TD) by improving methods of extracorporeal hemocorrection in the acute phase of a purulent-destructive process using thiotriazoline.

Materials and methods. A comparative analysis of the results of a comprehensive examination and treatment of 28 patients with severe forms of acute infectious destruction of the lungs in the late period (TD) was carried out. 62.5% of patients were people of the most working age – from 20 to 50 years. They were mostly men – 80.5%. In addition to drainage, sanitation of purulent cavities and traditional conservative therapy, these patients used extracorporeal hemocorrection (EHC) methods to relieve progressive endotoxicosis.

The severity of endotoxicosis was assessed based on the general condition of the patients, the level of endotoxemia, systemic inflammatory response (SIRS), the state of oxygen homeostasis, and changes in free radical oxidation. The signs of SIRS were determined according to the criteria of the Chicago Consensus Conference on Sepsis (Bone R.C. et al., 1992). Along with the use of clinical, laboratory, functional and radiological research methods widespread in practice, a number of original ones were used. Toxemia was judged by determining the content of "average weight molecules" (AVM) in plasma and erythrocytes of venous blood according to the method of M.Ya. Malakhova and S.V. Obolensky (1989). In addition, the total blood toxicity (RT of blood, conventional units) was calculated by summing the toxicity of plasma and toxicity of erythrocytes, and the coefficient of distribution (CD) of this class of endogenous toxic substances between the plasma and erythrocyte pool (CD plasma / erythrocytes) as the ratio of toxicity of plasma to toxicity of erythrocytes. To assess the state of oxygen homeostasis, the tension and saturation of arterial and venous blood gases were determined using a laboratory complex "Synthesis 45" (USA). Oxygen tension (PO2), hemoglobin saturation (SatO2), arteriovenous difference for oxygen tension (ΔP (a-v) O2) were determined.

The total oxidative activity (OA) was estimated by the formation and accumulation in the model system of the final product of lipid peroxidation (LPO), malondialdehyde (MDA).

Indications for extracorporeal detoxification in patients with acute infectious lung destruction were: persistence of signs of severe toxemia and systemic inflammatory reaction with the development of "organopathies" against the background of adequate drainage of the purulent cavity and conservative treatment, ineffectiveness of complex

Table 1

Distribution of patients depending on the form of pulmonary suppuration

Patient group	Acute purulent abscess	Limited gangrene (gangrenous abscess)	Common gangrene	Total
I (control)	2	7	4	13
II (thiotriazoline)	4	6	5	15
Total	6	13	9	28

detoxification therapy of patients for 7-10 days, and identification of signs of severe sepsis in patients.

As a detoxifying extracorporeal aid, as a rule, a combination of plasma exchange and plasma sorption was used. These patients were divided into two groups, depending on the characteristics of the pre- and post-perfusion therapy. In patients of the control (I) group, standard pre-perfusion and post-perfusion therapy regimens were used, aimed at optimizing the functioning of the detoxification organs and creating "imposed maximum endotoxemia" before the EGC session, and standard pre-perfusion preparation was carried out. Isotonic, hypertonic and hyperosmolar infusion solutions have been used consistently, causing "lymphatic drainage" of tissues. At the final stage of pre-perfusion preparation, an extracorporeal detoxification operation was performed. Patients of group II included "Thiotriazoline" in the pre-perfusion preparation program.

Thiotriazoline was used as part of infusion-transfusion therapy in pre-perfusion preparation 30–40 minutes before starting the infusion of crystalloid solutions. This period of time was necessary for the inclusion of substrates in the metabolic reactions of cells. Thiotriazoline was used in a volume of 10 ml per 400 ml of 5% glucose solution.

Extracorporeal operations were performed on PF 05 fractionators.

At the first stage of combined extracorporeal detoxification, plasmapheresis was performed with an exfusion volume of 60–75% of the CPV. Blood cells were combined with donor plasma in a volume of at least 70% of the volume of exfused plasma and plasma-substituting media. At the second stage, after the separation chamber, the plasma was directed into a container, from which it was directed to the sorption column. The latter contained 4–5 g of the "Aktilen" adsorbent. After passing through the mass exchanger, the depurated plasma was combined with cellular elements for further reinfusion to the patient.

Research results. There were no significant differences in most clinical and laboratory parameters in patients of groups I and II in the pre-perfusion period.

When studying the signs of SIRS, indicators of oxygen homeostasis and toxemia in patients of groups I and II before carrying out extracorporeal detoxifying perfusions, the revealed indicators were also comparable (Tables 2–5).

Table 2

Laboratory indicators of SIRS in patients of group II compared with the control (I) group before EGC (M ± m)

	Group of patients	
Indicators	**Group II (n=15)**	**Group I (n=13)**
Leukocytes, × 109 / l	16,2±0,9	15,5±1,2
Lymphocytes, × 109 / l	1,18±0,08	1,14±0,05
LII, conv. units	4,7±0,09	4,5±0,09
ESR, mm / hour	50,2±1,16	52,4±1,22
Albumin / Globulin	0,72±0,06	0,78±0,06
CRP, conventional units	++	++

Table 3

Oxygen homeostasis indicators in group II patients compared with the control (I) group before EGC (M ± m)

	Group of patients	
Indicators	**Group II (n=15)**	**Group II (n=15)**
Hemoglobin, g / l	93,3±1,4	92,7±1,5
Hematocrit l / l	0,30±0,03	0,32±0,03
PaO_2, mm Hg	67,7±0,7	68,6±0,8
Sat O_2a, %	87,7±0,5	88,4±0,6
$\Delta P(a\text{-}v)O_2$, %	26,9±0,4	27,4±0,5

Table 4

Indicators of endotoxinemia in patients of group II compared with the control (I) group before EGC (M ± m)

Indicators	Group of patients	
	Group II (n=15)	Group II (n=15)
Plasma toxicity, conventional units	30,2±0,8	31,6±0,4
Toxicity erythr., conventional units	21,5±0,4	21,2±0,2
KD pl / er	1,32±0,06	1,37±0,01
General toxicity, conventional units	53,8±0,5	54,6±0,5
E260/280	0,73±0,03	0,78±0,01
LII, conventional units	4,5±0,08	4,5±0,09

The presented data show that the analyzed parameters of SIRS and endotoxemia in patients of groups I (control) and II were comparable.

The dynamics of endotoxemia and systemic inflammatory response indicators after a session of extracorporeal hemocorrection (EGC) is presented in Tables 5 and 6.

The postoperative period was characterized by regression of SIRS in both groups, however, in group II, leukocytosis, LII decreased faster, and the level of lymphocytes increased compared to group I. The study of laboratory markers of endogenous intoxication revealed a significant decrease in the concentration of ETS after surgery. In both groups, the predominance of the plasma sector of the ETS was noted. However, over the next days in patients of group I, there was an increase in AVM in the blood up to 2 weeks of treatment.

Patients of group II showed a significantly faster decrease in plasma toxicity and general blood toxicity after EGC. The positive dynamics of these parameters in this group appeared already from the 3rd day. From day 3 in patients of group II, the plasma pool of ETS decreased significantly faster than in patients of group I. Taking into ac-

Table 5

Laboratory indicators of SIRS in patients of group II compared with the control (I) group after extracorporeal hemocorrection (M ± m)

Parameters	Group	Before EGC	Time after EGC		
			1 day	3 days	14 days
Leukocytes, × 109 / l	I	15,5±1,2	14,8±0,8	13,8±0,9	7,5±1,1
	II	16,2±0,9	15,4±0,9	12,7±0,8*	6,9±0,9*
Lymphocytes, × 109 / l	I	1,14±0,05	1,28±0,06	1,32±0,04	1,46±0,05
	II	1,18±0,08	1,26±0,05	1,38±0,07	1,82±0,06*
LII, conv. units	I	4,5±0,09	4,1±0,12	4,3±0,07	1,7±0,07
	II	4,7±0,09	4,3±0,09	4,5±0,08	1,4±0,09*
ESR, mm / hour	I	52,4±1,22	51,4±1,16	49,6±1,32	32,6±1,18
	II	50,2±1,16	49,6±1,20	48,2±1,14	30,2±1,15*
Albumin / Globulin	I	0,78±0,06	0,74±0,05	0,86±0,04	0,92±0,06
	II	0,72±0,06	0,72±0,06	0,90±0,07	0,98±0,05*
CRP, conventional units	I	++	++	++	+
	II	++	++	++	+

The indicator significantly differs from the one in the top line: * –p <0.05, ** –p <0.01

Table 6

Laboratory indicators of endotoxemia in patients of group II compared with the control (I) group after extracorporeal hemocorrection (M ± m)

Parameters	Group	Before EGC	Time after EGC		
			1 day	3 days	14 days
Plasma toxicity, conventional units	I	31,6±0,4	24,7±0,4	28,6±0,3	22,5±0,4
	II	30,2±0,8	24,3±0,5	23,7±0,5**	16,9±0,4**
Toxicity erythr., conventional units	I	21,2±0,2	22,6±0,2	23,2±0,3	23,8±0,3
	II	21,5±0,4	22,8±0,2	21,8±0,4*	22,5±0,2*
KD pl / er	I	1,37±0,01	1,20±0,01	1,22±0,01	1,21±0,01
	II	1,32±0,06	1,23±0,01	1,19±0,03	1,11±0,02*
General toxicity, conventional units	I	54,6±0,5	51,4±0,6	53,7±0,6	49,6±0,7
	II	53,8±0,5	50,6±0,5*	49,6±0,5**	36,8±0,6**
E260/280	I	0,78±0,01	0,70±0,02	0,76±0,03	0,72±0,01
	II	0,73±0,03	0,72±0,01	0,68±0,01*	0,54±0,02*
LII, conventional units	I	4,5±0,09	4,1±0,12	4,3±0,07	1,7±0,07
	II	4,7±0,09	4,3±0,09	4,5±0,08	1,4±0,09*

The indicator significantly differs from the one in the top line: * –p <0.05, ** –p <0.01

count this distribution pattern, it can be assumed that in patients of group I during the first few days of the postperfusion period, the predominantly catabolic direction of metabolic reactions was preserved with the continuation of the production of ETS into the bloodstream.

Table 7

Oxygen homeostasis indicators in group II patients compared with the control (I) group after extracorporeal hemocorrection (M ± m)

Parameters	Group	**Before EGC**	Time after EGC		
			1 day	3 days	14 days
Hemoglobin, g / l	I	92,7±1,5	94,8±1,2	94,6±1,4	116,5±1,4
	II	93,3±1,4	95,2±1,2	95,4±1,2	118,9±1,3*
Hematocrit l / l	I	0,32±0,03	0,38±0,02	0,36±0,03	0,41±0,03
	II	0,30±0,03	0,36±0,02	0,34±0,02	0,42±0,03
PaO2, mm Hg	I	68,6±0,8	76,6±0,6	70,8±0,6	75,2±0,6
	II	67,7±0,7	75,2±0,8	72,1±0,4**	76,8±0,7*
Sat O_2a, %	I	88,4±0,6	92,1±0,8	91,4±0,8	96,8±1,1
	II	87,7±0,5	91,8±0,8	91,6±0,5	97,9±1,2*
ΔP(a-v)O_2, %	I	27,4±0,5	38,5±0,4	34,8±0,4	29,2±0,6
	II	26,9±0,4	38,2±0,4	36,7±0,5*	32,2±0,4**
Δ$SatO_2$ (a-v), %	I	28,8±0,2	35,6±0,5	34,2±0,8	29,9±0,5
	II	28,5±0,3	35,3±0,5	34,8±0,4	32,4±0,6**

The indicator significantly differs from the one in the top line: * –p <0.05, ** –p <0.01

Table 8

Distribution of patients treated with extracorporeal hemocorrection according to the outcomes of the disease

Nosological the form	Outcome of the disease			Total
	recovery	transition in a chronic form	fatal outcome	
Acute lung abscess	1/3	2/2	-	3/5
Gangrenous lung abscess	4/5	2/1	-	6/6
Lung gangrene	3/4	1/-	-	4/4
Total	8/12	5/3	-	13/15

Note: patients in group I / patients in group II

Arterial hypoxemia relieved significantly faster in patients of group II. In patients of this group, already from day 3 after EGC, the coefficient ΔP (a-v) O2 significantly increased, which indicated more active tissue metabolism with increased oxygen extraction from arterial blood (Table 7).

Extracorporeal hemocorrection had a beneficial effect on the severity of systemic and tissue hypoxia.

In the postoperative period, patients of group II continued to receive thiotriazoline as part of basic intensive care. The total duration of drug administration was 7–10 days.

In the future, in patients in whose complex therapy thiotriazoline was included, a more favorable course of the disease was noted, which was reflected in the results of treatment (Table 8).

Conclusions.

Thus, in patients receiving thiotriazoline (in pre-perfusion preparation and as part of intensive treatment of the post-perfusion period), a more favorable course of the disease was noted (rapid positive dynamics of indicators of systemic inflammatory response, toxemia, and indicators of oxygen homeostasis, compared with patients receiving traditional therapy), which helped to reduce the time and improve the quality of treatment of patients.

The revealed changes indicate the advisability of using thiotriavzoline as part of preperfusion preparation and the basic program of complex treatment in patients with acute infectious lung destruction in the late period of TB.

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