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Article name: **Влияние артрофоона и СКЭНАР-терапии на показатели ПОЛ и антиоксидантной системы крови больных перитонитом в послеоперационном периоде**

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Summary: Administration of artrofoon in combination with SCENAR therapy to patients with localized suppurative peritonitis in the postoperative period considerably reduced plasma MDA level, stabilized ceruloplasmin activity, and increased catalase activity in erythrocytes compared to the corresponding parameters in patients receiving standard treatment in combination with SCENAR therapy.

Effect of Artrofoon and SCENAR Therapy on Parameters of LPO and Antioxidant System of the Blood in Patients with Peritonitis in Postoperative Period

Pronounced endogenous intoxication accompanying suppurative peritonitis (SP), mixed-type hypoxia, and hypovolemia lead to significant activation of free-radical LPO processes, which becomes a leading component in the pathogenesis of cell alteration [6,7]. The course of the inflammatory process is interrelated with the state of plasma membranes, which undergo destructive changes [8,12]. Destruction of membranes under the effect of endogenous and exogenous factors triggers pathochemical processes affecting the functions of various systems and the whole organism [3]. LPO processes play a role of a molecular trigger mechanism during the formation of adaptation mechanisms; activation of these processes is a universal response of the organism to extreme exposures. Antioxidant system regulates the intensity of LPO processes in the blood and cells and the concentration of endogenous lipoperoxides [1,18].

Correction of LPO is an essential, but little studied method of SP treatment. Apart from drug therapy, other methods of LPO correction are known. For instance, information influence by means of bioregulated low-frequency pulse electrotherapy, in particular, with self-controllable energoneuroadaptive regulator SCE-NAR [11] is a promising method [11].

Acute suppurative infection is accompanied by enhanced production of cytokines and LPO activation. TNF-α, one of the most active mediators, triggers a cascade of proinflammatory cytokines. It activates macrophages and interferes the process of respiratory burst in phagocytes. Addition of artrofoon, a preparation containing antibodies to TNF-α in ultralow doses, to complex therapy of patients with SP is advisable against the background of excessive inflammatory process. We found no published data on the use of artrofoon in SP, administration of this preparation in short courses, and its effect on the parameters of LPO and antioxidant system.

Here we studied the effect of artrofoon as a component of complex therapy with the use of SCENAR on parameters of LPO in the blood and erythrocytes and activity of the main antioxidant enzymes in patients with suppurative appendicular peritonitis in the postoperative period.

MATERIALS AND METHODS

We examined 99 patients (76 men and 23 women, age 17-74 years) operated for acute appendicitis complicated by localized SP. The diagnosis was made on the basis of clinical examination and biochemical blood tests. The patients were randomly divided into 3 groups. During the postoperative period, group 1 patients (n=42) received standard therapy; in group 2 patients (n=38) this standard treatment was supplemented with SCENAR-therapy. Group 3 patients (n=19) received artrofoon (1 sublingual tablet 4 times a day, every 6 h) in addition to complex therapy prescribed to group 2 patients. Artrofoon treatment was performed until elimination of fever (5 days on average) and attaining clinical improvement. SCENAR procedure consisted in stimulation of the skin on palms (thenar and hypo thenar) and feet (zone under fingers regio plantaris pedis) with remote electrodes (12 cm2) in the F-Sw mode (10 min for each zone) followed by treatment of the skin projection of the liver (including F13 и F14 points of the liver meridian). The strength of stimulation was chosen individually [11].

The control group comprised 38 age-matched healthy individuals.

Blood plasma, 1% hemolysate, and erythrocyte suspension were analyzed. Chemiluminescent (CL) analysis in the H2O2–luminol system [13] was used; the intensity of LPO was evaluated by accumulation of molecular products in chloroform extract of lipids [16]; the content of diene conjugates (DC) [9], MDA [10], and Schiff bases [15] and activity of SOD [17], catalase [5], and ceruloplasmin by the method of Re-vin with modifications [4] were measured. The studies were carried out in biochemical laboratory of Research Institute of Biology, South Federal University, on days 3-5 after surgery (initial data) and on day 5 after the start of complex treatment.

The data were processed statistically using Student t test.

RESULTS

The initial biochemical parameters in 3 groups reflected enhanced generation of reactive oxygen species, potent LPO inductors (Table 1). In all groups, the amplitude of fast fl ash, parameter of induced CL, surpassed the normal value by 29.9-42.6%. The total CL yield reflecting the rate of utilization of lipid radicals due to their interaction with other lipid radicals or endogenous antioxidants was significantly elevated only in groups 1 and 2.

The plasma level of DC in all groups before the start of treatment was significantly elevated by 43.4-55.1%. In groups 1-3, the content of MDA was significantly increased by 60.8, 82.8, and 55.1%, respectively, and the content of Schiff bases was increased by 51.5, 61.6, 24.2%, respectively.

MDA-type LPO products are bifunctional cross-linking agents inducing the formation of high-molecular weight end-products, Schiff bases. This leads to considerable and sometimes irreversible changes in the structure and function of membranes.

More pronounced changes in LPO intensity were observed in erythrocytes (Table 2). In contrast to blood plasma, where the initial scatter of data was observed, parameters of erythrocytic LPO in all groups underwent pa rallel changes. The plasma level of DC in all groups before the start of treatment was significantly elevated by 123.6, 112.8, and 133.2%. MDA content surpassed the control by 53.1, 48.2, and 53.1%, respectively, and the content of Schiff bases was increased by 26.3, 22.8, 28%, respectively. Excessive peroxidation considerably modulated cell functions [2].

In patients with SP transferred from intensive care unit to surgical ward, the generation of reactive oxygen forms possessing a wide range of cytotoxic effects remained elevated, the intensity of LPO considerably increased. LPO induced a vicious circle of disturbances in cell bioenergetics and homeostasis, which, if not broken, leads to cell disintegration.

The intensity of free-radical oxidation reactions depends on the state of the antioxidant system in tissues and biological fluids, e.g. blood plasma. In our study, components modulating the mechanisms of sanogenesis were added to the complex treatment of patients of groups 2 and 3.

Table 1.

Intensity of H_2O_2-Luminol-Induced CL, LPO, and Activity of Antioxidant Enzymes in Blood

Parameter	Control	Group 1		Group 2		Group 3	
		initial value	after 5 days	initial value	after 5 days	initial value	after 5 days
Fast CL flash amplitude, mm	43.8±4.1	62.5±11.0	71.9±7.5*	60.9±7.5*	53.5±4.2	56.9±4.1*	47.4±8.3
CL yield, $x10^4$, rel. units	84.1±2.1	120.0±30.6	164.5±21.3*	136.1±13.3*	153.3±33.7*	93.7±11.9	83.7±9.9
DC, nmol/ml	14.5±1.8	20.8±1.0*	20.3±1.6*	21.1±1.4*	18.2±0.5*$^+$	22.5±1.1*	19.2±2.6
MDA, nmol/ml	25.0±1.8	40.2±2.9*	47.2±2.9*	45.7±2.2*	39.6±2.0*$^+$	36.8±2.8*	29.7±2.2^{+o}
Schiff bases, rel. units/ml	0.99±0.05	1.5±0.1*	1.30±0.07*	1.6±0.2*	1.3±0.1*	1.23±0.09*	1.34±0.08*
Ceruloplasmin, μmol/liter	1.2±0.1	1.4±0.1*	0.90±0.08*$^+$	1.1±0.1	1.0±0.1	1.6±0.1*	1.5±0.1*o
Catalase, nmol H_2O_2/ml	14.9±0.9	11.8±1.1*	14.5±2.0	12.4±1.7	17.2±3.2	10.90±1.81*	15.4±0.40$^+$

Note. Here and in Table 2: $p<0.05$ compared to:*control, $^+$initial value, ^{o}group 2.

Table 2.

LPO Intensity and Activity of Antioxidant Enzymes in Erythrocytes in the Studied Groups (*M±m*)

Parameter	Control	Group 1		Group 2		Group 3	
		initial value	after 5 days	initial value	after 5 days	initial value	after 5 days
DC, nmol/mg Hb	7.16±0.72	16.01±0.49*	14.43±0.48*$^+$	15.24±0.72*	10.22±0.81*$^+$	16.7±1.1*	10.30±1.52$^+$
MDA, nmol/mg Hb	3.46±0.36	5.32±0.31*	4.53±0.24$^+$	5.13±0.31*	4.21±0.19$^+$	5.30±0.31*	3.90±0.20$^+$
Schiff bases, rel. units/mg Hb	0.57±0.05	0.72±0.04*	0.60±0.06	0.7±0.1	0.59±0.04	0.73±0.06*	0.60±0.03$^+$
SOD, U/mg Hb	3.35±0.11	3.10±0.23	3.41±0.15	2.80±0.21*	3.24±0.21	3.22±0.20	3.54±0.12
Catalase, nmol H_2O_2/mg Hb	26.40±1.07	31.60±3.28	31.10±1.34*	34.5±3.9*	30.80±1.82*	34.90±4.30	37.60±3.90*o

Standard therapy (group 1) did not eliminate oxidative stress in blood plasma on day 5. CK further increased to 64.1% compared to the normal and to 15% compared to initial value. In groups 2 and 3, this parameter tended to decrease by 12.1 and 16.6%, respectively. The concentrations of DC and MDA also decreased in groups 2 and 3 (in group 1 these parameters did not decrease). Significant contribution to these changes was made by artrofoon: on day 5, the content of MDA in group 3 only insignificantly surpassed the control level (by 18.8%)

This decrease was accompanied by significant changes in activity of antioxidant enzymes. In group 1, initial ceruloplasmin activity was increased by 16.6%, but after 5 days this parameter significantly decreased (-25%). In group 3, this activity was initially high (+33.3%) and remained elevated at later terms (+25%). Increased activity of ceruloplasmin is a defense and compensatory reaction, because it regulates LPO intensity by entrapping both superoxide anion radical and

hypochlorite; moreover, ceruloplasmin ex hibits ferroxidase activity and reduces the level of Fe2+. Catalase activity in groups 2 and 3 returned to normal and surpassed it, which was not observed in group 1.

Acute process during the development of localized ap pendicular SP against the background of satisfactory general health status determines more rapid recovery of the status of LPO and antioxidant system. In all groups, the content of MDA and Schiff bases significantly decreased (Table 2). DC production remained high in group 1 and decreased by 32.9 and 38.3% in groups 2 and 3, respectively.

SOD activity increased in all groups. In group 3, the pronounced increase in catalase activity made a great contribution into the effect of treatment. In groups 1 and 2, catalase activity decreased by day 5, while in group 3 it significantly increased by 7.7% compared to baseline and 22.1% compared to group 2 ($p<0.05$).

Thus, postoperation period of localized appendicular SP was characterized by enhanced generation of reactive oxygen species, which was seen from consider ably increased parameters of induced CL and elevated content of molecular LPO products in the plasma and erythrocytes; catalase activity in the plasma and SOD activity in erythrocytes decreased under these conditions.

Standard therapy did not eliminate the symptoms of oxidative stress, which was confirmed by high CL parameters and increased MDA content in the plasma. SCENAR therapy decreased oxidative stress by day 5 and decreased the content of DC and MDA in the plasma and erythrocytes.

The use of SCENAR therapy and artrofoon in the complex treatment reduced oxidative stress in the blood, significantly decreased plasma MDA, content, and increased plasma catalase activity. The contribution of artrofoon consisted in a significant decrease in MDA content in the plasma, maintenance of ceruloplasmin activity, and elevation of catalase activity in erythrocytes.

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