Effect of Artrofoon on Parameters of Endogenous Intoxication and Activity of Myeloperoxidase in Leukocytes from Patients with Postoperative Peritonitis

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We studied the possibility of using artrofoon in the treatment of patients with localized suppurative postoperative appendicular peritonitis. A significant inhibiting effect of the preparation on endogenous intoxication parameters was demonstrated. Inhibition of myeloperoxidase hyperactivity is considered as a possible mechanism of the therapeutic effect of artrofoon as a component of complex therapy.

Key Words: *suppurative appendicular peritonitis*; *artrofoon, endogenous intoxication; myeloperoxidase; self-controllable energoneuroadaptive regulator (SCENAR)*

Treatment of suppurative peritonitis remains an important problem due to extensive volume of surgical interventions, decrease in general reactivity of patients, and increase in the number of antibiotic-resistant strains of microorganisms [1,4,15]. The incidence of peritonitis as a complication of acute appendicitis is about 50% [12].

Intoxication plays the leading role in the pathogenesis of peritonitis. Suppurative process developing in the peritoneal cavity rapidly saturates the organism with toxins of both bacterial and non-bacterial (endogenous) origin, which is accompanied by drastic immunological shifts.

It was demonstrated that any surgical intervention is accompanied by enhanced synthesis of cytokines in response to tissue damage and bacterial contamination. Of them, TNF-α exhibits the most potent proinflammatory properties [8]. Artrofoon contains antibodies to TNF-α in ultralow doses. In light of this, it is quite reasonably to use this preparation in complex therapy of patients with supurrative appendicular peritonitis. We found no published data on the use of artrofoon in suppurative peritonitis, its administration by a short course, and its effects on parameters of endogenous intoxication and activity of leukocytic myeloperoxidase (MPO), an important element of oxygen-dependent phagocytosis [2].

The development of complex methods of therapy is an urgent problem of modern surgery. In light of this, the method of information influence by means of bioregulated low-frequency pulse electrotherapy, in particular, with self-contollable energoneuroadaptive regulator SCENAR, is a perspective approach [7,11].

Here we studied the effect of artrofoon as a component of complex therapy with the use of SCENAR on parameters of endogenous intoxication and MPO activity 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 suppurative peritonitis. The patients were randomly divided into 3 groups. During the postoperative period, group 1 patients (n=42) received complex standard antibacterial, infusion, and symptomatic therapy; in group 2 patients (n=38) this standard treatment was supplemented with SCENAR-

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therapy. Group 3 patients (n=19) received artrofoon (1 sublingual tablet 4 times a day) in addition to complex therapy prescribed to group 2 patients.

The diagnosis was made on the basis of clinical examination and biochemical blood tests. We also measured the content of medium-molecular-weight molecules (MMWM) and circulating immune complexes (CIC), which are considered as highly informative markers of endogenous intoxication in suppurative peritonitis [5, 13, 14]. The content of MMWM was measured as described previously [10] at 210, 238, 246, 254, and 280 nm.

Inflammation as a typical pathological process plays a defense role via activation of microbicidal and cytotoxic mechanisms. In light of this, we measured MPO activity in peripheral blood leukocytes as one of the major enzyme systems producing activated oxygen metabolites [6].

The control group comprised 38 age-matched healthy individuals.

Artrofoon treatment was performed until elimination of fever (5 days on average). SCENAR procedure consisted in stimulation of the skin on palms and feet with remote electrodes (12 cm^2) in the F-Sw mode (10 min for each zone) followed by treatment of the skin projection of the liver. The strength of stimulation was chosen individually [11]. The tests performed on days 3-5 after surgery were used for the analysis (initial data). The patients were then repeatedly examined 1 and 5 days after the start of complex treatment.

The data were processed statistically using Student t test.

RESULTS

Significant increase in MMWM and CIC by 1.2-2.0 times was observed in practically all patients during the postoperative period, which attested to considerable changes in the metabolic status of the organism.

Standard therapy practically did not reduce endogenous intoxication. Fractions MMWM (210) and MMWM (280) remained unchanged, fractions MMWM (238) and MMWM (254) continued to increase, and only fraction MMWM (246) significantly decreased

TABLE 1. Parameters of Endogenous Intoxication in Patients with Peritonitis ($M\pm m$)

Parameter	Control	Group 1		Group 2		Group 3	
		initial	after 5 days	initial	after 5 days	initial	after 5 days
MMWM(210), U/ml	19.5±0.8	24.6±0.9 p_1<0.001	24.70±1.06 p_1<0.001	26.5±1.1 p_1<0.001	23.1±1.2 p_1<0.02 p_2<0.05	24.5±0.7 p_1<0.001	23.0±0.2 p_1<0.02 p_2<0.05
MMWM(238), U/ml	4.50±0.41	5.6±0.6	6.70±1.09	7.2±1.3 p_1<0.05	6.2±1.1	10.0±2.4 p_1<0.05	8.2±2.4
MMWM(246), U/ml	4.6±0.4	11.70±0.62 p_1<0.001	6.90±1.13 p_2<0.001	9.9±1.4 p_1<0.001	6.4±1.1 p_2<0.05	12.5±0.5 p_1<0.001	11.0±0.4 p_1<0.001 p_2<0.02 p_3<0.001
MMWM(254), U/ml	2.3±0.2	4.70±0.61 p_1<0.001	5.20±0.72 p_1<0.001	5.8±1.2 p_1<0.01	4.6±0.8 p_1<0.01	8.7±0.7 p_1<0.001	5.8±1.5 p_1<0.01 p_2<0.05
MMWM(280), U/ml	2.4±0.3	5.40±0.31 p_1<0.001	5.30±0.17 p_1<0.001	5.2±0.3 p_1<0.001	3.7±0.2 p_1<0.001 p_2<0.001	6.4±0.8 p_1<0.01	3.9±0.4 p_1<0.01 p_2<0.01
CIC, arb. units/100 ml	106.6±9.1	182.8±16.2 p_1<0.02	147.2±15.1	232.0±29.7 p_1<0.001	150.6±21.7 p_2<0.05	171.1±22.9 p_1<0.01	102.1±15.4 p_2<0.02 p_3<0.005

Note. p_1 compared to the control, p_2 compared to initial values, p_3 compared to group 2.

by 41% compared to the initial level. CIC content decreased insignificantly and did not attain the control level by day 5.

In patients receiving SCENAR therapy in addition to standard treatment, the dynamics of these parameters was different. In group 2, the content of MMWM(210), MMWM(246), and MMWM(280) significantly decreased by 12.8, 35.3, and 28.8%, respectively, the content of CIC decreased by 35% from the initial values. The content of other MMWM fractions also decreased. These changes attest to a significant decrease in intoxication level, which correlated with clinical symptoms and blood parameters.

In group 3, metabolic homeostasis was more pronouncedly restored by day 5. A significant decrease in the content of all MMWM fractions, except MMWM(238), was noted. The content of CIC practically returned to the control.

For evaluation of artrofoon contribution into complex therapy we compared the parameters of endogenous intoxication in groups 3 and 2 on day 5 of treatment and their dynamics compared to the initial levels. In group 3 we observed a decreased in the content of 3 of 5 MMWM fractions (238, 254, and 280). The content of CIC decreased to the control level and significantly differed from that in group 2.

The initial MPO activity in blood leukocytes in group 1 patients surpassed the normal by 130.7% ($p<0.05$; Fig. 1). This parameter considerably increased after the first day of therapy and attained 150%. After 5 days, MPO activity slightly decreased by 11.3% compared to initial data.

In group 2, MPO activity on day 2 considerably increased more than 2-fold compared to the initial value. This is often clinically interpreted as aggravation of the disease. However, on day 5 MPO activity in leukocytes practically returned to initially elevated level, which also correlated with clinical symptoms.

Administration of artrofoon to group 3 patients prevented excessive MPO activation induced by SCENAR procedure after 1 day and decreased its activity after 5 days by 50.1% ($p<0.001$). This coincided with elimination of intoxication symptoms and acceleration of wound healing.

Kalf-Kalif formula for calculation of the leukocytic index of intoxication (LII) [9] is the most acceptable prognostic criterion for the development of wound infection. In all patients, blood tests revealed shifts indicating pronounced inflammation: leukocytosis with a shift towards stab neutrophils, lymphopenia, and high LII. Before treatment, LII in groups 1, 2, and 3 significantly surpassed the normal by 340, 400, and 420% (Fig. 2). After 1 day, changes in this parameter were 260, 300, and 280% in groups 1, 2, and 3, respectively. On day 5, LII in groups 1 and 2 was still above

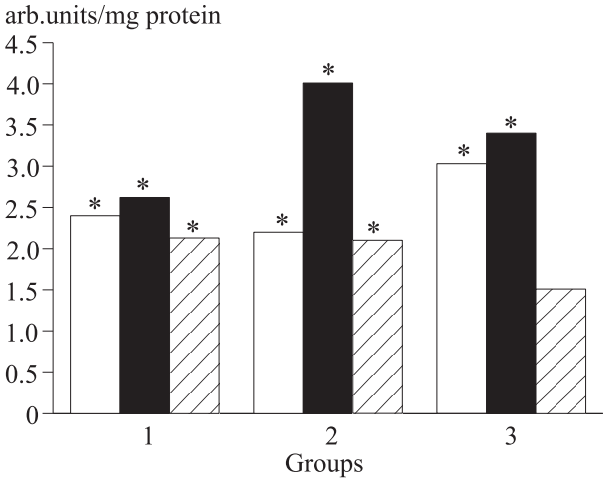

Fig. 1. Dynamics of MPO activity in groups. Here and on Fig. 2: light bars: initial data; dark bars: after 1 day; shaded bars: after 5 days. *$p<0.05$ compared to the control.

the normal by 280 and 120%, respectively. In group 3 LII decreased and was 140% of normal.

The complex positive effect of SCENAR and artrofoon manifested in not only biochemical changes, but also more rapid improvement of general patient's state and disappearance of paleness of the skin and dryness of mucosae. Body temperature returned to normal and intestinal peristalsis recovered more rapidly.

Short-term course of artrofoon considerably potentiated the effect of transcutaneous neurostimulation with SCENAR apparatus. Thus, postoperation period after localized suppurative appendicular peritonitis was characterized by increased LII and accumulation of products of impaired metabolism in the blood (MMWM fractions and CIC).

The use of SCENAR therapy and artrofoon produced a more potent biochemical sanation effect, which manifested in a decrease in endotoxicosis marker con-

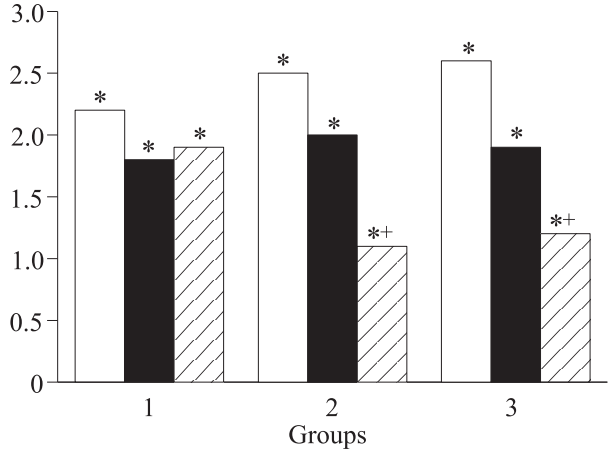

Fig. 2. Dynamics of LII in groups. $p<0.05$ compared to: *control, +initial values.

tent (MMWM and CIC) and LII; administration of artrofoon led to normalization of CIC content.

Artrofoon prevented excessive MPO activation on day 2 of treatment caused by SCENAR therapy and led to a more pronounced decrease in MPO activity by day 5 of treatment against the background of clinical improvement.

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