GENERAL PATHOLOGY AND PATHOPHYSIOLOGY

Prooxidant and Antioxidant Systems of the Blood during Experimental Bile Peritonitis

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Intensification of lipid peroxidation against the background of exhaustion of the antioxidant protective system was demonstrated in 70 rats with experimental bile peritonitis. Free radical oxidation primarily concerned free lipids and fatty acids in the plasma and to a lesser extent erythrocyte membrane lipids.

Key Words: *bile peritonitis; lipid peroxidation; antioxidant system*

Pathologies of the hepatobiliary zone occupy special place among pathological process in the abdominal cavity. Bile peritonitis is the most severe complication of these diseases. The mortality rate of patients with bile peritonitis reaches 12.4% [1,9,10].

The pathogenesis and thanatogenesis of bile peritonitis are associated with the syndrome of endogenous intoxication [2] resulting from activation of free radical oxidation and overproduction of lipid peroxidation (LPO) products [5,8].

The evolutionary antioxidant mechanisms maintain a constant level of oxidation and protect the organism from adverse effects of free radical oxidation. An imbalance between oxidation and antioxidant system is accompanied by progressive oxidative damage and development of oxidative stress.

Here we studied changes in the prooxidant and antioxidant system during experimental bile peritonitis.

MATERIALS AND METHODS

Experiments were performed on 70 male rats weighing 200-220 g.

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The animals were divided into groups. Group 1 rats (n=35) served as the control. Group 2 animals (n=35) were examined 24 h after modeling of bile peritonitis.

Experimental bile peritonitis was modeled as described elsewhere [6].

LPO intensity was estimated by measuring the contents of primary (isolated double bonds, IDB; and conjugated dienes, CD), secondary products (conjugated trienes, CT; and conjugated hydroxydienes, CHD), malonic dialdehyde (MDA), and final products (Schiff bases, SB) in the plasma and erythrocytes [3]. Antioxidant function was determined by activities of erythrocyte catalase [4], blood peroxidase [7], and plasma ceruloplasmin (CP) [3].

RESULTS

Parameters of LPO in the plasma and erythrocytes increased 24 h after the onset of bile peritonitis (Table 1). The content of IDB, CD, CT, CHD, MDA, and SB in the plasma increased by 3.1, 4.4, 2.4, 3, 2.3, and 3.1 times, respectively (p<0.05).

The content of other LPO products increased proportionally, while the concentration of CD most significantly exceeded the control level (Table 1). The

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considerable accumulation of primary LPO products (peroxides) in the plasma of animals with peritonitis was probably related to activation of arachidonic acid metabolism and intensive biosynthesis and oxidation of catecholamines under pathological conditions.

In group 2 animals the intensity of LPO in erythrocytes considerably increased: the contents of IDB, CD, CT, CHD, MDA, and SB increased by 2.2, 2.4, 2.3, 2.4, 2.3, and 2.8 times, respectively ($p<0.05$).

We should emphasize more pronounced accumulation of primary LPO products (IDB and CD) in the plasma compared to that in erythrocytes in group 2 rats and proportional accumulation of secondary and final LPO products in the plasma and erythrocytes. These findings probably attest to more early exhaustion of the plasma antioxidant system in animals with 24-h bile peritonitis.

Bearing in mind that quantitative and qualitative changes in oxidized lipids during bile peritonitis can modulate physicochemical properties of the blood, it seems important to evaluate the degree of oxidation of lipids. This parameter can be estimated by 232/220 ratio, or $K_{232/220}$ oxidation index, *i.e.* the ratio of UV absorption at 220 nm (maximum absorption of lipids) and 232 nm (maximum absorption of primary LPO products, CD) and by 440/220 ratio, or $K_{440/220}$ oxidation index (440 nm, maximum absorption of final LPO products).

Twenty-four hours after modeling of bile peritonitis $K_{232/220}$ for plasma lipids increased by 1.41 times, while $K_{440/220}$ for the plasma decreased by 1.32 times (Table 2). The rapid formation of primary LPO products in the plasma was probably associated with sharp metabolic activation developing as a part of the compensatory and adaptive reaction. Similar changes in the content of plasma lipids with different degrees of oxidation confirm accumulation of LPO products (IDB and CD).

$K_{232/220}$ and $K_{440/220}$ in erythrocytes tended to increase 24 h after modeling of bile peritonitis (compared to intact rats). However, intergroup differences were statistically insignificant ($p>0.05$). The absence of pronounced changes in the index of erythrocyte oxidation suggests that the disease is not accompanied by serious oxidative damage to erythrocytes.

It can be hypothesized that the development of bile peritonitis is accompanied by LPO activation, primarily due to plasma components.

Hydrogen peroxide is a reactive oxygen species possessing moderate oxidizing activity. This compound in high concentrations produces a cytotoxic effect. Intracellular hydrogen peroxide is inactivated by catalase and peroxidase. The catalase pathway is most effective in the presence of hydrogen peroxide in high concentrations and serves as the major mechanism protecting cells from oxidative stress. The peroxidase pathway is most effective at low concentration of hydrogen peroxide. It should be emphasized that activity of antioxidant enzymes depends on the amount of hydrogen peroxide and LPO products in the blood.

In animals with 24-h bile peritonitis blood catalase activity increased by 2.5 times compared to intact rats ($p<0.05$), which probably represent an adaptive reaction to activation of free radical processes and enhanced generation of hydrogen peroxide and peroxidation products (Table 3). However, blood peroxidase activity in rats with bile peritonitis decreased from 438 to 218 μmol/liter/min ($p<0.05$).

Compounds binding transition metals and preventing their involvement in the formation of high-reactivity hydroxyl and alkoxyl radicals (*e.g.* CP) are important components of the antioxidant system. Serum CP oxidizes Fe^{2+} to Fe^{3+} and inhibits production of hypohalous compounds.

CP is a direct reactant of acute-phase inflammation. It can be hypothesized that the concentration of CP will increase in animals 24 h after modeling of bile peritonitis. However, we revealed a significant decrease in plasma CP concentration in treated rats (37.85±3.66 *vs*. 49.79±1.66 mg/100 ml in intact animals, $p<0.05$, Table 3). These changes are probably related to complete disappearance of CP and reflect impairment of the antioxidant protection 24 h after modeling of bile peritonitis.

TABLE 1. Concentration of LPO Products 24 h after Modeling of Bile Peritonitis ($M\pm m$)

Group	IDB	CD	CT	CHD	MDA	SB
Plasma						
1	1.88±0.10	1.19±0.06	0.67±0.05	0.51±0.07	2.36±0.28	0.33±0.03
2	5.80±0.38*	5.18±0.17*	1.61±0.09*	1.54±0.14*	5.54±0.41*	1.03±0.12*
Erythrocytes						
1	3.48±0.34	2.95±0.40	1.86±0.13	0.91±0.08	11.84±0.44	2.46±0.22
2	7.86±0.33*	7.11±0.50*	4.30±0.48*	2.19±0.12*	27.0±0.83*	6.95±0.20*

Note. Here and in Table 3: *$p<0.05$ compared to group 1.

TABLE 2. Indexes of Lipid Oxidation in Animals 24 h after Modeling of Bile Peritonitis (*M*±*m*)

Index	Group 1		Group 2	
	plasma	erythrocytes	plasma	erythrocytes
$K_{232/220}$	0.63	0.85	0.89	0.93
$K_{440/220}$	1.26	3.40	0.96	3.52

TABLE 3. Indexes of Oxidation of Plasma and Erythrocyte Lipids 24 h after Modeling of Bile Peritonitis (*M*±*m*)

Group	Blood catalase, mmol H_2O_2/ 10^9 er/min	Blood peroxidase, μmol/liter/min	CP, mg/100 ml
1	4.76±0.36	438.10±29.95	49.79±1.66
2	11.77±0.50*	218.00±16.65*	37.58±3.66*

Thus, activation of lipid peroxidation and exhaustion of the antioxidant protective system occurred 24 h after modeling of bile peritonitis. Free radical oxidation primarily concerned free lipids and fatty acids in the plasma and to a lesser extent erythrocyte membrane lipids. The content of primary LPO products increased most significantly under these conditions.

These data indicate that postoperative therapy should include nonspecific detoxification treatment and administration of preparations inhibiting free radical oxidation of lipids.

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