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Changes in the Blood Lipid-Transporting System in Rats over the First Day of Experimental Peritonitis

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Changes in the lipid spectrum of blood plasma and composition of high-density lipoproteins in outbred albino rats were studied during early stages of experimental peritonitis. We revealed an increase in lecithin:cholesterol acyltransferase activity, activation of lipolytic production of high-density lipoproteins from very-low-density lipoproteins, and substitution of arachidonic acid in cholesterol esters for dihomo-γ-linoleic acid 7 h after induction of peritonitis. After 24 h the protein composition and functional activity of high-density lipoproteins was modified and the amount of saturated fatty acids in cholesterol esters increased.

Key Words: *high-density lipoproteins; phospholipids; cholesterol; fatty acids*

Peritonitis is a severe complication of abdominal surgery. The mortality rate of patients with generalized purulent peritonitis reaches 70-100%. Therefore, studies of the pathogenesis and etiology of peritonitis are of considerable importance. Our previous experiments revealed changes developing 4 h after induction of experimental peritonitis [1]: increased concentration of high-density lipoprotein (HDL) cholesterol resulting from activation of lecithin:cholesterol acyltransferase (LCAT), enhanced lipolytic production of HDL, and accumulation of dihomo-γ-linoleic acid in cholesterol esters. Dihomo-γ-linoleic acid is a precursor of class 1 prostaglandins. These compounds exhibit lower proinflammatory activity compared to prostaglandins synthesized from arachidonic acid [4]. Since cholesterol esters and LCAT are involved in the transport of polyunsaturated fatty acids in tissues [2], it was interesting to study changes in these parameters during experimental peritonitis.

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MATERIALS AND METHODS

Peritonitis was modeled by single intraperitoneal injection of *E. coli* (strain O-26, 4×10^9 microbial cells per animal) to 15 male outbred albino rats weighing 180-200 g. The control group included 12 intact rats. The animals were decapitated 7 and 24 h after administration of *E. coli* cells. The blood was collected into tubes with citrate. The total content of plasma cholesterol, concentration of HDL cholesterol and total HDL phospholipids, spectrum of HDL phospholipids (lysophosphatides, sphingomyelins, phosphatidylcholines, phosphatidylethanolamines, and polyglycerol phosphatides), LCAT activity, spectrum of fatty acids in cholesterol esters, and content of HDL protein were assayed [1]. The results were analyzed by Student's *t* test.

RESULTS

The total cholesterol concentration increased 7 h after induction of peritonitis (p=0.008, Table 1), which was related to an increase in the content of HDL cholesterol (p=0.018) and low-density lipoprotein (LDL)

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TABLE 1. Lipid Spectrum of Blood Plasma (*M*±*m*)

Parameter		Intact rats (*n*=12)	Treated rats	
			after 7 h (*n*=9)	after 24 h (*n*=9)
TG, mmol/liter		0.86±0.06	0.63±0.04*	0.99±0.08^{+}
Cholesterol, mmol/liter	total	2.24±0.09	2.59±0.05*	2.58±0.12*
	LDL	0.39±0.07	0.65±0.05*	0.64±0.04*
	VLDL	0.39±0.03	0.29±0.02*	0.45±0.03^{+}
	HDL	1.47±0.06	1.65±0.18*	1.48±0.03^{+}
LCAT activity, μmol/liter^{-1}/h^{-1}		3.77±0.62	21.96±3.90*	10.57±3.50*^{x}
Total HDL phospholipids, mmol/liter		3.42±0.23	2.70±0.09*	2.98±0.35
Phospholipid spectrum, %	LP	33.12±0.87	35.30±0.85^{x}	29.31±1.67*$^{+}$
	SPM	11.74±0.61	12.90±0.83	13.44±0,65^{x}
	PC	44.22±0.81	40.10±0.52*	45.32±1.01^{+}
	PGP	6.38±0.37	7.22±0.66	6.10±1.09
	PEA	5.21±0.44	3.88±0.26*	5.75±0.84^{x}
Total protein, g/liter		78.18±2.35	74.11±2.90	70.24±0.84*

Note. LP, lysophosphatides; SPM, sphingomyelins; PEA, phosphatidylethanolamines. Here and in Table 2: significant differences: *compared to intact animals; $^{+}$compared to 7 h after induction of peritonitis. ^{x}Tendency.

cholesterol (p=0.02). It should be emphasized that the content of triacylglyceride (TG) and very-low-density lipoprotein (VLDL) cholesterol decreased under these conditions (p=0.018). The observed changes can be related to activation of lipoprotein lipase. This enzyme satisfies energy requirements in tissues and provides lipolytic transformation of TG-rich lipoproteins into HDL. The concentration of HDL phosphatidylcholines (PC) and polyglycerol phosphatides (PGP) decreased (p=0.0009 and p=0.038, respectively).

The decrease in the concentration of PGP was probably associated with consumption of these phospholipids for the formation of mitochondrial apparatus and determine the decrease in the concentration of total HDL phospholipids (p=0.04). The decrease in PC content can be related to high LCAT activity (p=0.0008). This assumption is confirmed by a tendency toward the increase in lysophosphatidylcholine content (p=0.09). Activation of LCAT also contributed into the increase in HDL cholesterol concentration. In the spectrum of fatty acids in cholesterol esters the contents of myristic (C14:0, p=0.012), linoleic (C18:2, p=0.03), and dihomo-γ-linoleic acids (C20:3, p=0.004) increased (Table 2), while the content of oleic acid (C18:1, p=0.03) decreased. Only trace amounts of arachidonic acid (C20:4) were revealed. Changes in the fatty acid spectrum of cholesterol esters can result from a deficiency of polyunsaturated fatty acids developing after activation of lipid peroxidation (LPO) and production of ω9-fatty acids. The decrease in Δ^5-desaturase activity contributes to inhibition of arachidonic acid production from γ-linoleic acid. The substitution of arachidonic acid with dihomo-γ-linoleic acid decreases the severity of inflammation via production of class 1 prostanoids.

The concentration of total plasma cholesterol remained high 24 h after induction of peritonitis (p=0.033), which was related to the increase in LDL cholesterol content (p=0.018). The concentration of HDL cholesterol did not differ in intact and treated rats. However, HDL cholesterol content in this period was lower than 7 h after treatment (p=0.002). These changes were probably related to inhibition of lipolytic modification of TG-rich lipoproteins. The contents of TG and VLDL cholesterol 24 h after the induction of peritonitis were lower than 7 h after treatment (p=0.002). LCAT activity in treated rats remained higher than in intact animals (p=0.048), but tended to decrease compared to the level observed 7 h after the induction of peritonitis (p=0.09). It was probably associated with accumulation of LCAT inhibitor sphingomyelin in HDL (p=0.08) [3]. Inhibition of lipolysis and decrease in LCAT activity led to accumulation of PC and PGP (p=0.0004 and p=0.05, respectively, compared to 7 h after treatment). We also observed a decrease in HDL protein content (p=0.01).

Our experiments demonstrated a decrease in the content of saturated fatty acids in HDL cholesterol esters, including myristic (C14:0, p=0.02), palmitic (C16:0, p=0.026), heptadecanoic (C17:0, p=0.014), and stearic acids (C18:0, p=0.03, Table 2). The content of dihomo-γ-linoleic acid (C20:3) significantly decreased (p=0.02), while the content of arachidonic acid slightly increased 24 h after induction of peritonitis,

TABLE 2. Fatty Acid Spectrum of HDL Cholesterol Esters (*M*±*m*)

Fatty acid	Intact rats (*n*=5)	Treated rats	
		after 7 h (*n*=5)	after 24 h (*n*=5)
14:0	15.40±1.41	27.07±2.30*	29.4±3.6*
15:0	1.04±0.28	0.38±0.10	Trace amounts
16:0	50.04±3.00	44.46±2.97	56.03±1.61+
17:0	0.82±0.17	0.68±0.15	3.78±0.69*+
17:1	0.73±0.11	0.78±0.11	Trace amounts
18:0	5.60±0.85	5.49±0.88	10.68±1.29*+
18:1	8.29±0.61	5.95±0.40*	Trace amounts
18:2	0.66±0.16	3.40±0.69*	Trace amounts
20:3	0.020±0.002	11.73±1.98*	0.040±0.009*+
20:4	17.35±2.30	Trace amounts	0.029±0.004*

but remained below the baseline level (p=0.001). We found only trace amounts of oleic (C18:1) and linoleic acids (C18:2). These changes can be explained by enhanced production of saturated fatty acids more resistant to free radical oxidation, deficiency of exogenous (essential) fatty acids, and reduced generation of endogenous polyunsaturated fatty acids.

Our study showed that the increase in total plasma cholesterol over the first 7 h after induction of peritonitis is mainly determined by accumulation of HDL cholesterol due to lipolytic modification of VLDL and LCAT activation. A deficiency of polyunsaturated fatty acids was compensated by increased production of ω9-fatty acids and accumulation of dihomo-γ-linoleic acid. The decrease in the severity of inflammation is mediated by production of class 1 prostanoids. Changes in the fatty acid spectrum of cholesterol esters 24 h after induction of peritonitis manifested in increased content of saturated fatty acids, which resulted from inhibition of endogenous polyunsaturated fatty acid production. It is followed by suppression of LPO and increase in the availability of cell energy substrates.

REFERENCES

1. S. S. Osochuk, *Byull. Eksp. Biol. Med.*, **134**, No. 8, 169-171 (2002).
2. V. N. Titov, *Klin. Lab. Diagnost.*, No. 12, 3-9 (2000).
3. A. Jonas, *Biochim. Biophys. Acta*, **1529**, No. 1-3, 245-256 (2000).
4. L. Zhou and A. Nilsson, *J. Lipid Res.*, **42**, No. 10, 1521-1542 (2001).