MORPHOLOGY AND PATHOMORPHOLOGY

Comparative Morphofunctional Study of Liver Acini in Peritonitis of Different Origin

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Structural and metabolic characteristics of liver acini are studied in the peritonitis patients. In peritonitis, changes in the activities of hepatocyte dehydrogenases in different acinus zones depend on its causes. The entry of gram-negative bacteria lipopolysaccharides into portal blood flow and liver is an important factor in the pathogenesis of progressing hepatic failure.

Key Words: *liver acinus; dehydrogenases; peritonitis*

The efficacy of treatment of patients with peritonitis is determined by timely surgery to eliminate the cause of peritonitis and to correct progressing poly-organ failure [7]. Restoration of the morphology and function of the liver, the first barrier organ preventing dissemination of intoxication in peritonitis [8,10], is an important therapeutic measure.

We compared the morphology and function of liver acini in patients with peritonitis of different genesis.

MATERIALS AND METHODS

Material was collected during 30 early autopsies from patients with peritonitis (16 women and 14 men aged 33-87 years). All cases were divided into 4 groups according to microbiological characteristics of exudation [4,9]. Group 1 included 5 patients with peritonitis complicating the course of gangrenous cholecystitis (four patients) or resulted from perforation of chronic gastroduodenal ulcer (one patient). Group 2 included 14 patients with peritonitis complicating diseases of the small intestine: gangrene resultant from acute thrombosis of mesenteric arteries (eight patients), adhesive ileus (three patients), and incarcerated hernias (three patients). Group 3 included patients with peritonitis which resulted from perforation of the sigmoid colon (three pa-tients) or was a complication of acute appendicitis (two patients). Group 4 consisted of 6 patients with pancreonecrosis complicated by peritonitis. Diffuse fibrinous purulent peritonitis was observed in all groups. Control group included 6 early forensic medical autopsies (4 men and 2 women aged 42-71 years): 4 sudden deaths and 2 traumas incompatible with life.

Autopsy was carried out 45-90 min after death had been certified. Fragments of the right lobe of the liver were frozen and stored in liquid nitrogen. The activities of succinate, malate, isocitrate, glutamate, 3-hydroxybutyrate, glucose-6-phosphate dehydrogenases and NAD and NADP diaphoreses were detected in cryostate sections by histoenzymatic methods [6]. Enzyme activities were measured in the first and third zones of liver acinus with Microvideomat TV image analyzer (Opton) controlled by a Wang 720c computer using software for photometric analysis of histological preparations [3]. The periportal-periventricular gradient of enzyme activities in the acinus (K) was calculated. Paraffin sections of liver tissue were stained with hematoxylin and eosin.

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Digital material was processed using the methods of parameterical and nonparametrical statistics. The index of hepatocyte morphology and function was calculated using multifactorial analysis.

RESULTS

Microscopic examination of liver preparations showed pronounced circulatory disorders in all groups: plethoric sinusoids, leukostasis, extended Disse's spaces, and small hemorrhagic foci more pronounced in peritonitis resulting from perforation of the large intestine. Protein and fatty dystrophy and monocellular, centrolobular, and triangular necroses of hepatocytes were observed.

Histophotometric analysis of dehydrogenase activities revealed structural and metabolic heterogeneity of hepatocytes in peritonitis of different origin (Table 1). The activity of glutamate dehydrogenase, which characterizes the protein and amino acid metabolism, was markedly decreased. The lowest activity was observed in the pancreonecrosis group: 26.6% of the mean normal level for the acinus, which was apparently due to the synergic effect of pronounced intoxication and hypoxia. The activity of glucose-6-phosphate dehydrogenase, a marker of pentose phosphate shunt of glucose and citric acid enzymes oxidation, was decreased. Changes in the Krebs' cycle enzymes were as follows: activities of succinate and isocitrate dehydrogenases decreased in the periventricular zones in all groups, while that of malate dehydrogenase decreased in the periportal areas of the acini. Suppression of glycolysis, as evidenced by low activity of lactate dehydrogenase, is another indicator of endotoxicosis. The decrease in lactate dehydrogenase activity in the acini in different groups was as follows: in group 1 the enzyme activity decreased in periventricular zones (by 17.8% *vs.* the control, $p<0.05$), in groups 3 and 4 in the periportal areas (by 25.2 and 22.3%, respectively, $p<0.05$), and in group 2 in all areas similarly (by 17% in the first zone and by 16.9 in the third, $p<0.05$). Low values of NAD and NADP diaphorase activities also indicate the suppression of energy production.

The resultant index of hepatocyte morphology and function objectively shows the extent of damage to the liver acini in the studied groups (Fig. 1). The minimal values and, consequently, the greatest injury to liver tissue, are observed in pancreonecrosis and peritonitis resulting from the large intestine perforation. In all groups the indices of the hepatocyte morphology and function are the lowest in the periventricular zones of acini, which corresponds to predominant localization of cellular dystrophy and necrosis.

Our results indicate that the liver damage is more pronounced in peritonitis caused by perforation of the large intestine. This may be due to the entry of numerous bacterial endotoxins released from destroyed bacterial cells into the abdominal cavity and portal blood flow. It was reported that

TABLE 1. Hepatocyte Dehydrogenase Activities in Acinus Zones 1 and 3 in Peritonitis (*M*±*m*, Arb. Units)

Group	Acinus zone	Succinate DH	Malate DH	Isocitrate DH	Lactate DH	3-Hydroxy-butyrate DH	Gluta-mate DH	Glucose-6-phos-phate DH	NAD	NADP
Control	1	547±15	606±20	512±23	770±10	497±13	511±13	430±18	678±18	678±15
	3	462±13	470±16	600±19	669±19	604±17	607±23	516±13	779±18	803±13
	K	1.18	1.29	0.85	1.15	0.82	0.84	0.83	0.87	0.84
1	1	263±12	245±12	247±12	672±21	229±10	220±11	384±14	522±14	521±14
	3	219±12	198±11	201±10	550±21	173±11	196±12	316±14	394±12	463±12
	K	1.2	1.24	1.23	1.22	1.32	1.12	1.22	1.32	1.13
2	1	244±11	239±12	243±12	639±19	216±12	217±12	379±14	517±16	523±15
	3	183±10	192±11	198±10	556±20	169±11	183±11	308±13	389±12	448±12
	K	1.33	1.24	1.23	1.15	1.28	1.19	1.23	1.33	1.17
3	1	214±13	204±10	221±13	576±18	179±11	173±10	349±14	509±14	509±14
	3	182±10	174±10	184±10	543±19	154±10	154±12	298±12	362±11	447±12
	K	1.18	1.17	1.2	1.06	1.16	1.12	1.17	1.41	1.14
4	1	210±14	206±10	226±12	598±18	183±13	168±13	341±15	502±13	493±13
	3	168±11	171±9	183±10	531±19	137±9	151±14	272±11	364±11	439±12
	K	1.25	1.2	1.23	1.13	1.34	1.11	1.25	1.38	1.12

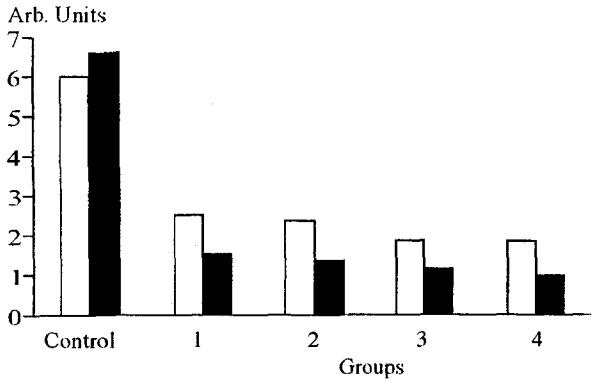

Fig. 1. The index of hepatocyte morphology and function of the first (light bars) and third (dark bars) acinus zones in peritonitis.

portal and systemic endotoxemia (with predominantly gram-negative microflora) occurs in all patients with peritonitis; its main sourse is the intestine, but not the abdominal cavity [1]. Endotoxin (lipopolysaccharide of the external wall of gram-negative bacteria), particularly together with gram-positive microflora, directly and indirectly affects the liver [2,14]. The presence of the endotoxin in subcellular hepatocyte structures and Kupffer's cells several minutes after intravenous injection confirmed the immediate effect of endotoxin [12,15]. Indirect damage to the liver by endotoxin is mediated by activation of neutrophilic polymorphonuclear leukocytes and macrophages. Low doses of endotoxin result in leukocyte adhesion in the periportal zones of the liver [11], while high doses lead to the involvement of the periventricular acinus zones, which was noted in microscopic examination of preparations. Activation of neutrophilic polymorphonuclear leukocytes (particularly in endotoxin shock) [13] results in pronounced damage to hepatocytes. Macrophages reacting with lipopolysaccharides release numerous transmitters, cytokines, and oxygen radicals, which trigger a cascade of pathological reactions leading to polyorgan failure. It is noteworthy that three zones of acini were severely damaged in all studied patients; the main detoxicating hepatocyte systems are localized in these zones [5]. This is probably the cause of generalization of intoxication and polyorgan failure in patients with peritonitis.

Thus, the detected structural and metabolic injuries to liver acini reflect the specific features of morpho- and pathogenesis of hepatic failure developing in peritonitis. The release of gram-negative bacterial lipopolysaccharides into the portal blood flow and liver is an important pathogenic factor.

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