Structural and Metabolic Characteristic of Nephrocytes during Peritonitis of Various Genesis

O. D. Mishnev, I. O. Tin'kova, T. S. Serdobintseva, and A. I. Shchegolev

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Structural and metabolic changes in nephrocytes during peritonitis were studied on early autopsy material. Unspecific morphological changes in the kidneys were presented by circulatory disturbances and damage to the tubular epithelium. The changes in dehydrogenase activity in nephrocytes of the proximal and distal tubules depended on the cause of peritonitis.

Key Words: *nephrocytes; dehydrogenases; peritonitis*

Despite significant progress in surgery and intensive therapy, treatment of general purulent peritonitis remains an actual problem, because peritonitis is a major cause of mortality associated with surgical diseases and abdominal trauma.

The general state of patients with general peritonitis largely depends on impairment of renal function and acute renal insufficiency. However, published data on morphofunctional state of the kidneys were obtained either on animal models of peritonitis or on autopsy material probably changed due to autolysis and postmortem blood redistribution. Structural and metabolic examination of early autopsy specimens of is a perspective method of pathological anatomy [3,4].

The purpose of the present study was comparative structural and metabolic examination of the kidneys in patients with peritonitis of various genesis.

MATERIALS AND METHODS

The study was based on 30 early autopsy specimens obtained from 14 men and 16 women aged 33-87 died of peritonitis. All cases were divided into 3 groups [7,9]. Group I included peritonitis due to pathology of the small intestine (gangrene of the small intestine caused by acute thrombosis of mesenteric arteries, n=8; adhesive intestinal obstruction, n=3; incarcerated hernia, n=3). Group II included peritonitis cased by sigma perforation (n=3) or complication of acute appendicitis (n=2). Group III (n=6) included cases of pancreonecrosis complicated by peritonitis. Control group included 6 early forensic autopsies (4 men and 2 women aged 42-71), of them 4 cases of acute cardiac death and 2 cases of life-incompatible trauma). The autopsy was performed 45-90 min after death. Histology was performed on 5-μ paraffin sections. The sections were stained with hematoxylin and eosin, elastic fibers and fibrin were visualized with Weigert resorcin fuchsin and by the method of N. Z. Slinchenko, respectively, amylase activity was evaluated by the method of Mac-Manus using periodic acid-Schiff reaction.

Histoenzyme assay was performed on cryostat sections. Succinate dehydrogenase (SDH), lactate dehydrogenase (LDH), and NAD- and NADPH-diaphorase activities were measured. Quantitative evaluation of enzyme activity in the proximal, distal, and collecting tubules was performed using a Mekos TV image analysis system. The results were processed using methods of parametric and nonparametric statistics.

RESULTS

Disturbances in microcirculation and damages to renal glomeruli and tubules were revealed in all patients

Department of Pathological Anatomy, Therapeutic Faculty of the Russian State Medical University, Moscow

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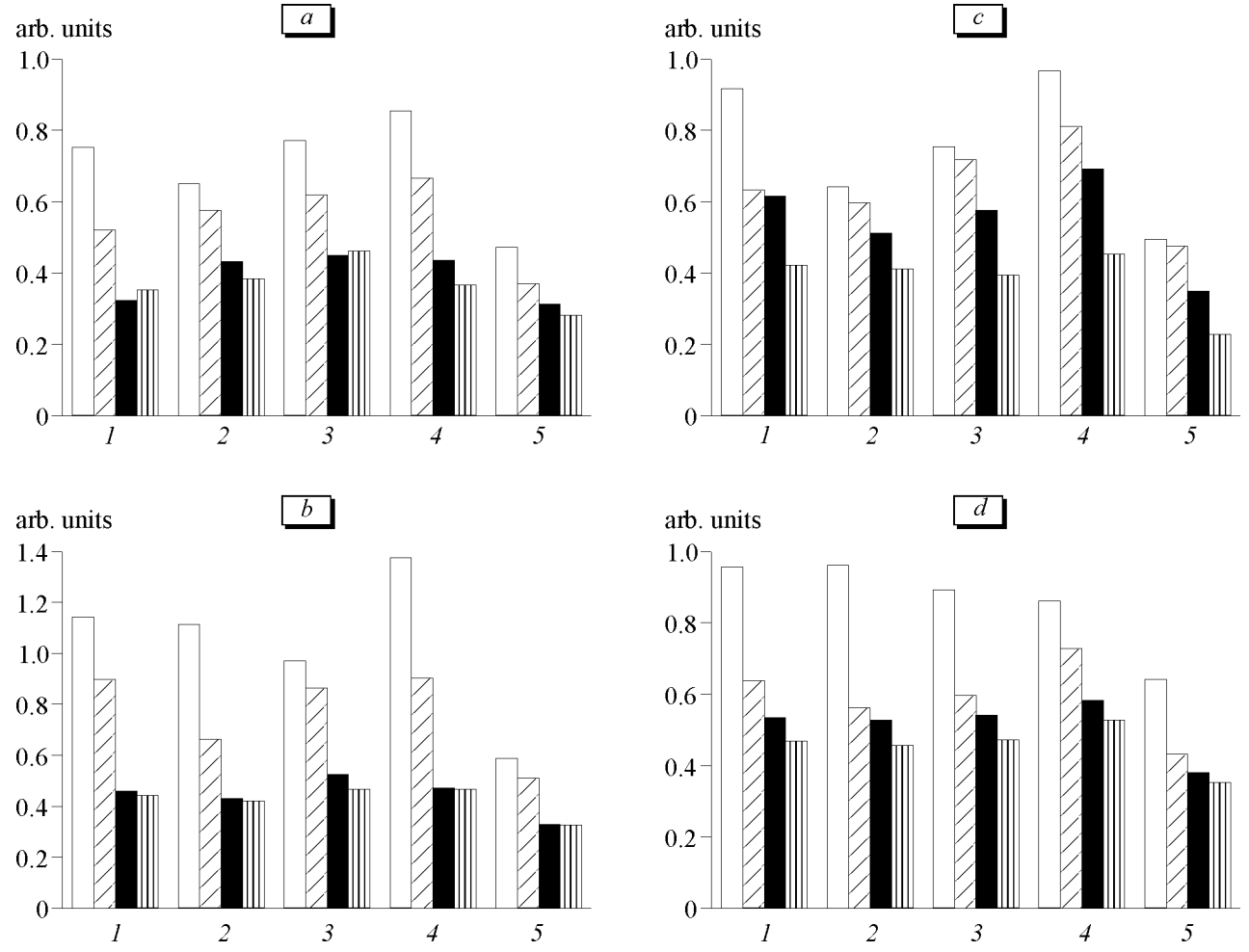

Fig. 1. Activity of SDH (*a*), LDH (*b*), NAD (*c*), and NADPH (*d*) in the kidneys of patients with peritonitis. Proximal tubules: *1*) convoluted, *2*) straight; distal tubules: *3*) straight, *4*) convoluted; *5*) collecting tubule. Open bars: control, oblique hatching: group I, dark bars: group II, vertical hatching: group III.

died of peritonitis. Circulatory disturbances manifested as irregular plethora of glomeruli and tubules in the renal medulla. In the majority of kidney preparations from patients with intestinal peritonitis (groups I and II), glomerular capsules were dilated and contained small amount of amorphous substance, while in group III their lumens looked like slits. In all preparations, artery sclerosis and hyalinosis and glomerular sclerosis were observed, abnormal glomeruli were most abundant in hypertensive patients. Arteries contained leukocytes adherent to the endothelium, solitary fibrin thrombi were seen in veins. Peritubular capillaries were sharply dilated and showed signs of stasis, in particular, erythrocytes and leukocytes aggregates, especially in cases of peritonitis caused by pathological processes in the small intestine. In some preparations, small hemorrhages in the renal cortex were seen. In group I patients, mononuclear perivascular, peritubular, and periglomerular infiltrates were found in the renal stroma. In some specimens, stromal edema (primarily in the medulla) was observed.

In almost all specimens, the proximal (strait and convoluted, PST and PCT, respectively) and distal (strait and convoluted DST and DCT, respectively) tubules were dilated, their epitheliocytes contained granular cytoplasm. Moreover, vacuolization of epitheliocyte cytoplasm was seen in PCT (patients with pancreonecrosis) and PST (small intestine pathology). Nephrocyte brush border was swollen and sometimes desquamated into the tubule lumen. Some proximal and distal tubules contained weakly eosinophilic amorphous or filiform substance; hyaline cylinders were seen in DST of group I patients. The lumens of collecting tubules were free, their endotheliocytes had transparent cytoplasm. Necrosis of the tubular epithelium of various degrees was found in all preparations. The most pronounced changes in nephrocytes, in particular necrosis of some tubules was found in pancreonecrosis.

More detailed picture of kidney damage in peritonitis patients was obtained by histoenzymatic analysis of the renal tissue, because quantitative histoenzy-

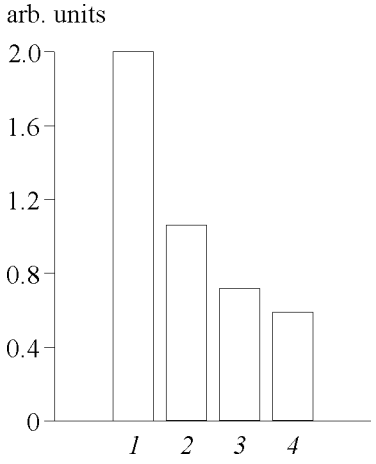

Fig. 2. Index of morphofunctional state of nephrocytes during peritonitis of different genesis. *1*) control; *2, 3,* and *4*) groups I, II and III, respectively.

matic study allowed to evaluate functional and morphological aspects of the type and degree of cell damage.

Histophotometry revealed structural and metabolic heterogeneity of various parts of the nephron manifested as different activities of dehydrogenases in the proximal and distal tubules (Fig. 1). In the control group, maximum SDH, LDH, and NAD activities were found in DCT, while NADPH showed maximum activity in PST. Minimum enzyme activity was revealed in collecting tubules.

Histoenzymatic study of the kidneys in patients died of peritonitis revealed decreased dehydrogenase activity in all nephron compartments (Fig. 1). Minimum enzyme activity was found in group III: LDH activity in DCT, PST, and PCT decreased by 66, 62.2, and 61.3%, respectively, compared to the control ($p<0.05$). This dramatic inhibition of glycolysis attests to severe endotoxicosis. Low NAD- and NADPH-diaphorase activity attests to impaired energy production. Minimum NAD-diaphorase activity was revealed in PCT and collecting tube (by 54 and 54.2% below control, respectively, $p<0.05$), while NADPH-diaphorase activity decreased by 51 and 52.5% ($p<0.05$) in PCT and PST, respectively. Activity of SDH, a key enzyme of the Krebs cycle, most significantly decreased in DCT and PCT (by 57.1 and 53%, respectively). Less pronounced but significant changes in dehydrogenase activities were revealed in the kidneys of patients died of peritonitis caused by small intestinal pathology. Thus, NADPH-diaphorase activity in PST and PCT decreased by 41.5 and 33.3%, respectively ($p<0.05$), while LDH activity in PST and DCT decreased by 40.5 and 34.3%, respectively ($p<0.05$). In PCT, NAD and SDH activities were below the control by 31.1 and 30.6%, respectively ($p<0.05$). It should be noted that, disturbances in the spatial organization of the nephron were found in all patients. This was confirmed by considerable changes in the intratubular gradient of dehydrogenase activity (Table 1).

TABLE 1. Changes in Intratubular Gradient of Dehydrogenase Activity in the Kidneys of Patients with Peritonitis

Gradient	Control	Peritonitis, group		
		1	2	3
PCT/PST				
SDH	1.16	0.9	0.75	0.92
LDH	1.03	1.35	1.06	1.05
NAD	1.43	1.06	1.2	1.02
NADPH	0.99	1.14	1.01	1.03
DCT/DST				
SDH	1.11	1.08	0.97	0.79
LDH	1.41	1.05	0.9	1
NAD	1.28	1.13	1.2	1.15
NADPH	0.97	1.22	1.07	1.12

Thus, pronounced structural and functional changes in the kidneys developed in patients with peritonitis. For detailed evaluation of the severity of degenerative changes in the kidneys in different groups, index of morphofunctional state of nephrocytes was calculated using factor analysis (Fig. 2). Higher values of this index in the proximal tubules in the control group attested to structural and metabolic heterogeneity of nephrocytes and can be explained by higher dehydrogenase and diaphorase activity in epitheliocytes. Low values of this index were found in patients with peritonitis caused by intestinal pathology. In patients with pancreonecrosis, this index dropped to a minimum, which indicate the necessity of additional correction for patients with endotoxicosis. Moreover, the lowest values of this index and, therefore, most pronounced pathological changes were revealed in PCT.

Thus, the revealed structural and metabolic changes in the renal tissue underlie the impairment of renal function (oligo- and anuria, protein- and cylindruria, and azotemia of various degrees). Our results show that pancreonecrotic and perforative peritonitis cause most severe damage to the kidneys, which can be explained by progressive hypoxia and pronounced intoxication. Decreased filtration pressure in the glomeruli due to circulatory hypoxia and juxtamedullary circulatory shunting can underlie anuria and progressive changes in tubular epithelium. Enzyme toxemia plays an important role during pancreonecrosis [2,11]. Activation of trypsin and lipolytic enzymes, in particular, phospholipase A_2 is a leading factor of endotoxicosis [8].

Distrophic changes in the proximal tubules associated with their dilation and accumulation of eosino-

philic substance are regarded as the signs of acute renal failure. Moreover, the presence of cylinders in DST observed mainly during intestinal peritonitis is a compulsory characteristic of oliganuria [5].

Microbial endotoxins expressed on the outer layer of plasma membranes of Gram-negative bacteria and released after the lysis of these bacteria, play a special role in the structure of endogenous intoxication [6]. B. R. Gel'fand *et al.* [1] showed that systemic endotoxemia originating from the intestine developed in all patients with peritonitis. Moreover, administration of endotoxin (LPS) to experimental animals induced acute renal failure associated with significant increase in serum urea and creatinine [15] despite preserved systemic hemodynamics [17]. The effect of endotoxin on the kidneys is mediated by various transmitters. It was shown that LPS appeared in systemic circulation induced synthesis and release of transmitters, cytokines, and oxygen radicals from polymorphonuclear neutrophils, macrophages, and endothelial cells, which triggered a cascade of pathological reactions culminating in acute renal and polyorganic insufficiency [12].

Quantitative histoenzymological studies revealed activation of dehydrogenases and diaphorases, which also can be induced by endotoxins. Experiments on rats [14] showed that the development of acute renal insufficiency induced by endotoxin shock is preceded by the impairment of energy metabolism in nephrocytes. More extensive changes in PCT agree with the data on the presence of LPS in the proximal renal tubules in patients died of acute renal failure [10]. Moreover, disturbed structural and metabolic heterogeneity of nephrons associated with changes in the intratubular enzyme activity gradient, most pronounced in group III specimens, is a morphological sign of impaired renal function and acute renal insufficiency.

Thus, the revealed structural and metabolic changes in the renal tissue reflect peculiarities of the morpho- and pathogenesis of renal insufficiency developing during peritonitis. The most pronounced changes are typical of pancreatogenic peritonitis.

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