POLYORGAN INSUFFICIENCY DURING OBTURATION OF GALLERY IN THE EXPERIMENT

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Abstract

Reologic condition of the blood in white female rats with obturation of bile ducts, as well as microcirculation of the liver, small intestine and kidneys, the process of free radicals.

Remarkable change in reologic blood features as hiperviscosity and blood flow decrease have been revealed.

Changes in microcirculation are observed both in the intestine and in the kidneys and liver.In kidneys they are more marked. In obturation of bile ducts the intense of free radicals oxidation along with the decrease of antioxidant enzymes activity, particularly superoxide dismutase (SOD) is observed.

These changes indicate the involvement of the liver, small intestine and kidneys in the pathology of the development of multiple organ failure during obstruction of the bile ducts.

Keywords: multiple organ failure, bile duct obstruction, rheological properties of blood, microcirculation, antioxidant protection (AOP)

Introduction. Multiple organ failure (MOF) is the leading cause of hospitalization of patients in intensive care units.

SNP is a set of failure of two or more organs and systems that are observed either simultaneously or sequentially, requiring prosthetics or complete replacement of the function of the affected organs, with the effects of mutual potentiation and a high probability of persistence and death [2,3,4]. This syndrome was first described in a series of articles by Baue and co-authors, who observed the sequential development of lung function failure and then liver and kidney function; the development of this syndrome was characteristic on the third day after aggressive surgical operations and without regard to shock. Autopsy revealed foci of inflammation in organs, microcirculation disorders, but inflammatory changes were

sterile, that is, did not have a primary infectious origin [5,6,7]. Despite the fact that in recent years, mortality due to multiple organ failure syndrome in developed countries has decreased both as a result of improved treatment methods and due to changes in approaches to diagnosis, this condition remains the main cause of death in intensive care units. Severe infections, major surgical interventions, severe burns and trauma,

severe pancreatitis, shock of any etiology, cardiopulmonary resuscitation are the main etiological factors of multiple organ failure syndrome in adults. Currently, the search and study of the effectiveness of various diagnostic and therapeutic technologies is ongoing, which make it possible to individualize the therapy of SPON and improve the prognosis.

The aim of this study was to assess the state of microcirculation in the liver, small intestine and kidneys, as well as the degree of free radical lipid oxidation in rats with acute obstruction of the biliary tract.

Material and methods

The experiments were carried out on white outbred male rats weighing 180-200 g. Obturation was reproduced by ligation of the common bile duct [10]. The mortality rate was 30.3%. Sham-operated animals, which underwent only laparotomy, served as control. The animals were sacrificed on days 1, 3, 7 and 15 after ligation of the common bile duct.

The rheological properties of blood were studied by determining the viscosity and shear rate of blood [13]. Biomicroscopic examination of the microcirculatory bed of the liver, kidneys and small intestine was carried out with a luminescent microscope "LYUMAM-IZ" using a contact objective 10x0.40 and 25x0.40. Intravital biomicroscopy was performed under general thiopental anesthesia at a dose of 70 mg / kg of animal body weight.

In the homogenate of the liver, kidneys and small intestine, the content of malondialdehyde (MDA) was determined according to [9], the activity of superoxide dismutase (SOD) according to [12], and catalase according to [11].

The digital data were subjected to statistical processing using the Excel-2000 statistical analysis software package.

The study of the dynamic viscosity of blood in acute obturation showed its increase only from the 3rd day of the experiment (Table 1), while the shear rate was already reduced by 1 day (Table 2). On the 7th day, violations of blood viscosity worsened even more. Only, on the 15th day, the blood viscosity almost returned to normal. In

this case, an increased viscosity value was observed only at an applied pressure of 4 mm. water Art. The latter suggests that disturbances in the peripheral circulation remain on the 15th day of the experiment. Changes in blood flow rate persisted throughout the experiment.

Table 1.

Dynamics of blood viscosity in rats with obstruction of the bile duct (M ± m), cps

Group	**Pressure, mm. water art.**			
	4	**8**	**12**	**16**
Intact	6,72±0,07	6,18±0,09	4,00±0,15	2,53±0,07
Obturation:				
	8,12±0,11[а]	7,00±0,08[а]	6,10±0,09[а]	4,67±0,06[а]
After 1 day	8,17±0,11[а]	6,80±0,04[а]	6,15±0,09[а]	4,68±0,03[а]
After 3 days	10,80±0,17[а,б]	7,95±0,20[а,б]	6,25±0,01[а,б]	4,79±0,06[а,б]
	7,00±0,08[а]	6,30±0,16	4,00±0,08	3,24±0,01[а]
After 7 days	13,63±0,11[а,б]	8,65±0,12[а,б]	6,15±0,03[а,б]	5,27±0,12[а,б]
	6,85±0,09	6,27±0,14	4,05±0,15	2,95±0,05[а]
After 15 days	8,65±0,06[а,б]	6,45±0,20	4,03±0,09	2,86±0,01[а]
	6,78±0,13	6,18±0,12	4,00±0,08	2,75±0,05[а]

The generalized nature of changes in the rheological properties of blood becomes one of the important reasons for the involvement of other internal organs in the pathological process, which should affect the severity of the course of the main pathological process. Changes in the rheological properties of blood should affect the state of the microvasculature and gas exchange at the “capillary-cell” level in different organs.

In this regard, the microcirculation system of the liver, small intestine and kidneys was studied in acute obstruction of the biliary tract.

There is a close structural and functional relationship between the bile capillaries and sinusoids of the hepatic parenchyma. This interaction suggests that a violation of the passage, and subsequently the formation of bile, will affect the activity of the vessels of the microvasculature of the liver.

In luminescent biomicroscopy, the liver tissue of intact animals appears greenish-blue, and the vessels have a dark shade. In the field of view, portal venules are clearly visible, from which sinusoids often branching and anastomosing between themselves are fanned out (Fig. 1).

Sinusoids are smooth-walled tubes, in the form of a cylinder, the blood flow rate in them varies greatly. So, in the sinusoids located in the center of the lobules, the blood flow rate is slightly higher compared to the sinusoids located along the periphery of the lobules. Along with the active sinusoids, a small number of non-functioning, plasma sinusoids is determined. Before the confluence of the sinusoids into the central collecting venule, occurring at a right angle or close to that, in most cases there is a narrowing of the lumen of the sinusoid. This indicates the presence of sphincters that regulate intraorganic circulation. The central collecting hepatic venules, in turn, are usually treelike. In cases when 2-3 collecting venules flow into them, they have a shape close to cylindrical. The walls of all vessels of the microvasculature of the liver have clear, even boundaries. The blood flow in the elements of the microvasculature of the liver of intact animals is continuous, jet-like.

In the control group of rats, which underwent only laparotomy, the microcirculatory bed of the liver reacted with a slight expansion of sinusoids and central collecting venules, a fine-grained nature of blood flow, and a slight slowdown in its velocity in them compared to the intact group of animals. Having begun on the first day, by the 3rd day, the changes were somewhat aggravated. Later, on the 7th and 15th days, the picture of the microvasculature of the liver of the control animals was characterized by an almost complete restoration of structural and hemodynamic parameters (Fig. 2), which is expressed in the restoration of the lumen of spasmodic microvessels, the nature and velocity of blood flow in them. The changes revealed in animals of the

control group are the result of laparotomy and are, as shown by studies, of a transient nature.

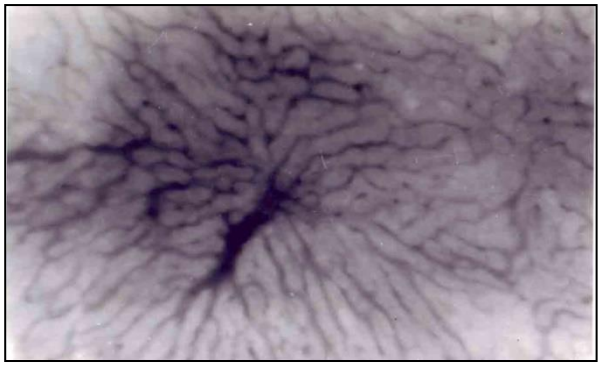


Fig. 1. Biomicroscopy of the microvasculature of the liver. Autofluorination of intact animals, magnification x 75

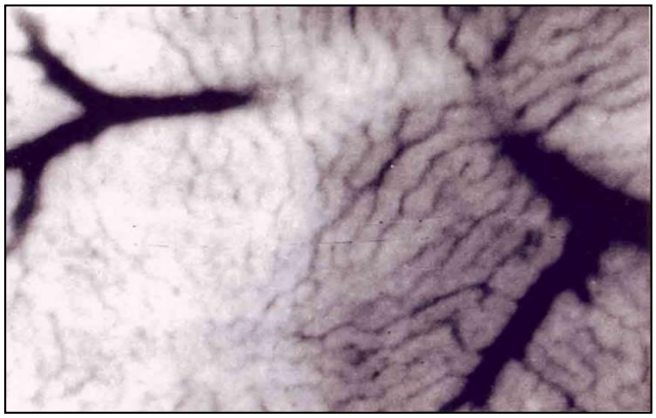


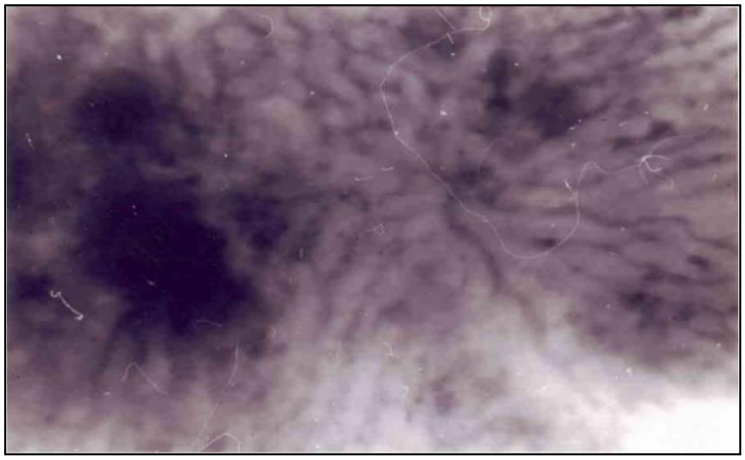
Fig. 2. Biomicroscopy of the microvasculature of the liver. Autofluorination of control animals, increase x 75

In animals with ligation of the common bile duct, in contrast to animals in the control group, significant changes were revealed in the system of the peripheral circulation of the liver. The changes were manifested by a complex of intravascular, vascular and paravasal changes.

By the 3rd day of the experiment, the liver is sharply increased in volume, its consistency is compacted, the surface is bumpy, there are also small-point subcapsular hemorrhages. During biomicroscopy, the angioarchitectonics of the liver is impaired due to a noticeable increase in the area of dystrophic changes in the parenchyma in the form of foci of posthemorrhagic organization, causing disorganization of the microvascular bed, deformation of sinusoids. The boundaries

of the vessels are blurred, individual sinusoids are filled with stagnant blood, and sharply expanded. Intersinusoidal anastomoses are also widened due to stagnant blood (Fig. 3).

Fig. 3. Biomicroscopy of the microvasculature of the liver. Autofluorination 3-day after ligation of the common bile duct of animals, increase x 75

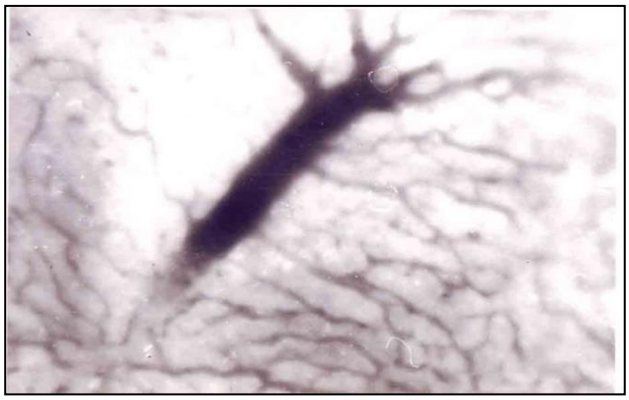


Individual areas of the parenchyma differ sharply by the nature of perfusion, which gives the microcirculatory picture shades of mosaicism. So, there is vasoconstriction and a decrease in the number of functioning terminal hepatic venules and sinusoids, their different blood filling (Fig. 4).

The blood flow is intermittent, coarse-grained due to aggregates, sharply slowed down. As the duration of cholestasis increased and hypertension in the bile ducts increased by the 7th day, microcirculation disorders progressed, which was expressed in the development of the so-called "nutmeg" liver. With biomicroscopy, the disturbances in angioarchitectonics by this time of research have become even more aggravated. This, first of all, was manifested by an increase in the degree of structural disorganization and disorientation of the elements of the microvascular bed of the hepatic parenchyma. The area of degenerative transformations in the liver increased, both due to an increase in the number of obliterated and deformed microvessels, and due to sclerotic changes in the parenchyma itself (Fig. 5). The blood flow in the functioning microvessels is sharply slowed down due to the pronounced phenomena

of aggregation and adhesion of blood corpuscles. Prestatic phenomena are widespread in the form of a pendulum-like nature of blood flow.

Fig. 4 Biomicroscopy of the microvasculature of the liver. Autofluorination 3-day after ligation of the common bile duct of animals, increase x 75



By the final period of the experiments - 15 days, the structural and hemodynamic disorders of the peripheral circulatory system of the liver were further aggravated. Violations of angioarchitectonics took on a pronounced character, which was manifested by the practical destruction of the structure of the hepatic parenchyma, an increase in the area of "silent" zones, in which there is no blood flow at all (Fig. 6). Along with single functioning microvessels, the presence of many fragments of microvessels is noted. The blood flow is preserved only in separate lobules, in the center of which portal venules are observed. The blood flow in these vessels is intermittent, often pendulum-like.

Fig. 5. Biomicroscopy of the microvasculature of the liver. Autofluorization on the 7th day after ligation of the common bile duct of animals, increase x 75

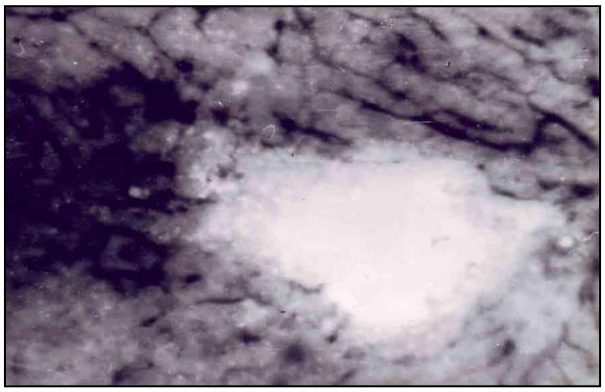


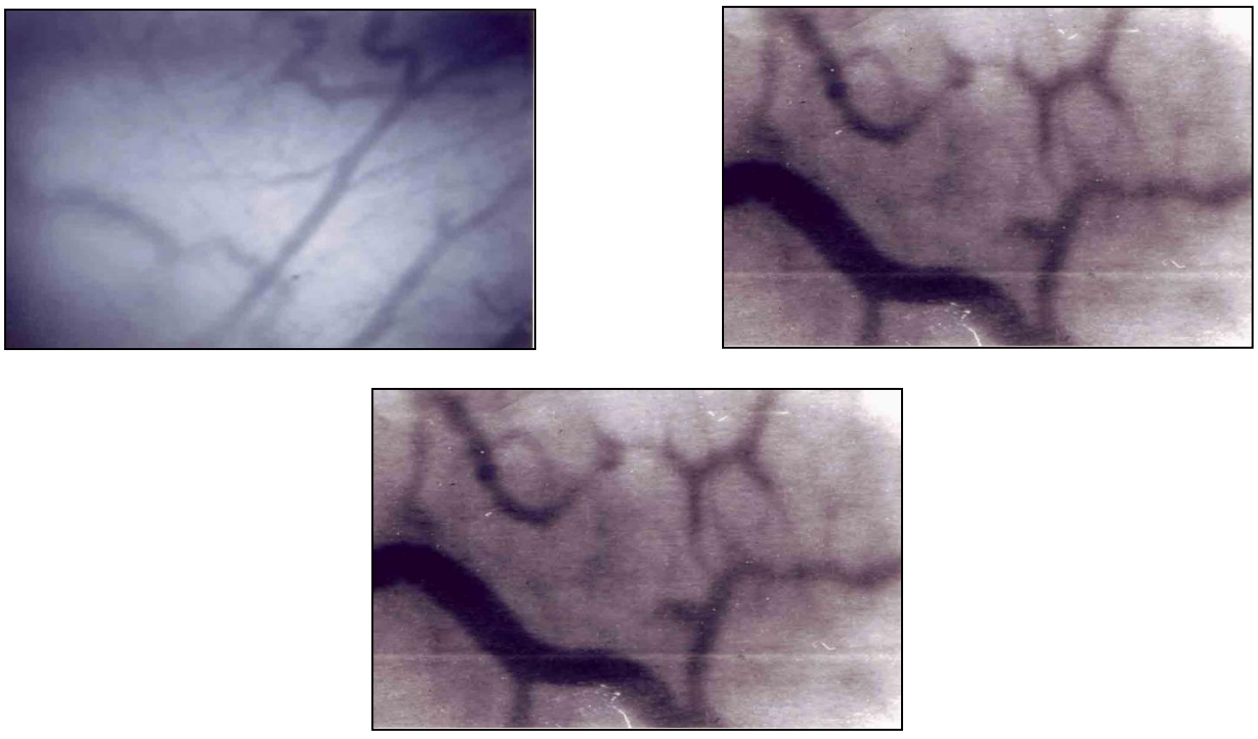
Fig. 6. Biomicroscopy of the microvasculature of the liver. Autofluorization 15 days after ligation of the common bile duct of animals, increase x 75

Thus, cholestatic syndrome leads to the development of a wide range of vascular, intravascular and extravascular changes in the peripheral circulation of the liver. As the studies have shown, an important factor in the genesis of microhemodynamic disorders is changes in the rheological properties of blood, since violations of the electrical and deformation parameters of shaped elements determine a high degree of their adhesion and aggregation with the development of blood hyperviscosity syndrome.

The vessels of the adventitia membrane and intramural vessels of the wall of the small intestine are available for biomicroscopy. In control animals, no significant changes were found on the part of the investigated vessels of the small intestine.

In animals of the experimental group, by the end of the first day, the vascular network of the wall of the small intestine changed somewhat. There was an expansion of the lumen of the capillaries and intramural venules. Blood stasis was noted in individual capillaries and intramural venules. Intramural arterioles did not undergo significant changes (microphoto 1, a). The blood flow in the functioning capillaries is somewhat slowed down, has an intermittent character, the tendency of blood corpuscles to aggregation is expressed. Day 3 was characterized by the aggravation of the revealed changes in the microvasculature of the wall of the small intestine. The number of capillaries and venules in which stasis was noted increased, microvessels with pendulum blood flow appeared (microphoto 1, b). The angioarchitectonics of the

vessels was generally preserved, there were changes caused by the expansion of capillaries, venules, their increased tortuosity, blurring of boundaries. Aggregation, adhesion of blood corpuscles acquired a more pronounced character in comparison with the previous period. The 7th day of the experiments was characterized by the preservation of the violations of the microcirculatory bed of the walls of the small intestine revealed in the previous periods (microphoto 1, c). The angioarchitectonics of the microvascular bed of the wall of the small intestine was preserved, although the presence of many tortuous, thickened capillaries, venules is noted. It should be noted that, despite pronounced intravascular and vascular changes, paravasal accumulations characteristic of parenchymal organs were not detected in the wall of the small intestine. The blood flow velocity was significantly reduced both in capillaries and intramural venules. The blood flow in these vessels was coarse-grained, intermittent.



Microphoto 1. Autofluorescence of the microcirculatory bed of the wall of the small intestine on the 1st (a), 3rd (b) and 7th (c) days after obturation of the common bile duct, uv. x 75.

Consequently, the microvasculature of the wall of the small intestine is involved in the pathological process, to a lesser extent in comparison with other parenchymal organs (for example, with the liver). This is possibly due to the fact that the vessels of the adventitia and intramural membranes of the wall of the small intestine have relatively less permeability. This is evidenced by the almost complete absence of paravasal accumulations of blood corpuscles throughout the experiments.

Peritubular capillaries of the renal cortex are available for vital microscopy. The only site in which the efferent vessel of a given glomerulus perfuses is in the region of the proximal convoluted tubule of the superficial renal cortex. Consequently, the state of the microvasculature of the renal cortex to a certain extent reflects the dynamics of changes in the glomerular capillaries. Studies in the group of control animals have shown that laparotomy does not significantly affect the microhemodynamic parameters of the kidneys. In experimental rats, on day 1 after ligation of the common bile duct, changes in the microcirculation of the cortical layer of the kidneys are characterized by intravascular aggregation of blood cells, intermittent and slowed down blood flow (microphoto 2, a). The angioarchitectonics of the renal cortical region is characterized by heterogeneity of the parenchyma due to the presence of separate groups of non-functioning capillaries. The contours of the vessels and tubules are preserved, except for areas of the parenchyma, where the luminescent glow of the epithelium of the tubules is somewhat erased. Day 3 of the experiment was characterized by an increase in discirculatory shifts, which was manifested by mosaic angioarchitectonics (microphoto 2, b). The number of non-functioning capillaries slightly increased in comparison with the previous study period. The boundaries of the tubules around the non-functioning capillaries are smoothed, probably due to the plasma impregnation of their walls. Around the non-functioning capillaries, foci of perivascular diapedesic hemorrhages were revealed. The blood flow in the capillaries is slowed down, is fine-grained, intermittent in places. 7 days after ligation of the common bile duct, the angioarchitectonics of the cortical region of the kidneys is characterized by slightly pronounced destruction, mainly due to

perivascular changes, plasma soaking and deformation of the walls of the proximal convoluted tubules (microphoto 2, c). The luminescence characteristic of the tubular epithelium was absent practically on the entire surface of the kidneys accessible for biomicroscopy. The latter, most likely, can be explained by the deposition of protein precipitate on the inner surface of the tubules and the imbibition of blood cells into the thickness of their wall. The nature of the blood flow practically did not change in comparison with the previous period, remaining slow and intermittent.

At the same time, the changes were more pronounced in rats with extrahepatic cholestasis. One day after the reproduction of the model, the catalase activity in the liver homogenate increases by 13.3% relative to the values of the control group of rats. Then it decreases slightly, approaching the values of the control group of rats. This decrease persists in the future (after 7 days), and during this period the activity of the enzyme reaches normal values. Subsequently, we observed a rise in the enzyme activity again (increase by 22.3%) in relation to the values of the control group of rats.

Changes in the activity of catalase in the kidney homogenate showed a tendency towards activation 1 day after the reproduction of cholestasis. However, these values did not differ significantly from those of the control group of rats. After 3 days, the enzyme activity decreased by 23.8 and 19.9% in comparison with the indicators of the previous period and the values of the control group of animals, approached the values of the control and the norm after 7 days and was statistically significantly inhibited by 41.7% by the end of the experiment.

Consequently, changes in catalase activity in homogenates of the liver, kidneys, and small intestine showed less variability.

Thus, on the basis of the data obtained, we can say that with obstruction of the bile duct, systemic disorders of the internal organs are observed. They are caused both by the action of cholemic toxins and the accumulation of intermediate metabolites, and by changes in the viscoelastic properties of the blood, which contribute to the development of extra-, intra- and vascular changes.

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