

STATE OF THE MONOOXYGENASE SYSTEM LIVER WITH ACUTE PANCREATITIS AND ITS CORRECTION WITH CYTOCHROME C

Alimbekova L.U., Sabirova R.A., Azizova D.M.

Резюме. В статье приводятся сведения об изменении показателей монооксигеназной системы печени при остром панкреатите и коррекции его цитохромом С, сандостатином и совместным применением обоих препаратов. Полученные результаты позволяют сделать вывод о более выраженном действии препаратов, для уменьшения действия патологических факторов на организм животных. Полученные результаты позволяют сделать вывод, что коррекция активности изученных ферментов цитохромом с в сочетании с сандостатином оказывает более выраженное действие чем отдельное их введение в организм экспериментальных животных с острым панкреатитом.

Ключевые слова: острый панкреатит, печень, монооксигеназная система, цитохром P-450-редуктаза, цитохром 1A1, глюкоза-6-фосфат-дегидрогеназа, антиоксидантная защита.

Summary. The article contains information about changes in the indicators of the liver monooxygenase system during acute pancreatitis and its correction with cytochrome C, sandostatin and joint application of both drugs. The results show a more pronounced effect of preparations to reduce pathological factors on animals. The results show that the correction of activity of the studied enzymes with cytochrome in combination with sandostatin has a more pronounced effect than the separate introduction of said enzymes into the body of experimental animals with acute pancreatitis.

Keywords: Oxidative stress, pancreatitis, liver, monooxygenase system, cytochrome P-450-reduction, cytochrome 1A1, glucose-6-phosphate-dehydrogenase, antioxidant protection.

Recently, the incidence of acute pancreatitis has remained relevant both in theoretical and practical terms. To date, many of the mechanisms underlying various factors at the subcellular and molecular levels have not been fully explored. Cross-

sectional and cross-system relationships remain unexplored under the influence of various factors, although it is known that exposure to the organism involves not only the pancreas but also other organs and systems, including the liver. The monooxygenase enzyme system is localized in almost all mammalian organs and tissues, some of which are as active as the liver [1-2]. The system of microsomal monooxygenase (MMO) is found in most animal tissues. Although the highest P450 microsomal cytochromes are found in liver cells, they are also present in lung cells, kidneys, the brain of the smooth muscles of blood vessels, the intestinal epithelium, the mucous membrane of the nose, the mammary gland and other tissues [3]. The MMO system can metabolize a large number of different substrates due to multiple forms of cytochrome P-450 with different substrate specificity [4]. Regardless of the damaging factor, one of the first links in the chain of pathological disorders (toxogenesis) is the membrane-mediating effect that results in a dysfunction of the cascade of microsomal and mitochondrial enzymes, participating in the maintenance of cell homeostasis, its repair and the elimination of xenobiotics (or their metabolites) [5-6].

In recent years, therefore, the functioning of microsomal monooxygenases and the influence of various factors on them have been studied intensively.

The aim of the research is to establish the pathogenic significance of the monooxygenase system in the mechanism of development of acute experimental pancreatitis and its correction by cytochrome c.

Materials and methods of research. Experiments have been conducted on 60 male nonmature male rats with a body mass of 120-140 g contained in the standard diet. The experiments were conducted in accordance with the «European Convention for the Protection of Vertebrate Animals, which are used for experiments and other scientific purposes» (Strasbourg, 1985). Acute experimental pancreatitis was induced in rats by P.S. Simovaryan [7]: Local freezing of pancreatic gland with ethyl chloride.

The extent of the pancreas was determined by the activity of amylase in the blood. The studies were carried out on the 7th and 10th day after the operation, determining the activity of cytochrome P-450-reductase, glucose-6-phosphate

dehydrogenase and cytochrome content 1A1. Six groups of rats were identified - 10 animals in each group:

- 1st - intact group (norm);
- Second, a false identification;
- 3rd - animals with 7- and 10-day acute pancreatitis;
- Animals with acute pancreatitis were administered with cytochrome with 0.15 mg/kg body weight daily (10 days) in the muscle;
- 5th, animals were given 0.007 mg/kg body weight sandostatin with acute pancreatitis;
- 6th - animals were injected simultaneously with cytochrome with and sandostatin.

The animals decapitated for 7 and 10 days after the operation.

The activity of cytochrome P-450-reductase, glucose-6-phosphate dehydrogenase and the content of cytochrome 1A1 in blood serum were determined by the method of quantitative solid-phase immunoforment analysis type «sandwich». The optical density was measured using the HUMAREADER HS (Human, Germany) computed immunoforment analyser at 450/620 nm, using standard test systems from Elabscience (USA).

Results and discussion thereof. The metabolic block of glucose-6-phosphate dehydrogenase (G6FD) in different tissues has consequences, the main consequence of the metabolic block of G6FD in different tissues is the development of oxidative stress against the background of the decrease of activity of the APS -antioxidant protection system [8-9].

The results of the G6FG activity study are presented in Table 1.

Table 1

State of the mono-oxygenase system for acute experimental pancreatitis

Rate	Intact group	False posse	Acute pancreatitis	
			7 th day	10 th day

Glucose-6-phosphate dehydrogenase (Pg/ml)	33.50±0,07	30.13±0,08	20.19±0,12	16.35±0,07
Cytochrome P450 reductase (Pg/ml)	7.24±0.06	8.50±0.07	16.08±0.09	20.19±0,08
Cytochrome 1A1(Pg/ml)	124.81±0,06	128.84±0.08	271.35±0,06	348,46±0,09

Note: In all cases $P < 0.05$

As can be seen from table 1, the activity of 6FGD in the falsified group of animals does not undergo a reliable change. In animals with acute pancreatitis for 7 and 10 days of the experiment, its activity decreases by 1.65 and 2.04 times respectively in comparison with animals of intact group.

The smooth endoplasmic reticulum is relatively rich in enzymes responsible for the oxidative metabolism of xenobiotics. They contain an important enzyme class known as mixed function oxidase (MFO) or monooxygenase. The activity of these enzymes requires the presence of both reducing agent (NADP-H) and molecular oxygen. In a typical reaction, one oxygen molecule per substrate molecule is consumed (reduced) and one oxygen atom appears in the product of the reaction and the other in the form of water [10-11].

Two microsomal enzymes play a key role in this oxidative-reducing process. The first of these is the flavoprotein NADPH cytochrome P-450-reductase, which is a multidomain protein, and its function requires certain inter-molecular and inter-domain interactions. Precise and specific interactions between the flavinmononucleotide (FMN) and flavinadeninucleotide (FAD) domains within the molecule, and between the FMN domain and the cytochrome P450 are necessary for electron transport, which provides the catalytic function of the cytochrome P-450 [12]. One mole of this enzyme contains one mole of flavinmononucleotide (FMN) and one mole of flavinadeninucleotide (FAD). Because cytochrome C can act as an electron acceptor, the enzyme is often referred to as NADP cytochrome of C-reductase. The second microsomal enzyme, hemoprotein, called cytochrome P-450, acts as a finite oxidase. In fact, the microsomal membrane contains many forms of this hemoprotein,

and this multiplicity increases with repeated administration of exogenous chemicals. The name cytochrome P-450 is associated with the special properties of this hemoprotein. In the reduced form it binds carbon monoxide to form a complex with maximum light absorption at 450 nm. The relative abundance of cytochrome P-450 compared to liver reduction makes the P-450 heme recovery a limiting stage in the process of oxidation of drugs in the liver [13-17]. Cytochrome P450-reductase activity in animals of false aligned group is reliably increased by 17.4% in comparison with animals of intact group (Board.1). In animals with acute pancreatitis for 7 and 10 days of the experiment, the activity of this enzyme increases by 2.22 and 2.78 times, respectively, compared to the animal intact group. We have established more pronounced increase of cytochrome 1A1 by 7 and 10 days of development of acute pancreatitis than animals of intact group and it was 2.17 and 2.79 times respectively.

Thus, the above data show that acute pancreatitis is characteristic of dysfunctional monooxygenase system.

In recent years it has been established that there is a sufficiently strong monooxygenase system in the liver to limit its resistance to endo- and exotoxins, toxic substances coming from food and formed in the body. The liver mono-oxygenase system increases its activity and can be regulated under the influence of various substances.

Cytochrome P-450-dependent liver monooxygenase system plays an important role in the regulation of endogenous metabolic processes in other organs, and hence resistance to damaging toxicants, changes in functional status of cytochrome P-The 450-dependent mono-oxygenase system may lead to metabolic disorders in the liver, with the accumulation of toxic products from disrupted metabolic processes that reduce the protective function of the liver and cause pathological changes [18-20].

In order to correct the detected changes, we used cytochrome c in our studies to eliminate the effects of the metabolic block G6FD. The results of the correction of the state of monooxygenase system at acute pancreatitis are given in Table 2.

Table 2

Effects of cytochrome c on the state of the monooxygenase system in acute

Experimental pancreatitis (Pg/ml)

Rate, Pg/ml	Intact group	False posse	in 7 days				in 10 days			
			Untreat ed	After treatment			Untrea ted	After treatment		
				with cytoch rome	sandos tatin	with cytoch rome		with cytoch rome	sandos tatin	with cytoch rome
Glucose -6- phospha te dehydro genase	33.50± 0,07	30.13± 0,08	20.19± 0,12	25.26± 0,119	23.89± 0,08	28.62± 0,08	16.35± 0,07	24.98± 0,08	22.60± 0,05	26.41± 0,08
Cytochr ome P450 reductas e	7.24±0 .06	8.50±0 .07	16.08± 0.09	10.36± 0,05	12.26± 0,05	9.04±0, 06	20.19± 0,08	13.15± 0,05	14.56± 0,101	12.36± 0,105
Cytochr ome 1A1	124.81 ±0,06	128.84 ±0.08	271.35 ±0,06	200.31 ±0,06	187.64 ±0,08	164.63 ±0,88	348,46 ±0,09	168.63 ±0,09	143.65 ±0,08	133.00 ±0,12

Note: In all cases P<0.05

As can be seen from table 2, treatment with cytochrome in animals with 7 10-day acute pancreatitis within 10 days increases the activity of G6FD by 25.11% and 52.78% respectively, compared to non-forest animals. Sandostatin increases the activity of 6FGD by 18.32% and 38.22% respectively in the same time periods, indicating a less corrosive effect on the activity of the enzyme. Combined administration of cytochrome with sandostatin within 10 days increased activity of this enzyme 41.75% and 61.52% respectively compared to non-forest groups.

Cytochrome P450 reduction activity in the treatment of cytochrome with animals with 7 and 10 days of acute pancreatitis is reduced by 35.58% and 34.87%, respectively, compared to the non-forest group. In this group of animals cytochrome

content of 1A1 is reduced by 26.2% and 51.61% respectively after cytochrome treatment compared to the non-forest group.

Treatment with sandostatin reduces cytochrome P450-reduction activity in animals with 7 and 10 days of acute pancreatitis by 23.76% and 27.89% respectively compared to the non-forest group. Their cytochrome content of 1A1 is reduced by 30.9% and 58.8% compared to the non-forest group.

Combined administration of cytochrome with and sandostatin for the correction of 7 and 10 acute pancreatitis has led to a decrease of P450-reduction cytochrome activity by 43.8% and 38.8% and cytochrome 1A1 by 39.3% and 61.9% respectively, compared to non-forest animals.

Thus, correcting the activity of the studied enzymes with cytochrome in combination with sandostatin has a more pronounced effect than their separate administration in experimental animals with acute pancreatitis.

The analysis and assessment of the state of microsomal oxidation shows the relevance of the assessment of their structural and functional status in the study of the influence of various factors on animals, especially when correcting them.

Thus, the experimental data obtained show a disturbance and an important role in the development of a pathological process in the liver with acute experimental pancreatitis, which increases the modern understanding of the subtle mechanisms of pathogenesis of the disease. The disruption of the function of the monooxygenase system in the liver is accompanied by an increased supply of toxic products, which increases the stress on the detoxification system and, As a result, it increases the severity and intensity of the pathological process both in this organ and in the organism in acute experimental pancreatitis.

Conclusions. The data obtained indicate the dysfunction of the MoE and its important role in the development of acute pancreatitis. Disruption of the function of the monooxygenase system in the microsoms of the liver results in an increased supply of toxic products, which increases the stress on the detoxification system and, As a result, it increases the severity and intensity of the pathological process, both in this body and in the body as a whole.

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