AJSIHD
GLOBAL RESEARCH NETWORK

AMERICAN Journal of Science on Integration and Human Development
Volume 01, Issue 07, 2023 ISSN (E): 2993-2750

Influence of Cytochrome on Antioxidant Defense of the Body in Acute Experimental Pancreatite

Shukurov Ilkhom Boltaevich
Professor of the Bukhara State Medical Institute named after Abu Ali ibn Sina

Abstract:

The article studied influence of cytochrome on the antioxidant defense of the body in acute experimental pancreatitis. The revealed significant disturbances in the mechanisms of natural detoxification in acute experimental pancreatitis, the possibility of preventing the provision of the body with antioxidants opens up a new promising direction in fundamental and practical medicine.

Keywords: Pancreatitis, antioxidant protection, pathogenesis, correlation.

Acute pancreatitis, being one of the most severe acute diseases of the abdominal organs, is accompanied by high mortality (3.6-23.5%), which reaches 80-100% in total destructive forms. Acute pancreatitis is characterized by a violation of one of the fundamental indicators of cellular homeostasis - intracellular processes. There is not an isolated lesion of any organ, but systemic membrane disorders that cause dysfunction of various organs and systems. The mechanism of these phenomena is rather complicated, but one of its elements can be considered the accumulation of products of lipid peroxidation (LPO) in membrane lipids. An uncompensated increase in lipid peroxidation can lead to disruption of membrane structures, which are the most sensitive to the action of reactive oxygen species.

The first ideas about the genetic determination of predisposition to pancreatitis were expressed in the middle of the twentieth century. Then for the first time they started talking about hereditary chronic pancreatitis .

Taking into account the leading role of enhancing lipid peroxidation processes in the development of acute pancreatitis and liver damage , it seems interesting to use the natural antioxidant --tocopherol αin the prevention of liver damage in acute pancreatitis, namely its effect on the mechanisms of natural detoxification in the liver in acute experimental pancreatitis.

Acute pancreatitis is accompanied by a cascade activation of kinins and cytokines, an increase in vascular permeability, an increase in blood viscosity, and a slowing of blood flow, which leads to a decrease in oxygenation and hypoxia. Under conditions of hypoxia, the processes of lipid peroxidation are intensified, damaging cell membranes and vascular endothelium. Violation of the energy-synthesizing function leads to the activation of pro-oxidant processes, and the failure of the antioxidant system. As a result, patients with pancreatic necrosis (PN) develop hypoxia of mixed genesis, which triggers a cascade of pathological processes that contribute to the progression of pancreatic destruction and systemic disorders .

In acute pancreatitis, in order to eliminate excessive production of pro-inflammatory cytokines, immunocompetent cells (ICCs) begin to produce anti-inflammatory mediators, the action of

which is aimed at suppressing the secretion of inflammatory mediators by macrophages and the activity of Th-1 cells, due to which a compensatory anti-inflammatory response syndrome is formed.

Thus, in acute pancreatitis, the mechanisms that provide pro- and anti-inflammatory response are disrupted. Such an imbalance leads to the depletion of ICC and severe immunodeficiency, which in the post-shock state becomes the leading pathogenetic link in acute destructive pancreatitis. Increasing endogenous intoxication causes suppression of the immune system, which, in turn, contributes to the progression of the local and systemic inflammatory process, the growth of intoxication and the development of purulent-septic complications.

In recent years, researchers have paid attention to genetic predisposition to severe forms of the disease. In this case, molecular genetic research methods are used to identify groups of patients in whom a tendency to develop severe forms of acute pancreatitis with septic complications is determined. Many works are devoted to the identification of gene polymorphism in chronic and acute pancreatitis. When analyzing the factors influencing the development of chronic pancreatitis, mutations in the cystic fibrosis gene (CFTR - with ystic ibrosis transmembrane conductance regulator), pancreatic secretory trypsin inhibitor. The literature also describes other mutations in the genes that affect the state of the pancreas - SPINK1 (serine protease inhibitor Kazal type 1), genes responsible for the synthesis of alcohol dehydrogenase and alpha-1-antitrypsin.

The pathogenesis of chronic pancreatitis also raises serious debate. A certain importance in the development of the disease is attached to the intensification of the processes of free radical oxidation of lipids. Thus, a study of the composition of the organic matrix of pancreatic stones showed that it includes modified lithostatin , albumin, and globulins with high molecular weight. Modification of albumin and other proteins in pancreatic and gastric juice is observed with the addition of end products of lipid peroxidation . This indicates, with a high degree of probability, the inducing role of LPO in the spontaneous modification of pancreatic proteins, with the formation of insoluble protein -calcium associates .

Chronic pancreatitis can also occur as a result of exposure of the pancreatic tissue to various chemical agents, among which drugs such as azathioprine are of great importance . hypothiazide, furosemide, estrogens, tetracyclines, sulfonamides and azo-couplings sulfanilamides with salicylic acid. The adverse effect of corticosteroids, non-steroidal anti-inflammatory drugs, metronidazole has been established . nitrofurans on the formation of chronic pancreatitis.

Among the etiological factors of chronic pancreatitis, a certain role belongs to viral lesions of the pancreas. Hepatitis B , Coxsackie , mumps, and infectious mononucleosis viruses have a pancreatic effect. The relationship between chronic pancreatitis and viral hepatitis is confirmed both by the isolation of HBsAg from the pancreatic secretion and the detection of markers of hepatitis B in pancreatic tissue, and by the detection of functional pancreatic insufficiency in patients with chronic viral hepatitis.

Lipid peroxidation determines the physicochemical properties of biological membranes (microviscosity , fluidity, membrane potential, polarity of the inner regions of the membrane, and others. According to E.B. Burlakova , this is achieved by changes in the fatty acid composition of membrane lipids: a decrease in the proportion of easily oxidized fatty polyunsaturated acids and an increase in the content of hardly oxidizable ... The accumulation of lipid peroxidation products leads to a redistribution of lipids in the membrane of the sarcoplasmic reticulum , resulting in an increase in the number of ordered clustered lipids in the bilayer due to a decrease in the proportion of liquid lipids and a decrease in the concentration of lipids interacting with the protein components of the membrane.

The main enzymes characterizing the activity of the antioxidant system are SOD and CAT. Determination of SOD activity is based on the ability of the enzyme to inhibit the reduction reaction of nitrotetrazolium blue in an alkaline environment.

The processes of lipid peroxidation against the background of the action of PAF, leukotrienes and proteases enhance the inflammatory response. It is believed that the accumulation of LPO products inhibits the respiratory function of mitochondria, changes energy metabolism and calcium permeability, which leads to a sharp increase in the concentration of calcium ions in the cell. Oxidized lipoproteins circulating in the blood system are referred to as destabilizing factors. The role of oxidized blood lipoproteins in the pathogenesis of acute and chronic diseases is now generally recognized. The reasons for the appearance of oxidized lipoproteins in the bloodstream include: their intake with food, synthesis and secretion by liver cells and activation of monocytes, neutrophils, and cells of the vascular wall. Reorganization of the native structure of blood lipoproteins during lipid peroxidation and oxidation leads to a change in the interaction of oxidized lipoproteins with biological membranes of blood cells and the vascular wall.

Antioxidants are a wide class of substances of various chemical nature that can inhibit or eliminate free radical oxidation of organic compounds by molecular oxygen.

Antioxidants are multifunctional compounds, depending on the mechanism of action , divided into antiradical inhibitors that interact with organic SRs; antioxidants that destroy organic peroxides; chelators - substances that bind oxidation catalysts - metal ions of variable valency; quenchers - substances that inactivate $0^{!}2$ without radiation

Antioxidant enzymes are also glutathione transferase , ceruloplasmin , etc. One of the most studied antioxidants is tocopherols, especially a-tocopherol (vitamin E), widely distributed in nature. Avitaminosis E in various animals (and hypovitaminosis E, which accompanies some pathological conditions in humans, causes a wide range of biochemical and physiological disorders, most of which are explained from the standpoint of the antioxidant concept of vitamin action. When using highly refined diets, only 1-7 mg / day of the vitamin is supplied with food E (with a need of 10 mg/day), which explains the deficiency of a-tocopherol in humans, leading to the development of free radical pathology, in particular: hemolysis of erythrocytes, neurological disorders, degenerative processes in internal organs.All these changes are due to destabilization of cell membranes, a decrease in the activity of enzymatic AO, an increase in the production of ROS and activation of lipid peroxidation. In this case, the processes of peroxidation proceed more intensively in lipids. Unsaturated fatty acids (linoleic , linolenic , etc.), being easily oxidized at double bonds, turn into peroxide, and then into hydroperoxide compounds. They are easily are destroyed, releasing active oxygen, which, apparently, is the main cause of metabolic disorders and damage.

Conclusions. In acute pancreatitis, the content of cytochrome P-450, microsomal protein, decreases , especially on the 7th, 10th day. Preliminary administration of vitamin E reduces the deficiency of microsomal hemoprotein . Its indicator increases by 1.6-2 times, but does not reach the norm.

In acute experimental pancreatitis, the content of LPO products (especially AGP) in the microsomal fraction of the liver and blood of rats increases significantly. Preliminary administration of vitamin E makes it possible to reduce these indicators by 1.6-1.9 times and bring them closer to the norm values.

In the microsomal cytosolic fraction of the liver and blood of rats with acute experimental pancreatitis, the activity of SOD and, especially, catalase is reduced. In contrast to the liver, in the blood of experimental animals, SOD activity slightly increases, while catalase sharply decreases. Vitamin E contributes to an increase in the activity of enzymes by 1.6-2.3 times, and if the activity of SOD slightly exceeds the control values, then the activity of CAT is still low.

Correlations between groups of experimental animals and at different times of the experiment are different and change their character with the preliminary administration of vitamin E.

LITERATURES

1. Pugaev AV Acute pancreatitis. Moscow: Profil , 2007. 335 p.].

2. Galperin EI Diagnostics and surgical treatment of pancreatic necrosis / / Surgery. 2003. No. 3. pp. 55-59.; Ermolov AS The main causes of lethality in acute pancreatitis in Moscow hospitals // Proceedings of the NV Sklifosovsky Research Institute of Emergency Medicine. 2001. T. 153. S. 4-14.].
3. Beger HG, Rau B., Isenmann R. Natural history of necrotizing pancreatitis // Pancreatology . 2003. Vol. 3, No. 2. P. 93–101].
4. Ursov SV Optimization of diagnostics and treatment of pancreatic necrosis / / Congress of Moscow surgeons: emergency and specialized surgical care: abstracts of reports. M., 2005. pp. 117-118., Uhl W., Warshaw A., Imrie C. [et al.]. IAP Guidelines for the Surgical Management of Acute Pancreatitis // Pancreatology . 2002 Vol. 2, no. 6. P. 565-573].
5. Savelyev VS, Filimonov MI, Gelfand BR, Burnevich SZ Destructive pancreatitis: an algorithm for diagnosis and treatment (project). 2001 Vol. 3, no. 6.pp. 373-379].
6. Vinnik Yu. s., Holman MI, Popov VO Acute pancreatitis: pathogenesis, clinic, treatment. - Krasnoyarsk- Zelenogorsk , 1997. - 208 p., Kubyshkin VA Pancreonecrosis : Dis.... doctor of medical sciences. - M., 1986 – - 384 p., Sotnikov AA Localization of foci of hemorrhagic necrosis with different variants of the ductal system of the gland // Questions of reconstructive plastic surgery. - 2002. - No. 2.-pp. 45-49 ., Howes N., V. Greenhalf , S. Rutherford, et al. A new polymorphism of the RI22H mutation in hereditary pancreatitis // Kishechnik . - 2001. - Vol. 48. No. 2.-pp. 247-250.
7. Rebours V., Levy P., Ruszniewski P. An overview of hereditary pancreatitis // Dig. Live Dis. 2012. Vol. 44, No. 1. P. 8–15 ..
8. Hirota M., Ohmuraya M., Baba H. Genetic background of pancreatitis // Postgrad. Med. J. 2006. Vol. 82, No. 974. P. 775–778.
9. Mayev IV, Kucheryavy Yu. A. Diseases of the pancreas. Vol. 2. M.: Medicine, 2008. 560 p., Lerch MM, Mayerle J., Aghdassi AA [et al]. Advances in the etiology of chronic pancreatitis // Dig. Dis. 2010. Vol. 28, No. 2. P. 324–329.
10. Truninger K., Witt H., Kock J. [et al.]. Mutations of the serine protease inhibitor, Kazal type 1 gene, in patients with idiopathic chronic pancreatitis // Am. J. Gastroenterol . 2002 Vol. 97, no. 5. P. 1133-1137.
11. Drenth JP, de Morsche R., Jansen JB Mutations in serine protease inhibitor Kazal type 1 are strongly associated with chronic pancreatitis // Gut. 2002. Vol. 50, No. 5. P. 687–692 ., Witt H., Luck W., Becker M. [et al.]. Mutation in the SPINK1 trypsin inhibitor gene, alcohol use, and chronic pancreatitis // JAMA. 2001. Vol . 285 , No. 21. P. 2716–2717.
12. Shukurov , I. B., & Umurov , F. F. (2020). Effect of tocopherol on glutathione metabolism in acute experimental pancreatitis. *Universum : chemistry and biology* , (3-1 (69)), 22-27.
13. Shukurov , IB, Khayrullayev , CK , Gulomova , M. T. , & Umurov , FF THE EFFECT OF VITAMIN E ON THE BIOCHEMICAL PARAMETERS IN THE EXPERIMENT .