Disorders of antioxidant defense in small intestine and its correction during acute necrotizing pancreatitis

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Key words: acute necrotizing pancreatitis, small intestine, glutathione, peroxidation, glutathione, N-acetylcysteine

Introduction. System hlutati onuyu (G) has a key role in antioxidant defense (AOP) tissues of the small intestine (TC) in acute surgical pathology of abdominal organs [1, 7, 8]. When excessive activation of lipid peroxidation (LPO) in patients with acute necrotizing pancreatitis (L D L) is quickly depleted supply of antioxidants (AO), including D, resulting in damage to the cell membrane of enterocytes and develop ment enteral insufficiency [4]. One of the few drugs that are capable of increasing endogenous contents recovered hlutati ONU (VG) is N-acetylcysteine (NAC) [1, 6].

The purpose of the work. Examine the breach antioxidant system of the small intestine in the HNP and evaluate the effectiveness of their correction NAC.

Material and methods. Work performed on white rats — males Wistar, weighing 200 — 250 g Animals are divided into 4 groups: control (I group), laparotomy (II group), induction of G N P L — arginine method P. Hegyi et al. (2004) [5] (III group), HNP and intraperitoneal administration NAC («F luimutsyl" firm Zambon grup, Italy) at the rate of 70 mg / kg / day in two administration (IV group). The animals were taken out of the experiment 6, 12 24, Jn 48 hours by an overdose of sodium thiopental. Experiments were conducted in accordance with the provisions of the Council of Europe Convention on the Protection of Vertebrate Animals used in Experiments and Other Scientific Purposes of 18.03.1986, the EU Emission Directive 609 of 24/11/1986 p. And MOH Ukraine from 13.02.2006 number 66 p. Conducted macroscopic and microscopic examination of tissues of the pancreas (pancreas) and small intestine (TC). Assessed degree of edema, infiltration and acinar cell necrosis [4]. Recycled hlutati one (VG) was determined in liver tissues (P), small intestine (TC), pancreas and enozniy blood. In the tissues T K determined and malondialdehyde (MD), diene conjugates (DC), catalase (K) [2]. All received digital data processed statistically using criterion (t) Student at normal distribution variables analyzed, And the Wilcoxon criterion — with deviation from the normal distribution.The difference between the comparative values was considered probable at P & lt; 0.05.

Results and discussion. In intact animals (I group) content in tissues SH P was significantly higher than in tissues pancreas and TC (Table. 1) and averaged 7,11 ± 0,17 mkmol / g tissue, which corresponds to the data [1, 5, 6], according to which almost 90% of circulating SH synthesized in Q and 50 — 60% of it comes from the bile in TC mucous which is utilized for detoxification. SH concentration in tissues TC Estates and La 2,62 ± 0,12 mmol / g. After laparotomy in animals II SH group content in tissues pancreas decreased by 21.6% (p <0.05) and TC tissues — on 26,25% (p <0, 05). At the same SH synthesis of P and its systemic circulation and practical ychno not disturbed (Table. 1). Qdonkey induction of T H P (III group) SH content decreases in P by 26.6% (p <0.05), due primarily to increased use of SH delivered by blood, by the second, including pancreas and fabrics TK. The concentration of SH si rovattsi blood decreased by 32, 4% (p <0.05) in tissue Pancreas 45.42% (p <0.02) and almost twice — TK tissue (p <0, 01). L D L fluid extravasation accompanied by a "third space", hypovolemia and circulatory shock [4]. Develops pancreas and ischemia of the abdominal cavity (PE), especially TC, due to the peculiarity of its blood supply. [4] In the following reperfusion in the first 48 hours of G N P form the ARE and accumulate reactive oxygen species (ROS) and lipoperoksyd and(LPO). Since the contents of the MD tissues TC has 6 hours increased by 35.6% (p <0.05) after 24 hours — by 48.3% (p <0.02) and remained higher (9,63 ± 0 16 n mol / g protein control — 5,61 ± 0,41 n mol / g protein; p <0.01) 48 hour experiment (Table. 2). These changes are intermediate products of lipid peroxidation — DC. Inactivation of lipid peroxidation products in the tissues was carried out on hlutati-dependent LPO recovery and hydrogen peroxide catalyzed hlutati onperoksydazoyu (GP) to form oxidized form D (GSSG), alcohols and water [8], and for atalaz th (K). This inventory AO TK tissues progressively fall after 48 hour experiment SH content was only 43.13% (P <0.02), and K -40.5% (p <0.01) indicators creature Eun control group (Table. 2). One of the factors limiting the restoration of HG content in P and other organs is the decrease of the biosynthesis rate of VH due to the deficiency of the amino acids precursors of VH. NAC Easily penetrates into cells and, as a result of deacetylation, becomes a cysteine that is a precursor of VH . Introduction of experimental animals of group IV NAC at a dose of 70 mg / kg / day increases the synthesis and restores, though not entirely, stock SH (Table. 1). Erez M 48 hours after induction of T H P SH content of P increased in comparison with the animals III Group 16 4 7% (p <0.05) in serum at 25, 93% (p <0.02), but remained below the prior control group. At the same time after administration of NAC was not significantly more recovery in tissues stocks AO TK (tab. 2), especially Br. The content of this peptide in the three tissues TC increased

progressively during the experiment was significantly (p <0.05) higher performance animals III d rupite, and at the end of the experiment was 2,37 ± 0, 07 mmol / g, which practically does not differ from the index etsya control group. Activity K 2.46 times (p <0.01) higher than the figure of animals IIIgroup. The restoration of the AO fund contributed to more effective neutralization of the products of the LP (Table 2), which prevents their toxin action on the tissues of TC and pancreas. Concentration MD and DC in tissues TC has dropped 6 hours after administration of NAC and throughout the experiment was within the parameters of the control group. In tissues pancreas cha stota decreased and the area of fat necrosis and hemorrhage, and cellular infiltration, swelling and ulceration wall mucosa TC (Table. 3).

Conclusions. In the first 48 hours of acute pancreatitis develops SH deficiency in the body, accompanied by toxic effects of lipid peroxidation products in the mucous membrane of TC and inflammation in the pancreas. N AC Input at a dose of 70 mg / kg / day of HNP animals leads to a rapid and significant increase in the content of education and SH lyzoviy with TC shell that reduces the degree of mucosal damage by free radicals and improves ysnyu for the course of inflammation in the pancreas.

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Experimental acute pancreatitis leads to deficit of reduced glutathione in pancreas, small intestine, liver and blood, which are caused by neutralization of lipoperoxides and active forms of oxygen. Administration of N-acetylcysteine 70 mg/kg/day increases amount of reduced glutathione in mucosal layer of small intestine, decreases level of its injury by free oxygen radicals and ameliorate inflammation process in pancreas.

Table 1

Metabolism of restored glutation experimental animal's acute pancreatitis (M ± m)

Animal Groups	Liver, Mmol / g	Pancreas, μmol / g	Small intestine, μmol / g	Blood serum, μmol / L
I	7.11 ± 0.11	5.24 ± 0.22	2.62 ± 0.12	92.6 ± 5.2
II	6.92 ± 0.28	4.11 ± 0.26 *	1.78 ± 0.18 *	89.6 ± 7.3
III	5.22 ± 0.22 *	2, 86 ± 0, 31 *	1 4 3 ± 0, 17 *	62.6 ± 6.5 *
IV	6.0 8 ± 0,15**	3.42 ± 0.25 *	2,37 ± 0,07 **	78.4 ± 8.4

Notes: I — Control group; II — animals after laparotomy; III — animals with HNP; IV — animals of the HNP, which introduced the N AC; * — p <0.05 compared with those in the control group of animals; ** — p <0,05 compared with those animals in group III.

Table 2

The evolution of the prooxidant and antioxidant systems of animals with acute pancreatitis in the treatment of N — atsetyltsy with tons eyinom (M ± m)

The term of observation	Malone dialdehyde Nmol / g protein		Dyne conjugates Nmol / g protein		Catalase, μmol / min / mg protein		Recovered glutathione, Mmol / g	
	I		I		I		I	
	5.61 ± 0.41		8.13 ± 0.91		542 ± 11.4		2.62 ± 0.12	
	III	IV	III	IV	III	IV	III	IV
6 hours later	7.61 ± ± 0 42 *	5.88 ± ± 0,29	9.54 ± ± 0,31	7.43 ± ± 1,11	305 ± ± 31,4*	455 ± ± 21,4**	1.93 ± ± 0,11 *	1.76 ± ± 0, 17 *
12 hours later	7.22 ± ± 0,72	6.08 ± ± 0,44	8.95 ± ± 0,44	7.49 ± ± 0,79	302 ± ± 28,8*	402 ± ± 17.9	1.86 ± ± 0,14 *	2.12 ± ± 0,12
24 hours later	8.32 ± ± 0,62*	5.76 ± ± 0,31**	9.62 ± ± 0,36	6.26 ± ± 0,91**	263 ± ± 14,7*	356 ± ± 22,3**	1.43 ± ± 0,12 *	2.19 ± ± 0,11**
48 hours later	9.63 ± ± 0,16*	5.46 ± ± 0,98**	9.44 ± ± 0,48	6.82 ± 0.56**	220 ± ± 32,4*	460 ± ± 41,7**	1.36 ± ± 0,09 *	2,37 ± ± 0,07**

Notes: I — Control group; III — animals with HNP; IV — animals with HNP, which introduced the N AC; * — p <0.05 compared with those in the control group of animals; ** — p<0,05 compared with those animals in group III.

Table 3

Effect of N AC on akroskopichni of us and microscopic tissue media and pancreas TC in animals with acute experimental pancreatitis (M ± m)

	Animal Groups			
	I (N = 7)	II (n = 7)	III (N = 7)	IV (n = 7)
The tissues of the pancreas, macroscopic signs				
Edema, points	0	1.7 ± 0.1	2.6 ± 0.3	2,1 ± 0, 1
Fat necrosis, scores	0	0	1.7 ± 0.2	0,7 ± 0, 3 *
Hemorrhages, scores	0	0	1,7 ± 0, 3	0,7 ± 0,2 *
The tissues of the pancreas, microscopic signs				
Edema, points	0	1,2 ± 0,1	2.5 ± 0.3	2.3 ± 0.2
Vascular changes, points	0	0	1.3 ± 0.2	0,5 ± 0, 1 *
Signs of inflammation, points	0	0.2 ± 0.1	0.7 ± 0.1	0.5 ± 0.2
Acinar necrosis, scores	0	0.5 ± 0.2	1.6 ± 0.1	1.3 ± 0.3
Fabrics of the small intestine, macro- and microscopic changes				
Edema, points	0	1,2 ± 0,1	2.8 ± 0.3	2.2 ± 0.2
Hemorrhages, scores	0	0	1.3 ± 0.2	0,5 ± 0, 1 *
Ulceration, scores	0	0	0.7 ± 0.1	0.5 ± 0.2
Ascites, ml	0	1.5 ± 0.6	6.6 ± 0.4	4,3 ± 0,3 *

Note. * — p <0.05 compared with the figures of animals III Groups