

and oxidized (OG) forms of glutathione were investigated spectrophotometrically.

Results and consideration. During the acute CAP period the production of proinflammatory cytokines IL-8, FNO α and OH group by neutrophils into the incubation medium increased ($p<0,05$) together with the activity increase of MP, which produced ClO $^-$ ions, that correlated with the pulmonary parenchyma inflammation intensity increase (the verification on the evidence of computerized tomography data). And with it the intracellular OAF amount in heterophilic leukocytes grew with protein oxidative modification (POM) processes promotion attended by the CP content increase and thiol-disulphide (TD) system balance shift towards oxygenized disulphide components formation. Against the OAF production increase in CAP patients the fact of total imbalance in glutathione-dependent neutrophil system has been registered, that was manifested in the GP activity inhibition, the decrease of DG amount and DG/OG integral factor characterizing the total TD potential capacity. The intracellular OG amounts' increase in neutrophils along with insufficient activity of GR and TRR reactivating reduction potential of the cell was registered. The HS/SS change is a repair moment in the processes of proteins oxidation and there can be no reparation in other OPM variants. Thus, the ratio of deoxidized thiol groups to oxidized ones and their ability to oxidative modification (buffer capacity) are important criteria of nonspecific cell resistance and enable their effective functioning. Antioxidative protection resources exhaustion and level increase of damaging functional proteins OAF leads to the creation of an oxidative stress situation in acute inflammation effector cells themselves. The redox potential decrease could promote the acceleration ($p<0,05$) of lethal program of neutrophils' apoptosis, which is registered in the acute CAP period.

Conclusions. The intra- and extracellular prooxidants production increase, POM with CP accumulation, glutathione-dependent system activity decrease against the expressed DG/OG index fall and reduction potential regeneration system's inhibition in neutrophils are the signs of oxidative imbalance of effector cells of acute inflammation developing in CAP debut, that worsens the clinical course.

Intracellular redox- potential modulation can take part in the regulation of programmed cell death of neutrophils in OS conditions.

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EVALUATION OF NEUTROPHILIC AND ERYTHROCYTIC PROTEINS' OXIDATIVE MODIFICATION IN OXIDATIVE STRESS CONDITIONS

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Protein molecules are not only objects, but also participants of regulation processes of cells' oxidative metabolism, the imbalance of which is registered in case of oxidative stress (OS) formation.

The purpose is to detect the features of neutrophilic and erythrocytic proteins oxidative modification (POM) processes on the model of OS, which is formed in acute period of community-acquired pneumonia (CAP).

Materials and methods. 47 patients with the verified CAP diagnosis have been examined; the control group was made up of 32 healthy donors matching on age and sex. Neutrophils were released on the Ficoll-Paque density bi-gradient; plasma was collected; erythrocytes were washed out and hemolysate was prepared (1:10). The oxidized carbonyl group proteins were detected in neutrophils by the enzyme immuno-detection method. In erythrocytes the proteins' carbonylation level, superoxide dismutase (SOD), catalase, glutathione peroxidase (GP) activity, deoxidized glutathione (DG) content were determined by spectrophotometric methods. The bitrosin formation and tryptophane oxygenation was evaluated in blood plasma by the fluorimetric method; the SOD, catalase activity, lipid peroxidation (LPO) products composition – diene (DC) and triene (TC) conjugates, malondialdehyde (MDA).

Results and considerations. In CAP patients in vivo the OS formation signs were registered. The LPO activation was attended by the increase of peroxide cascade toxicants in blood plasma: the DC, TC, MDA indexes were higher than the control ones ($p\leq0,01$) against the background of catalase, SOD antioxidant enzymes' activity decrease ($p\leq0,01$). The LPO products' excess lead to the mobilization and following degradation of antioxidants, creating their deficit in cells. The DG level in erythrocytes decreased at the GP, SOD, catalase activity combined inhibition against those in the control ($p\leq0,05$), being indicative of these cells' reduction potential inhibition. In parallel, the restoration capabilities of disulfide cross-links, provoking the inhibition of a range of key SH-containing enzymes, turned out to be suppressed in red blood cells. The oxidative metabolism imbalance in the CAP debut promoted the activation of POM processes: the carbonylation increased ($p\leq0,05$) both in acute inflammation effector cells (neutrophils) and in target cells (erythrocytes). Simultaneously the carbonylated proteins amount in plasma increased; the

proteins' oxidizability in vitro in conditions of incubation with the Fenton system components appearing to be increased: the carbonyl proteins increase was higher than in the group of control ($p \leq 0,05$). In the OS conditions at CAP the non-repair bitirozin cross-links and oxidized tryptophan – redox sensitive amino acids' oxidation products, accumulation in plasma was registered.

Conclusion

The accumulation of POM carbonyl products in plasma and blood cells, DG content and antioxidant enzymes decrease testifies to the expressed oxidative imbalance, developing in the CAP debut, in the system of functional proteins of the cell, that influences the pulmonary parenchyma state and worsens the disease course.

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UREA AND α -KETOGLUTARAT SPONTANEOUSLY FORM DEHYDROHYDANTOIN-5-PROPIONIC ACID IN VITRO

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By development of solutions for organs preservation we have found out, that solution EWS-1 (electrolyte water stabilization) does not prevent slices swelling in the test 24 hour incubations at +4°. Nevertheless, after addition 5mM α -ketoglutarat in EWS-1 and storages of this solution 24 hours at +4°C, it prevented a cortical kidney slices swelling authentically more effectively, than just prepared [1, 2]. Therefore we have assumed, any EWS-1 solution components enter a chemical reaction with formation of one or several derivatives possessing antiedematous action. The most probable candidates to us seem carbamide and α -ketoglutarat as carbamide falls into chaotropic compounds and it is inclined to formation ureid group. The ureid group, in particular, is present at all basic anticonvulsants of some derivatives of a hydantoin and in Karbamazepinum. All these compounds possess uniform property of chaotropic connections: to change physical and chemical properties of biological membranes, and to correct membranes permeability for Na^+ and K^+ . Besides hydantoins, possibly, prevent the brain swelling it previous development of the next epileptic attack.

Our experiments with the same medium, but for the lack of one of these compounds have appeared the indirect demonstration of what urea and α -ketoglutarat enter chemical reaction and form new compound. The solution containing both and urea and α -ketoglutarat preventioned a cortical kidney slices swelling at a hypothermal incubation (24 h at +4° C) whereas in a solution without one of these two compounds slices have swelled. [1, 2]. Us were it is carried out the given research with the purpose of revealing of this hypothetical substance.

Materials, methods and research volume

Synthesis of required compound has been carried out in several ways:

- 1) urea (extra pure (EP)) and α -ketoglutarat (EP) (on 0,1 M of each compound) containing equimolar quantities the solution has been heat uped on a water bath up to 80°C with the subsequent cooling on air;

- 2) urea and α -ketoglutarat equimolar quantities were incubated 24 hours at ambient temperature;

- 3) urea and α -ketoglutarat equimolar quantities were incubated 24 hours at +4°C;

The synthesized bond has received working name KM-1. The synthesized compound chemical structure has been certain by a NMR 1H spectroscopy method. For this purpose crystals KM-1 have been received by means of spontaneous evaporation within 2-3 months. The NMR 1H spectrum has been registered on device Bruker DRX-500 with a working frequency 500,13 MHz as the dissolvent has been used DMSO – d6. The internal standard was GMDS.

The experience with kidneys slices hypothermal incubation. As mother substances are natural animal metabolites their not enzymatic or enzymatic interaction in vivo with formation studied is possible KM-1. For check of this assumption we have spent experience on a hypothermal incubation (+4°C, during 24 hour) rats kidney cortical slices in mediums EWS-1 and EWS-1b (Tab. 1). On 5 mm either α -ketoglutarat (EP), or L-arginine (EP), or an ornithine (EP) have been brought in these solutions. Besides the hypothermal incubation of sections in medium EWS-HT with a concentration gradient has been spent KM-1 (0,1; 0,5; 1,0; 2,0; 5,0; 10,0 mM). pH mediums measurement has been carried out by means of pH-meter Piccolo plus. In total for experiences of 20 white not purebred rats-mans have been used, it a kidney mass was 140-160 g. Rats contained on a vivarium standard ration. Rats have been subjected to an ethereal euthanizing before kidney withdrawal. Rats' decapsulate kidneys quickly have been cut on thin cross-section at ambient temperature. Up to 20 sections have been prepared from each kidney on the average. Immediately after a rifling all sections have been weighed on torsion balances and, besides after an incubation.