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CERTAIN UNSOLVED QUESTIONS OF PATHOGENETIC INTERRELATION BETWEEN GASTROESOPHAGEAL REFLUX DISEASE AND CHRONIC FORMS OF ISCHEMIC HEART DISEASE (REVIEW OF THE REFERENCES)

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Abstract. The article deals with correlation links of developmental mechanisms and progressing of gastroesophageal reflux disease in patients with chronic forms of ischemic heart disease. The problem of treatment under conditions of comorbidity of these diseases is described.

Key words: gastroesophageal reflux disease, chronic forms of ischemic heart disease, comorbidity.

Success of modern diagnostics and pharmacotherapy are progressing as never before, but the problem of comorbid diseases still remains urgent. It refers to one of the most complicated parts of therapy. Availability of several diseases with chronic course provokes difficulties in making diagnosis, elaboration of therapeutic tactics and considerably worsens overall health [16, 17]. Today investigation of socially important diseases is rather topical including ischemic heart disease (IHD) and gastroesophageal reflux disease (GERD). Rapid increase of life style, negative influence of environmental factors contribute to general manifestation of morbidity for GERD among Ukrainian population. The topicality of the problem of gastroesophageal reflux increases in case of atypical manifestation of the disease and its complications which diminish the quality and provoke untimely diagnostics, and complicate the selection of an adequate therapeutic tactics respectively [1, 2]. In addition, the cases of comorbid course of GERD and hypothyroidism become more frequent.

In case of thyroid hormones deficiency, essential for normal functioning of practically every cell, pathologic changes develop in all the organs and systems including the digestive one [15, 24]. Hepatomegaly, dyskinesia of the bile ducts and colon, flatulence and inclination to constipation, poor appetite and atrophic gastritis [3, 10]. All these factors together with hypodynamia (lack of motion) and gaining body weight creates favourable preconditions for the development of GERD and ischemic heart disease. As a result, it leads to comorbidity of these diseases [18, 27].

Literary analysis does not provoke any doubt in that increased production of NO, its metabolites and melatonin accelerates the development and progressing clinical manifestation of GERD. NO promotes activation of guanylate cyclase which in its turn leads to increased content of cGMP of the muscular fibers, reducing the level of intracellular calcium and thus promotes relaxation of the posterior esophageal sphincter (PES) being a central mechanism in the development of GERD. On the contrary, melatonin inhibits cGMP action and possesses a stimulating effect on the tonus of PES limiting a negative influence of GERD on the course of IHD [13, 14, 19]. Besides, melatonin has a property to regulate the activity of NO-synthase and neutralize free radicals appearing in the process of synthesis and metabolism of nitrogen oxide [9, 11, 12].

Certain evidence is found in the studies of the scientists performed at T.M. Mala Institute of Therapy, the Academy of Medical Science of Ukraine in Kharkiv. They consider that the level of stable NO metabolites increases as far as erosive processes in the esophageal mucus are removed. This tendency is found more obvious in patients with comorbid conditions. The concentration of melatonin metabolites depends also on the pronounced lesion of the mucous membrane of the esophagus. The more pronounced the lesion is, the lower is melatonin concentration.

Oxidative-antioxidative imbalance being a link of pathogenesis of many internal diseases plays an important role in the development of pathogenetic changes [20, 23, 26, 29]. Although, today the state of the systems of lipid peroxide oxidation (LPO), protein oxidative modification (POM) and antioxidant defense (AOD) in patients with gastroesophageal reflux disease (GERD) and chronic forms of ischemic heart disease (IHD) remain insufficiently studied [21, 22, 25, 28]. Increased concentrations of oxygen active forms (OAF) and their metabolites are known to cause POM resulting in changes of the structural-functional properties of cells. Increased LPO intensity is found simultaneously. The influence of a destructive action of OAF in the tissues depends on the possibilities of the body concerning AOD mobilization. AOD disorders under the influence of toxic action of free radical products leads to structural and metabolic disorders in cells with further necrosis. Being aware of the fact, that increased concentration of OAF and intensification of LPO and POM processes reduce regeneration properties of the mucous membrane in case of erosive-ulcerous lesion of the digestive tract, one should modify GERD therapy by means of administration of antioxidant agents in the complex of therapeutic means [4].

The genes of II phase enzyme detoxication of the superfamily glutathione S-transferase (GST), especially GSTM1 and GSTT1 classes, play a key role to ensure cellular resistance to lipid peroxide oxidation, influence of free radicals on alkylation of proteins, prevention of DNA breaking, transport of

bilirubin, hormones, and biosynthesis of prostaglandins [1, 6], responsibility for the activity of oxidative stress in the continuum of cardio-vascular link in pathogenesis of diabetic complications [8]. GST-M1gene deletion is found to be the risk factor for coronary artery disease and arterial hypertension, and as a result, genotoxic lesion of chromosome by the products of thermal decay of tobacco with an appropriate expression on the endothelium [5, 9, 10]. Although, there are no data concerning the influence of mutation genotypes of the above mentioned genes of detoxication and antioxidant protection on the occurrence of gastroesophageal reflux disease (GERD), its complications (erosion, ulcer, bleeding etc.) in patients with GERD [5].

One more unsolved problem is changes in the system of fibrinolysis and proteolysis under conditions of comorbidity of these diseases. Proteolytic enzymes and their inhibitors take part in maintenance of the body homeostasis, blood clotting, metabolism, inflammation and digestion. Proteolytic activation is treated as the body reaction to lesion and results in resistance disorders of the digestive mucous membrane. Proteolytic condition depends on specific proteins-inhibitors inactivating proteolytic enzymes [1, 4, 6]. At the same time, proteolysis is in the basis of such vital physiological processes as blood clotting, fibrinolysis, regulation of blood pressure etc. Affliction of the epithelial and endothelial cells of the digestive tract mucous membrane due to increased proteolytic activity of blood plasma is accompanied by the activation of coagulation and platelet links of hemostasis leading to disorders of rheological properties of blood [6]. Therefore, the search of previously unknown mechanisms of development and progressing of gastroesophageal reflux disease (GERD) in patients with IHD and the means of effective correction of disorders found is certainly topical.

The question concerning the influence of disorders of psychic status and vegetal dysfunction on clinical course and efficacy of treatment of GERD is still studied. Certain authors indicate etilogical role of stress factors, peculiarities of psychological “portrait” of an individual, physical activity and/or occupational belonging in the course of the disease. One of the mechanisms in the development of motor esophageal dysfunction is considered disorders of cholinergic innervation of the cardioesophageal zone caused by functional imbalance of the parasympathetic and sympathetic links of the autonomous nervous system (ANS) [8]. Pathological changes in psycho-neurological status due to close relations between the hypothalamus-pituitary-adrenal system, ANS and neuroepithelial cells of APUD-system can cause motor-evacuatory dysfunction and development of GERD through disorders of topical endocrine regulation at the expense of the changes in the production of motilin, gastrin, somatostatin, vasoactive intestinal hormone and nitrogen oxide. In these conditions specially urgent problem is investigation of the role of dysfunction of the central and autonomous nervous systems in the initiation of reflux activity, clinical course of various variants of GERD and their effective correction, as imbalance of these two systems provokes the development of disorders of the cardio-vascular system function [8].

Positive results concerning the influence on the vegetal disorders in patients with cardio-vascular pathology have demonstrated the use of the medicine Noophen (hydrochloride beta-phenyl-gammaaminobutyric acid). Vegetal-vascular disorders are characterized by a great number of subjective symptoms such as emotional disorders, vegetal signs, internal tension, anxiety etc. Noophen possesse anti-anxiety, nootropic, tranquilizing, vegetostabilizing action, improves condition of patients improving their quality of life [7]. Practical absence of side effects especially peculiar for muscle relaxants of a central action and tranquilizers makes Noophen safe in its use in the treatment of vegetal disorders in patients with different pathology of the internal organs including patients with gastroesophageal reflux disease [7].

Conclusion can be drawn that both pathogenic mechanisms of development, diagnostic methods and strategy of treatment are not studied completely and requires urgent correction for successful development of internal medicine.

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НЕКОТОРЫЕ НЕРЕШЕННЫЕ ВОПРОСЫ ПАТОГЕНЕТИЧЕСКОЙ ВЗАИМОСВЯЗИ ГАСТРОЭЗОФАГЕАЛЬНОЙ РЕФЛЮКСНОЙ БОЛЕЗНИ И ХРОНИЧЕСКИХ ФОРМ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА (ОБЗОР ЛИТЕРАТУРЫ)

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Резюме. В статье освещаются корреляционные связи механизмов развития и прогрессирования гастроэзофагеальной рефлюксной болезни у больных хроническими формами ишемической болезни сердца. Описывается проблематика лечения в условиях коморбидности этих болезней.

Ключевые слова: гастроэзофагеальная рефлюксная болезнь, хронические формы ишемической болезни сердца, коморбидность.

ДЕЯКІ НЕВИРІШЕНІ ПИТАННЯ ПАТОГЕНЕТИЧНОГО ВЗАЄМОЗВ'ЯЗКУ ГАСТРОЕЗОФАГАЛЬНОЇ РЕФЛЮКСНОЇ ХВОРОБИ ТА ХРОНІЧНИХ ФОРМ ІШЕМІЧНОЇ ХВОРОБИ СЕРЦЯ (ОГЛЯД ЛІТЕРАТУРИ)

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Резюме. У статті висвітлені кореляційні зв'язки механізмів розвитку та прогресування гастроезофагальної рефлюксної хвороби у хворих на хронічні форми ішемічної хвороби серця. Описується проблематика лікування за умов коморбідності цих хвороб.

Ключові слова: гастроезофагальна рефлюксна хвороба, хронічні форми ішемічної хвороби серця, коморбідність.

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