

significantly higher in comparison with the control group of patients (by 2.1, 1.4 and 4.9 times, respectively). Similar results were observed when comparing levels of neopterin, TNF α and CRP in patients with IHD with hypothyroidism with a group of patients with IHD without structural and functional changes in thyroid gland: their concentration was by 2.2; 1.3 and 3.1 times higher than the corresponding indicators, respectively ($p < 0.05$). This indicates a clear immune activation in patients with IHD in the context of concomitant hypothyroidism. The question of the relationship between markers of immune activation, inflammation and endothelial dysfunction in patients with IHD with thyroid pathology is also an interesting one. Significant positive correlation relationships were established between the level of neopterin and TSH ($r = +0.36$; $p < 0.05$), ET-1 and TSH ($r = +0.46$; $p < 0.05$) and inverse correlation interactions between the neopterin level concentration and free T4 ($r = -0.29$; $p < 0.05$). The obtained data testify that hypothyroidism increases the risk of complications of atherosclerosis, provokes the progression of IHD both due to the development of endothelial dysfunction, stimulation of systemic inflammation and increased secretion of proinflammatory cytokines [4]. Thus, patients with IHD, which occurs on the background of hyperthyroidism, had an increase in markers of immune activation and endothelial dysfunction compared with patients with IHD without thyroid disease. The presence of correlations between the levels of neopterin and ET-1 with the hormones of the pituitary-thyroid system suggests the involvement of hypothyroidism in stimulating systemic inflammation and the development of endothelial dysfunction in patients with IHD.

Prospects for further research: Further scientific research will deal with the development of optimally substantiated schemes of differentiated combined treatment of patients with IHD on the background of hypothyroidism, taking into account changes in immune-inflammatory and endothelium dysfunction markers.

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INHIBITION OF MARKERS OF THE IMMUNE INFLAMMATION IN BRONCHIAL ASTHMA INFLUENCED BY FULLERENE C₆₀ NANOPMATERIALS

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Bronchial asthma (BA) is a chronic disease associated with local tissue inflammation and remodeling of the airway [1, 2]. Inflammation is a complex immune response which involves immune cells as regulators and effectors of the immune function and, therefore, may play critical role in pathophysiological processes. Recent studies have suggested the possible effect of dysfunction immune cells and/or their products on inflammation process in BA. Fullerene C₆₀ is the most promising nanomaterial in

modern medicine due its key properties, small size, enhanced permeability, surface modification and retention effect [3, 4]. Fullerene C₆₀ and some of its derivatives as potent antioxidants are capable of effective ROS inactivation and lack of immunogenicity [5, 6]. However, little is known about the effect of fullerene C₆₀ on immune mechanisms in the pathogenesis of BA. Therefore, further studies of fullerene C₆₀ will be required for the development of specialized target treatment strategy in BA. The purpose of our work was to determine the effect of fullerene C₆₀ on markers of immune inflammation in experimental model of BA.

Materials and Methods. Balb/c 24 mice aged 6 weeks were divided into 4 groups: intact, control and two experimental. Experimental BA sensitization of mice were induced by the ovalbumin (OVA; Sigma, USA) intraperitoneal solution in a sterile physiological saline at the start of the study and at day 14, and by inhalation of the OVA solution at 24, 25, and 26 days. Animals of the experimental groups were intraperitoneally injected with an aqueous dispersion of fullerene C₆₀ or a fullerene C₆₀ solution conjugated with OVA in an amount of 0.05 ml at 24, 25, 26 days, one hour before OVA inhalation. Evaluated the level of CD4 + and CD8 + lymphocytes by flow cytometry, cellular composition in the lungs by the method of tissue imprints, histological analysis was conducted light microscopy (Axio Lab.A1, Carl Zeiss, Germany).

Results. CD4⁺ T lymphocytes expression was significantly increased to $38.5 \pm 1.05\%$ and CD8⁺ T lymphocytes expression was significantly decreased to $21.2 \pm 1.2\%$ in mouse with experimental BA compared to intact group. After administration of fullerene C₆₀ CD4⁺T lymphocyte expression was significantly reduced to $30.83 \pm 0.6\%$ compared to animals with BA. After administration of fullerene C₆₀ conjugated with OVA only CD8⁺ T lymphocyte expression was significantly increased compared to animals with BA.

In the study of lung tissue imprints in animals with experimental BA, eosinophils and lymphocytes quantity were increased, while neutrophils and alveolar macrophages quantity were significantly decreased in the lung. After administration of fullerene C₆₀ and its conjugated to OVA form macrophages quantity were significantly increased in the lumen of the airways compared to animals with BA. A morphological study of large and medium-sized bronchi in animals with experimental BA revealed that there are areas with goblet cell hyperplasia, an increased number of cells, dystrophy and atrophy of the epithelium. Marked infiltration of the submucosa and muscle plate by mononuclear cells (lymphocytes) was revealed. Various forms of fullerenes contributed to the normalization of the state of tissue structure. The bronchial epithelium is predominantly cylindrical, a decrease in bronchial secretion was noted. The lumen of the bronchioles and bronchi were free. A decrease in infiltration by mononuclear cells was noted.

Conclusions. These results suggest that fullerene C₆₀ effectively prevents immune inflammation in a mouse model of BA by decreasing the level of CD4 +T lymphocytes expression and the number of eosinophils, increasing the number of neutrophils and macrophages as cells of non-specific immune protection. Fullerene C₆₀ significantly decreases tissue inflammation and airway remodeling. In conclusion, fullerene C₆₀ acts as potential anti-inflammatory and immunomodulatory agent via inhibition of NF- κ B- and MARK-dependent signaling pathways [7] and, therefore, may prevent inflammatory responses during BA.

Prospects for further research. Further studies are needed to characterize the effects of nanoparticle-based drugs on the prevention of immune inflammation and the development of a treatment strategy for bronchial asthma.

Recommendations. Markers of immune inflammation are an important goal in the study of the pathogenetic course of AD. Our results lay the foundation for further study on the use of fullerene C₆₀ as an anti-inflammatory agent in the treatment of bronchial asthma.

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NEUTROPHILIC EXTRACELLULAR TRAPS IN TISSUES WITH DIFFERENT TREATMENT MODES OF COLORECTAL CANCER

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An important feature of malignant tumors is their relatively autonomous growth, regulated by locally produced factors, which include “microenvironment factors” of tumors produced by both the tumor cells themselves and the cells of the stroma surrounding them. A permanent component in the structure of microenvironment of tumors are neutrophilic granulocytes. But their role in oncogenesis is not fully established. There is evidence that in addition to antitumor activity neutrophils can demonstrate antitumor activity, provoking metastasis. In response to microbial and non-microbial stimuli, neutrophils actively form network-like structures in the extracellular space consisting of nucleic acids and enzymes – neutrophil extracellular traps (NET). Fibrous structures of NET represent the main DNA chain containing histones and proteins – products of neutrophil granules. The main protective function is the destruction of pathogens [1]. Views about the role of neutrophil traps in Oncology vary greatly. On the one hand, there is evidence of anticarcinogenic properties of NET associated with direct destruction of tumor cells and stimulation of the immune system. Cytotoxicity in relation to tumor cells is manifested by the components of NET (myeloperoxidase, proteinase and histones), while DNA strands are considered as a kind of tool for capturing tumor cells and limiting their further spread [2, 3]. On the other hand, NET can promote migration and immune avoidance of tumor cells. The possible role of the flow of neoplastic process As a prognostic biomarker in NET is suggested [4, 5]. The aim of this study was to investigate extracellular neutrophil traps in colorectal cancer.

Materials and Methods. The study is carried out within the framework of the scientific and technical program “Personalized approach in the management of a number of significant diseases”, developed by the NAO “Medical University of Karaganda”. A set of patients with cancer of the colon and rectum was carried out under the conditions of the KGP “Regional Oncology center” of Karaganda, Kazakhstan. The clinical diagnosis was established according to ICD 10, for the classification of
