INFLUENCE OF INCREASED GLUCOSE CONCENTRATIONS ON OXYGEN-INDEPENDENT METABOLISM OF NEUTROPHILS

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Influence of simulated conditions of hyperglycemia (6.5 mM, 8.0 mM, 11.0 mM) on spontaneous and induced myeloperoxidase activity of azurophilic granules of polymorphonuclear leukocytes has been researched. It was established that the spontaneous and receptor-induced activity of myeloperoxidase of azurophilic granules of neutrophils in hyperglycemia condition increases with the increase in the amount of glucose in the pre-incubation environment.

Keywords: hyperglycemia, myeloperoxidase, neutrophils, atherosclerosis, oxidative stress, Staphylococcus aureus, azurophilic granules, glucose.

It has been figured out recently that MPO is an important factor in the initiation and development of a variety of diseases associated with the related to a chronic or acute inflammatory process. In clinical practice, the activity of neutrophil myeloperoxidase serves as a marker for the intensity of inflammatory processes, and is also a promising diagnostic and prognostic indicator for a number of diseases and pathological conditions. The biological effect of MPO is largely determined by the balance between the effectiveness of the secretion of this enzyme in the extracellular space at the stage of neutrophil degranulation, on the one hand, and its inactivation and utilization in tissues, as well as degradation of oxidants formed in reactions involving MPO, on the other hand. In the secretory degranulation or death of neutrophils, the pathological action of the enzyme may be manifested.

Elevated systemic level of MPO is associated with the presence of coronary arterial diseases and may provoke the risk of developing adverse cardiological events (myocardial infarction, sudden death, etc.) among patients with chest pain and acute coronary syndrome. In addition, elevated levels of MPO can play a decisive role in atherosclerosis, oncological, neurodegenerative diseases, impaired lung respiratory function, kidney disease, systemic vasculitis, rheumatoid arthritis, etc.

Increased glucose content is able to reduce the immune response, lead to suppression of phagocytic activity of neutrophils, metabolic changes occur including glycosylation of proteins, metabolism of polyol (converts glucose to sorbitol), activation of protein kinase C (increased activity of this enzyme in hyperglycemia is accompanied by activation of lipid peroxidation processes), the formation of free radicals of oxygen, nitrogen oxide, cyclic guanosine-3’-5’ monophosphate, the reaction of glycolysis. In this case, the strong oxidants that result from the functioning of MPO initiate lipid peroxidation, the modification of proteins and nucleic acids (including halogenation, nitration, oxidation and cross-linking), thereby damaging the own tissues in the inflammation points.

In the experiments physiologically recorded glucose concentrations of 6.5 mm, 8.0 mm, 11.0 mm. have been used. To induce myeloperoxidase degranulation the daily culture of St. aureus have been used. With mild hyperglycemia (6.5 mM), the increase in spontaneous myeloperoxidase activity was increased at 1.2 times. In hyperglycemia of moderate degree (8.5 and 11.0 mm), the increase in spontaneous myeloperoxidase was observed at 1.6 and 2 times, respectively, and the induced activity was increased at 1.2 and 1.6 times in relation to intact cells.

It is obvious that glucose in concentrations of 6.5, 8.0 and 11.0 mm stimulates the processes of glycolysis and Krebs cycle, leading to the increase in the synthesis of ATP molecules and to the hyperactivation of neutrophils. Spontaneous and induced release of myeloperoxidase triggers the formation of free forms of oxygen and oxidative radicals, but in this case, it promotes the development of oxidative stress and leads to an increase in the bioaggressive potential of neutrophils.

Thus, the incubation of neutrophils under simulated hyperglycemia results in a nonspecific increase in the activity of myeloperoxidase cells, which promotes the generation of active oxygen species and the development of oxidative stress.

BIBLIOGRAPHY