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FEATURES OF THE PHARMACOLOGICAL ACTION AND USE OF DIPYRIDAMOLE IN THE PREVENTION AND TREATMENT OF VIRAL INFECTIONS

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Abstract: The review presents current information on the molecular mechanisms of antiplatelet, vasodilatory, angioprotective, antifibrotic and immunomodulatory effects of dipyridamole. The paper presents data from domestic studies devoted to testing the efficacy and safety of dipyridamole (Curantil) in the prevention of acute respiratory viral infections and the treatment of recurrent stress-induced opportunistic infectious diseases, which show that dipyridamole is an effective combination drug with a good safety profile and the ability to exert a positive effect on blood vessels in metabolic disorders in patients with a complicated medical history, and allows for effective prevention of acute respiratory viral infections in high-risk patients.

Keywords: dipyridamole, molecular mechanisms of action, prevention and treatment of acute respiratory viral infections, organoprotective action.

INTRODUCTION

The most common infectious disease is acute respiratory viral infection (ARVI). The number of complications with ARVI, especially with influenza, reaches 20-30% during epidemics. The main causes of complications are dysfunction of the body's immune system with a decrease in antibacterial resistance and the addition of a bacterial infection in high-risk patients. Etiotropic antiviral therapy exists only for the treatment of influenza: neuraminidase inhibitors (oseltamivir), M2 protein blockers (adamantanes) and a fusion inhibitor (umifenovir). For other types of ARVI, drugs of pathogenetic and symptomatic types of action are used [1].

MATERIALS AND METHODS

The best way to combat complications of ARVI is to prevent the disease itself. The development of infection can be prevented by targeted activation of one of the most ancient mechanisms of the body's defense - the interferon system (IFN). IFN is a family of local regulation proteins that can activate intracellular processes and intercellular interactions that ensure the body's resistance to viral infections, enhance the innate and acquired immune response, and modulate the processes of development and death of unchanged and tumor cells. The body's resistance to viral infections and a number of other diseases largely depends on the activity of IFN genes. The effects of IFN are indirect – activation of IFN specific receptors causes a cascade of cellular processes leading to the induction of genes encoding the synthesis of many proteins that provide the antiviral effects, antitumor and antiproliferative action of IFN. Proteins induced by IFN include: enzymes, receptors, transporters, cytokines, chemokines and other factors. The production of IFN by cells is transient, temporary – normally “silent” IFN genes are induced under the influence of products of viral and microbial origin and chemical inductors (high- and low-molecular) [2].

RESULTS AND DISCUSSION

For the prevention of ARVI, IFN preparations, IFN inducers and other immunomodulators are often used. Popular IFN preparations have a number of drawbacks from a pharmacological point of view, the most important of which is the problem of bioavailability (this does not apply to injectable IFN, but this method of administration is not used for the prevention of ARVI). A fairly large peptide molecule of IFN will be destroyed and lose its properties when taken orally, and when applied locally, it will not be able to overcome tissue barriers. Nevertheless, local use of IFN has a right to exist, since in the mucous membrane they stimulate local immunity, thereby

strengthening the protection of potential infection gates. A more popular class of drugs for the prevention of viral infections are low-molecular IFN inducers, which can be taken orally. The problem of drug prevention and treatment of ARVI is that high-risk patients, i.e. For those who especially need medications, medications included in the treatment standards are often contraindicated. In particular, pregnant women, overweight patients and patients with diabetes, older patients, and children are at risk of severe and complicated influenza. Therefore, among IFN inducers, a special place is occupied by dipyridamole, a well-studied drug with a favorable safety profile, which is widely used in clinical practice as an antiplatelet agent, vasodilator, and IFN inducer. To exhibit IFN-inducing activity, dipyridamole must be administered in significantly smaller doses (4–8 times smaller than generally accepted therapeutic doses) according to a special regimen adopted for most low-molecular IFN inducers (once a week) [3].

The antiplatelet effect is associated with several events. Firstly, dipyridamole causes an increase in the concentration of adenosine in tissue by inhibiting the reuptake of adenosine by cells (nucleoside transporter ENT1) and blocking its catabolism – adenosine desamenase (P. Gresele, 1986; P. Ferrandon, 1994; C. Wang, 2013). Adenosine exhibits the properties of a platelet inhibitor (stimulates adenylate cyclase – AC through A2A receptors). Secondly, in human platelets, dipyridamole enhances the nitric oxide – NO/cyclic guanosine monophosphate – cGMP signal and its consequences, such as phosphorylation of serine 239 VASP, inhibition of thromboxane synthase and serotonin secretion (B. Aktas, 2003). Thirdly, there is inhibition of the intracellular PDE enzyme – non-selective in high doses and selective – PDE type 5 (cGMP) and PDE type 8 (cyclic adenosine monophosphate – cAMP) – in therapeutic (V. Ahn, 1989; S. Francis, 2011), responsible for the breakdown of cyclic nucleotides. The accumulation of cGMP and cAMP in the cell (platelet) causes a decrease in the concentration of free Ca2+ ions, as a result of which contractile proteins (microtubules and microfilaments) do not polymerize, which is absolutely necessary for the transport of receptorosomes to the membrane and the exposure of IIb/IIIa receptors on the cell surface (actually, platelet activation) [4].

CONCLUSION

Dipyridamole is an effective drug with complex action, its effects include antiplatelet, anti-ischemic and immunomodulatory action. The drug improves the rheological properties of the blood, promotes angiogenesis and the development of collaterals, has an angio- and organoprotective effect (neuro- and nephroprotection). It is used not only for cardiovascular diseases, but also in obstetrics. Its immunomodulatory effect is successfully used for the prevention of acute respiratory viral infections, influenza and the treatment of opportunistic infections.

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