CURRENT METHODS AND PROMISING WAYS OF THE GAUCHER DISEASE TREATMENT

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Introduction. Gaucher disease (GD) is the most common hereditary disease, classified as an autosomal recessive genetic disorder. The development of the disease is based on a defect in the enzyme β-D glucosidase, which leads to the accumulation of glucocerebrosides (complex glycolipids) in the cells of the reticuloendothelial system (lysosomes of cell-macrophages). The prevalence of GD is approximately 1: 40.000, in the general population, rising to 1:800 among Ashkenazi Jews. GD has a multisyndromic character with predominant damage to the nervous system, bone tissue, liver, spleen, and bone marrow. The high disabling potential of GD encourages the search for new ways of its treatment, including innovative directed drugs.

Aim. Based on the obtained experimental and clinical data, as well as information about the disease and its treatment, to predict and highlight promising areas of therapy for the Gaucher disease.

Materials and methods. The literature was reviewed, which describes the treatment of GD including pharmacotherapy options for the disease. A search was conducted for relevant publications on the PubMed and Medscape portals from September 2018 to March 2020.

Results and discussion. Among the currently available treatment methods, they are widely used nowadays; we can distinguish Enzyme Replacement Therapy (ERT) and Substrate Reduction Therapy (SRT). The ERT method is based on the use of Imiglucerase, Velaglucerase and Taliglucerase. The principle of action of which is to replace the lack of the β-D glucosidase enzyme and stop the initial pathophysiological changes. The occurrence of secondary pathological transformations in the body is overlapping. There are some visible disadvantages of this treatment: lifelong intravenous administration, high cost, and not entering to the nervous system. SRT is presented by drugs Eliglustat and Miglustat. They minimize the synthesis of excess cell material by inhibiting intracellular synthesis. The most significant advantages of the SRT method are the possibility of oral administration of the drug, the relatively easy penetration of active substances through the blood-brain barrier and the effective penetration into tissues and organs.

One of the most progressive strategies in treatment of GD is concomitant therapy, based on the use of molecular chaperones. Molecular chaperones are small molecules that enable proteins to take on the specific molecular configuration which determines their functional efficacy. They also protect proteins by preventing inappropriate aggregation, that facilitate their passage through the cell membranes and thus their transport into lysosomes, when dealing with lysosomal enzymes. Molecular chaperones can therefore help the production of functional enzymes and thus even restore the intracellular activity of mutant GCase. This approach is especially applicable in GD because only a modest increase in residual GBA should be sufficient to ameliorate the phenotype. Moreover, these small molecules should be able to cross the blood-brain barrier. The effect is thought to be responsible for the positive results of pilot studies with ambroxol. The development of this type of treatment for GD is still in the early stages. Another promising approach to treating GD is the use of induced pluripotent stem cells by transplantation. A donor bone marrow transplant was used to treat lysosomal accumulation diseases. In this case, monocytes from peripheral blood migrate through the blood-brain barrier and turn into microglial CNS cells, which in turn take on the function of further cross-metabolic correction.

Conclusions. Summing up, the current state of development and improvement of the treatment of one of the most common hereditary diseases of accumulation, Gaucher Disease, was helded.

NEW METHODS IN IMMUNOTHERAPY OF ALLERGIC DISEASES

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Introduction. Allergen-specific immunotherapy (ASIT) is a method of treating allergic diseases, which consists in introducing into the patient's body in increasing doses the allergen that causes the disease. Its aim is to induce a tolerogenic response against the allergen of interest. Moreover, ASIT reduces the risk of developing asthma, at least in the short term, in patients with allergic rhinitis. ASIT is also effective in patients with IgE-mediated food allergy and insect venom allergy, with allergic asthma and rhinoconjunctivitis.

Aim. The aim of this review is to provide an overview of the current knowledge on the mechanisms and new methods of allergen immunotherapy based on the recent publications and clinical trials.