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.

Materials and methods. Data analysis of literature and Internet sources.

Results and discussion. The complex mechanism of action of ASIT occurs in 3 phases: rapid desensitization, early tolerance, and sustained tolerance. Rapid desensitization is characterized by an early fall in degranulation of mast cells and basophils, probably due to rapid upregulation of histamine type 2 receptor. The second phase, early tolerance, includes a decrease in interleukin (IL) 4–secreting TH2 cells and increases in IL-10–secreting Treg cells and Breg cells. Finally, sustained tolerance implies that Treg cells stimulate B cells to produce allergen-specific IgG4, a tolerogenic highaffinity blocking antibody that competes with allergen-specific IgE, thus avoiding the allergen-induced release of mediators by mast cells and basophils. These sequentially activated mechanisms induce immune tolerance that attenuates or even abolishes both the acute (early) phase of allergic reaction and any subsequent immunologic event. Over the last decade, there have been increasing interests in developing and modifying ASIT to strengthen its efficacy while maintaining or improving its safety profile. The goal of using adjuvant molecules is to enhance the immunological and thus also the clinical efficacy of ASIT. An ideal adjuvant should be able to accomplish 2 goals. First, to modify the nature of the immune response by inducing a robust Th1 response and/or suppressing Th2 responses arising from the allergic state. Second, to amplify the primary immune response to ASIT, thus requiring lower doses of allergen to achieve therapeutic effect.

Allergoid vaccines are allergen extracts which have been modified chemically by substances such as glutaraldehyde or formaldehyde. The chemical modification causes irreversible intra- or intermolecular polymerization of the protein, disrupting the conformational IgE epitopes of the allergen. Immunostimulatory sequences are oligodeoxynucleotide DNA sequences containing unmethylated CpG motifs, which are recognized by Toll-like receptor 9 (TLR 9), an important member of the TLR family of transmembrane signaling molecules that play an important role in the initiation of innate immune responses. ISS induce interferon (IFN)-α and convert a Th2 immune response to a Th1 response. Omalizumab (anti-IgE monoclonal antibody) is a recombinant humanized monoclonal antibody which binds to free IgE, preventing it from binding to the $Fc_{\varepsilon}R1$ and decreasing the number of FcεRI receptors on basophils. Aluminium hydroxide (carrier) is now being used as a safe carrier adjuvant in ASIT. It induces a strong Th2 response by stimulating the activation of antigen presenting cells, independent of TLR signaling. Advances in molecular cell biology have allowed for the development of standardized and effective recombinant allergen preparations for both sublingual immunotherapy and subcutaneous immunotherapy. A handful of studies on the successful use of probiotics as adjuvants in ASIT have been reported. The use of probiotics as adjuvants in ASIT is likely to be strain-specific, given that different strains of bacteria. Fungal compounds, specifically fungal immunomodulatory proteins (FIPs), have been shown to have immunomodulatory properties such as the ability to inactivate the innate immune system, such as dendritic cells, NK cells, monocytes/macrophages, as well as induce cytokine/chemokine production which in turn activate the adaptive immune system by polarizing the Th1 or Th2 effector cells and stimulating the differentiation of B cells for antibody production. Helminths (parasitic molecules) use several immunomodulatory strategies to evade or modify the host immune response in order to survive in the host. These including suppression or inactivation of host antigen-specific immune response. Vitamin D may act as an adjuvant by activating specific regulatory immune cells to prevent atopic disease. In addition to finding an optimal adjuvant, the discovery of an optimal window period for ASIT and an optimal mode of delivery may also be important in optimizing the outcomes of ASIT. It may be desirable to start ASIT earlier in life or even in the antenatal period, at a time when the immune system is still naïve and before any structural complications of allergy have occurred, such as lung remodelling in asthma, or chronic sinusitis in allergic rhinitis. New routes of ASIT administration now include administration of allergens via tissues which have a high density of antigen-presenting cells such as via the skin and lymphatics.

Conclusions. Overall, there has been increasing interests in the use of novel approaches to augment the effects of ASIT for atopic disease. There is a need for more robust, larger-scale randomized clinical trials in humans to thoroughly evaluate the safety, clinical efficacy and cost effectiveness of the use of these various modalities across age and disease spectrums.