Pro Index | Journal of Science in Medicine and Life

Volume: 2 Issue: 6 Year: 2024

http://journals.proindex.uz

Allergic Reactions to Drugs in Children

Yomgurova Ozoda Rajabturdiyevna

Bukhara state medical institute after named Abu Ali ibn Sino

Abstract: Drug allergies are characterized by the occurrence of hypersensitive reactions to medications that have an immune mechanism of development. In such reactions, antibodies and/or activated T cells are directed against drugs or their metabolites. This problem is very relevant for practical healthcare, since more than 7% of the population suffers from drug allergies.

Key points: drug allergy, diagnosing drug allergy, drug hypersensitivity reactions, child.

In addition, severe life-threatening allergic reactions may develop, requiring hospitalization and long-term treatment. Immunological reactions to drugs (drug hypersensitivity reactions) are considered in category B of adverse drug reactions, the mechanism of which is associated with an abnormal response to drugs. This distinguishes them from type A reactions, which can occur in any patient and are usually related to the underlying mechanism of action of the drugs and their dosage.

Theoretically, allergic reactions can be caused by all drugs, but the most common causes are antibiotics, anticonvulsants, nonsteroidal anti-inflammatory drugs (NSAIDs), and anesthetics. The risk of developing a drug allergy and its clinical features depend on the individual properties of the immune system, the dose of medication, duration of treatment, route of administration, gender of the patient, as well as unique HLA characteristics, which are increasingly being described.

It is possible to develop both immune and non-immune (pseudoallergic) forms of hypersensitive reactions to drugs, often having identical clinical manifestations. Non-immune variants of undesirable adverse reactions to drugs can have different origins, for example: nonspecific degranulation of mast cells or basophils with the release of histamine (x-ray contrast agents, vancomycin), changes in the metabolism of arachidonic acid (non-steroidal anti-inflammatory drugs - NSAIDs), pharmacological action of substances that cause bronchospasm (beta blockers).

Drug hypersensitive reactions, depending on the time of their manifestation from the start of treatment, are divided into immediate and delayed (delayed). Immediate drug hypersensitivity reactions occur predominantly within the first hour (first six hours) after drug administration and are induced primarily by an IgE-mediated mechanism. Their typical symptoms are urticaria, angioedema, rhinoconjunctivitis, bronchospasm, nausea, vomiting, diarrhea, abdominal pain, anaphylaxis. Delayed-type hypersensitive reactions can occur at any time 1 hour after drug administration, but usually occur later than 6–72 hours from the start of drug administration and are associated primarily with T-cell mechanisms of the allergic reaction. Their clinical manifestations are very diverse and may include maculopapular exanthema, exfoliative dermatitis, erythroderma, DREss syndrome (drug-related eosinophilia with systemic symptoms), toxic epidermal necrolysis, and other bullous reactions. System-wide effects may include the development of hepatitis, nephritis, cytopenia, etc.

Drug hypersensitivity reactions have been around for as long as drugs themselves have existed. However, many of the mechanisms of their formation have not yet been disclosed, and for a large number of types of drug hypersensitive reactions there are still no approved diagnostic procedures. Medicines can cause the development of all types of immunopathological reactions described by

P.G.N. Gell and R.R.A. Coombs [21], but IgE-mediated and T-lymphocyte-mediated reactions are the most common ones.

Immediate allergic drug hypersensitive reactions are based on the hyperproduction of IgE antibodies by antigen-specific B lymphocytes. The binding of specific IgE antibodies to high-affinity receptors on the surface of mast cells and basophils, their interaction with the drug antigen leads to the release of preformed mediators (histamine, tryptase), tumor necrosis factor and newly formed mediators (leukotrienes, prostaglandins, kinins, cytokines). These mediators can be used as diagnostic biomarkers of drug hypersensitivity. Clinically, these reactions manifest themselves in the form of urticaria, angioedema, rhinitis, conjunctivitis, bronchospasm, gastrointestinal disorders or anaphylaxis, anaphylactic shock. Their development can be observed with the use of foreign serums, beta-lactam antibiotics, sulfonamides, analgesics, and NSAIDs.

The second type of drug allergic reactions is cytotoxic. It is based on the interaction of predominantly IgG or Igm with an antigen fixed on cell membranes, followed by the development of complement-mediated damage to these cells. Clinically, it manifests itself predominantly as immunopathological reactions from blood cells, for example, immune hemolytic anemia.

The occurrence of some clinical forms of drug allergies may be due to immunocomplex reactions (type III according to Gell and Coombs). They are based on the formation of immune complexes, their deposition in the vascular bed on the endothelial membranes of small-caliber vessels, with the subsequent occurrence of tissue damage and microcirculation disorders. Immune complex reactions occur with the involvement of complement in the pathological process, the resulting anaphylotoxins C3a and C5a cause the release of histamine, proteolytic enzymes, and vasoactive amines from mast cells and basophils. This mechanism is leading in the development of serum sickness, vasculitis, systemic lupus erythematosus, glomerulonephritis, Arthus phenomenon, and some exanthems of drug origin. The most common cause of the immune complex variant of drug allergy is the use of antibiotics, serums, vaccines, sulfonamides, anesthetics, NSAIDs, and modern immunobiological drugs (drugs based on monoclonal antibodies).

However, in recent years, special attention has been focused on delayed allergic reactions to drugs that are mediated by T lymphocytes. The most common target for drug-responsive T cells is the skin, but other organs may also be involved. First, the drug antigen is processed by dendritic cells, then the antigen is transported to regional lymph nodes, where it is presented to T cells. Subsequently, antigen-specific T-lymocytes migrate to the target organ; after exposure to the antigen, they are activated and secrete proinflammatory cytokines, which cause the development of inflammation and tissue damage. Clinically, delayed drug hypersensitivity reactions most often manifest themselves in the form of symptoms of skin lesions: the occurrence pruritic maculopapular rash, fixed drug eruptions, vasculitis, toxic epidermal necrolysis, Stevens-Johnson syndrome, generalized bullous fixed drug eruptions, acute generalized eczematous pustulosis and symmetrical drug-related intertriginous and flexor exanthems.

Internal organs can also be involved in the pathological process (isolated or in combination with skin symptoms, resulting in hepatitis, kidney damage, hypersensitivity pneumonitis, cytopenias.

It was also noted that the development of allergic reactions to pharmacological drugs in the same patient may involve the participation of several types of immunological reactions. Thus, the involvement of both IgE-mediated and cell-mediated reactions has been proven in the development of insulin allergy.

Many drugs and/or their metabolites are haptens, but when they bind to proteins they form a complete antigen. Such newly formed antigens can cause the development of both IgE-mediated and T-cell-mediated drug hypersensitivity reactions.

Of great interest are modern studies indicating an undoubted connection between the risk of developing both immediate and delayed allergic drug reactions with genetic factors. This is evidenced, in particular, by the identified relationship between Stevens-Johnson syndrome, epidermal toxic necrolysis induced by carbamazepine, and the HlA-B*1502 antigen, as well as the

association of IL-4 and IL-10 gene polymorphism with immediate drug hypersensitive reactions to beta- lactam antibiotics.

In recent years, it has been established that viral infections, including all herpesviruses, can provoke a drug hypersensitive reaction and the appearance of skin rashes if the medicine (most often antibiotics) is used during the infectious process. Clinical manifestations can be very serious - in the form of DREss syndrome (drug-induced eosinophilia with systemic symptoms) and other systemic manifestations.

Hypersensitive reactions to drugs occur more often in patients, including children, who suffer from allergic diseases. This may be due to a change in the metabolic functions of the body in the biotransformation of medicinal compounds and, in particular, a change in the activity of their acetylation and the formation of antigenic determinants when interacting with body proteins.

As mentioned above, clinical manifestations of drug hypersensitivity can be immediate or delayed relative to the time of taking the drug. In addition, there are systemic (anaphylaxis, drug fever, serum sickness) and organ-specific variants of drug allergic reactions. Modern literature emphasizes that the main target organ for drug hypersensitivity is the skin, however, other organs may also be involved in the pathological process: the hematopoietic system (eosinophilia, cytopenia, hemolytic anemia), the respiratory system (rhinitis, bronchospasm, laryngeal edema, eosinophilic pulmonary infiltrate), urinary system (glomerulonephritis, nephrotic syndrome, interstitial nephritis), hepatobiliary system (hepatocellular lesions, cholestasis).

Let us consider the features of the main syndromes characteristic of drug hypersensitivity, including those described relatively recently. The most common symptoms of drug allergies are skin symptoms, which is due to the high immune activity of the skin. The rashes are polymorphic in nature. They are accompanied by itching, most pronounced with measles-like and scarlet-like rashes. Maculopapular rash. Papular and/or morbilliform rashes account for 75–90% of drug-induced skin rashes. The onset of the rash is usually observed 1 week after the start of treatment [55]. In the absence of other manifestations, these rashes are usually not dangerous. The predominant cell type in this case is cytotoxic CD4+ T cells. However, it is possible for the rash to progress to more serious manifestations, including toxic epidermal necrolysis, which is mediated primarily by CD8+ cytotoxic T cells.

In general, these skin changes disappear a few days after stopping the drug, which is often accompanied by extensive exfoliation of the epidermis, which can leave areas of depigmentation.

References:

1. Demoly P., Adkinson N.F., Brockow K., Castells m., Chiriac A.m., Greenberger P.A., Khan D.A., lang D.m., Park H.s., Pichler W., sanchez-Borges m., shiohara T., Thong B.Y. International Consensus on drug allergy. Allergy 2014; 69(4): 420–437, http://dx.doi.org/10.1111/all.12350.
2. Gomes E., Cardoso m.F., Praca F., Gomes l., marino E., Demoly P. self-reported drug allergy in a general adult Portuguese population. Clin Exp Allergy 2004; 34(10): 1597–1601, http://dx.doi.org/10.1111/j.1365-2222.2004.02070.x.
3. Dao R.-l., su s.-C., Chung W.-H. Recent advances of pharmacogenomics in severe cutaneous adverse reactions: immune and nonimmune mechanisms. Asia Pac Allergy 2015; 5(2): 59–67, http://dx.doi.org/10.5415/apallergy.2015.5.2.59.
4. Балаболкин И.И., Булгакова В.А. Клиническая аллергология детского возраста с неотложными состояниями. М: МИА; 2011; 264 с. Balabolkin I.I., Bulgakova V.A. Klinicheskaya allergologiya detskogo vozrasta s neotlozhnymi sostoyaniyami [Clinical allergology of childhood with urgent conditions]. moscow: mIA; 2011; 264 p.
5. Rawlins m.D., Thompson J.W. mechanisms of adverse drug reactions. In: Textbook of adverse drug reactions. Davies D.m. (editor). Oxford: Oxford University Press; 1991; p. 18–45.