Classification, etiopatogenesis and clinical studies of drug hypersensitivity

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Abstract: In recent years, the safety of pharmacotherapy has become of particular relevance for practitioners. The reason for this is the prevalence of complications of drug therapy. Quite often, patients receiving drugs develop toxic and allergic reactions, there are hereditary adverse reactions. Drug allergy occupies a special place in this structure. According to WHO data for 2001, the lethality from drug allergies was more than 5 times higher than the lethality from surgical interventions. The frequency of allergic reactions tends to increase and is 17% in people who regularly take medications.

Keywords: drug allergy, drugs, drug biotransformations, polypharmacy

Numerous diagnostic errors, the frequency of which reaches 30%, are also due to the polymorphism of the clinical picture of drug allergy, incorrect assessment of the anamnesis and errors in the interpretation of clinical and laboratory data, as well as difficulties in identifying the drug allergen. This may also be due to the appointment of several drugs (MP) at the same time, without taking into account their interaction with each other, a change in the reactivity of the patient's body, as well as the widespread, often uncontrolled use of drugs by the patients themselves.

Etiology, pathogenesis, classification.

Drug allergy (DA) can develop to any drug. The most common allergens are antibiotics, vitamins, non-steroidal anti-inflammatory drugs, local anesthetics, radiopaque agents, plasma substitutes, hormones, vaccines and sera, as well as auxiliaries used in the preparation of drugs. It is known that the ability to sensitization depends not so much on the chemical structure of the drug, but on the characteristics of its biotransformation in the body. This makes it clear why people with impaired drug biotransformation processes, with liver and kidney diseases, have an increased likelihood of developing not only toxic, but also allergic reactions to drugs. Summarizing the above, we can distinguish the following factors that determine the high rate of development of drug allergies:

• growth in drug consumption by the population;

• widespread self-treatment due to the availability of drugs (possibility of acquiring them without prescriptions);

• insufficiency or delay of medical information about the side effects of medicines;

• polypharmacy;

• pollution of the environment by industrial waste;

• diseases of an infectious, parasitic, viral or other nature. Which in themselves are not allergic, but, due to the peculiarities of pathogenesis, create the possibility of the formation of sensitization and the production of allergic antibodies in response to a wide variety of allergens, including medicinal ones (for example, allergic reactions to penicillin often occur in patients with foot mycoses);

• the use of antibiotics, vitamins, hormonal drugs and other drugs for the treatment and fattening of livestock, creating the possibility of sensitization of the population due to impurities contained in food products (meat, milk) obtained from these animals.

The reaction develops after a period of sensitization with either the active substance or an "inert" substance (fillers, stabilizers) used in drug preparation technology. Sensitization can occur with any route of administration of the drug: oral, parenteral or topical. The rate of development of sensitization depends on the route of administration of the drug. Local application and inhalation application most often and quickly causes sensitization, but less often leads to the development of life-threatening conditions. Intravenous administration sensitizes somewhat less than intramuscular and subcutaneous. For example, parenteral administration of β-lactam antibiotics is more likely to cause anaphylaxis than oral agents.

The most important signs of true allergy to drugs are sensitization and immune response only upon repeated contact with the allergen. An exception may be the so-called "latent" sensitization, due to the fact that the organism, predisposed to allergic reactions, had previously air or food contact with this drug or chemically related substances, i.e. we are talking about the cross-antigenic properties of LP.

It is possible to activate the complement system in an alternative way (bypassing the stage of the immunological response). In this case, the side effect of drugs is associated with the direct release of mediators without a previous period of sensitization (i.e. at the first dose of the drug), the presence of specific IgE antibodies, or the formation of an antigen-antibody complex on the membrane of mast cells / basophils. Conventionally, these reactions were called non-specific reactions or pseudo-allergic.

True allergic reactions go through three stages:

I. The stage of immune reactions (immunological) - begins with the first contact of the body with the drug and consists in the formation and accumulation of allergic antibodies or sensitized lymphocytes in the body. When the drug enters the body again, the allergen-antibody complex (or allergen-sensitized lymphocyte) is formed, which determine the next stage of the allergic reaction.

II. Stage of biochemical reactions (pathochemical). As a result of complex biochemical processes triggered by allergen-antibody or allergen-sensitized lymphocyte complexes, ready-made and new biologically active substances (allergy mediators) are released. From this stage, the interaction of allergy target cells, carrying complexes of IgE, IgG or antibodies of other classes, with a specific allergen begins to occur.

III. Stage of clinical manifestations (pathophysiological). An increase in the level of mediators in the blood leads to the development of a number of clinical symptoms (skin hyperemia, itching, skin rashes, a feeling of heat, headache, shortness of breath, etc.).

The classification of drug allergy (LA), based on the pathogenetic principle of P.Gell and R.Coombs (1969), has become widespread. According to this classification, LA can proceed according to any of four types of immunological reactions. Often in patients with LA there is a combination of several types of drug allergic reactions, one of which prevails. This can be explained by the general mechanism of initiation of IgE and IgG synthesis by B cells. In 1998, Snow R. E. et al. published the results of studies convincingly showing that in patients with LA, individual B-lymphocytes producing specific antibodies are able to selectively intensify the synthesis of both IgE and IgG4. At the same time, the severity of the course of an allergic disease depends on the level of the balance existing between them.

Clinic

The most common manifestations of LA are general allergic reactions (anaphylactic shock, erythema multiforme and Stevens-Johnson syndrome, bullous epidermolysis, including epidermal necrolysis - Lyell's syndrome). Various skin reactions are not uncommon (urticaria, contact dermatitis, fixed erythema, eczema and eczema-like lesions, acneiform rashes, lichenoid rash, etc.), lesions of the mucous membranes of the oral cavity, tongue, eyes, lips (stomatitis, gingivitis, glossitis, cheilitis, etc.).) and the gastrointestinal tract (gastritis, gastroenteritis). From the hematopoietic system in LA, all three links of hematopoiesis can be involved. Most often, allergic leukopenia and agranulocytosis occur, less often - thrombocytopenia and anemia. The most severe form of these pathological conditions is pancytopenia - total oppression of hematopoiesis, which occurs as an allergic complication during therapy with acetylsalicylic acid, quinine, chlorpromazine, heavy metal compounds, gold preparations, streptomycin, sulfonamides and some other drugs.

Less commonly, LA is identified as the cause of myocarditis, nephropathy, systemic vasculitis, periarteritis nodosa, and systemic lupus erythematosus (SLE). LP can cause autoimmune reactions. The literature provides examples of Coombs-positive hemolytic anemia caused by methyldopa and mefenamic acid, SLE - similar manifestations after the use of novocainamide and apressin. Perhaps the development

of generalized lymphatic hyperplasia with a wide range of autoantibodies (to erythrocytes, lymphocytes, nucleoprotein, etc.). In this case, interference of the drug substance with the lymphocyte membrane was noted. When furadonin is used, the formation of autoantibodies to albumin, IgG - lupus syndrome can be observed.

The most common symptoms of LA are vascular lesions, which manifest themselves differently in different cellular and organ territories: in the kidneys they lead to the development of nephritis, in the lungs - to pneumonia, in the skin - to the appearance of exanthema. Many drugs can cause a form of vascular disease known as Henoch-Schonlein thrombocytopenic purpura. Thrombocytopenic purpura may be due to the use of drugs such as acetylsalicylic acid, quinine, chlorpromazine, isoniazid, iodine, gold preparations, tetracycline, penicillin, sulfanilamide preparations, etc. Allergic reactions to drugs may develop in the myocardium and in the coronary vessels, as a result which causes transient disorders of the coronary circulation - up to a typical picture of a heart attack described after the administration of sera and streptomycin. Allergic myocarditis may occur after the use of antihistamines and PAS.

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