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SECTION 2.

MEDICAL SCIENCE

THE MODERN TREND OF THE ANTIALLERGIC PHARMACOLOGICAL THERAPY

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Antihistamines H1-receptor blockers — drugs that eliminate or reduce the effects caused by the interaction of histamine with the receptors of this type: smooth muscle spasm, increased capillary permeability, the development of edema, tachycardia, and so forth Today, there are several classifications of drugs which refer to this group. As one of the most common blockers all H1 receptors are divided into formulations of the I, II and III generation [3—10].

The I generation preparations (Diphenhydramine, Diazolin, Suprastine

The III generation preparations — fundamentally new remedies, active metabolites of the previous generations. Their main feature is the lack of cardiotoxicity (do not change the interval QT). In addition, the above mentioned drugs do not penetrate the blood-brain barrier and thereforedoes not have side effects from the CNS (no sedative), have important additional antiallergic effect: reducing the expression of adhesion molecules (ICAM-1) and inhibit eosinophil-induced secretion of interleukin (IL-8), cytokines (GM-CSF) and sICAM-1 in epithelial cells (anti-inflammatory properties). They are also characterized by high bioavailability and long half-life, which allows a single receiving and storing action effect during the day [3—10].

Drugs belonging to a modern third generation are: Cetirizine, Fexofenadine, Dezloratadin and Norastemizol. Let us consider them in detail.

Cetirizine is the first example of the synthesis of qualitatively new H1-blocker, an active metabolite generation antihistamine I — Hydroxyzine. From its predecessor Cetirizine is characterized bythe presense of the hydroxyl group in its structure, which gives it a number of additional important physico-chemical and pharmocological properties. Thus, the negative charge of the molecule Cetirizine, provision by hydroxyl group, it dramatically reduces the possibility of penetration through the BBB. As a result, there is practically no blocking H1-receptors in the central nervous system that manifests a decrease sedation [2; 7—10].

Some clinical studies have shown that Cetirizine at usual doses (10 mg/day) can cause adverse reactions from the CNS (drowsiness, fatigue, headache and dizziness), but they are not obvious and temporary. Furthermore, Cetirizine is highly selective peripheral H1-blocker, even at high doses, it does not interact with other receptor types, thereby aliminating side effects, able to have its predecassors less active (disorders of the gastrointestinal tract, mucosal dryness, blurred vision).

Also Cetirizine at therapeutic doses has potent antiallergic activity associated with inhibition of expression at epithelial cells adhesion molecule (ICAM-1) that prevents from adhesion migratory cells (eosinophils, basophils), endothelial and epithelial cells with subsequent penetration into tissues and cavities and development allergic inflammation. In addition, the mentioned above drug inhibits the cytotoxic activity of the platelets. Clinical studies of Cetirizine therapeutic influence investigated on the basis of the classical manifestations of allergy (allergic rhinitis and rhinokonyuktivity, chronic urticaris) have shown its high efficiency.

Modern registered preparations containing Cetirizine in its composition are: Allertek, Tsetrin, Amertil, Zyrtec, Zodak, Cetirizine-Sandoz, Cetirizine-Astrofarm.

Dezloratadin — active metabolite of Loratadin. Its distinctive quality is the ability to stabilize the membrane of mast cells basophils. It inhibits production of histamine, tryptase, prostaglandins. An important pharmacologic effect of Dezloratodin is its ability to inhibit the secretion of proinflammatory effector cells of bioactive substances: proinflammatory cytokines, chemokines, adhesion factors. It is a long-acting drug: the half-life is approximately 21—24 hours, which allows you to prescribe the drug 1 time per day. Similar to the preparations described before, Dezloratodin also does not cause adverse changes in the cardiovascular system and other organs, no sedative action. The advantages of dezloratodin over other antihistamines in allergic rhinitis and idiopathic urticaria were proved by means of the clinical experiments, including several multi-center, double-blind studies in which a total of about 48 000 patients took part It is a constituent of such drugs as: Aerius, Lourdes, Allergostop, Edem [1; 2; 8—10].

Fexofenadine — antihistamine designed by American scientists in 1993, it is a racemic mixture, which includes two reactive metabolite of the drug isomer of the II generation — terfenadine. The preparation is similar to cetirizine, it does not penetrate the BBB, a sedative effect is not observed even at taking it in doses of 2 times the standard. This determines the uniqueness of this drug of its kind and allows assignment of it to people whose work is related to the management and transport mechanisms

At doses higher than therapeutic, even repeatedly, Fexofenadine, according to clinical studies does not affect the slow potassium channels infarction, hence does not affect the functioning of the heart and has no cardiotoxicity. A positive aspect is the fact that after entering the body, Fexofenadine hardly undergoes any change, because it is a metabolite and thus — displays rapid pharmacologic effect. It has been shown in 80 % of patients with allergic rhinitis, complete disappearance of all symptoms observed for 30 minutes of the oral usage.

Fexofenadine may be widely used in combined therapy, since it does not interact with other drugs (except antacids that contain aluminum or magnesium hydroxides, which reduces its bioavailability). As the active ingredient, it is a part of such drugs as: Altiva, Feksofast, Allergo, Tigofast, Telfast [3—10].

Thus, the appearance of antihistamines of the III generation allows to expand the range of their application. Due to the higher activity, better security and a more rapid onset of clinical effect, they are chosen for many serious diseases, including bronchial asthma. And thanks to indicators such as more predictable level in blood, increased therapeutic index and better tolerability, absence of drug interactions due to the fact that drugs are not

metabolized in the liver, the can be administered in the complex therapy of patients with concomitant diseases and the elderly people.

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