

CLINICAL PHARMACOLOGICAL APPROACH TO THE USE OF ANTIHISTAMINES IN CHILDREN UNDER 3 YEARS OF AGE

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ABSTRACT

This article discusses the clinical and pharmacological aspects of using antihistamines in children under three years of age. The focus is placed on the pharmacokinetics, pharmacodynamics, and safety profiles of commonly used antihistamines in pediatric patients. Special attention is given to age-specific physiological factors that influence drug metabolism and efficacy. The article also highlights the importance of individualized treatment approaches, considering the potential side effects and contraindications in young children. Recommendations for the appropriate selection and dosing of antihistamines are provided, supported by recent clinical guidelines and evidence-based studies.

Keywords: Antihistamines, pediatric pharmacology, children under three, clinical pharmacology, drug safety, pharmacokinetics, pharmacodynamics.

INTRODUCTION

Histamine is one of the most important mediators of various physiological and pathological processes in the body, including allergic reactions. Histamine is released from mast cell granules under the influence of various physical and chemical irritants, but most actively – during the interaction of an allergen with antibodies on the surface of mast cells. Histamine released by mast cells during allergic reactions interacts mainly with H1 receptors. An increase in its concentration causes spasm of smooth muscles and bronchi, dilation of blood vessels, increased permeability of the vascular wall, release of plasma from the vascular bed, tissue edema, decreased blood pressure, etc. [1, 2].

Over the past few years, the number of patients with bronchial asthma (BA), allergic rhinitis, atopic dermatitis (AD) has been increasing. These conditions are usually not life-threatening, but require active therapeutic intervention, which should be effective, safe and well tolerated by patients. The appropriateness of using antihistamines in various allergic diseases (urticaria, AD, allergic rhinitis, conjunctivitis, etc.) is due to the wide range of effects of histamine [2, 3].

MATERIALS AND METHODS

H1-receptor blockers prevent the development and alleviate the course of allergic reactions. This group of drugs prevents or eliminates excessive physiological effects of endogenous histamine in the body by reducing its concentration in tissues, as well as by blocking histamine receptors. Most of the antihistamines used have a number of specific pharmacological properties, such as anti-allergic, antipruritic, anti-exudative, antispasmodic, anticholinergic, sedative-hypnotic, etc., and also reduce capillary permeability, prevent the development of tissue edema, relieve smooth muscle spasms [2, 3]. In the same year, the pharmacological

effect of histamine on animals was established, which made it possible to consider it as an important physiological mediator. A series of studies conducted in the 1920s allowed us to formulate the idea that histamine is the most important mediator of such allergic manifestations as anaphylactic shock, rhinitis, asthma, and urticaria [5].

RESULTS AND DISCUSSION

In recent years, the list of these drugs has been constantly updated, new compounds of H₁-histamine receptor blockers are synthesized, which, while exhibiting a pronounced antihistamine effect, are distinguished by the peculiarities of their pharmacokinetic and pharmacodynamic properties.

Despite the emergence of 2nd generation antihistamines, 1st generation drugs will continue to remain in the arsenal of drugs for widespread use due to:

- the constant receipt of new clinical data based on long-term experience in the use of these drugs and the possibility of a differentiated approach to their administration;

- the presence of certain pharmacological effects in 1st generation H₁-antagonists (such as antiserotonin activity, sedative effect, anticholinergic effect, etc.). Suprastin is a classic first-generation antihistamine drug with pronounced antihistamine and M-anticholinergic effects.

In recent years, new data on the mechanisms of action of Suprastin have appeared, due to which it has found wide application in medical practice. Thus, in 2013, a meta-analysis of comparative studies on the sedative effect of first- and second-generation H₁-blockers was published in the April issue of the journal *J Allergy Clin Immunol*. According to the authors of this publication, the difference in the frequency of sedative action between first- and second-generation antihistamines is not as significant as previously assumed. Data from 18 clinical studies showed that the results of the studies varied significantly, with the level of sedation in some studies in patients taking 1st generation drugs being lower than in patients taking placebo or 2nd generation antihistamines. New data on the pharmacokinetics of 1st generation antihistamines have appeared: in particular, it has become known that this indicator for chlorpheniramine, brompheniramine and hydroxyzine in adults exceeds 14–20 hours, so they can be used 1 or 2 times a day without reducing efficacy and with a decrease in the frequency of side effects [2].

Unlike second-generation H₁-blockers and first-generation drugs that do not have anticholinergic activity (mebhydroline and quifenadine), the mechanism of action of Suprastin is associated with both its ability to block H₁-histamine receptors and competitive antagonism with respect to muscarinic receptors, which mediate parasympathetic stimulation of nasal gland secretion and vasodilation. In addition, due to the ability to penetrate the blood-brain barrier, Suprastin affects the receptor formations of the medulla oblongata and hypothalamus and acts on the sneezing center, blocking the parasympathetic cascade in relation to the nasal glands and blood vessels. Clinically, Suprastin effectively reduces rhinitis symptoms such as mucosal edema and nasal congestion, rhinorrhea, itching and sneezing in acute respiratory viral infections [3].

Prescribing Suprastin 2 times a day at a daily dose of 50 mg (25 mg per dose) for 5 days already on the 2nd day of administration reduces nasal congestion, discharge and sneezing. On the 4th–5th day of treatment with Suprastin, nasal breathing is practically restored, nasal

discharge, sneezing and itching in the nose cease. Analysis of the dynamics of the disease in groups comparable in gender, age and the nature of the pathological process showed that in patients receiving Suprastin, rhinitis symptoms regress 1.6–2.3 times faster than in the group of patients receiving vitamins and herbal preparations. Against the background of relief of rhinitis manifestations, the general condition of the patient improves, the intensity of sore throat decreases, and the severity of cough syndrome caused by discharge from the nasal cavity flowing into the larynx and trachea decreases. In addition, the use of Suprastin allows in certain cases to avoid the use of nasal vasoconstrictors, which, with prolonged use, can cause drug-induced rhinitis. Patients already using nasal decongestants manage to significantly reduce the frequency of their use (by 40%) [3].

Prevention of acute subglottic laryngitis ("false croup") in children with acute respiratory infections

Suprastin as an antihistamine is prescribed for acute respiratory viral infections, since the allergic component plays an important role in the mechanism of development of laryngeal mucosal edema, especially with "false croup". In addition, Suprastin has an M-cholinolytic effect, due to which it also eliminates mucosal edema. It is important for pediatric practice that Suprastin is approved for use in children starting from the 1st month of life [4].

AD and other itchy allergic dermatoses (eczema, chronic recurrent urticaria, etc.)

The main and invariable symptom of allergic dermatoses, primarily AD, is itching of the skin. Discomfort associated with skin itching leads to significant disturbances in sleep, daily activities, and social relationships [5]. The use of H₁-receptor antagonists as basic drugs for the treatment of AD is justified by the critical role of histamine in the mechanism of skin itching in AD, which leads to skin damage, the formation of erosions, excoriations, crusts, lichenification, scars, hyper- and hypopigmentation and, as a consequence, to an increase in the release of inflammatory mediators, which in turn intensify it; an itching-scabies cycle is formed. Itching leads to sleep disturbances and the development of a neurotic state. In this regard, skin itching significantly affects the quality of life of patients and determines the severity and course of AD [2]. The presence of a sedative effect makes first-generation antihistamines indispensable in some clinical situations, for example, in AD, accompanied by debilitating skin itching, which intensifies at night and significantly disrupts sleep. The existence of an injectable form of these drugs allows them to be included in detoxification regimens for patients with severe forms of AD. They can be administered parenterally - intramuscularly, in acute severe cases - intravenously (under the supervision of a physician), which is especially important in the treatment of children, patients suffering from severe and widespread forms of allergic dermatoses and having concomitant pathology of the gastrointestinal tract [3].

Leading American dermatologist, Harvard University professor T. Fitzpatrick also recommends giving preference to antihistamines with a sedative effect in case of severe itching [4]. According to the French allergist A. Didier, not only antihistamine but also anticholinergic action is necessary for the treatment of allergies. "The release of acetylcholine and substance P from presynaptic nerve endings can maintain the allergic inflammation reaction at the level of the cholinergic nervous system in the late phase of the anaphylactic reaction.

Anticholinergic action blocks the late phase of the anaphylactic reaction (absent in selective antihistamines) [5].

CONCLUSION

The use of first-generation antihistamines in clinical practice has not lost its relevance. Many years of positive experience in the clinical use of Suprastin in children gives grounds to assert that the drug has broad indications for use in various areas of practical medicine and remains a reliable and proven remedy for the treatment of allergic and infectious-inflammatory diseases of the respiratory tract in children.

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