Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/alergo

Review/Praca poglądowa
Experts' guidelines/Zalecenia ekspertów

The role and choice criteria of antihistamines in allergy management – Expert opinion

Piotr Kuna [1,*], *Dariusz Jurkiewicz* [2], *Magdalena M. Czarnecka-Operacz* [3], *Rafał Pawliczak* [4], *Jarosław Woroń* [5], *Marcin Moniuszko* [6,7], *Andrzej Emeryk* [8]

[1] *Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Faculty of Medicine, Medical University of Lodz, Lodz, Poland*
[2] *Department of Otolaryngology with Division of Cranio-Maxillo-Facial Surgery, Military Institute of Medicine, Warsaw, Poland*
[3] *Department and Division of Dermatology, Poznan University of Medical Sciences, Poznan, Poland*
[4] *Department of Immunopathology, Division of Allergology, Immunopathology and Dermatology, Faculty of Biomedical Sciences and Postgraduate Training, Medical University of Lodz, Lodz, Poland*
[5] *Department of Clinical Pharmacology, Faculty of Medicine, Medical College Jagiellonian University, Krakow, Poland*
[6] *Department of Allergology and Internal Medicine, Faculty of Health Sciences, Medical University of Bialystok, Bialystok, Poland*
[7] *Department of Regenerative Medicine and Immune Regulation, Medical University of Bialystok, Bialystok, Poland*
[8] *Department of Lung Diseases and Rheumatology, 2nd Faculty of Medicine, Medical University of Lublin, Lublin, Poland*

Reprint of article published in "Postępy Dermatologii i Alergologii". doi:10.5114/pdia.2016.63942, Copyright: © 2016 Termedia Sp. z o. o. *This article should be cited as:* Adv Dermatol Allergol 2016;33 (6):397–410.

Przedruk pracy opublikowanej w „Postępach Dermatologii i Alergologii". doi:10.5114/pdia.2016.63942, Copyright: © 2016 Termedia Sp. z o. o. *Pracę należy cytować jako:* Adv Dermatol Allergol 2016;33 (6):397–410.

ARTICLE INFO

Article history:
Received: 29.08.2016
Accepted: 18.09.2016
Available online: 10.02.2017

Keywords:
- Antihistamines
- Bilastin
- Allergic rhinitis
- Urticaria
- Allergy

ABSTRACT

Allergic diseases are the most common chronic conditions lasting throughout the patient's life. They not only cause significant deterioration in the quality of life of patients but also lead to significant absenteeism and reduced productivity, resulting in very high costs for society. Effective and safe treatment of allergic diseases is therefore one of the main challenges for public health and should be carried out by all the specialists in family medicine, internists and paediatricians in collaboration with allergists, otorhinolaryngologists and dermatologists. Antihistamines are most commonly used in the treatment of allergies. Several dozen drugs are available on the pharmaceutical market, and their generic forms are advertised widely as very effective drugs for the treatment of allergic diseases. What is the truth? What are the data from clinical trials and observational studies? Are all drugs equally effective and safe for the patient? According

* *Corresponding author at*: Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Faculty of Medicine, Medical University of Lodz, ul. Kopcińskiego 22, 90-153 Łódź, Poland. Tel.: +48 42 677 69 51.
E-mail address: piotr.kuna@umed.lodz.pl (P. Kuna).
http://dx.doi.org/10.1016/j.alergo.2017.02.001
2353-3854/

to a panel of experts representing various fields of medicine, inappropriate treatment of allergies can be very risky for patients, and seemingly equally acting medications may differ greatly. Therefore, a panel of experts gathered the latest data from the entire scientific literature and analyzed the latest standards and recommendations prepared by scientific societies. This paper provides a summary of these studies and highlights the importance for the patient of the proper choice of drug to treat his allergies.

Which antihistamines should be chosen according to current standards and recommendations?

In the last few decades the incidence of allergic diseases has grown to epidemic status. According to the current data, more than 600 million people suffer from allergic rhinitis worldwide, approximately 25% of them in Europe. In the ECAP trial (Epidemiology of Allergic Diseases in Poland) as many as 30% of respondents reported allergic rhinitis, less than 7% mentioned urticaria, but over 40% of patients had positive skin tests with common inhaled allergens (e.g. plant pollen, dust mites, mould and animal hair). Despite this huge number of patients, these data are frequently underestimated, since allergic diseases are generally believed to be trivial and non-hazardous. However, it has already been proven that allergic rhinitis, asthma and urticaria are associated with a significant socioeconomic burden all over the world – regardless of region, development level and financial status. The total cost of allergic diseases brings both reduced quality of life and also direct costs of drugs and health services as well as indirect social costs such as the absence from work; it also decreases productivity and concentration and generates learning disorders and concomitant diseases. As allergic diseases occur mainly in the young population (which supports the senior population), their consequences are much more costly than those of diabetes, coronary heart disease or myocardial infarctions. In the USA alone, the costs of allergic rhinitis morbidity are estimated at over 25 billion dollars per year, of which approximately a half consists of indirect costs, resulting from insufficient disease control. In light of these studies it is not difficult to notice multidirectional benefits from effective management of allergic diseases, which improve both the patients' activity, productivity and quality of life and ultimately decrease the financial burden of healthcare systems. Efficient therapy of the most common allergic diseases is based mainly on oral antihistamines which are administered simply and, as a result, have the best compliance among the drugs recommended for the treatment of allergic rhinitis.

Histamine plays an important role in human physiology, influencing immunoregulation of the acute and chronic inflammatory response through 4 different types of receptors, called H1, H2, H3, and H4. Drugs classified in the first generation of antihistamines (sometimes called "classical" antihistamines) act non-selectively. Apart from all histaminic receptors they also block muscarinic, adrenergic (or adrenoreceptors) and dopaminergic receptors, causing cardiovascular, urinary and gastrointestinal adverse reactions. High lipophilicity and consequently easy crossing of the blood–brain barrier additionally intensify the most dangerous adverse events from the central nervous system, including drowsiness, decreased concentration, vigilance and psychomotor efficiency as well as reduced ability to learn and memorize, which is not related to sedation. However, in histamine-dependent allergic diseases the most important role is played by the H1 receptor, whose stimulation by histamine results in e.g. constriction of smooth muscles (obturation of inhalatory tract), increased permeability of endothelium (oedema) and stimulation of sensory nerves and cough receptors (pruritus, sneeze attacks, rhinorrhoea). Therefore, the discovery of compounds selectively acting on H1 receptors, currently called second generation drugs, could be considered the greatest breakthrough during more than 70 years of the history of antihistamines (Fig. 1). On top of the high efficacy, the most important feature of these drugs is the incomparably better safety profile: some of them have the same (or even lower) number of adverse reactions as placebo. Due to the selective mechanism of action, low penetration of the central nervous system (CNS) and lack of interaction with adrenergic, muscarinic and dopaminergic receptors, the second generation drugs are devoid of the majority (if not all) of the side effects mentioned above; however, some of them could cause other serious adverse reactions, including body mass gain, inter-drug interactions or potentially life-threatening cardiotoxicity (in the majority of countries, these preparations have been withdrawn from the market) (Fig. 2). Due to selective antagonism with H1 receptors, these drugs are highly effective in reduction of allergic rhinitis and urticaria symptoms, and the wide therapeutic index makes it possible to use them in very high doses without any concerns related to overdosing toxicity, which with the first generation drugs could lead to consciousness disturbances, coma, respiratory distress, and even death.

The described characteristics and easy usage as well as affordable price led to the inclusion of the second generation antihistaminic drugs in all global and local recommendations as the drugs of choice in all forms of allergic rhinitis and urticaria. The most frequently cited are ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines, which discusses pharmacotherapy and presents the second generation anti-H1 drugs in the first place, recommending them in all adults and children [1]. Additionally, they highlight that the first generation drugs are not recommended wherever newer drugs are available. Almost the same recommendations could be found in the current EAACI/GA(2)LEN/EDF/WAO guidelines of urticaria management, in which non-sedative second generation antihistamines are recommended not