

Second generation antihistamines: assessment of the efficacy of treatment and tolerance of some preparations of this group (preliminary studies)

Leki przeciwhistaminowe II generacji – ocena skuteczności leczenia i tolerancji wybranych preparatów tej grupy (badania wstępne)

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Słowa kluczowe: leki przeciwhistaminowe, rupatadyna, bilastyna, lewocetyryzyna, feksofenadyna.

Abstract

Introduction: Second generation antihistamines are key medicines in the treatment of allergic diseases such as allergic rhinitis and allergic conjunctivitis.

Aim of the research: To compare the effectiveness of selected antihistamines and frequency of side effects in the course of their therapy in the patient opinion.

Material and methods: The study was conducted on a group of 40 patients taking rupatadine, bilastine, levocetirizine and fexofenadine. The method of diagnostic survey was used, having the character of a preliminary examination in view of the small number of people involved in the study.

Results: Among the 40 patients, side effects of the medicines only appeared in 3 respondents, which is 1.2%.

Conclusions: The new generation antihistamines in light of our studies appear to be safe and associated with few side effects. Due to the small number of surveyed people we treat these tests as preliminary to further analysis of the effectiveness of selected antihistamines.

Streszczenie

Wprowadzenie: Leki przeciwhistaminowe II generacji są podstawowymi lekami w leczeniu schorzeń alergicznych, takich jak alergiczny nieżyt nosa i alergiczne zapalenie spojówek.

Cel pracy: Porównanie skuteczności działania wybranych leków przeciwhistaminowych oraz częstości występowania działań niepożądanych po ich przyjmowaniu w ocenie pacjentów.

Materiał i metody: Badanie przeprowadzono u 40 pacjentów otrzymujących rupatadynę, bilastynę, lewocetyryzynę i feksofenadynę. Zastosowano metodę sondażu diagnostycznego, wykorzystując ankietę. Badania mają charakter wstępny ze względu na niewielką liczbę osób biorących w nich udział.

Wyniki: Objawy uboczne po zastosowaniu leków pojawiły się zaledwie u 3 spośród 40 chorych, co stanowi 1,2%.

Wnioski: Leki przeciwhistaminowe nowej generacji wydają się bezpieczne i wiążą się z niewielką liczbą działań ubocznych. Ze względu na niewielką liczbę przebadanych osób badania te traktujemy jako wstępne do dalszej analizy skuteczności wybranych leków przeciwhistaminowych.

Introduction

Antihistamines are now often used mainly in allergic diseases [1, 2]. This is primarily because histamine affects all stages of allergic inflammation and thus antihistamine in these conditions is the most important. It not only works in the early phase of inflammation but also participates in the chronic phase. Antihistamines have become the mainstay of treatment of these diseases. In certain allergic diseases such as allergic rhinitis they may be the only drug, while in others such as allergic contact eczema they provide supportive treatment [1–3]. Various publications have reported [1, 2, 4] their effectiveness, but few studies have compared the efficacy of treatment. They are indicated for persistent and intermittent allergic rhinitis, seasonal allergic conjunctivitis, and chronic idiopathic urticaria. There are also many types of diseases in which antihistamines are supportive therapy and complementary [2].

Allergic rhinitis (AR) – More than 500 million people worldwide suffer from allergic rhinitis [4]. In genetically predisposed individuals it is due to the IgE-dependent response to a variety of allergens. These include both inhalants in the external environment as well as indoor, while food allergens rarely cause isolated AR [4]. In this disease there is inflammatory infiltration of the nasal mucosa by different cells: eosinophils, mast cells (in an increased number) CD4 T lymphocytes, Langerhans cells and release of a variety of mediators – histamine, cysteinyl leukotrienes, nitric oxide and cytokines (IL-5). Also these are the mediators released in allergic asthma [4, 5]. Histamine is one of the most important and earliest release mediators affected by these drugs.

Allergic conjunctivitis – The conjunctivitis allergic reaction is mainly IgE-dependent, usually accompanying AR. Symptoms of the disease are itching, watery, bloodshot eyes; they may be accompanied by swelling of the conjunctiva and eyelids [6]. Allergic conjunctivitis often occurs in allergic rhinitis [4].

Asthma – We know that in most patients with asthma, rhinitis coexists. Thus, inflammation of the lower respiratory tract is accompanied by inflammation of the upper respiratory system – this confirms the concept of one path of the diseases, and it is inter alia related to the similarity of the nasal mucosa and bronchi [4, 5]. In asthma there has also been found subclinical inflammation of the lining of the gastrointestinal tract, and food allergy differently expressed in airway hyperresponsiveness. These observations suggest to us that allergic diseases are committed to the mucosal system [7–9]. Hence, in asthma coexisting with AR in the next course of asthma control medications antihistamines are used to combat the symptoms of rhinitis [10]. To summarize the treatment of allergic diseases one should begin to eliminate or limit their contact with allergens. But it is not always

possible [11]. Then you need to implement pharmacotherapy. H1 antihistamines of the second generation are among the first used in rhinitis and allergic conjunctivitis.

Aim of the research

The aim of the study was to compare the effectiveness of selected antihistamines and frequency of side effects in the course of their therapy in the patients' opinion.

Material and methods

The study used a survey method with a diagnostic study group of 40 patients. The study was attended by 34 women and 6 men, aged 18 to 82 years: 24 with isolated allergic rhinitis (8 seasonal, 16 year-round); the second group consisted of 12 patients with coexisting allergic rhinitis with asthma (all of them had year-round type); the third consisted of 4 patients with allergic rhinitis coexisting with allergic conjunctivitis (2 of them – seasonal, 2 year-round). Inclusion criteria: 1) age between 18 and 82 years, 2) male and female, 3) diagnosis: isolated allergic rhinitis, allergic rhinitis coexisting with asthma, AR coexisting with allergic conjunctivitis. In current use is a division of allergic rhinitis into periodic (symptoms persist for less than 4 days per week or less than 4 consecutive weeks) and chronic (symptoms persist for more than 4 days per week and more than 4 consecutive weeks). Previously, allergic rhinitis was divided into seasonal (connected with allergy to seasonal allergens) and year-round (caused by IgE-mediated reaction to year-round allergens). However, in this paper, the previous division is applied in order to enable patients comprehension of this study.

Among the patients 16 (45%) were taking rupatadine, 8 (20%) bilastine, 6 (15%) levocetirizine and 8 (20%) fexofenadine at standard doses. The time on medication varied from a few months to several years. Patients filled out a questionnaire with 21 questions. These were Outpatient Specialist – Allergy patients in Kielce. Exclusion criteria from the study were: smoking, chronic diseases that may affect the course and outcome of treatment of allergic disease, the use by the patient in addition other medications for allergic rhinitis or conjunctivitis (intranasal α -agonists, nasal or conjunctival chromones and antihistamines, nasal steroids) as well as drugs used to maintain control – steroids and β -mimetics of inhaled antileukotriene drugs.

Answers to the questions used in the questionnaire by Kaszyński and associates in their own modifications were analyzed and summarized using descriptive statistics.

Questionnaire evaluating the efficacy of antihistamine therapy:

1. How old are you?
2. Gender: a) female, b) male.

Table 1. Characteristics of the study group

Parameter	Result
Gender	34 (85%) women 6 (15%) men
Median age [years]	27
AR	24 (60%)
AR + allergic conjunctivitis	4 (10%)
AR + asthma	12 (30%)
Positive family history of allergic disease	28 (70%)
Work exposure to allergenic factors	8 (20%)

3. Where do you live? a) City, b) Village.
4. Where do you work? a) Do not work, b) Working – where?
5. Was anyone in the family sick/suffering from allergic diseases? a) The parent, b) siblings, c) the child, d) other family member.
6. Do you have any animal? a) Yes (if so, since when and what), b) no.
7. Where were you treated? a) General Clinic, b) Allergy Clinic, c) take drugs on my own.
8. What are the reasons you take an antihistamine? a) Allergic rhinitis, b) allergic conjunctivitis, c) coexistence of both diseases, d) coexistence of allergic rhinitis with asthma.
9. How long have you taken an antihistamine?
10. What antihistamine do you take?
11. Have you taken from the beginning the same antihistamine medicine – if not when and what was taken?
12. In what dose do you take medicine?

13. Do you take other drugs because of allergic disease – if so, what?
14. Is your treatment: a) seasonal, b) year-round?
15. Did you take during treatment medicines in accordance with medical indications?
16. Are you allowed to stand during treatment preparation? If yes, please specify for what reason.
17. How do you assess the currently taken antihistamine in terms of effectiveness? a) Very good, b) good, c) average, d) weak.
18. How do you assess the currently taken drug in terms of the duration? a) Very good, b) good, c) average, d) weak.
19. While taking this medication did there occur major side-effects – if so, what?
20. Are you being treated due to some other illness? If so, what?
21. Do you take chronically other drugs? If so, what?

Results

This research was conducted through questionnaires evaluating the effectiveness of the selected second generation antihistamines and the occurrence of complications during therapy. Because the study involved 40 patients it was treated as preliminary to further discussion on the effectiveness of these drugs (Table 1).

Among the 40 patients side effects of the medicines taken only appeared in 3 respondents, representing only 1.2%; they were somnolence after bilastine, increased levels of glucose, which the surveyed connected to the use of levocetirizine, and general weakness and dizziness after fexofenadine. None of the patients taking rupatadine after it reported side effects.

According to 15 (37.5%) of the respondents antihistamines are very effective, to 17, good (42.5%). As many as 15 (37.5%) respondents stated that they have a very good time of action, according to 14 (35%)

Table 2. Global assessment of efficacy of all medicines

Parameter	Criteria for assessment			
	Very good	Good	Average	Poor
Effectiveness	15	17	6	2
Speed	15	14	8	3

Table 3. Side effects of drugs used

Side effects	Drug		
	Bilastine	Levocetirizine	Fexofenadine
Somnolence	1 (0.4%)		
Hyperglycemic		1 (0.4%)	
Weakness of vertigo			1 (0.4%)

good, while 6 (15%) patients rate their antihistamine as average according to its effectiveness and 8 (20%) according to speed. Only 2 (5%) patients rated it as weak according to the effectiveness, 3 (7.5%) as weak, also because of the speed (Tables 2 and 3).

Discussion

This study was conducted through questionnaires evaluating the effectiveness of the selected second generation antihistamines and the occurrence of complications during therapy. Because the study involved 40 patients it was treated as preliminary to further discussion on the effectiveness of these drugs.

In our study, only 3 patients reported the presence of side effects after using antihistamines – very few in comparison with the study by Kaszyński, in which as many as 60% of respondents reported side effects [2]. It is possible that drugs taken by patients had an impact on the results. In our study, many of the respondents have used rupatadine (45%), bilastine (20%), levocetirizine (15%) or fexofenadine (20%). All the while these drugs have a negligible impact on the CNS, while in the study by Kaszyński *et al.* [2] cetirizine, loratadine and fexofenadine were most studied. The study by Martinez comparing the efficacy of rupatadine and cetirizine for allergic rhinitis showed higher efficiency of the first of these drugs with fewer side effects recorded [12]. Also, when it comes to assessing the effectiveness of it in our study, a majority of respondents assessed the efficacy of drugs and rated their performance as very good – in total 30 (75%) and good – 31 (77.5%) patients. For comparison, the study by Kaszyński *et al.* indicates that these drugs are not well rated by patients [2]. Perhaps these differences affect both other drugs used by respondents, and another selection of patients – in our study there are mainly patients with allergic rhinitis isolated or coexisting with allergic conjunctivitis or asthma.

In the study by Kaszyński *et al.* [2] the main indications for use of antihistamines were allergic conjunctivitis, urticaria and atopic dermatitis. More comparable to our study, the study by Layton *et al.* [13] also indicated a low risk of side effects such as sedation – but it was also carried out on later generation drugs (levocetirizine and desloratadine). Similarly, studies by Reinartz showed high efficacy of desloratadine in reducing symptoms of allergic rhinitis co-morbidity of asthma [14]. Other studies by Singh-Franco showed the high efficacy of levocetirizine for the treatment of allergic rhinitis and chronic urticaria in adults and children, and its good tolerability [15]. And Miyabe's studies confirmed that fexofenadine may be successfully used to suppress the symptoms of allergic rhinitis [16]. The majority of Japanese research also emphasizes the high efficacy previously shown for antihistamine therapy [17]. Interestingly, there are also studies comparing the effectiveness of

old drugs – the now withdrawn terfenadine with loratadine; evidence of their effectiveness, however, is not related to their safety profile [18]; or efficacy of cetirizine and loratadine, after challenge, showing an advantage of cetirizine in reducing symptoms of the skin [19]. In a similar way, Eloy's studies confirm high effectiveness of taking rupatadine in a treatment of allergic rhinitis symptoms [20]. Therefore, in our study it was found to be the safest of the compared drugs, especially as the proportion of patients taking it was highest (45%). Also, studies by Maiti comparing rupatadine and levocetirizine in allergic rhinitis indicate the superiority of rupatadine both due to higher efficacy and a better safety profile [20]. Similarly, Eloy's study confirmed the high efficacy of rupatadine in addressing the symptoms of allergic rhinitis [21].

Conclusions

Antihistamines of the new generation according to our initial study appear to be safe and associated with a small number of side effects. They are also highly rated by patients for efficacy and speed. Due to the small number of surveyed people we treat these tests as preliminary to further analysis of the effectiveness of selected antihistamines.

However, it seems that each drug should be individualized for the specific patient.

Conflict of interest

The authors declare no conflict of interest.

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