ORIGINAL ARTICLE

CONTENTS

Evaluation of the treatment strategy for complicated allergic rhinitis

Lilia Buria, Nataliia Moisieieva, Anna Kapustianska, Andrii Vakhnenko, Iryna Zviagolska, Olena Vlasova, Mariia Rumiantseva

POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

Aim: To carry out a comprehensive evaluation of treatment modification for patients with seasonal allergic rhinitis (SAR) complicated by anxiety-neurotic disorders.

Materials and Methods: Patients with SAR in the acute stage on the background of anxiety disorders were studied. Immunological studies were carried out, an assessment of the dynamics of indicators of the quality of life of patients, the level of anxiety / depression was assessed. In the clinical group, a variant of therapy modification was proposed.

Results: Significant changes in the subpopulation ratio of lymphocytes, an increase in the immunoregulatory index, which indicated the severity of the immunological process, were revealed in SAR patients in the acute stage against the background of anxiety disorders. At the same time, a significant activation of the humoral link of immunity was observed: an increase and a significant increase in IgE in the blood serum and an increase in the content of sIgA in the nasal secretion. In most patients, eosinophilia was found in the peripheral blood and in the rhinocytogram before treatment. In the study of the quality of life of patients, changes in many parameters were found.

Conclusions: The combination of "Nazafort Allergy Protection" and Atarax seems to be the most successful, which significantly improved the physical and psycho-emotional state of patients with SAR, complicated by anxiety and neurotic disorders. This combination led to an increase in the stress resistance of patients.

KEY WORDS: seasonal allergic rhinitis, pollinosis, complex therapy of SAR, barrier antiallergic drugs

Wiad Lek. 2024;77(1):62-67. doi: 10.36740/WLek202401109 DOI

INTRODUCTION

In modern world with its rapid development and transformations, climatic and social changes, health care system reforms, one of the global problems remains - allergic diseases, which have a tendency to increase significantly over the last decade [1,2]. Today, according to various data in different countries of the world, frequency of allergic diseases is 25-40% of total population morbidity, and this percentage constantly grows. In some countries, over the past 10 years, number of patients with various forms of allergic reactions has doubled [2-4].

Allergic rhinitis (AR) remains one of the most common diseases in the general structure of allergy pathology. Depending on climate, social and household characteristics of different countries, its prevalence varies in range of 4-32%. Moreover, even mild and short-term symptoms of AR have an undesirable effect on psychological state, disrupt a person's social life, and also limit his professional activity [3,5].

Among ARs, seasonal allergic rhinitis (SAR) or pollinosis has a specific weight. It is characterized by seasonality, symptoms develop at a certain time of the year, which are caused by contact of mucous membrane with plant pollen. Thus, SAR is an allergic disease that is manifested by allergic inflammation of nasal cavity mucous membrane and is caused by an ethiologically significant allergen [2,6]. In climatic zone of central Ukraine, there are three regional peaks of pollinosis symptoms: spring, summer and summer-autumn.

The generally used tactics of SAR treatment include three main components: elimination measures, pharmacotherapy (local and systemic) and antigen-specific immunotherapy (ASIT) [1,3,5,7,8]. In modern allergology, quite a lot of approaches and various recommendations for ASIT and pharmacotherapy have been developed. But pharmacological drugs, along with desired clinical effect, have numerous side effects that limit their use for certain groups of patients. And conducting ASIT is combined with being under the supervision of an allergist, which is not always possible in today conditions. Elimination measures in many program documents, unfortunately, are either insufficient or absent at all. At the same time, elimination of causative factors belongs

to etiopathogenetic treatment methods, especially treatment of allergic diseases. It becomes especially important in cases where patient has serious limitations for pharmacotherapy (pregnancy, childhood, comorbid pathology, old age). But it is almost impossible to limit person's contact with an allergen (plant pollen, household allergens, professional allergens). Therefore, alternative methods of therapy and prevention remain very relevant today for treatment of allergic diseases [8]. The method that would be aimed at creating a barrier and preventing contact, action of the allergen on the mucous membrane targeted, is very relevant for prevention and treatment of SAR.

Among existing modern medical measures for treatment and prevention of SAR, the drug "NAZAFORT allergy protection" (Great Britain) attracts special attention. "Nazafort Allergy Protection" is a spray for local application, which ensures the limitation of nasal mucosa contact with ethiologically significant allergen and prevents development of an allergic reaction, in particular SAR, acting as a barrier to inhaled allergens. Micronized hydroxypropyl methylcellulose reacts with the moist surface of nasal mucous endothelium, where it forms a transparent, gel-like protective barrier that does not interfere with breathing. This prevents mast cell degranulation and the release of immunoglobulin E (IgE) and histamine. As a result, it is possible to avoid an allergic reaction and development of allergic rhinitis symptoms. In addition, with SAR, it is possible to start using "NAZAFORT allergy protection" in advance, 1-2 weeks before expected start of pollination season, or it can be used situationally 15-30 minutes before expected contact with an allergen.

When analyzing literary sources on the effectiveness of "Nazafort protection against allergies", collected data on the dynamics of subjective symptoms in patients with allergic rhinitis is very limited. Decreased release of total IgE and changes in the number of eosinophils in peripheral blood are described, but there is no evidence as laboratory data on the drug effect on local immunity.

On the other hand, it is impossible not to note the psycho-emotional state of a patient with SAR, especially during exacerbation of disease [9,10]. When symptoms of SAR emerge and progress, it very often leads to the development of anxiety, neurotic states in patients, and are most often manifested in emotional lability, reduced concentration of attention, restlessness, anxiety, fear, sometimes obsessive states, very often in the form of migratory itching [11-13]. Thats when the question arises of prescribing additional drugs to combat these conditions [12,14]. From a wide range of sedatives, tranquilizers, anxiolytics, Atarax (hydroxyzine dihydrochloride) (Code: ATX N05B B01) attracts special attention. Which, due to its sedative, tranquilizing and antihistamine properties, is indicated for anxiety states symptomatic treatment in adults and the symptomatic therapy of allergic itching.

AIM

Aim of this study was to carry out a comprehensive evaluation of treatment modification for patients with SAR complicated by anxiety-neurotic disorders.

MATERIALS AND METHODS

The research program included 63 patients with established SAR, persistent, moderate-severe course with clinical manifestations of rhinoconjunctival syndrome, disease course of 2-5 years, with annual exacerbations. All patients have established sensitization to tree, cereal and couch grass pollen, as well as varying degrees of anxiety disorders. 56 patients (89%) complained of periodic, migrating itching that appeares at any time of the day. Age group of patients was 17-50 years. According to the treatment protocol, all patients received intranasal glucocorticosteroids 1 dose in each nasal passage 2 times a day. All patients were divided into 3 groups: 1 group - control (11 patients) received only basic therapy: intranasal glucocorticosteroids and the antihistamine desloratadine; 2nd group - (26 patients) received basic therapy and additionally "NAZAFORT allergy protection" one injection into each nostril 3 times a day; 3rd group - (26 patients) received intranasal glucocorticosteroids, "NAZAFORT allergy protection", and desloratadine was replaced with Atarax 25 mg 2 times a day. Duration of observation was 30 days.

All patients, in addition to general clinical and biochemical studies, were examined by an ENT doctor with X-ray examination of paranasal sinuses, rhinocytogram, nasal peakflowmetry, as well as examination by an ophthalmologist. Immunological and allergological diagnostics were carried out, which included scarification skin tests, the phenotypes of CD4+, CD8+, CD22+ cells and the immunoregulatory index (IRI) of the CD4+/CD8+ ratio [15, 16], general and specific IgE [16,17] and the level of secretory IgA (sIgA) in nasal secretions.

During the entire study, dynamics of patients quality of life indicators were evaluated. To study patients quality of life in different periods: exacerbation of SAR, treatment, rehabilitation using the general questionnaire MOS SF-36 (MOS SF Item Short Form Health Survey). To determine the impact of therapy on patients quality of life, global assessment of the state of treatment quality was performed by doctor and patient. Test results were evaluated according to the point grading system. Pa-

tients independently filled out the SF-36 questionnaire: first, treatment upon admission to the hospital, that is, during the exacerbation phase; at the end of inpatient treatment (on day 12-14); and also for 30 days. The HADS questionnaire and the CES-D self-questionnaire were used to assess the level of anxiety/depression. Severity of the patient's condition was assessed using the Hospital Anxiety and Depression Scale (HADS) [18]. Psychological status was determined on the day of hospitalization and at discharge.

Statistical calculations were performed using the "STATISTICA for Windows 8.0" program package. Non-parametric methods of statistical analysis are applied. The Mann-Whitney test was used to compare quantitative indicators in unrelated groups, and the Wilcoxon test was used in dependent groups. Fisher's test was used to compare the frequencies of a binary feature in two unrelated groups; in cases where the frequencies were less than 10 - criterion 2 with Yates correction. The analysis of the relationship between two traits was carried out by the Spearman method. Differences were considered reliable at a statistical significance level of less than 0.05.

RESULTS

When conducting an allergological examination, sensitization to pollen allergens was established in all patients (100%): tree pollen - 13 patients (20.63%), cereal grass - 9 (14.29%), couch grass - 11 (17.46%), trees and couch grass – 12 (19.05%), cereal and couch grass – 18 (28.57%). The main signs of therapeutic effectiveness were considered to be: positive dynamics of AR course (disappearance of nasal congestion, sneezing, rhinorrhea, mucus running down the back wall of the pharynx, hyperemia and swelling of nasal mucosa according to anterior rhinoscopy). Also, the effectiveness of treatment was determined according to the positive dynamics of clinical and laboratory indicators, which were evaluated on a four-point scale. Treatment quality indicators were: in 1 group (control): excellent result – 2 patients (18.18%), good – 6 (54.55%), unchanged 2 (18.18%), negative – 1 (9.09%); in group 2: excellent - 10 (38.46%), good - 14 (53.85%), unchanged - 2 (7.69%), negative - 0 (0%); in group 3 excellent – 20 (76.92%), good – 5 (19.23%), unchanged – 1 (3.85%), negative – 0 (0%).

Patients of 2nd and 3rd groups noted improvement on the 2nd day of treatment, as nasal congestion and swelling of the mucous membrane decreased. In these groups, on the 10th day of treatment, a full therapeutic effect was achieved, basic therapy was shortened by reducing the frequency of use or completely canceling intranasal glucocorticosteroids. Groups who completely refused intranasal glucocorticosteroids: group 1 - 0 patients (0%), group 2 - 18 (69.23%), group 3 - 20 (76.92%), but continued to use "NAZAFORT allergy protection" for 3 weeks. When comparing clinical courses, it can be noted that in 2nd and 3rd groups the effect came 2 days faster. In control group, 3 patients required additional use of decongestants and antileukotriene drugs.

During a general clinical examination, eosinophilia was detected in peripheral blood in 54 (85.71%) patients, the average rate was 9.26±2.6%. The content of eosinophils in the rhinocytogram was increased in 49 (77.78%) patients, the average content was 8.9±3.5%. It should be noted that after the treatment in group 1, blood eosinophilia and rhinocytogram remained in 3 (27.27%) patients, in group 2 in 9 (34.62%), in group 3 8 (30.77%). Most likely, this is due to the fact that groups 2 and 3 canceled or significantly reduced the intake of intranasal glucocorticosteroids.

During the immunological examination before the treatment, significant changes in the subpopulation ratio of lymphocytes were detected, an increase in CD4+ cells up to 49.39±13.06% was noted; CD8+ decreased to 17.06±9.02% compared to the norm, the average value of the immunoregulatory index (IRI), as one of the key integral indicators of immunity, increased, which indicated the expressiveness of the immunological process. At the same time, a significant activation of the immunity humoral link was observed: an increase in proportion of antibody-producing CD22+ to 40.17±7.62% and a significant increase in IgE in the blood serum to 281.83±98.18 IU/ml, and an increase in the content of sIgA in the nasal secretion to 18.97±4.65 mg/l.

Analysis of changes in immunological parameters in patients before and after treatment showed in the control group: CD4+ from 49.39±13.06 to 42.75±12.94; CD8+ from 18.81±9.63 to 18.21±9.46; IRI from 2.63±0.99 to 2.3±0.93; IgE from 275.73±92.21 to 196.87±97.64; sIgA from 17.83±6.49 to 16.26±5.83, which had no significant changes and only CD22+ significantly decreased from 39.38±12.22 to 25.23±10.86 ($p \leq 0.05$). In group 2, almost all indicators changed reliably: CD4+ from 50.94±12.9 to 39.87±11.18 ($p \leq 0.05$), CD8+ from 17.06±9.02 to 19.82±9, 13 ($p \leq 0.05$), IRI from 2.99±1.21 to 2.01±1.17 ($p \leq 0.05$), CD22+ from 39.5±10.35 to 36.14±11, 88 ($p \leq 0.05$), IgE from 281.83±98.18 to 183.76±83.53 ($p \leq 0.05$), except for the content of sIgA in the nasal secretion from 18.71±7.37 to 15 .43±6.78. We observed a similar pattern in group 3: CD4+ from 50.35±9.86 to 38.95±8.16 ($p \leq 0.05$), CD8+ from 17.23±7.04 to 20.19±4, 15 ($p \leq 0.05$), IRI from 2.92±1.4 to 1.93±1.97 ($p \leq 0.05$), CD22+ from 40.17±7.62 to 36.02±9, 85 ($p \leq 0.05$), IgE from 279.54±84.76 to 187.65±85.38 ($p \leq 0.05$), sIgA in nasal secretion from 18.9±4.65 to 15.38 ±7.12.

When studying patients quality of life, changes in many parameters were found. Thus, in the control group, only the vital activity index (VAI) changed reliably. In clinical group 2, only "NAZAFORT allergy protection" was connected to the treatment, significantly improved indicators of vital activity (VA), physical functioning (PF), general health (GH). However, indicators of the psychological status of patients: manifestation of anxiety (HADS scale, scores), manifestation of depression (HADS scale, scores), manifestation of depression (questionnaire CES-D scores) did not have reliable changes. In the control group, all these indicators also had no significant changes.

In group 3, modification of therapy led not only to a significant improvement in the index of general health (GH), vital activity (VA), role functioning (RF), physical functioning (PF), as well as normalization of mental health (MH), emotional functioning (EF), which led to an increase in stress resistance of patients. Indicators of the psychological status of patients: the manifestation of anxiety, depression according to the scales of specialized questionnaires, also had reliable improvements.

Long-term studies confirmed a steady increase in stress resistance of patients in group 3, which was confirmed by a decrease in the number of manifestations of anxiety.

DISCUSSION

Analysis of treatment modification showed that in groups using "NAZAFORT allergy protection" clinical effect came 2 days faster, a significant number of patients reduced the basic therapy, mainly due to intranasal glucocorticosteroids and continued the use of the drug in complex therapy until the end of the observation.

It should be noted that most patients had eosinophilia in the peripheral blood and in the rhinocytogram before treatment, but after treatment in group 1, eosinophilia persisted in blood and rhinocytogram in fewer patients than in groups 2 and 3, which is most likely due to withdrawal or a significant decrease in use of intranasal glucocorticosteroids.

Before the treatment, significant changes in the subpopulation ratio of lymphocytes were detected: an increase in CD4+ lymphocytes, a decrease in CD8+, an increase in the immunoregulatory index (IRI), as one of the key integral indicators of immunity, which indicated the expressiveness of the immunological process. At the same time, a significant activation of the humoral link of immunity was observed: an increase in CD22+ cells and a significant increase in IgE in the blood serum, and an increase in the content of sIgA in the nasal secretion. As a result of the treatment in the control group with basic therapy, only the number of CD22+ lymphocytes significantly changed, in group 2 and in group 3 with the modification of therapy "NAZAFORT allergy protection" a similar picture was observed, when almost all immunological indicators had reliable positive changes, including IgE in blood serum, except for sIgA in nasal secretions.

In the group with the modification of Atarax treatment, the most pronounced improvement in the psycho-emotional state of patients was observed, the general health, vital activity, role functioning, physical functioning, as well as the normalization of mental health and emotional functioning, which caused an increase in the stress resistance of the patients, significantly improved. Indicators of the psychological status of patients: manifestation of anxiety, depression according to the scales of specialized questionnaires, also had reliable improvements.

Long-term studies confirmed a steady increase in stress resistance of patients in group 3, which was confirmed by a decrease in the number of anxiety manifestations. What was not observed in 1st and 2nd groups.

Thus, modification of the basic therapy of SAR "NAZAFORT allergy protection" led to the modulation of the immune response in the form of a decrease in the allergic reaction, an increase and faster achievement of the clinical effect, and a decrease in the need for the use of inhaled glucocorticosteroids. Although, even though it is effective protection against allergen contact with the shock organ (mucous membrane of the nasal cavity) and can be recommended for use in the treatment of SAR of varying degrees of severity, its separate use does not achieve a sufficient effect on the psycho-emotional state of patients. Therefore, combination "NAZAFORT allergy protection" and Atarax appears to be the most successful, and significantly improving the physical and psychoemotional condition of patients with SAR complicated by anxiety disorders. Such a combination led to an increase in stress resistance of patients.

CONCLUSIONS

Analysis of the modification of the treatment showed that in the groups of application of «Nazafort Allergy Protection» the clinical effect occurred earlier, the basic therapy was reduced due to inhaled glucocorticosteroids. In the groups with the modification of therapy with «Nazafort Allergy Protection», almost all immunological parameters had significant positive changes, with basic therapy, single indicators improved. In the Atarax treatment modification group, the most pronounced improvement in the psycho-emotional state of patients was observed, indicators of the psychological status

had significant positive changes. Long-term studies confirmed a steady increase in the stress resistance of patients, which was confirmed by a decrease in the number of anxiety manifestations. Modification of the basic ATS therapy «Nasafort Allergy Protection» led to the modulation of the immune response and a decrease in the allergic reaction, an increase and a faster achievement of the clinical effect, and a decrease in the need for the use of inhaled glucocorticosteroids. Despite the fact that it is an effective protection against contact of the allergen with the shock organ (nasal mucosa) and can be recommended for use in the treatment of SAR of varying severity, however, its isolated use does not lead to a sufficient positive effect on the psycho-emotional state of patients. Therefore, the combination of «Nazafort Allergy Protection» and Atarax seems to be the most successful, which significantly improved the physical and psycho-emotional state of patients with SAR, complicated by anxiety and neurotic disorders. This combination led to an increase in the stress resistance of patients.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Lilia Buria
Poltava State Medical University
23 Shevchenko st., 36000 Poltava, Ukraine
e-mail: burya.lilia@gmail.com

ORCID AND CONTRIBUTIONSHIP

Lilia Buria: 0000-0003-3137-6783 A D F
Nataliia Moisieieva: 0000-0001-8901-3710 B D
Anna Kapustianska: 0000-0001-9150-8472 D F
Andrii Vakhnenko: 0000-0003-1040-7042 C
Iryna Zviagolska: 0000-0001-7531-3966 C
Olena Vlasova: 0000-0002-4175-5341 E
Mariia Rumiantseva: 0000-0001-7247-9792 E

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 27.09.2023
ACCEPTED: 01.12.2023