Dynamics of the immunological and clinical parameters in patients with chronic polyoid rhinosinusitis in the course of specific immunotherapy using fungal antigens

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Abstract

The article contains the results of dynamic changes in the clinical course and immunological parameters in patients with polyoid rhinosinusitis on the background of fungal sensibilization in the course of specific immunotherapy using fungal antigens.

Keywords: Polyoid rhinosinusitis, fungal sensibilization, Specific immunotherapy, Immunological status

1. Introduction

According to the European Position Paper on Rhinosinusitis (EPOS) about 2-4% of the European population suffer from nasal and paranasal sinus polyposis. Recurrence of nasal polyps after surgical treatment is common in about 30-50% of patients as a result of significantly reduced quality of life. Quality of life in CPRS is compared with quality of life in chronic obstructive pulmonary disease (COPD) [1, 2].

In recent years, a special role in the occurrence of polyposis has been given to the fungal flora as the primary cause of inflammatory process including polyposous one [3, 4].

Decades of scientific research leave no doubt that potentially pathogenic fungi are quite often causative factors for developing allergic diseases in both adults and children. In addition to the increased prevalence of fungal infections changes in their typical clinical manifestations are also observed [5, 6, 7].

Fungal antigens are known as being able to modify the type and nature of the immune response significantly reducing a full immune response to opportunistic microflora and structure of the mucous membrane of the nasal cavity [8, 9, 10, 11]. At present, in the scientific literature there are insufficient data on the role of fungal sensibilization in maintaining chronic polyposus process in the nasal cavity in order to arrive at a firm evidence-based conclusion providing practical recommendations for clinical practice. Therefore, it has been advisable to conduct research to determine the role of fungal sensibilization in developing chronic inflammatory diseases of the nasal cavity associated with polyyp formation and develop effective treatment options for this severe disease.

The Aim of the Research

The aim of the research was to assess the dynamic changes in the clinical course and immunological parameters in patients with polyoid rhinosinusitis on the background of fungal sensibilization in the course of specific immunotherapy using fungal antigens.

2.1. Materials and Methods

90 patients at the age of 20-55 years with CPRS secondary to fungal sensibilization were examined. Basic and additional clinical examinations were performed to investigate the features of the clinical course and immunological status of all patients. They included identifying the chief complaints, medical history, physical examination, if necessary-an X-ray and/or computed tomography of the paranasal sinuses, assessing the serum levels of total IgE, IgG4 and interleukin-1β. Sensibilization to fungi was confirmed by allergy skin testing (skin prick test with fungal allergens), and detection of allergen-specific IgE.

According to the prescribed treatment all the patients were divided into two groups – Group 1a and Group 1b. Patients of Group 1a (36 people) underwent allergen-specific immunotherapy (ASIT) using fungal allergens (Sevapharma, Czech Republic), patients of Group 1b (54 People) received standard treatment of CPRS (pharmacotherapy). The intensity of clinical
Symptoms and the efficacy of treatment were evaluated based on the analysis of their dynamics on a IV-point scale: I—absence of complaints and any symptoms; II—minor manifestations; III—clinically apparent manifestations; IV—an absence of positive dynamics of treatment effect.

An assessment of the patients’ complaints at the beginning of our investigation has revealed that the most common complaints among patients of both groups included violation of nasal breathing or its complete absence. In addition, most patients complained of a decreased sense of smell, rhinorrhea, conjunctival symptoms, sneezing, periodic headaches, increased fatigue, and nasal discharge of a mucous character.

The serum levels of IgE and IgG4 were determined by the ELISA method. The serum concentrations of total IgE and IgG4 in patients of both groups were significantly higher than those in healthy controls. The presence of IgE antibodies to fungal allergens in patients’ serum samples with an allergen was determined using basophil degranulation test following L.A. Diuhovska’s recommendations (1975). The result was expressed as a percentage of the degree of spontaneous degranulation of tissue basophils in patients’ serum samples without any allergen. Fungal antigens Alternaria altern (Al), Botritis cinerea (B), Aspergillum (As), Penicilium (Pn), and Monilia (M) were used. Determination of fungal allergen-specific IgE has revealed that hypersensitivity (p<0.02) to all fungal allergens increased by more than twice. Among proinflammatory cytokines only the serum level of interleukin-1β was significantly higher than that in healthy controls.

3. Results and Discussion

Before the treatment the clinical status of patients with CPRS secondary to fungal sensitization was evaluated. The results have revealed that none of the patients had the maximum point score of I point (a IV-point scale), 10 (11.1%) patients had II points, and most patients (62.2%) had IV points after being examined (Graph 1).

The evaluation of the clinical status in patients of Group 1a after treatment has revealed that there was a positive dynamics, namely, 17 (47.2%) patients developed minor manifestations of the disease (II points), 14 patients received a score of I point when assessing their clinical status (an absence of complaints and any symptoms), and only 5 (13.8%) patients had III points.

The evaluation of the clinical status in patients of Group 1b who received standard treatment using a IV-point scale has revealed that 27 (50%) patients received a score of III points indicating a significantly larger number of patients involved compared to Group 1a (p<0.05) and clinically apparent manifestations remaining after treatment. 12 (22%) patients received a score of II points indicating a significantly smaller number of patients involved compared to Group 1a (p<0.05) (minor manifestations). 8 (14.8%) patients were treated effectively (I point), however, no positive dynamics was observed in 7 (12.9%) patients indicating the ineffectiveness of treatment (Graph 1).

The most significant deviations in the evaluation of immunological status when performing both ASIT and pharmacotherapy included a reduction in the serum levels of total IgE, fungal allergen-specific IgE, IgG4 and interleukin-1β. In patients with CPRS receiving ASIT the serum level of total IgE reduced by 76% (160 IU/ml before treatment and 38.4 IU/ml after treatment), and in patients receiving standard treatment the serum level of total IgE reduced by 59.8% (160 IU/ml before treatment and 64.3 IU/ml after treatment) (Graph 2).
patients who received standard pharmacotherapy. Difference in the severity of clinical symptoms was also statistically significant.

Positive dynamics of immunological status was also observed in patients with CPRS. Thus, elevated serum IgE level being about three times higher in patients with CPRS than that in the control group was significantly lower after specific immunotherapy compared to that in patients who received standard pharmacotherapy. This peculiarity has proved the involvement of allergic reactions in developing and progressing CPRS. Moreover, considering the ability of IgE to affect the production of vasoactive amines and its major role in developing immediate hypersensitivity it can therefore be concluded that the use of specific immunotherapy when treating patients with CPRS is pathogenetically justified. Namely, the impact on the allergic genesis will contribute to reducing clinical symptoms, alleviating disease symptoms, slowing down the course of the disease, and increasing the effectiveness of treatment.

Serum interleukin-1β level has also proved that the use of specific immunotherapy when treating patients with CPRS is much more effective compared to the use of standard treatment. Thus, serum interleukin-1β level was found to be about four times higher in patients with CPRS than that in the control group. After treatment in patients who additionally received specific immunotherapy serum interleukin-1β level was found to be significantly lower compared to that before treatment. However, in patients with CPRS who received standard pharmacotherapy serum interleukin-1β level was also significantly lower than that before treatment and did not differ from that in patients who underwent specific immunotherapy. Interleukin-1β is known to be a multifunctional cytokine with a broad spectrum of activities playing a key role in the development and regulation of nonspecific defense and specific immunity. Statistically identical reduction in IL-1β levels can be considered as one of the criteria of effective treatment of patients with CPRS indicating reducing inflammatory and immune processes as a result of treatment.

4. Conclusions

1. Patients with chronic polyoid rhinosinusitis on the background of fungal sensitization developed clinically apparent manifestations being accompanied by significant nasal dysfunction which were rated on a IV-point severity scale as severe condition.

2. Chronic polyoid rhinosinusitis in patients with allergy to fungi was accompanied by significantly elevated serum levels of IgE, fungal antigen-specific IgE and anti-inflammatory cytokine IL-1β.

3. When performing ASIT a reduction in serum levels of total and specific IgE antibodies was determined in a wider range of allergens being significant regarding the degree of desensitization compared to the same values obtained in patients with CPRS when using pharmacotherapy indicating that therapy was pathogenetic.

4. The obtained results have revealed that the use of allergen-specific immunotherapy when treating patients with polyoid rhinosinusitis secondary to fungal sensitization provides a greater and statistically significant reduction in negative clinical symptoms and improvement of immunological parameters compared to patients receiving standard treatment of chronic polyoid rhinosinusitis.

5. References


