www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2015; 4(7): 94-97

www.thepharmajournal.com
Received: 31-07-2015
Accepted: 04-08-2015

Olesya Gerych
Department of Otorhinolaryngology, Ophthalmology-Head and Neck Surgery Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine.

Correspondence:
Olesya Gerych
Department of Otorhinolaryngology, Ophthalmology-Head and Neck Surgery Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine.

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

Olesya Gerych

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

Keywords: Polypoid 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 polypous 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 polypous 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 polyp 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 polypoid 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-an 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 the 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.

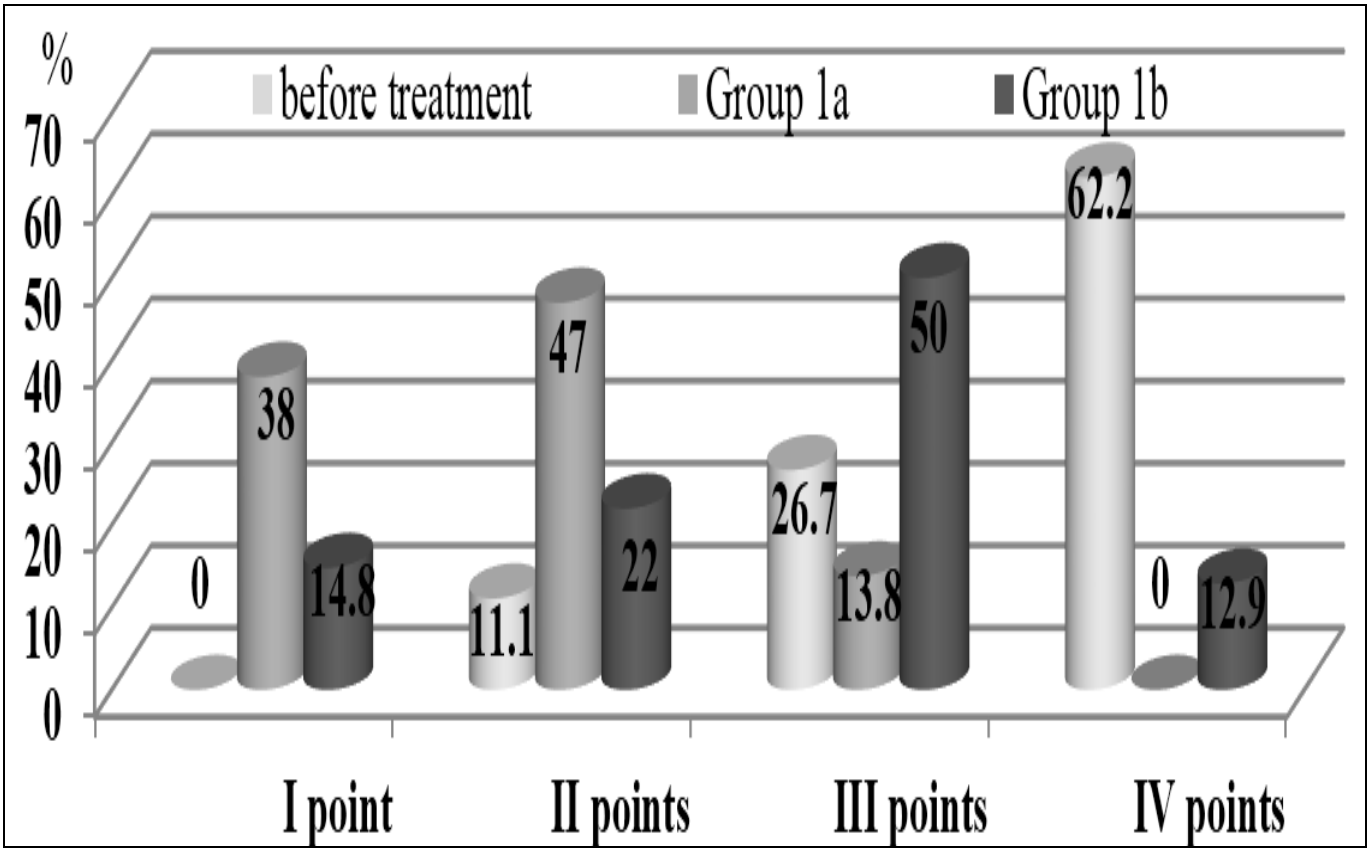
The serum levels of IgE and IgG4 were determined by the ELISA method. The serum concentrations of total IgE and IgG4 in patients of both groups were significantly higher than those in healthy controls. The presence of IgE antibodies to fungal allergens in patients' serum samples with an allergen was 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), Aspergilium (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 sensibilization 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).

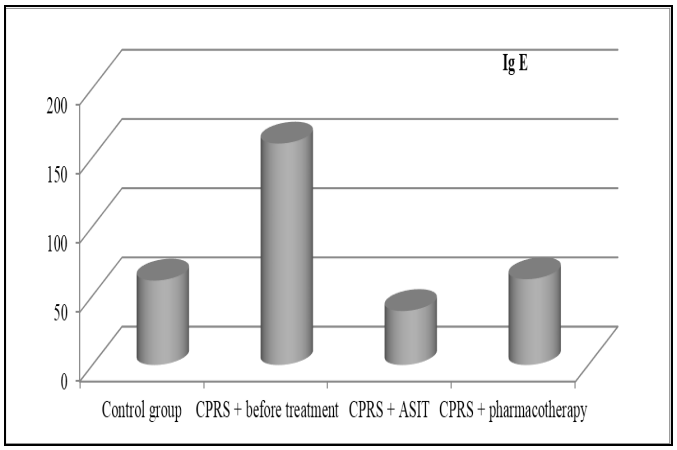
The evaluation of the clinical status in patients of Group 1a after treatment has revealed that there was a positive dynamics, namely, 17 (47.2%) patients developed minor manifestations of the disease (II points), 14 patients received a score of 1 point when assessing their clinical status (an absence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



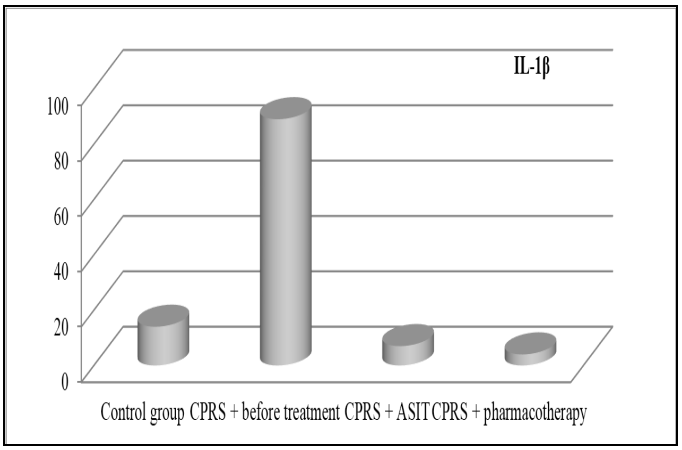
Graph 1: The number of patients with a different number of scale points for the dynamics of the clinical symptoms on a IV-point scale

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, IgG4and 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).



Graph 2: Serum IgE levels in patients with CPRS secondary to fungal sensibilization when using different treatment methods

After performing ASIT serum level of interleukin-1β was 7.1 pg/ml being 91.87% less compared to that before treatment, and when using standard treatment serum level of interleukin-1β reduced by 95.5% (3.9 pg/ml) (Graph 3).



Graph 3: Serum interleukin-1β levels in patients with CPRS secondary to fungal sensibilization when using different treatment methods

The results of the research have revealed that most patients with CPRS developed clinically apparent manifestations including significant violation of nasal breathing accompanied by a decreased sense of smell, rhinorrhea, conjunctival symptoms, and sneezing. Medical regimens used to treat patients have provided a certain level of reduction in clinical symptoms, however, there has been found that patients with CPRS who underwent specific immunotherapy had fewer complaints after treatment and diagnosed clinical manifestations became less frequent compared to those in 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 polypoid rhinosinusitis on the background of fungal sensibilization developed clinically apparent manifestations being accompanied by significant nasal dysfunction which were rated on a IV-point severity scale as severe condition.
2. Chronic polypoid 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 polypoid rhinosinusitis secondary to fungal sensibilization provides a greater and statistically significant reduction in negative clinical symptoms and improvement of immunological parameters compared to patients receiving standard treatment of chronic polypoid rhinosinusitis.

5. References

1. Aak AV. Fungal allergens. Features of fungal sensitization (review). Problems in Medical Mycology 2005; 7(2):12-16.
2. Ahapkyna IG. Hypersensitivity and environmental microorganisms. Immunology 2010; 4:212-215.
3. Barskiy OB, Yaremchuk SE, Volska OG. Fungal infections of ENT-organs: etiology, diagnosis, treatment. Medicine of Railway Transport 2004; 4:41-43.
4. Bezshapochny CB, Puhlyk SM, Loburets VV. Modern aspects of polypoid rhinosinusitis. Clinical Immunology, Allergology, Infectology 2008; 1:40-45.

5. Volkov AG. Trophimenko SL. Chronic Polypoid Rhinosinusitis: Pathogenesis and Treatment. Manual, Rostov-on-Don, 2007, 46.
6. Dzublik O Ya, Zaykov SV, Grishilo PV, Grishilo AP. Fungal allergy (Part I). Respiratory fungal allergies: features of bronchial asthma with fungal sensitization, Clinical Immunology, Allergology, Infectology 2010; 1:36-40.
7. Dzublik O Ya, Zaykov SV. Grishilo PV. Grishilo AP. Fungal allergy (Part IV). Allergic fungal rhinosinusitis. Clinical Immunology, Allergology, Infectology 2010; 4:22-25.
8. Zabolotniy DI, Yurochko FB. Nasal polyposis. Theory and Practice, 2006, 143.
9. Zavadsky NV, Zavadsky AV, Zavadska EA. Comparative study of medical history and clinical data in patients with nasal polyposis. Journal of Ear, Nose and Throat Diseases. 2008; 5:2-10.
10. Zarytska IS, Gogunska IV. Features of the pathology of the nasal cavity and paranasal sinuses on the background of allergic rhinitis with polyvalent sensitization to fungal and household allergens. Journal of Ear, Nose and Throat Diseases. 2010; 2:33-37.
11. Lopatin AS. Modern theories of the pathogenesis of polypoid rhinosinusitis, Pulmonology 2003; 5:110-115.