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# IMPLEMINTATION OF AUTOVACCINE TREATMENT IN PATIENTS WITH POLYPOUS RHINOSINUSITIS

Andrii Lupyr[1], Victoriia Alekseeva[1,2], Yeugenia Domina[1], Marina Yashchenko[1], Nadiia Yurevych[1], Oleksandr Karchynskiy[1], Alla Dzyza[1], Olga Bondarenko[1], Rozana Nazaryan[1]

[1]Kharkiv National Medical University, 4 Nauky Avenue, 61022, Ukraine

[2]Kharkiv International Medical University, 38 Molochna str. 61001, Ukraine

*vik13052130@gmail.com

**Abstract**

One of the most important aspects of the polypous rhinosinusitis problem is insufficient efficacy of its anti-relapse treatment. The goal of our study was to improve anti-relapse treatment efficacy of polypous rhinosinusitis by distinguishing of the core meaningful factors of the disease's development.

**Material and Methods.** Comprehensive evaluation of the data of three hundred patients with PRS aged 18-77 which have been hospitalized to the otorhinolaryngological clinic is done by means of factor analysis by the method of the main components with subsequent varimax-rotation of the factor axes (rotation of the coordinate system in such a way that factors become orthogonal, that is, minimally correlated with each other and maximally with real variables).

**Results.** The analysis of data demonstrated that among the variables some constellations took place - 46.47% of all fluctuations and changes observed in empirical data were due to two latent causes of higher degree, that is, the effect of two factors (and six factors explained more than a half of variability).

**Conclusions.**

1. Thus, as a result of the factorial analysis, 6 main factors were identified, the joint action of which explains 53.72% of the variability of indicators for the polypous rhinosinusitis.

2. The factor analysis allowed to distinguish the groups of indicators and estimate the specific weight of individual pathogenetic factors in the development of polypous rhinosinusitis, which might be conditionally combined under the general names of "clinic-immune", "clinic-pathomorphological", "immunoregulatory", "clinical-microbiological", "violation local protection "," epidemiological and demographic "factors.

3. The effect of two of the most powerful factors ("clinical-immune" and "clinic-pathomorphological factor") is explained by 46.47% of the variability of indicators.

4. Factor estimates for the most potent "clinically-immune-causative factor" with a high degree of reliability distinguished groups of patients with the first identified polypous rhinosinusitis and its relapse.

**Keywords**: *paranasal sinuses, recurrent polypous rhinosinusitis, autovaccine, CD4 cells*

## Introduction

The polypous rhinosinusitis is an old and at the same time very actual problem of the modern otophynolaryngology.

One of the topical aspects of the polypous rhinosinusitis problem is insufficient efficacy of its anti-relapse treatment [1]. The distinguishing of the core meaningful factors (including inflammatory, infectious, immunological, social and other factors)of the disease's development is important in terms of threatment modernization [2, 3, 4].

The goal of our study was to improve anti-relapse treatment efficacy of polypous rhinosinusitis by distinguishing of the core meaningful factors of the disease's development.

## Methods

In order to integrate the evaluation of clinical, clinical and epidemiological, immunological, general morphological, immunohistochemical and biochemical parameters, as well as the results of practical testing of the use of bacterial autovaccine in the system of anti-relapse therapy of polyposis rhinosinusitis, a logical and statistical analysis of the data of the examination of 300 patients with polypous rhinosinusitis aged 18-77 years on the basis of the otorhinolaryngological clinic of the Kharkiv National Medical University, the communal healthcare institution "Regional Clinical Hospital - Center of urgent care and disaster medicine" of Kharkov during the 2000-2009 period has been performed as the basis of development of new diagnostic and preventive measures.

Comprehensive evaluation of the data is done by means of factor analysis by the method of the main components with subsequent varimax-rotation of the factor axes (rotation of the coordinate system in such a way that factors become orthogonal, that is, minimally correlated with each other and maximally with real variables) [5].

A standard set of investigations have been performed. In order to evaluate the immune recognition as one of main lymphocyte functions the lymphocyte interaction parameter which is based on an ability of lymphocytes to recognize foreign substances and produce a cytokine capable to limit in vitro E-rosetting [6].

Some qualitative (categorical) indicators have been converted quantitatively to their score. Thus, the points assessment of the degree of polyposis was expressed according to the prevalence of polyps in the nasal cavity: 1 point - middle nasal meatus, 2 points - middle and common nasal meatus, 3 points - obstruction of the nasal cavity on both sides or any half of the nose.

The points assessment of the type of excretions was the following: 0 points in their absence, 1 point - for their mucous character, 2 points - serous, 3 points -purulent. The morphological degree of maturity of a polyp was expressed through its rank number: 1 point –"young", 2 points–"mature", 3 points –"old".

Partly main results of factor analysis superficially have been represented in our earlier publication [7], now we describe the fundamentals.

The critical value of p-level has been 0.05.

## Results

61 variables were included in the analysis. On the basis of the interconnections between them, 6 factors were identified, which together explained 53.72% of the empirical data variation.

At the same time, the ranking of the detected factors by the power of their influence (by descendent order) showed that factor 1 (the most powerful) explained 34.26% of the variability of the variables, while the remaining five factors had significantly less influence (Table 1). The analysis of data in the table 1 demonstrated that among the variables some constellations took place - 46.47% of all fluctuations and changes observed in empirical data were due to two latent causes of higher degree, that is, the effect of two factors (and six factors explained more than a half of variability).

Table 2 shows the factor loads of the six selected factors (only variables with loads ≥ 0.46 are presented, while cross-correlations began with lower values of indicators, i. e. one variable was included in several factors).

## Discussion

Taking into account the factors that were loaded with the most powerful factor 1 (number of operations on polypous rhinosinusitis in past, functional condition of the nasal breathing, degree of olfactory analyzer dysfunction, motor activity of the ciliated epithelium, the number of T-lymphocytes (CD2, CD3, CD4, CD8),CD19lymphocytes, total number of leukocytes, lymphocytes interaction parameter, phagocytic parameter, phagocytic index, immunoglobulins A, M, G, natural killers activity, circulating immune complexes, C3 and C4 complement components), it was named "Clinical and immune-causative factor". At the same time, the indicators, which were at the positive pole of the factor, acquired high values (increased), and indicators at the negative pole of the factor had low values.

The combined effect of factor 1 together with the second on factor significance (factor 2) was explained by almost half (46.47%) variability of indicators.

Taking into account the variables included in factor 2 (points of the degree of polyposis intensity,morphological degree of polyp maturity, the contents of CD4, CD8, CD4/CD8, CD16, HLA-DR antigen carriers, cells producing Ig M, Ig G, Ig Ein polyps stromal infiltrates, activity of hexokinase, phosphofructokinase, lactate dehydrogenase, creatinphsphokinase in polyp tissue), it has obtained the descriptive name of "Clinical and pathomorphological factor".

Factors 3, 4, 5 and 6, to a lesser extent, influenced the variability of the indicators, however, it is interesting that they were loaded with certain groups of indicators.

Thus, factor 3, called "Immunoregulatory factor", was loaded with indicators of concentration of interleukines 1β, 2, 6, 10, interferon γ and prostaglandin E2 cytokines in serum.

Taking into account that the factor 4 load included mainly the characteristics of the etiological infectious factor and the corresponding clinical manifestations (points assessment of excretions character,mean quantity of Klebsiella pneumoniae, Staphylococcus aureus, Streptococcus pyogenesin the nasal meatus, antibody titers to Klebsiella pneumoniae lipopolysacharides, Staphylococcus aureus, Streptococcus pyogenes, immunoglobulin Etiter to K. pneumoniaeand S. aureus,migration inhibition index to Klebsiella pneumoniaelipopolysaccharide, Streptococcus pyogenesstreptolysin-O, Staphylococcus aureus protein A), it was given the name of "Clinico-microbiological factor".

Factor 5 was characterized by a load of indices of predominantly local immune and non-immune protection (contentsof:secretory Ig A, monomeric Ig A, Ig G, lactoferrin, interferon γin oropharyngeal secretion), because ofwhat it was called "Violation of local defense factor".

Finally, factor 6 was loaded mainly with clinical, anthropodemographic and epidemiological parameters (age, duration of history of polypous rhinosinusitis, number of acute respiratory diseases exacerbations last year, polypous rhinosinusitis prevalence in a region of living), it was called "Epidemiological and demographic factor".

At the next stage, the intensity of the factors in the groups of patients with the newly diagnosed polypous rhinosinusitis and the recurrent course of the disease has been studied (Table 3).

Taking into account the variables that loaded the factors, these provisions can be interpreted as follows: for patients of the group for the first time diagnosed polypous rhinosinusitis characterized by high levels of intensity of immune inflammation, changes of microbiocenosis due to low values of local defense dysfunction and clinical and epidemiological parameters. On the contrary, during the next relapse of polypous rhinosinusitis, along with the unchanged dominance of immune-inflammatory shifts, the importance of the clinical-morphological factor, the depression changes of specific and nonspecific local protection, and the immunological factor in general.

Perspectives of further investigations are related to mathematical modeling of the pathological process using artificial neural networks or some other new diagnostic methods [8, 9, 10, 11].

PRS may be attached with development of antibiotic resistance [12].

At the same time perspectives of our further investigations are related to wider clinical approbation of bacterial autovaccine use in complex treatment of PRS maybe in cases of its combinations with other disorders in the orofacial zone [13, 14] or other organs and systems [15].

The effectiveness of the treatment can be displayed by new promising diagnostic procedures [16, 17, 18] in different cohorts of patient maybe with presence 3of comorbidities [19, 20, 21], levels of hormones or immune response [22, 23, 24], experience of previous antibiotic administration [25-27].

## Conclusions

1. Thus, as a result of the factorial analysis, 6 main factors were identified, the joint action of which explains 53.72% of the variability of indicators for the polypous rhinosinusitis.

2. The factor analysis allowed to distinguish the groups of indicators and estimate the specific weight of individual pathogenetic factors in the development of polypous rhinosinusitis, which might be conditionally combined under the general names of "clinic-immune", "clinic-pathomorphological", "immunoregulatory", "clinical-microbiological", "violation local protection "," epidemiological and demographic "factors.

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**Table 1.** Ranking of the most powerful factors influencing the variability of the parameters in patients with polypous rinosinusitis

| Factors | The power of the explained influence on the variability of indicators,% |
|---|---|
| Factor 1 | 34.26 |
| Factor 2 | 12.21 |
| Factor 3 | 2.15 |
| Factor 4 | 2.87 |
| Factor5 | 1.31 |
| Factor6 | 0.92 |
| Total | 53.72 |

**Table 2.** Characteristics of factor loading of parameters in patients with polyposis rinosinusitis

| Parameters | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 | Factor 6 |
|---|---|---|---|---|---|---|
| Age | | | | | | 0.750 |
| Duration of polypous rhinosinusitis history, years | | | | | | 0.952 |
| Operations forpolypous rhinosinusitisquantity in past | 0.947 | | | | | |
| Degree of polyposis intensity, points | | 0.941 | | | | |
| Acute respiratory diseases quantity per last year | | | | | | 0.938 |
| Points assessment of excretions character | | | | 0.864 | | |
| Functional condition of the nasal breathing, mm of water | 0.938 | | | | | |
| Degree of odor perceprion disturbances | 0.951 | | | | | |
| Motor activity of the ciliated epithelium, minutes | 0.894 | | | | | |
| Polypous rhinosinusitis prevalence in a region of living, per 10000 of population | | | | | | 0.815 |
| T-lymphocytes CD2 count, % | -0.911 | | | | | |
| T-lymphocytesCD3 count, % | -0.887 | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| T-lymphocytesCD4 count, % | 0.815 | | | | | |
| T-lymphocytesCD8count, % | -0.837 | | | | | |
| B-lymphocytesCD19 count, % | 0.953 | | | | | |
| Totalleukocytescount, $\times 10^9$/l | 0.864 | | | | | |
| Lymphocytes interaction parameter | -0.823 | | | | | |
| Phagocytic parameter | -0.724 | | | | | |
| Phagocytic index | 0.719 | | | | | |
| Immunoglobulin A, g/l | -0.937 | | | | | |
| Immunoglobulin M, g/l | 0.815 | | | | | |
| Immunoglobulin G, g/l | 0.871 | | | | | |
| Natural killers activity, % | -0.784 | | | | | |
| Mean quantity of *Klebsiella pneumoniae*in nasopharynx, colony forming unit per ml | | | | 0.996 | | |
| Mean quantity of *Staphylococcus aureus*in nasopharynx, colony forming unit per ml | | | | 0.975 | | |
| Mean quantity of *Streptococcus pyogenes*in nasopharynx, colony forming unit per ml | | | | 0.957 | | |
| Antibodies to *Klebsiella pneumoniae*lipopolysaccharide titer, $log_2$ | | | | 0.935 | | |
| Antibodies to*Staphylococcus aureus* titer, $log_2$ | | | | 0.923 | | |
| Antibodies to *Streptococcus pyogenes* titer, $log_2$ | | | | 0.896 | | |
| Ig E to*K. pneumoniae* | | | | 0.937 | | |
| Ig E to*S. aureus* | | | | 0.941 | | |
| Migration inhibition index to *Klebsiella pneumoniae*lipopolysaccharide | | | | -0.703 | | |
| Migration inhibition index to*Streptococcus pyogenes*Streptolysin O | | | | -0.722 | | |
| Migration inhibition index to Staphylococcus aureus protein A | | | | -0.914 | | |
| Circulating immune complexes, units of optical density | 0.891 | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Complement C3 component | -0.753 | | | | | |
| Complement C4 component | -0.760 | | | | | |
| Interleukin 1β serum concentration, pg/ml | | | 0.927 | | | |
| Interleukin 2 serum concentration, pg/ml | | | -0.726 | | | |
| Interleukin 6 serum concentration, pg/ml | | | 0.769 | | | |
| Interleukin 10 serum concentration, pg/ml | | | -0.737 | | | |
| Interferon γ serum concentration, pg/ml | | | -0.965 | | | |
| Prostagrandin $E_2$serum concentration, pg/ml | | | 0.738 | | | |
| Secretory Ig A contents in oropharyngeal secretion, g/l | | | | | -0.895 | |
| Monomeric Ig A contents in oropharyngeal secretion, g/l | | | | | 0.872 | |
| Ig G contents in oropharyngeal secretion, g/l | | | | | 0.914 | |
| Lactoferrin contents in oropharyngeal secretion, mkg/ml | | | | | -0.967 | |
| Interferon γ contents in oropharyngeal secretion, pg/ml | | | | | -0.955 | |
| Morphological degree of polyp maturity | | 0.710 | | | | |
| T-lymphocytesCD4contents in polyps stromal infiltrates, % | | 0.797 | | | | |
| T-lymphocytesCD8contents in polyps stromal infiltrates, % | | 0.711 | | | | |
| CD4/CD8ratio in polyps stromal infiltrates | | 0.724 | | | | |
| CD16contents in polyps stromal infiltrates, % | | 0.742 | | | | |
| HLA-DR carrier cells contents in polyps stromal infiltrates, % | | 0.774 | | | | |
| Ig M-producer cellscontents in polyps stromal infiltrates, % | | 0.793 | | | | |
| Ig G-producer cellscontents in polyps stromal infiltrates, % | | 0.809 | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Ig E-producer cellscontents in polyps stromal infiltrates, % | | 0.787 | | | | |
| Hexokinase activity in polyp tissue, mkmol/gprotein/hour | | 0.753 | | | | |
| Phosphofructokinase activity in polyp tissue, mkmol/gprotein/hour | | 0.803 | | | | |
| Lactate dehydrogenase activity in polyp tissue, mkmol/gprotein/hour | | 0.766 | | | | |
| Creatinphosphokinase activity in polyp tissue, mkmol/gprotein/hour | | 0.708 | | | | |

**Table 3.** Averaged factor estimates in the groups of patients with newly diagnosed and recurrent polypous rinosinusitis

| Groups | Factor 1 | Factor 2 | Factor 3 | Factor 4 | Factor 5 | Factor 6 |
|---|---|---|---|---|---|---|
| Primarilydiagnosedpolypous rhinosinusitis | 0.517 ± 0.025 | 0.071 ± 0.062 | 0.157 ± 0.081 | 0.238 ± 0.107 | 0.217 ± 0.092 | 0.053 ± 0.009 |
| Recurrentpolypous rhinosinusitis | 0.623 ± 0.047 | 0.156 ± 0.092 | 0.023 ± 0.026 | 0.063 ± 0.033 | 0.101 ± 0.054 | 0.139 ± 0.037 |

**Table 4.** Differences between groups of patients with newly diagnosed and recurrent polyposis rhinosinusitis by factors

| Groups | Distances between groups | | p-level value |
|---|---|---|---|
| Primarily diagnosed polypous rhinosinusitis – recurrent polypous rhinosinusitis | Factor 1 | 1.507 | p<0.01 |
| | Factor 2 | | p>0.05 |
| | Factor 3 | 1.059 | p<0.01 |
| | Factor 4 | | p<0.05 |
| | Factor5 | 3.072 | p<0.01 |
| | Factor6 | | p<0.01 |