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Possibilities of Application of Bacterial Immunomodulators in Polyposis Rhinosinuitis

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Abstract To date, the immunological aspects of the pathogenesis of nasal polyps attract close attention. As a result of numerous studies, irrefutable evidence has been obtained for the existence of three main clinical and morphological directions in the development and course of PRS: allergic, detected in 60% of patients, immunodeficiency (hypoimmune) - up to 50% and autoimmune - up to 14%. It has also been established that chronic PRS is an infectious and inflammatory process that is supported by immunological mechanisms - antibodies, including reagins, immune complexes and cytokines, including chemokines of the interleukin—8 type. Currently, immunomodulators of a new class in the form of immunocorrectors of bacterial origin and synthetic vaccines are increasingly being used. These are IRS-19, VP-4, bronchoimmunal, which are purified bacterial lysates; ribomunil, represented by bacterial ribosomes; lycopid, which is the main structural fragment of the cell wall of almost all known bacteria. The use of these drugs for the treatment of chronic infectious and allergic diseases was characterized by an increase in the level of T-lymphocytes, serum Ig, secretory ID, phagocytic activity of neutrophils, lysozyme and complement activity.

Keywords: polyposis rhinosinusitis, prevalence, immunocomplex therapy, immunomodulators.

Introduction. The results of many epidemiological studies conducted in different countries of the world indicate that the prevalence of polypous rhinosinusitis (PRS) ranges from 1-40% [1]. Morbidity data based on patients seeking medical care do not reflect the actual prevalence of this disease, since this does not take into account the huge number of patients who did not apply, patients with initial manifestations, as well as persons who were not correctly diagnosed.

To date, the immunological aspects of the pathogenesis of nasal polyps attract close attention. As a result of numerous studies, irrefutable evidence has been obtained for the existence of three main clinical and morphological directions in the development and course of PRS: allergic, detected in 60% of patients, immunodeficiency (hypoimmune) - up to 50% and autoimmune - up to 14%. It has also been established that chronic PRS is an infectious and inflammatory process that is supported by immunological mechanisms - antibodies, including reagins, immune complexes and cytokines, including chemokines of the interleukin—8 type [2].

The literature provides data confirming that allergy is one of the most common causes of polypous ethmoiditis (PE) and rhinosinitis. This is evidenced by frequent relapses of PRS in patients with bronchial asthma (BA), as well as information that 40% of patients with nasal polyps have a history of BA or allergic diseases. According to various authors, PRS develops against the background of allergies in 18-80% of cases. So, according to S. E. Yaremchuk et al. [3], the examined patients with PRS revealed an allergic reaction to household dust in 57.14% of cases, to

food allergens — in 5.71%, drug allergy — in 32.86%, polynosis — in 4.28% of cases. It is well known that eosinophilia is a characteristic sign of allergies. Rinia A.V. and co. [4] revealed that in patients with nasal polyposis, the polyps tissue is infiltrated mainly by eosinophils, lymphocytes, plasmocytes and mast cells. At the same time, activated eosinophils that infiltrate the tissue produce a large number of toxic proteins, such as eosinophilic cationic protein and the main protein with basic properties. In addition to these toxic mediators, eosinophils are capable of producing many cytokines, in particular IL-5, chemokines (RANTES) and colony stimulating growth factor of granulocytes and macrophages. Thus, eosinophils autocrinally continue their own life and contribute to an increase in tissue infiltration.

Analysis of the results of studies of the state of general immunity in PA patients over the past decade has shown an inhibition of the quantitative and functional activity of the cellular link of immunity, a decrease in phagocytosis, as well as a decrease in the number of populations of B lymphocytes. According to some authors [5], it has been established that it is violations on the part of immunity that play a leading role in the suppression of resistance in PE, i.e. there are significant changes in the state of natural nonspecific protection, and this causes a severe picture of the clinical course with frequent development of relapses of the disease.

Taking into account the existence and the huge role of the inflammatory theory in the pathogenesis of PRS, based on the fact that this disease is a manifestation of immune inflammation, the development of which is dominated by viruses and various pathogenic bacteria, we have investigated modern aspects of the use of bacterial immunomodulators in this pathology.

Since PRS often occurs against the background of upper respiratory tract allergies, the use of specific immunotherapy (SIT) with causal allergens as an anti-relapse treatment of patients with this pathology may have prospects. This technique has been successfully used for the treatment of respiratory allergoses since the beginning of the last century and to date continues to be widely used in the treatment of atopic diseases of the upper respiratory tract [6].

So, V. P. Sitnikov et al. [7], considering the determining role of autoallergia in the development of PRS, an autoextract of polyps was used for the treatment of nasal polyposis with a course of treatment of 10 injections according to an increasing scheme. The authors noted a direct correlation between the repetition of the course of specific desensitization and the lengthening of the remission period.

It is known that allergy pharmacotherapy does not always lead to the desired results and predicts almost lifelong use of the drug. Currently used antiallergic drugs affect only certain pathogenetic links of allergic inflammation. Causing certain pathogenetic and symptomatic effects, they have little effect on the immunological phase of allergic inflammation. In this regard, there is the use of sieves as an anti-relapse treatment for allergic nasal polyposis. The experience of using SIEVES has shown that this method affects all pathogenetically significant links of the allergic process and is able to naturally change the course of an allergic disease. In recent years, the efforts of scientists from many countries have succeeded in establishing a variety of immunological mechanisms of SIT, which can be represented by 1) an increase in the number of rosette-like T- and B-lymphocytes; 2) an increase in the production of blocking antibodies; 3) a decrease in the release of allergy mediators; 4) an increase in the activity of suppressor cells and mechanisms; 5) enhancement of the function of Th-1 helpers and a decrease in Th-2; 6) switching CD4+ cells from Th-2 to Th-1 phenotype; 7) increased functional activity of T-lymphocytes; 8) reduction of lymphocyte blastogenesis under the influence of a specific antigen; 9) induction of tolerance of B-lymphocytes that produce IdE; 10) decrease in the reactivity of mediator-producing cells.

As a result of these effects, there is a preservation of long-term (sometimes for decades) remission; prevention of deterioration of the course of the disease and the expansion of the spectrum of allergens to which hypersensitivity is formed; reduction of the need for pharmacological drugs.

In the second half of the last century, attempts were made to carry out sieves with bacterial allergens in infectious allergic rhinosinuitis, including in the polypous form. For this purpose, N. G. Mitrokhina and V. B. Bureva [8] used standard bacterial allergens that were administered intradermally in constantly increasing doses twice a week for 3-4 months. The same authors tested the sieving technique by aerosol spraying of bacterial allergens into the nose and throat daily for 10 days, and then once a week for 1 month. The effectiveness of such treatment with aerosol administration of the allergen was 86%.

Currently, immunomodulators of a new class in the form of immunocorrectors of bacterial origin and synthetic vaccines are increasingly being used. These are IRS-19, VP-4, bronchoimmunal, which are purified bacterial lysates; ribomunil, represented by bacterial ribosomes; lycopid, which is the main structural fragment of the cell wall of almost all known bacteria. The use of these drugs for the treatment of chronic infectious and allergic diseases was characterized by an increase in the level of T-lymphocytes, serum Ig, secretory ID, phagocytic activity of neutrophils, lysozyme and complement activity.

Of great interest are the issues of combined use of sieves with allergens and immunocorrecting drugs. B. A. Molotilov et al. [9] the effectiveness of sieves with bacterial allergens in combination with lycopide was studied in patients with infectious allergic rhinosinitis, which amounted to 86.4%.

The problem of treating fungal lesions of the paranasal sinuses, in particular allergic fungal sinusitis (AS), according to A. S. Lopatin [10], is a world-class problem today. This disease is almost always accompanied by a polypous process in the nasal cavity, and its treatment is carried out mainly surgically, followed by long-term therapy with corticosteroids (CS).

The possibility of treating patients with AgS by the SIT method with fungal allergens was discussed by R. L. Mabry et al. [11]. For the entire period of their observations (from 7 to 17 months), patients remained in remission.

Taking into account the significant prevalence of allergic diseases of the upper respiratory tract and considering nasal polyps as a stage in the course of allergic rhinitis, A. G. gadzhimirzaev et al. [12] applied the technique of sieving with household and pollen allergens in the treatment of PRS in children. The use of this method was characterized by the same positive dynamics as in the treatment of topical CS. In addition, there was an improvement in the respiratory function of the nose and the cytological picture of smears of the nasal mucosa after a course of SIT treatment. Indicators of humoral and cellular immunity shifted towards normalization. The X—ray picture was normalized - the air permeability of the paranasal sinuses resumed, the cyst-like shadows in the maxillary sinuses disappeared. During a dynamic examination of the nasal cavity, the resorption of small polyps in the middle nasal passages was observed.

Thus, given the increase in the number of allergic diseases and a significant part of patients with PRS, in whom this disease occurs against the background of allergies, the use of SIEVES in the treatment of this pathology may be promising and has a special scientific interest. The search for new methods of anti-relapse treatment of patients with PRS is one of a number of issues that are being studied in almost all leading ENT clinics. However, the only methodological approach to treatment that would be as effective as possible and cause minimal side effects has not yet been found.

The use of bacterial vaccines to prevent the recurrence of infectious and inflammatory diseases of different localization is one of the promising methods that are intensively studied and developed by both clinicians of different specialties and representatives of various scientific fields and schools [13]. The high clinical efficacy of vaccinating drugs obtained from upper respiratory tract

microorganisms in PRS, as well as an increase in some immunological indicators of a local and systemic nature with parenteral administration of a bacterial vaccine, has been shown. Filatov et al. [14] successfully used an autovaccine, which consists of a suspension of killed bacteria isolated from the nasal cavity of patients with PRS, in combination with tissue homogenate of removed polyps. The course of treatment consisted of two stages: the first — 10 injections every 2-3 days, the second — 7 one month after the first. This method of treatment, according to the authors, contributes to the regulation of micro- and macroorganism relations, stimulation of specific and non-specific protection factors and, possibly, suppression of immunopathological reactions of the nasal mucosa. The described technique is recommended mainly for the infectious-allergic form of PE.

D. I. Zabolotny et al. [15] in an experiment, the active effect of vaccines from microorganisms vegetating on the mucous membrane of the upper respiratory tract of a person on various manifestations of immune reactions was established. The formol-warmed vaccine significantly exceeds the vaccine obtained by lysing microorganisms in its effect, especially in the formation of antibodies to the microorganisms contained in the vaccine (streptococcus, staphylococcus, klebsiella) and to their toxins. The study of factors of innate immunity during animal immunization showed that the formol-heated vaccine caused greater stimulation of leukocytes than the lysate of microorganisms, and also enhanced the phagocytic activity of these cells. At the same time, the immunization of animals with lysate of microorganisms was accompanied by a more effective increase in the number of Fcr+ cells and the activity of natural cytotoxic cells.

Significant progress in understanding the mechanisms of the occurrence and development of allergic processes has made it possible to achieve significant success in the pharmacotherapy of allergic diseases. However, in some cases, pharmacotherapy does not allow either to suspend the course of the disease or to prevent its transformation into more severe forms in the event of discontinuation of drug treatment. According to modern ideas about the pathogenesis of allergic diseases and their immunological aspects, an imbalance of Thl/Th2 lymphocytes plays an important role in this pathology, which is characterized by a shift in the cytokine profile towards the production of IL-4, 5, 13, which induce the formation of IgE by B cells [16].

G. L. Osipova [17] based on the available evidence of a violation of immune processes in atopy, admits that the use of drugs that contribute to the normalization of the immune system function with its switching to IL-2 and gamma interferon synthesis will lead to a decrease in IgE synthesis. The use of drugs normalizing the function of Th1 lymphocytes in basic therapy may become a new strategy that will allow to achieve an increase in clinical efficacy and long-term rehabilitation of patients with allergic diseases. The author believes that modern ideas about the immunological mechanisms of the pathogenesis of allergies allow for a revision on a new theoretical basis of the existing opinions about the role of bacterial vaccines in the treatment of allergic diseases. If there is sufficient evidence of clinical efficacy in controlled trials, they can be included in the basic therapy of allergic diseases.

Immunotherapy affecting pathogenetically significant links of the allergic process is possible when conducting specific hypo-sensitizing therapy with allergens or other specifically active drugs (allergoids, allergovaccines, etc.) or when using broad-spectrum immunomodulators, which are bacterial vaccines from antigens of causally significant pathogens. At the same time, protection against conditionally pathogenic bacteria is formed, which initiate triggers for many manifestations of allergic pathology. Protection is created during the formation of protective immunity against specific pathogens by correcting secondary immunodeficiencies that are associated with allergic diseases.

If specific hyposensitizing immunotherapy has a long history and the positive and negative sides of its effects have been established, then the use of bacterial vaccines to increase the

effectiveness of therapy for allergic diseases is in its infancy. For this purpose, ribomunil (France), bronchovax and its analogues (Switzerland), as well as the multicomponent VP-4 vaccine developed at the I. I. Mechnikov Research Institute of Medical Sciences were used [17]. The use of VP-4 for the treatment of AD patients who received the vaccine intranasally-subcutaneously showed an excellent positive effect throughout the year in more than 66.7% of patients. With intranasal-oral administration of the vaccine, a positive effect was obtained in 74.2% of patients. There was a long-term (for a year or more) decrease in the frequency and severity of exacerbations, prolongation of remission, which made it possible to reduce the volume of medications used, especially systemic COP. Immunotherapy provides correction of the composition of subpopulations of lymphocytes with CD3, CD4, CD72 markers and the increase in titers of antibodies to antigens that are part of the drug. The use of therapeutic multicomponent vaccine VP-4 in patients with latent allergy provides a state of long-term remission. Referring to the results of the conducted studies, the author [17] considers it possible to use the therapeutic multicomponent vaccine VP-4 in the basic therapy of allergic diseases, and the significant degree of influence of these drugs on different parts of the immune process and factors of nonspecific resistance allow predicting the possibility of achieving a positive effect in the treatment of various nosological forms of allergic diseases.

Currently, as noted by T. Y. Zaporozhets and I. V. Loskutova [18], clinicians are increasingly attracted to the issues of the influence of changes in the biocenosis of the human body in various diseases and their treatment. The biocenosis of the organism constitutes integral ecological systems that maintain a dynamic balance between the micro- and macroorganism. Activation of autoflora occurs as a result of the influence of various negative factors on the human body (hypothermia, fatigue, etc.), while non-pathogenic microorganisms of biological cavities become pathogenic, which causes the development of diseases. A decrease in antimicrobial resistance is not the only reason for the development of endogenous intoxication. The suppression of natural immunity factors causes a violation of associative connections in microbiocenoses, which leads to dysbiosis and changes in the biological properties of microorganisms of the autoflora [19]. In addition, secondary infections join the PRS, and asymptomatic forms of persistent infection are also observed, which contributes to the progress of the disease.

Modern treatment of PRS consists of surgical and conservative stages. However, with surgical intervention, it is impossible to remove all polypous tissue, as this can cause the development of relapses, and as a result of the use of general and local anesthesia and the use of systemic antibiotics, secondary immunodeficiency, which can provoke relapses of polyposis of the paranasal sinuses and will require repeated polypotomies. Thus, surgical intervention can be symptomatic, depriving the patient only of the symptoms of the disease, but not affecting the links of pathogenesis.

To solve this issue, immunomodulatory agents for the correction of systemic immunity disorders are included in the comprehensive treatment of recurrent forms of PRS.

The authors [18] studied new modern immunoactive drugs — subalin and immunomax, which are used in the treatment of chronic viral (herpetic) and bacterial infections [21]. The immunopharmacological properties of the drug activate tissue macrophages, stimulate the production of antibodies against foreign antigens and cause an increase in the synthesis of anti-inflammatory cytokines.

Subalin is a drug created by genetic engineering based on a bacterium of the genus Bacillus. It affects the immune system, enhancing cellular and humoral immunity. In this case, the immunoactive substance immediately enters the lymphatic system, and not into the bloodstream, which reduces immunization against interferon (IFN), as it happens with parenteral administration of the IFN drug and its inducers. The physiological and genetic similarity of the mucous membranes of all organs and systems explains the activation of immune reactions throughout the body. As a result

of the studies, it was found that IFN-α2, which is synthesized by Bacillus subtillis during the presentation of the antigen to Th0-lymphocytes, induces the expression of a specific IL-12 receptor stimulating the IL-18 receptor on T-lymphocytes, which is also synthesized by B. Subtillis with IFN-β, which is necessary for the development of Th-1 immune response and activation of macrophages for cytolysis [22]. It has been proven that subalin is effective not only for the correction of the microflora of the gastrointestinal tract (gastrointestinal tract), but also for the therapeutic effect on chronic inflammation outside the gastrointestinal mucosa. When using a combination of subalin and immunomax in the treatment of patients with PRS, a positive effect on the state of microbiocenosis of the nasal mucosa was determined: in most patients, a decrease in the quantitative composition of conditionally pathogenic microflora was noted.

The study of the main aspects of the use of bacterial immunomodulators in polypous rhinosinitis has shown that the problem of using immunomodulatory therapy in polypous rhinosinitis at the moment still needs improvement.

Among the various methods of treating this disease, the effectiveness of the use of specific immunotherapy is quite high, and during anti—relapsing treatment - bacterial immunomodulators.

References:

1. Эпидемиология полипозных риносинуситов / А. А. Ланцов, С. В. Рязанцев, Б. М. Цецарский, В. И. Кошель.— СПб.: Аг-во мед. информации «РИА-АМИ», 1999.— 95 с.
2. Типы аллергических реакций на различные микроб-ные, тканевые и аутотканевые антигены у больных полипозным риносинуситом / Д. И. Заболотный, О. Ф. Мельников, Д. И. Безбах, Т. В. Сидоренко // Журн. вушних, носових і горлових хвороб.— 2001.— № 3.— С. 204–205.
3. Яремчук С. Я., Волосовец Л. И., Голобородько О. П. Роль аллергии в развитии полипозного риносинусита // Журн. вушних, носових і горлових хвороб.— 2001.— № 3.— С. 234–235.
4. Rinia A. B., Ebbens F. A., Fokkens W. J. Полипоз носа: клеточный подход к ответам на вопросы // Клінічна імунологія. Алергологія. Інфектологія.— 2007.— № 5 (10).— С. 74–79.
5. Запорожець Т. Ю. Стан макрофагально-моноцитарної системи крові у хворих на поліпозний етмоїдит // Журн. вушних, носових і горлових хвороб.— 2009.— № 3.— С. 71–72.
6. Нестерчук В. І., Заболотна Д. Д. Лікування хворих на алергічний цілорічний риніт неінвазивними методами специфічної імунотерапії // Ринологія.— 2002.— № 1.— С. 39–41.
7. Ситников В. П., Новиков Д. К. Использование ау-тоэкстракта полипов в лечении больных рецидивирующим полипозным риносинуитом // 4-й съезд отоларингологов республики Беларусь: тезисы докладов.— Минск, 1996.— С. 122–123.
8. Митрохина Н. М., Бурева В. Б. Полипоз носа и не-которые аспекты иммуноспецифического лечения // Журн. ушных, носовых и горловых болезней.— 1975.— № 2.— С. 42–45.
9. Новый подход к лечению инфекционно-аллергиче-ского риносинуита / Б. А. Молотилов, Е. М. Костина. Н. К. Починина, Н. И. Баранова // Материалы I межрегиональной научно-практической конференции «Иммунологические аспекты ринологии».— Самара, 1999.— С. 119–124.

10. Лопатин А. С., Сидоренко И. В. Хирургическое лечение аллергического риносинусита // Materia Medica.— 1999.— № 3.— С. 72–81.
11. Mabry R. L., Mabry C. S. Immunotherapy for allergic fungal sinusitis: The second year // Otolaryngology —Head and Neck Surgery.— 1997.— Vol. 117, № 10.— P. 367–371.
12. Гаджимирзаев Г. А., Гамзатова А. А., Багомедов М. М. Особенности полипозных риносинуситов у детей // Вестн. оториноларингологии.— 1997.— № 1.— С. 27–31.
13. Исследование эффективности применения рибомунила для лечения детей, страдающих частыми ОРВИ и воспалительными заболеваниями ЛОР-органов г. Э. Тимен, Д. И. Заболотный, И. В. Кузык и др. // Журн. ушных, носовых и горловых болезней.— 2001.— № 6.— С. 26–32.
14. Филатов С. В. Некоторые аспекты патогенетического воздействия аутовакцинации при полинозе носа // Журн. ушных, носовых и горловых болезней.— 2003.— № 3.— С. 225.
15. Заболотный Д. И., Лупырь А. В., Мельников О. Ф. Влияние микробных вакцин на основные реакции иммунитета экспериментальных животных при их системной иммунизации // Мат. X съезда отоларингологов Украины (22–25 мая, 2005).— К., 2005.— С. 27–28.
16. Хаитов Р. М. Физиология иммунитета // Аллергия, астма, клинич. иммунол.— 2000, № 2.— С. 3–16.
17. Осипова Г. Л. Поликомпонентная вакцина ВП-4 в терапии аллергических заболеваний // Журн. микробиологии, эпидемиологии и иммунологии.— 2003.— № 1.— С. 36–42.
18. Запорожець Т. Ю., Лоскутова І. В. Ефективність лікування хворих на хронічний поліпозний етмоїдит при дисбіотичних порушеннях слизової оболонки порожнини носа // Журн. вушних, носових і горлових хвороб.— 2010.— № 1.— С. 58–63.
19. Микробные ценозы носоглотки /Е. М. Бабич, И. В. Елисеева, В. И. Белозерский и др. // Мікробіол. журн.— 1999.— Т. 61, № 3.— С. 63–68.
20. Тищенко А. Л., Сергеева Н. С., Кралин М. Ю. «Им-муномакс» в терапии рецидивирующей генитальной папилломавирусной инфекции // Рус. мед. журн.— 2003.— Т. 11, № 27.— С. 1526–1527.
21. Буданов П. В., Вороной С. В., Асланов А. Г. Принципы лечения папилломавирусной инфекции // Вопр. гинекологии, акушерства и перинатологии.— 2005.— Т. 3, № 4.— С. 70–75.
22. Адъювантные свойства рекомбинантного пробиотика субалина, продуцирующего интерферон / В. А. Белявская, г. М. Игнатьев, Н. В. Литвяков и др. // Журн. микробиол.— 2001.— № 6.— С. 77–82.