MODERN TREATMENT METHODS OF POLYPOID RHINOSINUSITIS

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Abstract.

Treatment of polyposis rhinosinusitis is currently an urgent problem of modern otorhinolaryngology. A significant increase in the prevalence of the disease with polypous rhinosinusitis (from 5 to 20%) and a high frequency of relapses are due to insufficiently studied pathogenetic mechanisms for the development of the polypous process and the lack of effective methods of treatment. The combination of this disease with bronchial asthma, the asthmatic triad and the addition of a purulent process significantly complicate the course and treatment of patients with polypous rhinosinusitis. In accordance with the multifactorial theory, the development of polyposis rhinosinusitis occurs as a result of mechanical, physical factors, as well as the penetration of microbial, fungal and viral agents on the surface of the nasal mucosa. This leads to the activation of the mechanisms of local immunity, which is a whole complex of specific and non-specific reactions that provide the barrier function of the mucous membrane. Long-term exposure to various agents leads to a decrease in the activity of the protective barrier of the nasal mucosa and stimulates the development of an infection-dependent allergic process. The latter is accompanied by a violation of immune homeostasis in the form of secondary immunodeficiency, the formation of persistent immune eosinophilic inflammation, leading to remodeling of the nasal mucosa and the development of polypous rhinosinusitis.

Keywords: polyps, nasal cavity, rhinosinusitis, allergy, bronchial asthma.

СОВРЕМЕННЫЕ МЕТОДЫ ЛЕЧЕНИЯ ПОЛИПОЗНОГО РИНОСИНУСИТА

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Аннотация.

Лечение полипозного риносинусита в настоящее время является актуальной проблемой современной оториноларингологии. Значительный рост распространенности заболевания полипозным риносинуситом (с 5 до 20%) и высокая частота рецидивов обусловлены недостаточно изученными патогенетическими механизмами развития полипозного процесса и отсутствием эффективных методов лечения. Сочетание этого заболевания с бронхиальной

астмой, астматической триадой и присоединением гнойного процесса значительно усложняют течение и лечение больных полипозным риносинуситом. В соответствии с многофакторной теорией развитие полипозного риносинусита происходит в результате действия механических, физических факторов, а также проникновения микробных, грибковых и вирусных агентов на поверхность слизистой оболочки носа. Это приводит к активации механизмов местного иммунитета, представляющего собой целый комплекс специфических и неспецифических реакций, обеспечивающих барьерную функцию слизистой оболочки. Длительное воздействие различных агентов приводит к снижению активности защитного барьера слизистой оболочки носа и стимулирует развитие инфекционно-зависимого аллергического процесса. Последнее сопровождается нарушением иммунного гомеостаза в виде вторичного иммунодефицита, формированием стойкого иммунного эозинофильного воспаления, приводящего к ремоделированию слизистой оболочки носа и развитию полипозного риносинусита..

Ключевые слова: полипы, полость носа, риносинусит, аллергия, бронхиальная астма.

POLIPOZ RINOSINUSITNI DAVOLASHNING ZAMONAVIY USULLARI

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Annotatsiya.

Polipozli rinosinusitni davolash hozirgi vaqtda zamonaviy otorinolaringologiyaning dolzarb muammosi hisoblanadi. Polipli rinosinusit bilan kasallikning tarqalishining sezilarli darajada oshishi (5 dan 20% gacha) va retsidivlarning yuqori chastotasi polipli jarayonning rivojlanishining patogenetik mexanizmlari etarli darajada o'rganilmaganligi va samarali davolash usullarining yo'qligi bilan bog'liq. Ushbu kasallikning bronxial astma bilan kombinatsiyasi, astmatik triada va yiringli jarayonning qo'shilishi polipli rinosinusit bilan og'rigan bemorlarning kursi va davolashini sezilarli darajada murakkablashtiradi. Multifaktorial nazariyaga muvofiq, polipoz rinosinusitning rivojlanishi mexanik, fizik omillar, shuningdek, burun shilliq qavati yuzasiga mikrobial, qo'ziqorin va virusli vositalarning kirib borishi natijasida yuzaga keladi. Bu shilliq qavatning to'siq funktsiyasini ta'minlaydigan o'ziga xos va o'ziga xos bo'lmagan reaktsiyalarning butun majmuasi bo'lgan mahalliy immunitet mexanizmlarini faollashishiga olib keladi. Turli xil vositalarga uzoq muddatli ta'sir qilish burun shilliq qavatining himoya to'sig'i faolligini pasayishiga olib keladi va infektsiyaga bog'liq allergik jarayonning rivojlanishini

rag'batlantiradi. Ikkinchisi ikkilamchi immunitet tanqisligi shaklida immunitet gomeostazining buzilishi, doimiy immun eozinofil yallig'lanishning shakllanishi bilan birga keladi, bu burun shilliq qavatining qayta tuzilishiga va polipli rinosinusitning rivojlanishiga olib keladi.

Kalit so'zlar: polip, burun bo'shlig'i, rinosinusit, allergiya, bronhial astma.

Introduction.

The chronic course of the inflammatory process in the paranasal sinuses leads to significant changes in the state of humoral immunity, changes in the concentration of class A, M, and G immunoglobulins, suppression of the phagocytic activity of neutrophils and macrophages [1–4]. The level of immunoglobulin E in the blood serum is a marker of "preclinical" registration of allergy in nasal polyposis, which can serve as a background for changes in the level of reactivity of the body [10-11]. According to a number of authors, dysfunction of the mucous membrane of the nasal cavity and paranasal sinuses is accompanied by metaplasia, desquamation of the epithelium and, as a result, a violation of its motor activity [5-9]. However, to date, the results of objective fundamental studies of the motor activity of the ciliated epithelium in chronic polypous rhinosinusitis are not available in the available literature. Over the past decade, corticosteroid drugs that affect the main links in the pathogenesis of the polypous process have been the most effective in the treatment of polypous rhinosinusitis [12]. The appointment of short courses of systemic corticosteroid therapy in the treatment of polypous rhinosinus, combined with bronchial asthma or the asthmatic triad, accompanied by frequent relapses of the polyposis process, allows achieving long-term remission and significantly improving the quality of life of patients [13-16]. However, due to the large number of side effects, systemic corticosteroid therapy is not widely used in clinical practice. According to the literature, long-term use of these drugs, due to a pronounced immunosuppressive effect, weakens the protective immune responses of the body due to inhibition of production and increased apoptosis of immature or activated T- and B-lymphocytes. This leads to a violation of the synthesis of IgA, IgG, IgM, since the latter are derivatives of B-lymphocytes [22]. The emerging deficiency of immunoglobulins becomes an additional factor stimulating the weakening of the phagocytic activity of neutrophils, since IgM and IgG direct phagocytes to the infectious focus, thereby regulating the stages of phagocytosis. At the same time, against the background of taking systemic corticosteroids, the work of the hypothalamic-pituitary-adrenal system is inhibited, which is accompanied by a progressive decrease in the synthesis of endogenous cortisol [14]. The concentration of this hormone is important in maintaining the functional state of the body's immune system [23,24]. A high level of cortisol is a necessary condition for a normal response to infection, while a low level

of the hormone can in some way contribute to the development of autoimmune reactions and lead to destabilization of the lysosome membrane, increased capillary permeability, a weakening of the anti-inflammatory effect of cortisol, and an increase in the likelihood of a secondary infection [17-21]. In this regard, the level of cortisol and its correlation with indicators of nonspecific resistance and immunoglobulins M, G and A are a prognostically important marker of the state of the body's immune system.

In this regard, the development of principles for choosing the tactics of treating patients with polypous rhinosinusitis using corticosteroid drugs based on the study of the functional state of the nasal mucosa and monitoring the indirect effect of cortisol concentration on the state of humoral immunity in patients with polypous rhinosinusitis is relevant and novel.

Material and methdos. The work was performed in the multidisciplinary clinic of the 3rd base of the TMA ENT department. We examined 128 patients with polypous rhinosinusitis aged 18 to 50 years, including 83 men and 45 women. Patients were divided into two groups: main and comparison. The main group consisted of 98 patients who were prescribed a course of treatment with methylprednisolone for 14 days, starting with 40 mg per day, then for 14 days the dosage was gradually reduced to a maintenance dose of 4 mg per day and simultaneously administered the topical steroid mometasone furoate, 2 inhalations per day. each nostril 2 times a day for 3 months. The comparison group included 30 patients who received only the intranasal corticosteroid mometasone furoate at the same dosage for 3 months.

Exclusion criteria from the study were: age under 18 years, presence of intolerance to corticosteroids, breast-feeding, purulent discharge from the nose, previous treatment with systemic corticosteroids less than 3 months ago, and a history of severe somatic diseases and immunodeficiency conditions in patients that are a contraindication to steroid therapy. Diagnosis of polyposis rhinosinusitis was carried out on the basis of patient complaints, history taking, objective examination data and instrumental methods of research: anterior active rhinomanometry on the RINO-SYS apparatus, endoscopy of the nasal cavity and computed tomography of the paranasal sinuses according to 4 stages of severity of paranasal sinus lesions according to G. Z. Piskunov (2002) [16].

The state of mucociliary clearance of the nasal mucosa was analyzed using television microscopy with registration of motor activity of cilia on the surface of the ciliated epithelium and subsequent computer and mathematical processing of the results [8, 21, 22]. To assess the state of humoral immunity of the body, patients underwent laboratory diagnostics of immunoglobulins A, M, G, determination of the phagocytic activity of neutrophils and the phagocytic index. For the purpose of differential diagnosis of allergic conditions, patients underwent a laboratory blood test

to determine the level of total immunoglobulin E in the blood serum. The modulating effect of the hypothalamic-pituitary-adrenal system on the state of humoral immunity was analyzed by recording the concentrations of the bound fraction of cortisol in the blood and the free form of the hormone in saliva and with simultaneous monitoring of the levels of specific antibodies and indicators of nonspecific resistance. Blood and saliva sampling was performed at 8–9 am, taking into account the peak of the physiological secretion of the hormone by the adrenal cortex [18]. To monitor the state of humoral immunity and the function of the hypothalamic-pituitary-adrenal system, on the 7th day of taking methylprednisolone and 2 weeks after the withdrawal of systemic corticosteroids in patients of the main group and the comparison group, venous blood and saliva were taken to determine the level of the bound fraction of cortisol and the free form of the hormone in saliva. The obtained parameters of the hormone were analyzed simultaneously with the concentrations of immunoglobulins A, G, E and M. Two weeks after the start of treatment, simultaneously with the registration of the levels of specific antibodies in the systemic circulation, nonspecific resistance indicators were recorded in both groups: phagocytic activity of neutrophils and phagocytic index.

Among the indicators of nonspecific resistance in both groups, there was a decrease in the phagocytic activity of neutrophils to 43.5±3.7% and a decrease in the percentage of neutrophils involved in phagocytosis to 2.55±0.65. At the same time, in patients with purulent-polypous rhinosinusitis, a statistically significant decrease in phagocytic activity of neutrophils to 32.5±1.5% and a phagocytic index from 0.96 to 1.66 compared to physiological parameters were revealed. The decrease in the phagocytic index, the phagocytic activity of neutrophils is primarily due to the long course of the polyposis process, leading to changes in the humoral immunity system, which, in turn, is a predisposing factor in the development of infectious processes.

In the comparison group, the main nasal symptoms were effectively stopped in 4 (13%) patients after 1 month from the start of therapy and in 6 (20%) patients - at the end of the course of treatment. Analysis of IgE parameters after systemic corticosteroid therapy in the main group showed a pronounced decrease in the level of this immunoglobulin in the blood serum to 67 ± 23 g/l in patients with bronchial asthma, in those examined without a aggravated allergic history, the concentration of IgE corresponded to the values before treatment. In the comparison group, all patients showed no statistically significant differences in the content of IgE in the blood ($p > 0.05$) before and after therapy. Control over fluctuations in the level of cortisol in the blood and saliva in the main group revealed on the 7th day of taking methylprednisolone a statistically significant decrease in the concentration of this hormone ($p < 0.05$) in the blood serum to 81.5 ± 23.4 nmol/l and a decrease in free fractions of cortisol in saliva up to 12.5±9.6 nmol/l, which indicates drug suppression

of the activity of the adrenal cortex. In the comparison group, on the 7th day of therapy and after 2 weeks of treatment, there were no statistically significant differences in relation to the initial values of cortisol in the blood and saliva ($p > 0.05$).

3 months after the course of treatment, 61 (62%) patients of the main group showed positive dynamics according to computed tomography of the paranasal sinuses and endoscopy of the nasal cavity. All subjects of the main group, who had stage I of the polyposis process according to the classification of G. Z. Piskunov (2002), after treatment, had satisfactory pneumatization of the paranasal sinuses, a significant reduction in the degree of damage to the paranasal sinuses by the polyposis process was noted in 12 (12%) patients with stage II polyposis and in 48 (49%) patients with stage III lesions of the paranasal sinuses by a polyposis process, in 9 (9%) patients with stage IV, a slight positive trend was registered according to CT of the paranasal sinuses and endoscopy of the nasal cavity, which made it possible to further reduce the amount of surgical intervention and reduce nasal symptoms. In 11 (11%) patients of the main group, the dynamics against the background of systemic corticosteroid therapy was not revealed, which is due to the predominance, according to endoscopy, of the presence of fibrous polyps. This category of patients subsequently underwent planned surgical treatment. In the comparison group, according to the data of computed tomography of the paranasal sinuses and endoscopy of the nasal cavity, positive dynamics was observed in 2 (7%) patients with stage I of the polyposis process and in 3 (10%) with stage II of the polyposis, in the rest of the examined patients - without changes. The follow-up period for patients ranged from 3 months to 2 years. During this time, the recurrence of the polyposis process in the main group was observed after 7 months in 8 (8%) patients in connection with the transferred ARVI, after 1.5 years, the exacerbation of the polyposis process was detected in 26 patients (26%). In the comparison group, 19 (63%) had a relapse of polyposis rhinosinusitis 3 weeks after the end of the course of treatment.

When conducting television microscopy after a course of treatment, a high motor activity of the cilia of the ciliated epithelium was established, which remained in the region of the nasal septum - up to 9.0 ± 0.2 Hz, the lower turbinates up to 8.0 ± 0.4 and $9.0 \pm 0,3$ Hz on the surface of polyps in patients of both groups. Thus, the appointment of systemic corticosteroid therapy in short courses in polyposis rhinosinusitis objectively improves the function of nasal breathing, relieves the main symptoms of the polyposis process, suppresses allergic reactions, does not have an inhibitory effect on the secretion of endogenous cortisol and a pronounced immunosuppressive effect on the humoral immunity system, but, on the contrary, contributes to the regulation mechanisms of nonspecific resistance of the body. In the presence of stages I and II lesions of the paranasal sinuses with a polyposis process, this method of conservative treatment allows you to control the course of the polyposis process and avoid surgical

intervention; in stages III and IV, systemic corticosteroid therapy is recommended for preoperative preparation of patients, as well as anti-relapse therapy after surgery.

Conclusion. Polyposis rhinosinusitis is accompanied by violations of humoral immunity. In chronic polypous rhinosinusitis, the ciliated epithelium is preserved with pronounced motor activity on the surface of the polypous tissue. A short course of systemic corticosteroid therapy in conjunction with topical intranasal steroids has a high therapeutic efficacy and safety in the treatment of nasal polypous sinusitis. Gradual monitoring of fluctuations in the concentrations of free and bound fractions of cortisol and the levels of immunoglobulins A, G and M and indicators of nonspecific resistance is a necessary condition for the appointment of systemic corticosteroids for nasal polyposis.

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