

MODERN ISSUES OF THE TREATMENT OF CHRONIC POLYPOUS RHINOSINUSITIS

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Abstract: Treatment of polypous rhinosinusitis should be considered from a therapeutic point of view, rather than as a disease that initially requires surgical treatment. The main problem is the recurrence of polyposis after surgery. Relapse rate reaches 60% on average 2 years after surgery. Comparing surgical and therapeutic methods of treatment, we can conclude that the use of even the latest achievements of rhinosurgery allows you to affect only the final result of the pathological process, without affecting the pathogenesis of polypous rhinosinusitis, i.e. surgical treatment is symptomatic. It does not interrupt the chain of development of polyposis sinusitis and therefore has little effect on the duration of remission. Treatment of polypous rhinosinusitis with steroid drugs is pathogenetic in nature, since it is aimed at blocking the effects of biologically active substances and cells directly involved in the development of the pathological process.

Keys words: chronic polypous rhinosinusitis, surgery, glucocorticosteroid, paranasal sinuses

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Introduction

Polypous rhinosinusitis (PRS) among inflammatory diseases of the nasal mucosa and paranasal sinuses is one of the most pressing problems of modern rhinology. In recent years, there has been an increase in the specific gravity of this disease in the structure of the pathology of the nose and paranasal sinuses. This is due to changes in the environmental situation, an increase in the number of bacterial, viral and occupational pathogenic factors [1].

To date, the etiology and pathogenesis of PRS remain the subject of discussion. In monographs and periodicals, reports of relapses of PRS are controversial and range from 19 to 60% [2,4,5,8,13,15]. Among the reasons that contribute to the development and recurrence of the polyposis process, the participation of allergies, bronchial asthma, chronic inflammatory processes in the paranasal sinuses caused by bacterial flora,



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and viral agents is discussed, the influence of various anatomical abnormalities contributing to the violation of aeration and the maintenance of the inflammatory process, and the presence of a genetic predisposition are discussed. However, there is no consensus on the nature of the origin of PRS and the main triggers for the activation of this pathology in the body [12,13].

The purpose of this publication is to study modern diagnostic methods and the treatment of chronic polypous rhinosinusitis.

In recent decades, diseases of the nose and the paranasal sinuses in terms of referral to the polyclinic and treatment in hospitals have firmly occupied the first place in the overall structure of the incidence of ENT organs [1, 3, 4]. Worldwide, chronic rhinosinusitis (CRS) affects 5–15% of the adult population [6] and over the past decade the incidence has increased 2-fold [7]. Chronic polypous rhinosinusitis (CPRS) is one of the most common forms of CRS and requiring the attention of specialists. [1, 12, 14, 15, 19].

CPRS is considered a serious problem of modern medicine, reducing the quality of life of patients due to worsening or complete blockade of nasal breathing, impaired sense of smell, and headaches as a result of chronic hypoxia [9, 14, 15]. The use of universal (not dependent on the nature of the disease) questionnaires (SF-36) showed that the quality of life in individuals with nasal polyposis is worse than in patients with arterial hypertension, migraine, angina, malignant head and neck tumors [4, 5]. The deterioration in the quality of life of patients with nasal polyposis is comparable to that in patients with chronic obstructive pulmonary diseases. [1, 3].

The purpose of this review is to study and evaluate modern methods of treatment of chronic polypous rhinosinusitis.

At present, conservative and surgical methods are used to treat nasal polyps [1, 7, 8]. Ideally, the conservative treatment of CPRS should be based on the causative factor [3, 6]. According to some author's [11], the pathogenetic therapy of nasal polyps is

determined by three provisions, including the fact that polyps are the result of chronic infectious rhinosinusitis, the basis of the formation of polyps is persistent immune eosinophilic inflammation and remodeling of the nasal mucosa, as well as the process develops against the background of impaired immune homeostasis as secondary systemic and mucosal immunodeficiency.

Considering the above, on the basis of numerous studies, the role of individual factors was clarified, and on this basis various schemes of CPRS drug treatment were developed, including corticosteroids, antibiotics, antifungal drugs, specific immunotherapy, antihistamines, anti-leukotriene drugs, decondensers, physiotherapeutic methods, etc. [15, 19, 23].

Some scientists in Europe, based on the document EPOS 2012 [10], proposed several types of conservative treatment in terms of evidence and degree of recommendation. In this regard, pathogenetically substantiated and proven conservative treatment of CPRS consists in prescribing glucocorticosteroid drugs [1, 5, 8, 12, 14, 15, 16, 17, 18, 20, 23]. These drugs have a pronounced anti-inflammatory and immunosuppressive effect, which is manifested by a decrease in eosinophilic infiltration and secretory activity of the glands of the nasal mucosa and paranasal sinuses, a decrease in vascular permeability, inhibition of the synthesis of leukotrienes, interleukins, controlling the expression of cell receptors and cell adhesion molecules; reduce swelling of the mucous membrane, leading to a decrease in the volume of polyps [21].

Systematic corticosteroids (SC) are also increasingly used in the preoperative period to reduce intraoperative bleeding and improve the long-term results of surgical intervention in patients with CPRS who are prepared for endoscopic sinus surgery [13, 15, 16, 18].

The introduction of deposited corticosteroids into the lower nasal concha was also used, but there is currently no reliable data regarding the efficacy and safety of this treatment method, since the injection

of depot preparations into the nasal concha is associated with the risk of retinal embolism and blindness.

Systemic treatment with steroids due to the risk of side effects is used for the purpose of short-term improvement. A significant number of side effects do not allow the widespread use of SC in the treatment of CPRS, therefore topical corticosteroids are increasingly used in practical otorhinolaryngology [19].

There is strong evidence in the form of randomized controlled studies that allow the use of topical intranasal SC [20, 22]. Topical SC can be used as a long-term therapy for mild cases of the disease as monotherapy or in combination with systemic corticosteroids for severe cases of CPRS. After cessation of treatment, recurrences of symptoms appear more slowly in patients with a mild form of the disease and faster in patients with massive polyps. Intranasal corticosteroid sprays have a limited effect on the improvement of decreased sense of smell in patients with nasal polyposis. In some cases, nasal sprays may not provide the desired dose of drug at the site of polyps formation [5].

Studies have been conducted to evaluate the effectiveness of the combined (local and systemic) treatment of nasal polyps with corticosteroids [1]. Information of some author's [9], in their prospective study, treated patients with CPRS with oral steroids for 16 days, followed by 2-month courses of topical CS. A clear involution of nasal polyps was observed in 76% of patients, while in 12% of patients, clearing of the paranasal sinuses from polyps was achieved [17].

Conducted control studies have shown that topical SCs can prevent the recurrence of polyps in the postoperative period and, at the same time, delay the need for repeated surgical intervention [16, 18, 22]. For example, some authors used to observe 162 patients for 52 weeks, revealed that the use of fluticasone furoate reduces the number of recurrences of polyps. In 2005, by some author's [13] in its 5-year follow-up, also used fluticasone spray in 109 patients, which

showed a decrease in the recurrence of the disease.

However, corticosteroid therapy is not always effective. According to some authors [22], one of the reasons for the body's immunity to topical steroids is their inadequate distribution in the nasal cavity, which sometimes leads to a lack of effect from the use of SC. He also notes that local edema, the development of granulation tissue and steroid inactivation by induction of resistant protein are of great importance [20].

In the treatment of CPRS, the use of antibacterial drugs with secondary bacterial contamination is fully justified both for local exposure to mucous membranes and in combination with systemic use of antibiotics [9].

The otolaryngology otolaryngologists also deserve close attention, which includes the long-term (3–6 months or more) use of macrolide antibiotics at low dosage [7, 9]. This effective use of macrolides in CPSD is due to erythromycin, roxithromycin, clarithromycin and azithromycin, in addition to the antimicrobial effect, have immunotropic and anti-inflammatory properties, and also strengthen the protective mechanisms of the mucous membrane of the nasal cavity and paranasal sinuses [22].

According to some author's [9], macrolide antibiotics not only destroy the virulence of colonizing bacteria, but also activate anti-inflammatory processes leading to a significant decrease in the size of a polyp in parallel with a decrease in the number of local IL-8, he also advocates the use of macrolides in patients which therapy SC was ineffective [12].

Studies have shown that macrolides have an immunomodulatory effect by suppressing the chemotaxis of inflammatory cells, reducing the production of pro-inflammatory cytokines (IL-8, IL-5, GM-CSF, TGF β , IL-6, TNF α), increasing the synthesis of anti-inflammatory cytokines (IL-10, IL-6 and IL-1) [10]. It has also been proven that macrolides induce neutrophil apoptosis, inhibit the expression of adhesion molecules and the production of free radicals, inhibit

eosinophilic inflammation, and inhibit the proliferation of T-lymphocytes [3]. The immunotropic properties of macrolides reach a maximum when they are taken for a long time (at least 12 weeks) in low doses [5].

Studying the effectiveness of antifungal therapy for CPRS, although they have been studied, but these results do not have a level of evidence [14, 16]. By some author's [9] to patients with CPRS were recommended for topical administration of Amphotericin B solution. The study showed that in 39% of patients who had used amphotericin irrigation for 4 weeks, polyps disappeared. It should be noted that in studies on the background of antifungal treatment, conventional therapy with topical SC continued.

Specific immunotherapy (SIT), of course, is shown to patients with CPRS who have sensitization to aeroallergens of the environment or dwellings confirmed by the results of an allergological examination [14]. SIT must be combined with a surgical revision of PNSs, removal of polyps and allergic mucin, otherwise it does not give effect or even leads to the progression of the disease [1].

The method of desensitization with aspirin is based on the phenomenon of the development of tolerance to the repeated use of nonsteroidal anti-inflammatory drugs (NSAIDs). It is still rarely used in the treatment of recurrent CPRS, but taking into account the results of a series of studies conducted by some author's [5], has good prospects. However, it is necessary to take into account that long-term use of large doses of aspirin in many patients causes side effects from the gastrointestinal tract.

At present, studying the role of leukotrienes in the pathogenesis of bronchial asthma and CPRS, it became clear that anti-leukotriene preparations should be used [10, 19]. There are isolated reports on the use of anti-leukotriene preparations for the treatment of polypous rhinosinusitis. Subjective improvement was noted by 72% of those examined, 50% stopped the growth of existing polyps, while at the same time 11% of patients were forced to stop taking the drug

due to side effects. Currently, researchers are unanimous that existing anti-leukotriene drugs are ineffective in the treatment of CPRS, even in aspirin-sensitized patients [10, 16, 19].

To date, antihistamines are prescribed to patients with CPRS for the relief of associated manifestations of AR, since mast cells and histamine secreted by them do not play a primary role in the pathogenesis of CPRS, and also do not have a significant impact on the size of nasal polyps [6,8].

Several studies have also been conducted on the intranasal use of capsaicin, lysine-acetylsalicylic acid and furosemide in patients with CPRS, which showed positive results in the form of a decrease in the frequency of polyp recurrences [14]. Intranasal furosemide has been used to minimize the postoperative recurrence of nasal polyps compared to intranasal mometasone [15]. However, there are no proven controlled studies in the world literature.

Changes in the immune system, of course, occupy a leading place in the pathogenesis of CPRS, and this fact has stimulated repeated attempts to use various immunomodulatory drugs in anti-relapse treatment [17]. The regimens included injections of splenin, intranasal bacterial vaccines (IRS-19, bronchomunal), licopid, polyoxidonium, cycloferon, thymalin, imunofan, Vilozen and others [3, 5, 10]. By stimulating B cells, these drugs increase the level of IgA and secretory immunoglobulin IgA in saliva and nasal secretion, increase the functional and metabolic activity of macrophages. When prescribing these drugs in patients suffering from CPRS, serum immunoglobulin M, G and A levels increase, the number of T-suppressors decreases (CD8+ cells), the immunoregulatory index increases (CD4 / CD8+), the functional activity of T-cells in the reaction that ultimately leads to a decrease in the frequency and severity of relapse of CPRS [10]. However, no controlled studies of the effectiveness of immunomodulators in CPRS have been conducted.

Attempts have been made to use various physiotherapeutic methods (helium-neon and infrared lasers, magnetic therapy, intranasal and intrapulsar microwave therapy, intranasal electrophoresis, etc.) in the treatment of chronic sinusitis, including its polypous form [6, 5, 18]. However, they were used in complex treatment, to assess the effectiveness of these methods, it is in CPRS, independent comparative studies are needed.

Despite the large number of existing schemes for the conservative treatment of CPRS, the main and in some cases the only method of treatment remains surgical [1, 8, 16, 12, 20]. Recently, functional endoscopic rhinosinusosurgery (FESS - Functional Endoscopic Sinus Surgery) has been widely used in rhinosurgery with the use of endoscopic techniques, ensuring maximum functional effect [5, 8, 7, 13, 22].

Endoscopic surgery undoubtedly offers excellent visualization and the possibility of precise operations. Today it is the favorite method of many surgeons. The advantages of endoscopic access consist in the absence of external incisions, precision removal of pathological tissues, revision of the natural sinuses of the sinuses, which in principle is impossible with classical approaches using the head-on reflector; aesthetics of endosurgery, when the surgeon sees in front of him not narrow nasal passages through the opening of the forehead reflector, but a full-color magnified image on the monitor, including the 3D visualization technique [23].

Despite the success of endoscopic surgery, patients with CPRS undergo repeated surgical interventions, and long-term follow-up of patients operated on CPRS allows us to state the recurrence of nasal polyposis in 85% of cases [16]. A positive effect and a stable remission in the treatment of CPRS are achieved in only 60% of patients [14].

In connection with the above, it has become generally accepted that the treatment of CPRS (with the exception of solitary polyps) should begin with medical therapy, and surgical intervention should be performed only if the conservative treatment fails [12].

The question of the volume and methods of surgical intervention for CPRS has remained controversial since the middle of the last century, when many specialists were committed to carrying out radical operations on the paranasal sinuses with complete removal of the mucous membrane. They considered such a volume of intervention appropriate because of the need to suppress allergic inflammation, which can cause a relapse of a polyposis; however, some authors argued that the affected mucous membrane should only be removed, since it cannot be cured [15].

Some experts have proposed a hypothesis of inflammatory tissue deposit ("inflammatory load hypothesis"), according to which it is necessary to completely and completely remove the affected mucosa of PNSs, including using combined approaches. Operational manuals on classical methods (radical sinus surgery, frontotomy, external ethmoidotomy) gradually fade into the background, since most of them are very traumatic and do not meet the basic principle of nose and sinus surgery - functionality. In case of nasal polyposis, two approaches to surgery are possible: full house FESS - the widest possible opening of all sinuses affected by polyposis with exposing the base of the skull and minimal invasive sinus technique (MIST) - when only polyps that are freely located in the nasal cavity are removed. Here the technical arsenal of the operating surgeon matters [7, 17].

Modern surgical methods pursue the following objectives: restoration of free nasal breathing, complete removal of polypous tissue, maximum preservation of the unchanged mucosa and improvement of the ventilation of the sinuses [5]. The choice of tactics of surgical treatment should be based on the data of visual assessment and analysis of the results of additional methods of verification of the pathological process [4].

At the same time, ensuring the rapid regression of postoperative inflammatory changes and the restoration of the functional activity of the nasal mucosa and PNSs at the early stages of the postoperative period is the

main condition for increasing the effectiveness of surgical treatment of CPRS [1,2]. However, the methods used in everyday clinical practice for the postoperative management of patients with CPRS do not fully respond to the variety of pathogenetic mechanisms in this disease.

According to some authors, 5-7% of all cases of CPRS are resistant to conservative treatment with steroids and do not recur after surgery. As a rule, they are combined with anatomical defects (curvature of the nasal septum, ridges and spines of the septum, bullous shell, additional fistula, etc.) [5, 14].

Surgical treatment is aimed at removing polypous tissue from the nasal cavity and PNSs with preservation of the anatomical structures and normal mucosa. Currently, the standard of surgical treatment of nasal polyps is functional endoscopic sinus surgery (FESS). Other methods include polypectomy, Caldwell-Luke sinus surgery, and intranasal ethmoidectomy. FESS has been proven to improve the quality of life of patients and is more effective in stopping the symptoms of the disease than other methods [1,7]. In a study conducted by foreign authors [9], 78-88% of patients showed improvement in symptoms after FESS, whereas among patients who underwent other surgical techniques, 43-84% improved. CPRS relapses after FESS accounted for 8%, after Caldwell-Luke sinusitis - 14%, after endoscopic ethmoidectomy - 28%, after polypectomy - 35% [3].

Local authors [2] believe that the main attention should be paid to the issues of postoperative management of CPRS patients, including individual characteristics of the organism, the presence of intraoperative risk factors that increase the volume and duration of the intervention or require re-implantation of auto-tissue, the use of stents, which increases the likelihood of postoperative complications and adversely affects the processes of restoration of the functional activity of the nasal mucosa [5].

Treatment success after functional endoscopic surgery has been reported. Some authors [15] (2004) studied the results of FESS in patients with chronic rhinosinusitis and nasal polyposis for 6 months. According to their data, previous sinus operations 6 months after the operation showed significantly worse results.

Local authors [9] believe that the results can be significantly worse if there is an allergy before the operation, and there were previously polypectomies. Several studies [8] conducted a cohort study in 65 patients who underwent FESS in the same institution. Massive relapses were observed in 3 patients, ahead of localized relapses occurred in 19 (31.7%). Bilateral normoplastic mucosa at the end of the study was observed only in 6 (10%) patients.

Foreign authors [19] conducted a study involving 118 patients who underwent extensive bilateral nasal polypectomy. They found that relapse over an average period of 40 months developed in 60% of patients. The presence of previous surgical interventions, allergies or asthma indicated the possibility of a high recurrence rate and revision operations [1,9].

Thus, the use of various methods of treatment does not allow to fully provide the expected results, in this regard, the search for effective methods of diagnosis and treatment is relevant. To do this, it is necessary to adhere to the primacy of drug treatment, minimal invasiveness of surgical intervention and its mandatory combination with preoperative drug preparation and postoperative treatment, which can help reduce the recurrence of the disease, normalize the mucous membrane of the nasal cavity and improve the quality of life of patients, therefore, to achieve the above goals we conducted this study.

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