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Research Article

TREATMENT OF CHRONIC POLYPOSIS RHINOSINUCYTES WITH CORTICOSTEROIDS

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Dr Abdurasul Botirov
Phd, Tashkent Medical Academy, Uzbekistan

ABSTRACT

The article provides general information about conservative treatment methods of chronic polyposis rhinosinusitis using corticosteroids. In accordance with modern recommendations, an integrated scheme of corticosteroid therapy was developed, according to which 245 patients with polyposis rhinosinusitis were treated in the ENT Department of the Bukhara Regional Multidisciplinary Medical Center. According to the results of the study, the high efficiency and safety of the use of a short treatment course of methylprednisolone combined with a 6-month course of intranasal corticosteroid therapy (Nasonex) and saline irrigation therapy were determined.

KEYWORDS

Polyposis rhinosinusitis, corticosteroids, cortisol, immunoglobulins.

INTRODUCTION

Treatment of chronic polyposis rhinosinusitis is one of the most pressing problems of modern rhinosinusitis, and long-term nasal congestion, reduced sense of smell, chronic hypoxia, frequent recurrence and exacerbation of the disease significantly reduce the quality of life of patients.

In Russia, 1.5 million people are infected with SPRS, in the United States, this figure reaches 30-35 million people [1], and in Uzbekistan, this disease is found in 1.2 million people. According to the consensus of the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2012), SPRS occurs in 2-4.3% of the European population.2]. In addition, subclinical forms of the disease are noted to be at a much higher level [3, 4]. In the early stages after surgical treatment, the percentage of recurrence of SPRS disease is observed from 19 to 60%, largely depending on whether this disease is accompanied by bronchial asthma or the asthmatic triad [2, 5-7]. This situation is primarily due to the aspects of the etiological and pathogenetic development of polypous rhinosinusitis that have not been fully studied. Currently, it is widely studied that the development and course of the polyposis process

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can be caused by allergies, disorders in the immune system, as well as bacteria, fungi, viruses, and occupational diseases. [8]. Today, treatment of patients with corticosteroids after functional sinus surgery is considered the "golden standard" in the treatment of SPRS, this fact is proven in the recommendations and standards developed by researchers of our country, as well as in the minutes of the 2012 EPOS foreign conference . The high efficiency of this group of drugs, such as eliminating the main clinical symptoms and reducing the size of polyposis tissue, is proven by their strong anti-allergic, immunodepressive and anti-inflammatory effects [9-10] .

Intranasal glucocorticosteroids (InGKS) are used as a basic therapy in polyposis rhinosinusitis, which was detected for the first time, as well as in order to prevent the recurrence of the polyposis process in the nasal and paranasal cavities after surgical treatment. These drugs are very effective and safe and have been confirmed in a number of clinical studies, allowing the use of InGKS in the form of monotherapy and in combination schemes in the treatment of SPRS [2, 5, 9-13].

The feasibility of using systemic corticosteroids for the treatment of polypous rhinosinusitis has been actively debated over the past decade due to the lack of a single safe algorithm for recommending systemic corticosteroid therapy (SCT). In many foreign countries, TKT is prescribed only for the treatment of polypous rhinosinusitis associated with bronchial asthma and aspirin-induced asthma, and is also used in severe forms of allergic rhinitis [14].

According to the recommendations of EPOS 2012, systemic corticosteroids are used in short courses, and in the later period, in stages III and IV of the polyposis process, long-term antibacterial therapy is used together with InGKS [2].

Joint reviews of The Cochrane Collaboration from 2011 and 2016 analyzed the effectiveness and level of evidence of studies on the use of oral short courses of corticosteroids in the treatment of polyposis rhinosinusitis, including the combination of these drugs with InGKS. However, research data are diverse in terms of methodological approaches and they often lack sufficient evidence, suggesting a need for more detailed studies of the effectiveness of TKT in patients with polypous rhinosinusitis [9, 11].

In the development of integrated treatment schemes for SPRS, it is important to make a rational choice of InGKS.

In the pharmaceutical market, the list of InGKS and their generics has increased significantly over the last ten years. However, for more than 10 years, Nasonex ® spray has been the undisputed leader among this group of drugs.

These InGKS are widely used for the treatment and prevention of SPRS, as well as for the treatment of moderately severe and severe seasonal and persistent allergic rhinitis, and for the treatment of acute and chronic sinusitis in adults and children over 12 years of age.

Nasonex® spray is produced by the American pharmaceutical company "MSD Pharmaceuticals" in the form of a dosed water aerosol (50 µg=1 dose), which is equipped with a convenient nozzle that allows the drug to be distributed evenly on the surface of the mucous membrane of the nasal cavity . The main active ingredient of this drug is mometasone furoate, it has been proven that it has high anti-inflammatory activity, as well as minimal systemic and local side effects, the

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fastest development of clinical effectiveness, that is, it is manifested 12 hours after taking the drug.

Long-term treatment with InGKS Nasonex® significantly reduces inflammatory infiltration of the mucous membrane and does not reduce the anti-inflammatory effect of corticosteroid therapy over time [15].

Repeated placebo-controlled studies have confirmed that the safety criterion of mometasone furoate spray is the absence of changes in the endogenous secretion of cortisol in the blood serum of patients, which indicates the preservation of the functional state of the hypothalamus-pituitary-adrenal gland system [16, 17].

The high safety profile of Nasonex ® spray is also due to the fact that during its long-term use, atrophic changes do not develop in the mucous membrane of the nasal cavity, and the movement activity of the floating epithelium is preserved. [18, 19].

Thus, at the current stage, corticosteroids are the main means of treatment for polypous rhinosinusitis all over the world, and the development of a unified scheme for the treatment of polypous rhinosinusitis is a promising and actively developing direction of modern rhinology.

The aim of the study is to improve the efficacy and safety of combined intranasal and systemic corticosteroid therapy for the conservative treatment of SPRS.

RESEARCH MATERIALS AND METHODS

Research It was conducted in the ENT department of the multidisciplinary medical center of Bukhara region, 245 patients with polyposis rhinosinusitis (131 men and 114 women) were examined. The average age of the patients was 46.12±13.99. All patients were divided into 2 groups.

Group 1 included 188 patients with polyposis rhinosinusitis, including 63 (33.5%) patients with bronchial asthma and 112 (59.6%) patients with housing, dust, epidermal and food allergens. cases of allergy were detected.

57 patients with purulent-polypous rhinosinusitis were included in the 2nd group of the study, including bronchial asthma in 27 (47.4%) patients and allergic conditions in 31 (54.38%) patients.

Group 1 patients were given L. According to the clinical recommendations of Vertkina et al. (1998), after functional endoscopic sinus surgery, which we used, an integrated corticosteroid treatment regimen was recommended, which included:

1. Systemic corticosteroid methylprednisolone 40 mg/day is taken daily for 14 days, gradually reducing the dose of systemic corticosteroid to 4 mg/day.

2. At the moment, InGKS Nasonex ® drug is prescribed, for two inhalations in each half of the nose (1 dose of 50 μg) 2 times a day, for 6 months.

3. Omeprazole 1 capsule (20 mg) to drink in the evening for 16 days as a "protective therapy" to prevent the ulcerogenic effect of methylprednisolone.

4. Nasal cavity with isotonic saline solutions for 6 months per day

Wash 2-3 times.

5. Diet: low-calorie, high-protein, potassium-, calcium-, and low-sodium foods.

A combined corticosteroid treatment scheme was also recommended for the treatment of group 2 patients,

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but from the 8th day of taking methylprednisolone, patients with polyposis-purulent rhinosinusitis were additionally given amoxicillin clavulanate 875 mg/day 2 times a day in order to prevent the exacerbation of the purulent process in the early stages after the cancellation of TKT. times for 7 days, [20].

The analysis of the effectiveness of the diagnosis and treatment of polyposis rhinosinusitis was carried out based on the data of the patient's complaints, objective vision and instrumental examination methods: endoscopy of the nasal cavity and computer tomography of the paranasal cavities, and their assessment was carried out by G. Z. Piskunov and S. Z. According to Piskunov (2002) [21], it was performed according to four stages of the spread of damage to the paranasal sinuses by the polyposis process. Severity of clinical signs was evaluated on a scale from 0 to 4 points. The structural and functional properties of the nasal mucosa in both groups of patients were studied using television microscopy , recording the activity of cilia movement on the surface of the floating epithelium, and the obtained results were processed on a computer. The assessment of nasal respiratory function was performed based on the registration of the main parameters of the previous active rhinomanometry performed on the RINO-SYS device, this method was not performed in patients with a complete blockage of the nasal passages with polyps or a perforation in the nasal septum.

Against the background of the treatment, dynamic monitoring of the humoral immunity of patients was carried out by determining the concentrations of IgA, IgM, IgG and total IgE immunoglobulins in blood serum. The safety of the treatment in relation to the hypothalamus-pituitary-adrenal gland system was evaluated by recording the concentrations of the bound fraction of cortisol in the blood and the free form of the hormone in saliva according to the method developed by us [22].

RESULTS AND DISCUSSION

Against the background of the treatment, a clear positive dynamics due to the reduction of the main clinical signs was observed in 166 (88.3%) patients of the 1st group on the 8th day of treatment, and in 49 (86.0%) patients with purulent-polyposis rhinosinusitis, statistically, nasal breathing and a significant improvement in the sense of smell was noted 16 days after the start of treatment.

At the end of the treatment course, 129 (73.9%) patients in group 1 and 39 (68.4%) patients in group 2 had a significant reduction in difficulty breathing through the nose, improved sense of smell, and decreased nasal discharge. Positive dynamics were not observed in 9 (4.8%) patients with polyposis rhinosinusitis and 10 (5.7%) with purulent-polyposis rhinosinusitis, this condition was noted in patients with fibrous polyps in the nasal and paranasal cavities, which later required surgery.

Laboratory diagnostic indicators of immunoglobulins (IgA, IgM, IgG) in the blood before and after 2 weeks of systemic corticosteroid treatment were found to not cause statistically significant changes in these indicators of humoral immunity in comparison with the physiological norms of specific antibodies in both groups A, M and G ($p > 0.05$). The recorded indicators of humoral immunity should be considered as one of the safety criteria of the applied treatment with respect to the humoral immune system. Analysis of serum total IgE levels 2 weeks after TKT treatment showed that this Ig level was significantly higher in group 1 patients (198.2 ± 34.4 ME/ml) and in patients of group 2 (113.3 ± 35.7 ME/ml) it is statistically significantly reduced ($r<0.05$).

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When pre-active rhinomanometry was performed 3 months after the start of treatment, the number of patients without nasal breathing disorders increased by 34.3% in group 1, the number of patients with moderate obstruction decreased by 11.4%, and the number of patients with high levels of nasal breathing disorders decreased by 11.4%. it was found that it decreased significantly by 55.8%. In group 2, there was a 27.9% increase in the number of patients with mild nasal obstruction and a 37.2% decrease in the prevalence of severe nasal obstruction among patients 3 months after treatment (Fig. 1).

In group 1, on the background of combined corticosteroid therapy, after 3 months, there was a 28% reduction in the number of patients with stage III lesions of the paranasal sinuses, and a 60% reduction in the number of patients with total polyposis due to a significant reduction in the size of polyps. In group 2, compared to the results of research before treatment, there was a 33.3% reduction in the number of patients with stage III lesions of the paranasal sinuses and a 20% reduction in the number of patients with total polyposis (stage IV). At the same time, the treatment made it possible to completely restore paranasal sinus pneumatization in 1 out of 4 patients (Fig. 2, 3).

In television microscopy , it was found that the average frequency of cilia movement in patients with polyposis rhinosinusitis increased statistically significantly ($r<0.05$) up to 12.8±0.4 Hz and in patients with polyposis-purulent rhinosinusitis - up to 10.8±0.5 Hz , which confirms that the violation of the activity of the floating epithelial movement is limited and has a functional nature, as well as the effectiveness and appropriateness of the selected conservative treatment method.

Determination of cortisol concentration in patients of groups 1 and 2 on the 8th day of receiving systemic corticosteroids showed that hormone secretion was 65.7 ± 29.6 nmol/l in blood and 8.98 ± 4.74 nmol/l in saliva ($r<0.05$). made it possible to determine its suppression in time. However, a gradual reduction of the dose of methylprednisolone on the 16th day of treatment, in patients of the 1st and 2nd groups, the concentration of total cortisol in the blood to 311.5±121.4 nmol/l and the concentration of free cortisol in saliva to 18.90±7.96 nmol caused a statistically significant increase to /l. These indicators recorded in blood and saliva on the 16th day of treatment were later compared to the initial cortisol concentrations before the start of corticosteroid therapy, as well as the reference values of this hormone in blood and saliva 1, 3 and 6 months after the start of the course of treatment with TKT ($r>0.05$). no statistically significant differences were observed between them, which indicates a reasonable and safe dosing regimen of systemic corticosteroids (Fig. 4).

A single course of corticosteroid therapy avoided surgery in 76.1% of patients with polyposis rhinosinusitis and 57.9% of patients with polyposis-suppurative rhinosinusitis, 27.1% of patients with stage IV polyposis rhinosinusitis - ida made it possible to significantly reduce the size of the planned surgical procedure due to the elimination of signs of inflammation in the mucous membrane of the nasal and paranasal cavities. A positive effect of combined corticosteroid therapy on the progression of concomitant disease - bronchial asthma was observed in 54 (85.7%) patients in group 1 and 22 (81.5%) in group 2.

The follow-up period of patients was from 3 months to 4 years. Recurrences of the polyposis process were observed 2 times more often in patients with the asthmatic triad, usually against the background of acute respiratory viral infections. At the same time,

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remission was longer in group 1 patients compared to polyposis-purulent rhinosinusitis. Figure 5 shows the percentage of recurrences of the polyposis process in both groups at different periods.

CONCLUSION

Thus, combined corticosteroid therapy, including long-term use of Nasonex® spray and saline solutions, short-term TKT with methylprednisolone, and in the case of polyposis-purulent rhinosinusitis - the appointment of additional systemic antibacterial therapy for polyposis and polyposis-purulent rhinosinusitis I, II and It is a reasonable, effective and safe method of conservative treatment in III stages. The presented scheme of treatment embodied in the IV stage of polyp spread can be recommended before preparing patients for surgery.

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