

Adherence to Intranasal Steroids in CRSwNP

Subjects: Otorhinolaryngology

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Adherence to treatment is essential in chronic rhinosinusitis with nasal polyposis (CRSwNP). Intranasal corticosteroids (INCS) are the first-line therapy, followed by systemic corticosteroids and surgery if needed. In cases of refractory disease, biologics are added to conventional treatment, making adherence to INCS crucial in assessing eligibility for these targeted therapies.

Keywords: adherence ; nasal polyposis ; chronic rhinosinusitis ; intranasal corticosteroids

1. Introduction

The WHO defines adherence as “the extent to which the persons’ behaviour (including medication-taking) corresponds with agreed recommendations from a healthcare provider” ^[1]. Adherence to medication is a crucial part of patient care and required for reaching clinical goals; it represents a critical issue in any chronic condition, even more in respiratory diseases. In the case of bronchial asthma and COPD, according to literature evidence, only 20–30% of patients regularly take the prescribed medication ^[2] and treatment underuse has been commonly described in both adults and children ^{[3][4]} ^[5]. Furthermore, when talking about severe asthma, a low adherence has been reported both before starting and during biologic therapy ^[6], although poor disease control and an increased risk of asthma exacerbation have been described as the consequence of inappropriate asthma management ^{[7][8]}. CRSwNP represents the most relevant comorbidity affecting severe asthma patients in terms of prevalence and the burden of the disease and it shares with asthma an eosinophilic inflammatory background as the major pathobiological driver ^{[9][10]}. Its prevalence in the general population is estimated to be around 3–4% with a variability based on geographical area, but it increases to 40–60% in patients suffering from severe eosinophilic asthma ^{[10][11]}. Though this is not a life-threatening condition, it heavily impacts the quality of life of affected patients, particularly because of the nasal obstruction with concomitant hypo/anosmia and sleep disturbances it causes ^[12]. Interestingly, a similar scenario can be observed in this condition compared to asthma regarding the adherence to therapy, specifically about the use of intranasal corticosteroids (INCS). A regular treatment with INCS is considered, in fact, the cornerstone of CRSwNP management according to recent guidelines ^[13]. Despite this, in a recent survey authors demonstrated that the general perception of ENT about the adherence to INCS of CRSwNP patients is quite variable and rather low, ranging between 50 and 70% ^[14]. Of note, monoclonal antibodies have been approved as add-on therapies to INCS in severe cases of CRSwNP, meaning that eligibility to biologic therapy implies an unsuccessful regular use of nasal steroids in addition to the contraindicated/unsuccessful use of OCS and/or surgery. In the case of no history of previous sino-nasal surgery, four criteria are required to start biologics according to EUFOREA consensus: evidence of type 2 inflammation, comorbid asthma, significant loss of smell, significant impaired quality of life or need for systemic CS (two or more courses in the past year) ^[15].

2. Treatment Options and Adherence in Current Guidelines

The management of CRSwNP is often challenging. According to the current guidelines, the cornerstone of the management of CRSwNP consists of treatment with intranasal corticosteroids due to their strong and multidirectional anti-inflammatory activity. There are different corticosteroid delivery options, including nasal sprays, irrigation, nebulization, a steroid-eluting stent and direct infiltration. Nasal sprays and rinses can be found over the counter, so they are easily affordable. At the same time, the delivery of corticosteroids through nasal spray and rinses may not be sufficient to reach some areas such as the frontal sinus. When comparing corticosteroid nasal irrigation to sprays, nasal irrigation was found to be superior to nasal sprays in post-surgical patients ^[16].

When inadequate to achieve disease control, short courses of oral corticosteroids (OCS) can be prescribed, even if in clinical practice systemic corticosteroids are commonly used for longer timeframes due to the high frequency of nasal polyps recurrence. OCS are often used in an abusive manner, exposing the patient to significant systemic side effects.

Based on an Italian survey, the most frequently observed adverse events related to the administration of systemic steroids are hypertension (57.6%), hyper-glycaemia (55.76%), insomnia (50%), anxiety (23.27%), diabetes (23.04%), mood changes (21.66%), increased appetite (12.67%) and glaucoma (10.83%) [14]. Patients sometimes describe the adverse effects related to the use of OCS as even more disabling than the CRSwNP symptoms themselves [17]. The International Consensus Statement on Allergy and Rhinology: Rhinosinusitis gives a grade A recommendation for the use of short-term OCS in the management of CRSwNP but does not recommend long-term use [18]. Likewise, the guidelines in the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) give a grade A recommendation, corroborated by level 1a evidence, for the use of OCS [13].

There is a need for high-level studies to define the safest and most effective regimen and dosage of OCS. A review by Ahmed et al. including seven articles shows that the daily doses vary for prednisolone from 15 mg to 1.3 mg/kg, with total doses ranging from 150 to 440 mg. In addition, several studies use the same regimen for both CRSwNP and CRSsNP [19].

As a further step, endoscopic sinus surgery (ESS) is considered for CRSwNP patients whose condition is not adequately controlled by the medical treatment. The aim of the surgical approach is to unblock the nasal cavities and widen the ostium of the paranasal sinuses in order to restore respiratory function and allow INCS to reach the sinuses' epithelium; however, the risk of disease recurrence cannot be effectively prevented by the surgical intervention, which does not impact the underlying inflammation [13][20]. Isaman et al. carried out a retrospective study to define the impact of functional endoscopic sinonasal surgery (FESS) in reducing OCS burden and healthcare resource utilization. They found that in real-world US practice, patients with CRSwNP undergoing FESS had a similar OCS burden to those not undergoing FESS, and with similar costs during follow-up, indicating a high treatment burden and unmet needs in both groups [21].

When standard of care fails, biologic agents represent the options in the presence of features suggestive of a type 2 inflammation. More than one biologic is currently marketed for CRSwNP, addressing different targets of the underlying immunological cascade, so that the identification of the best biologic drug for each patient implies a careful endo-phenotyping of the inflammation profile [22]. FDA-approved biological therapies for nasal polyps are omalizumab, mepolizumab and dupilumab. Currently, there are neither head-to-head trials nor guidelines available to help decide between these FDA-approved biological treatments. In addition, the high cost of biologics for the health care system, even in the light of their life-long schedule, requires careful patient selection including a detailed evaluation of previous treatments and clinical responses [11]. Importantly, most biological therapies approved for CRSwNP used intranasal corticosteroid sprays in the control arm as a standard of care [23].

In the comprehensive management of CRSwNP, adherence to nasal corticosteroid therapy is critically emphasized in the latest guidelines, and the targeted therapy is not intended to replace traditional treatment, which is recommended on a regular basis as a concomitant medication during biological treatment. The European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) 2020 [13] positions intranasal corticosteroids as the central therapeutic approach, stressing their importance for the sustained, long-term management of CRS symptoms. Notably, the guidelines favor corticosteroids such as mometasone furoate, fluticasone propionate and fluticasone furoate due to their minimal systemic absorption and lower risk of adverse effects. This choice reflects the understanding of the balance between efficacy and safety in chronic conditions.

EPOS 2020 also underlines the proven effectiveness and safety of the long-term use of nasal corticosteroids in CRSwNP. These medications have shown significant benefits in terms of improving patients' quality of life, reducing nasal polyp size, and even preventing the recurrence of polyps when used postoperatively. This recommendation is particularly notable, even though direct evidence in the postoperative setting is somewhat lacking, indicating a strong consensus on their utility based on indirect evidence and clinical experience.

Beyond the choice of medication, EPOS provides detailed recommendations on the optimal administration of nasal corticosteroids. This includes practical tips such as priming the bottle before use, shaking the bottle to reduce the viscosity of the drug suspension, and correct techniques for spraying to ensure effective drug delivery and minimize risks such as nasal bleeding or septum irritation. Special considerations are given for patients with physical limitations or coordination challenges, highlighting the need for individualized patient education and support.

The European Forum for Research and Education in Allergy and Airways Diseases (EUFOREA) [24] complements these recommendations by emphasizing the broader context of patient education in disease management. It underscores the role of nasal rinsing and corticosteroids as foundational in the EUFOREA management flowchart for CRSwNP, underscoring these as initial and secondary steps in treatment. This approach implicitly involves a commitment to patient

adherence, recognizing that the success of the overall management plan hinges on the consistent and correct use of these baseline therapies.

Moreover, both EPOS and EUFOREA guidelines acknowledge the multifaceted nature of CRSwNP management. They highlight the need for personalized approaches, considering factors like phenotyping and endotyping in surgical prognosis and postoperative care.

The ARIA-ITALY multidisciplinary consensus on nasal polyposis defines biologic drugs as a possible beneficial integration or improvement of the standard therapy ^[25]. It suggests starting treatment with a biologic drug in case of relapse after surgery despite therapy with nasal steroids.

Guidelines always consider biologic drugs as an add-on therapy, so standard-of-care therapy consisting of intranasal saline irrigations and INCS should be continued. At present, the length of time of treatment with biologics has not been well defined, and there are no indications about reducing the dose of INCS over time.

In summary, the guidelines provide a robust and detailed framework for the use of nasal corticosteroids in CRSwNP. They emphasize not only the clinical efficacy and safety of these treatments but also the crucial roles of patient education, adherence, and personalized care in achieving optimal therapeutic outcomes in managing this complex and chronic condition.

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