Exploring Adherence to Treatment in Nasal Polyposis

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Chronic rhinosinusitis with nasal polyps (CRSwNP) is an inflammatory respiratory disorder with a significantly deleterious impact on quality of life. Intranasal corticosteroids (INCS) and saline irrigation are the mainstay of treatment [1].

The World Health Organization (WHO) defines adherence to treatment as the extent to which a person’s behavior (ie, taking medication) corresponds with agreed recommendations from a health care provider [2]. In developed countries, adherence to long-term therapy for chronic illness is around 50%; consequently, the effectiveness of treatment is severely compromised [2].

As in other respiratory diseases [3-4], analysis of adherence in CRSwNP reveals infrequent use of INCS and discontinuation [5]. Rudmik et al [6] reported that 80% of patients with CRS failed to use a single unit of INCS spray during the previous year. Philpott et al [7] analyzed 1243 questionnaires, where only 18% of patients used INCS, and Phillips et al [8] found that only 44.3% of 174 patients reported use of INCS for ≥6 days per week.

As in previous studies, we evaluated adherence to INCS among CRSwNP in a health district of 447 600 inhabitants receiving care at Fundación Jiménez Díaz, a public university hospital in Madrid, Spain. A cross-sectional, retrospective, observational study was performed by searching electronic medical records of the allergy and ENT departments that contained the terms “nasal polyps” and/or “nasal polyposis” for the period spanning 2016 to 2019. We selected those patients with CRSwNP diagnosed based on nasal endoscopy findings and related symptoms [1] who were prescribed INCS through the electronic prescription programme of the Spanish public health system during 2019. The system reimburses 60% of the cost (the mean cost of a generic INCS is €3). Saline irrigation solutions are over-the-counter products, with the result that their use cannot be tracked. We recorded the number of vials obtained from pharmacies in Spain during 2019 (January-December) and compared the amount of medication prescribed during the most recent visit to the ENT/allergy department with the amount of medication withdrawn at the pharmacy.

Patients were arbitrarily classified into 4 groups according to the vials collected, as follows: ≥0-50%, ≥50-<90%, ≥90-100%, and >100%.

In addition, we collected demographics, polyp grade according to Meltzer et al [9], symptom scores using a visual analog scale (VAS) [1], peripheral blood eosinophils, association with asthma, allergy, and aspirin-exacerbated respiratory disease (AERD). The study was approved by the local ethics committee.

Categorical variables were expressed as frequencies and percentages. Continuous variables were expressed as mean (SD). We used a 2-sided Fisher exact test to compare the frequencies. Continuous variables were compared using the Kruskal-Wallis test. Normality was analyzed using the Shapiro-Wilk test and Kolmogorov-Smirnov test. P values of <.05 were considered significant. The statistical analyses were performed using GraphPad Prism 8 (GraphPad Software Inc, San Diego, California, USA).

A total of 789 patients had a confirmed diagnosis of CRSwNP between 2016 and 2019. Only 248 individuals (31.43%) were prescribed INCS before/during 2019. The average age at diagnosis was 61.18 years (range, 23-93 years), and the mean number of years since diagnosis was 7.53 (4.56) years, with a male predominance (Table). Fifty-four patients (22%) had received systemic corticosteroids for CRSwNP in the previous year. Ninety-two (37%) patients had undergone endoscopic endonasal surgery (EES).

Seven patients (2.8%) failed to collect their INCS. Twelve patients (4.8%) obtained more bottles than they had been prescribed, 40 (16.1%) withdrew 90%-100% of INCS, 83 (33.5%) withdrew 50-90%, and 106 (42.7%) withdrew less than 50% of the vials prescribed (Table). No statistically significant differences were found between the 4 groups in terms of age, years since diagnosis of CRSwNP, polyp stage according to Meltzer et al [9], VAS score [1], previous use of systemic corticosteroids, previous EES, peripheral blood eosinophils, positive prick tests with aeroallergens, and presence of asthma and AERD (Table).

In summary, consistent with other authors, we found adherence to INCS adherence to be low: 43% of patients had less than 50% adherence despite the low cost of these prescriptions. This rate is similar to that recorded by the WHO for other chronic diseases, such as asthma, in which nonadherence ranges from 6% to 44% [2]. Philpott et al [7]...
found that only 18% of patients reported current use of INCS, and Rudmik et al [6] found that 80% failed to use a single unit of INCS during the previous year. Our findings show better results, as 97% of the study population withdrew at least 1 bottle.

We found that adherence to INCS was not associated with years since diagnosis, VAS score, or comorbidities. Although ours is a descriptive study, we can conclude that there do not seem to be differences between patients with polyposis grade 1 or 2 and patients with grade 3 or 4 in terms of the percentage of bottles collected.

Additional explanations for low adherence may include a perceived lack of rapid improvement in nasal symptoms with INCS and incorrect information from physicians on the disease, treatment, and associated adverse effects. The low cost of a generic INCS did not explain the low adherence.

This study is limited by its retrospective, single-center design, as well as its small sample, which only includes patients receiving specialist care. Additionally, patient educational level was not assessed. However, the pharmacy data used are reliable, as they were obtained from an electronic prescription system. We do not know whether the patients administered the appropriate dose at home or used INCS for other purposes (ie, allergic rhinitis). The low frequency of prescription of INCS (31.4%) is probably because the electronic prescription program in Madrid was established in October 2018. Therefore, 2019 was a period during which specialists were being trained and this new tool was gradually being implemented in daily practice.

In conclusion, adherence to INCS in patients with CRSwNP is low and not related to disease severity. Through the present study, we show the need for new research aimed at discovering the relevant nonclinical reasons for poor adherence to treatment in patients with CRSwNP.

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**Conflicts of Interest**

Dr Valverde-Monge reports personal fees for lectures from GSK, outside the submitted work. Dr Betancor is supported by a Rio Hortega Research contract. Dr Sastre reports grants and personal fees from Sanofi and personal fees from GSK, Novartis, AstraZeneca, Mundipharma, Fas Farma outside the submitted work.

**References**

Evaluation of Fractional Exhaled Nitric Oxide During SARS-CoV-2 Infection

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Fractional exhaled nitric oxide (FeNO) is a noninvasive marker of type 2 inflammation. It is increasingly measured in the diagnosis and follow-up of allergic diseases such as asthma. High levels of FeNO are correlated with asthma attacks and are being evaluated in other respiratory diseases. Respiratory infections also have a significant effect on FeNO through an as yet unknown mechanism [1-3]. The increase or decrease in FeNO during viral infection is unclear, although it seems to be virus-dependent [4]. The unknown and variable clinical progress of SARS-CoV-2 infection from asymptomatic to death has forced us to investigate new biomarkers that could predict the natural course of the disease.

Aiming to assess the potential role of FeNO as a marker of severity in cases of COVID-19, we included consecutive patients over 18 years of age who received care in the emergency department (ED) at Fundación Jimenez Diaz Hospital, Madrid, Spain for SARS-CoV-2 infection from January to June 2021. All patients had a positive reverse transcriptase-polymerase chain reaction (RT-PCR) result and/or positive antigen test result. We included a control group consisting of patients with respiratory symptoms and a negative RT-PCR result for SARS-CoV-2. The local ethics committee approved this study. All patients provided their written informed consent to be included.

FeNO was measured in duplicate using the Evernoa device (Eversens) [5]. The first measurement was taken at baseline, before any therapeutic intervention in the ED; the second was performed at least 10 days later (recovery from infection). The data collected included demographic, clinical, and disease-related characteristics, presence of atopy (patient-reported), as well as comorbidities (eg, pneumonia), treatment, hospital and intensive care unit (ICU) admission if required, blood analysis, and chest x-ray findings. If the patient was admitted, FeNO was measured every 48-72 hours until discharge. The control group included 18 patients.

Quantitative variables were expressed as mean (SD), and qualitative variables as absolute and relative frequencies.

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