
Exploring Adherence to Treatment in Nasal Polyposis

Valverde-Monge M^{1,2*}, Barroso B^{1,2*}, Ortega-Martin L¹,
Betancor D¹, Santillan J³, Villacampa JM³, Sastre J^{1,2}

¹Department of Allergy, Hospital Universitario Fundación
Jiménez Díaz, Madrid, Spain

²Department of Medicine, Universidad Autónoma de Madrid,
Madrid, Spain, CIBERES, Instituto de Salud Carlos III, Spain

³Department of Otorhinolaryngology, Hospital Universitario
Fundación Jiménez Díaz, Madrid, Spain

*Contributed equally as first authors

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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]

Table. Comparison of Demographics and Characteristics of Patients with CRSwNP and Adherence to Treatment

% Adherence	Total population	Adherence to treatment ^a				No adherence to treatment
		>0<50%	≥50<90%	≥90-100%	>100%	
No. (%)	248 (100)	106 (42.7)	83 (33.5)	40 (16.1)	12 (4.8)	7 (2.8)
Males, No. (%)	147 (59)	60 (57)	54 (65)	27 (67.5)	6 (50)	NS 4 (57)
Mean (SD) age, y	61 (15)	60 (14)	62 (14)	63 (16)	63 (17)	NS 55 (12)
Median no. of years since diagnosis	7.5	7	6	6	4.5	NS 8
NP grade 1-2, No. (%)	125 (50.4)	51 (48)	41 (49)	26 (65)	4 (33)	NS 3 (43)
NP grade 3-4, No. (%)	123 (49.6)	49 (52)	42 (51)	14 (35)	8 (67)	NS 4 (57)
VAS ≤5, No. (%)	108 (43.5)	51 (48)	36 (43)	18 (45)	3 (25)	NS 1 (14)
VAS >5, No. (%)	140 (56.5)	62 (58.5)	47 (57)	22 (55)	9 (75)	NS 6 (86)
Systemic corticosteroids for CRSwNP in the previous year, mean (SD)	54 (22)	25 (24)	15 (18)	9 (22.5)	5 (42)	NS 2 (29)
Previous EES, mean (SD)	92 (37)	43 (41)	32 (39)	14 (35)	3 (25)	NS 4 (57)
Eosinophils×10 ³ , median	396	335	344	324	354	NS 286
Asthma, No. (%)	110 (44)	48 (45)	44 (53)	15 (37.5)	3 (25)	NS 2 (29)
AERD, No. (%)	36 (14.5)	17 (16)	15 (18)	3 (7.5)	1 (8)	NS 1 (14)
Positive allergy tests, No. (%)	81 (33)	33 (31)	34 (41)	11 (27.5)	2 (17)	NS 2 (29)

Abbreviations: AERD, aspirin-exacerbated respiratory disease; CRSwNP, chronic rhinosinusitis with nasal polyps; EES, endoscopic endonasal surgery; NP, nasal polyposis; NS, nonsignificant; VAS, visual analog scale.

^aAdherence percentage: described as the ratio of intranasal corticosteroid bottles withdrawn to those prescribed.

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.

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References

1. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*. 2020;58(Suppl S29):1-464.
2. WHO | ADHERENCE TO LONG-TERM THERAPIES: EVIDENCE FOR ACTION [Internet]. WHO. World Health Organization; [Accessed 2021 Feb 28]. Available from: http://www.who.int/chp/knowledge/publications/adherence_report/en/
3. Plaza V, Giner J, Curto E, Alonso-Ortiz MB, Orue MI, Vega JM, et al. Assessing Adherence by Combining the Test of Adherence to Inhalers With Pharmacy Refill Records. *J Investig Allergol Clin Immunol*. 2021;31(1):58-64.

4. Baiardini I, Paoletti G, Malipiero G, Giua C, Keber E, Canonica GW, et al. Validation of the Italian Version of the Test of Adherence to Inhalers. *J Investig Allergol Clin Immunol*. 2020;30(6):450-2.
5. Ortega-Martin L, Betancor D, Barroso B, Valverde-Monge M, Santillan J, Villacampa JM, et al. Where Has All The Nasal Polyposis Gone? *J Investig Allergol Clin Immunol*. 2021;31:500-2.
6. Rudmik L, Xu Y, Liu M, Bird C, Kukec E, Quan H. Utilization Patterns of Topical Intranasal Steroid Therapy for Chronic Rhinosinusitis: A Canadian Population-Based Analysis. *JAMA Otolaryngol Head Neck Surg*. 2016;142(11):1056-62.
7. Philpott C, Erskine S, Smith R, Hopkins C, Kara N, Farboud A, et al. Current use of baseline medical treatment in chronic rhinosinusitis: Data from the National Chronic Rhinosinusitis Epidemiology Study (CRES). *Clin Otolaryngol*. 2018;43(2):509-24.
8. Phillips KM, Hoehle LP, Caradonna DS, Gray ST, Sedaghat AR. Intranasal corticosteroids and saline: Usage and adherence in chronic rhinosinusitis patients. *Laryngoscope*. 2020;130(4):852-6.
9. Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Nicklas RA, et al. Rhinosinusitis: developing guidance for clinical trials. *J Allergy Clin Immunol*. 2006;118(5 Suppl):S17-61.

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Blanca Barroso García
Allergy Department
University Hospital Fundación Jiménez Díaz
Avenida Reyes Católicos, 2
28040 Madrid, Spain
E-mail: blanca.barroso@quironsalud.es