

Exploring adherence to treatment in nasal polyposis

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

The World Health Organization (WHO) defines treatment adherence as the extent to which “a person's behaviour (i.e., taking medication) corresponds with agreed recommendations from a health care provider” [2]. In developed countries, adherence to long-term therapies for chronic illness is around 50%, which severely compromises treatment effectiveness [2].

As in other respiratory diseases [3-4], adherence to treatment has been previously explored in CRSwNP, finding low use of INCS and abandonment [5]. Rudmik et al. describe that 80% of patients with CRS failed to use a single unit of INCS spray during the last year [6]. Philpott et al. analysed 1243 questionnaires where only 18% of patients used INCS [7] and Phillips et al. found that only 44.3% of 174 patients reported a use of INCS for ≥ 6 days per week [8].

Similarly, to previous studies, we evaluated INCS therapy adherence among CRSwNP in a health area of 447,600 inhabitants receiving care at the 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 by nasal endoscopy and related symptoms [1] who were prescribed INCS through the electronic prescription programme of the Spanish public health system during

2019, which reimburses 60% of the cost (the mean cost of a generic INCS is 3 euros). Saline irrigations are over-the-counter products and their use cannot be tracked. We recorded the number of vials obtained from any pharmacy in Spain during 2019 (January-December) and compared the amount of medication prescribed during the most recent ENT/allergy visit with the amount of medication withdrawn in any pharmacy. Subjects were arbitrarily classified into 4 groups according to the vials collected as prescribed: >0-50%, $\geq 50 < 90\%$, $\geq 90-100\%$ and >100%.

In addition, we collected demographics, data on polyps grade according to Meltzer [9], symptoms described by visual analogue scale (VAS) [1], peripheral blood eosinophils, association of asthma, allergy and aspirin-exacerbated respiratory disease (AERD). The study was approved by the Institutional Ethical Committee Board.

Categorical variables were described as frequencies and percentages. Continuous variables were summarized as mean \pm standard deviation (SD). To compare the frequencies, we used two-sided *Fisher's* exact test. Continuous variables were compared by Kruskal-Wallis test for non-parametric data. Normality was analyzed using the Shapiro-Wilk test and Kolmogorov-Smirnov test. $P < 0.05$ was considered significant. Statistical analyses were performed using GraphPad Prism 8 (GraphPad Software Inc, San Diego, CA, USA).

A total of 789 patients had a confirmed diagnosis of CRSwNP between 2016 and 2019. Only 248 individuals (31.43%) had INCS prescribed before/during 2019. The average age at diagnosis was 61.18 years of age (range 23 to 93years), the mean years since diagnosis was 7.53 ± 4.56 years, with a male predominance (Table 1). Fifty-four subjects (22%) had received systemic corticosteroids for CRSwNP in the last year. Ninety-two (37%) patients had been previously treated with endoscopic endonasal surgery (EES).

Seven subjects (2.8%) failed to collect a single bottle of INCS. Twelve patients (4.8%) obtained more bottles than they had been prescribed, 40 (16.1%) withdrew 90-100% of INCS, 83 (33.5%) patients, 50-90%, and 106 (42.7%) withdrew less than 50% of the vials prescribed (Table 1). No statistical differences were found among the four groups in terms of age, years since diagnosis of CRSwNP, polyp stage according to Meltzer [9], VAS [1],

previous use of systemic corticosteroids, previous EES, peripheral blood eosinophils, positive prick tests with aeroallergens, and presence of asthma and AERD (Table 1).

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

In this study, adherence to INCS was not associated with years since diagnosis, VAS and comorbidities. Although it is a descriptive study, we can extract that there do not seem to be differences between patients with polyposis grade 1 or 2 and 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 physician-provided information on the disease and treatment and to adverse effects related to ICNS. The low cost of a generic INCS did not explain the low adherence.

This study is limited by its retrospective, single-centre design as well as its small sample, which includes only patients undergoing specialist care. Additionally, patient educational level was not monitored. However, the pharmacy data used are quite reliable as they were obtained from an electronic prescription system. Nevertheless, we do not know if our patients have administered the appropriate dose at home or if the use of INCS could be also for other purposes (i.e., allergic rhinitis). The low ratio in INCS prescription (31.4%) is probably due to the fact that the electronic prescription program in Madrid was established in October 2018. Therefore, 2019 was a period of training of specialists and a progressive adaptation of this new tool in to the daily consultation.

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 non-clinical reasons for poor adherence to treatment in patients with CRSwNP.

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Conflicts of interests

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Table 1

Comparison of demographics and characteristics of patients with CRSwNP and adherence to treatment.

% Adherence: described as the ratio of INCS bottles withdrawn to those prescribed. NP (nasal polyposis). VAS (visual analogue scale). EES (endoscopic endonasal surgery). AERD (aspirin-exacerbated respiratory disease). n.s. (not statistically significant).

% Adherence	Total population	Adherence to treatment					No adherence to treatment
		>0<50%	≥50<90%	≥90-100%	>100%		
N (%)	248 (100)	106 (42.7)	83 (33.5)	40 (16.1)	12 (4.8)		7 (2.8)
Male, n (%)	147 (59)	60 (57)	54 (65)	27 (67.5)	6 (50)	n.s.	4 (57)
Age years, mean±SD	61±15	60±14	62±14	63±16	63±17	n.s.	55±12
Years since diagnosis, median	7.5	7	6	6	4.5	n.s.	8
NP Grade 1-2, n (%)	125 (50.4)	51 (48)	41 (49)	26 (65)	4 (33)	n.s.	3 (43)
NP Grade 3-4, n (%)	123 (49.6)	49 (52)	42 (51)	14 (35)	8 (67)	n.s.	4 (57)
VAS ≤ 5, n (%)	108 (43.5)	51 (48)	36 (43)	18 (45)	3 (25)	n.s.	1 (14)
VAS > 5, n (%)	140 (56.5)	62 (58.5)	47 (57)	22 (55)	9 (75)	n.s.	6 (86)
Systemic corticosteroids for CRSwNP in last year, mean±SD	54 (22)	25 (24)	15 (18)	9 (22.5)	5 (42)	n.s.	2 (29)
Previous EES, mean±SD	92 (37)	43 (41)	32 (39)	14 (35)	3 (25)	n.s.	4 (57)
Eosinophils x10³, median	396	335	344	324	354	n.s.	286
Asthma, n (%)	110 (44)	48 (45)	44 (53)	15 (37.5)	3 (25)	n.s.	2 (29)
AERD, n (%)	36 (14.5)	17 (16)	15 (18)	3 (7.5)	1 (8)	n.s.	1 (14)
Positive allergy tests, n (%)	81 (33)	33 (31)	34 (41)	11 (27.5)	2 (17)	n.s.	2 (29)