Where Have All The Nasal Polyposis Gone?

Ortega-Martin L[1*], Betancor D[1*], Barroso B[1], Valverde-Monge M[1], Santillan J[2], Villacampa JM[2], Sastre J[1,3]

[1]Department of Allergy, Fundación Jiménez Díaz, Madrid

[2]Department of Otorhinolaryngology, Fundación Jiménez Díaz, Madrid

[3]Department of Medicine, Universidad Autónoma de Madrid, Madrid, Spain, CIBERES, Instituto de Salud Carlos III, Spain ORCID 0000-0003-4689-6837

[*]Contributed equally as first authors

Corresponding Author

Dr. Marcela Valverde-Monge

Allergy Department, University Hospital Fundación Jiménez Díaz

Avenida Reyes Católicos, 2, 28040, Madrid, Spain

E-mail: marcela.valverde@quironsalud.es

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.18176/jiaci.0679

Key Words: Nasal polyps. Nasal polyposis. Eosinophils. Asthma. Non-steroidal anti-inflammatory drug hypersensitivity.

Palabras clave: Pólipos nasales. Poliposis nasal. Eosinófilos. Asma. Hipersensibilidad a antiinflamatorios no esteroideos.

Nasal polyposis (NP) is a benign chronic inflammatory disease. However, the significant impact of the disease resides in a decrease in quality of life, in particular, the loss of sense of smell, an increase in socioeconomic burden, and other associated comorbidities [1]. The exact prevalence of Chronic rhinosinusitis with NP (CRSwNP) in the general population is scarcely documented [2]. The objective of this study was to describe the characteristics of patients attended with NP at a health area in Madrid, Spain.

A cross-sectional retrospective and observational study was performed through a search of electronic medical records at our university hospital of patients from our health area containing the terms “nasal polyps” or “nasal polyposis” during the years 2016, 2017, and 2018. Secondly, we continue to confirm that the subjects previously selected, corresponded to a diagnose of nasal polyposis by comments of symptoms and a nasal endoscopy [1]. Third, we select patients with at least one visit at the outpatient clinic (Allergy and ENT) during 2016, 2017, and 2018. Data collected included patient demographics, presence of atopy based on positive skin tests to common aeroallergens, association with asthma and non-steroidal anti-inflammatory drug hypersensitivity, use of healthcare resources such as CT scans, visits/year, and treatment administered (both drugs and surgery). The polyp grading system used was described by Meltzer et al. [3] and in all cases. The Hospital Research Ethics Board approved the study. ENT specialists

doi: 10.18176/jiaci.0679

and allergologists participated in the study since this entity is often co-managed by both specialties.

Our health area includes 447 600 citizens, of whom 393 418 individuals are more than 18 years of age. A total of 667 individuals resulted from the initial search based on terms and with a diagnose of confirmed NP; we excluded 272 patients with a confirmed NP diagnosis because they did not attend ENT or allergy clinics during the selected years. Therefore, identified patients with NP in our electronical records was of 0.14% among the general population and 0.16% among the population over 18 years.

A total of 144 new patients fulfilled the criteria consecutively for three years. Overall, 59 new patients were included in 2016, 53 in 2017, and 32 in 2018. The annual incidence of patients with NP attended on our tertiary hospital was 0.7 to 1.3 per 10.000 (0.013 per 100 in 2016, 0.012 in 2017 and 0.007 in 2018).

The average age at diagnosis was of 58.7 years, with a range from 23–96 years with a higher prevalence of males (Table I). A total of 190 subjects whom underwent endonasal surgery, 66 (34%) had a grade 0 in the follow-up.

Other results are summarized in Table I. Although this study was not designed to calculate prevalence and annual incidence, our data on NP attended at our tertiary hospital is much lower than prevalence of NP reported in other studies [4-6]. Johansson et al. [4] calculate a prevalence of 2.7% (95% CI:1.9–3.5) with an annual incidence of one and 20 per 1000 population from a random sample of 1,900 inhabitants over 20 years old in Sweden diagnosed by nasal endoscopy versus 0.07-0.13 per 1000 in our study. A similar prevalence was found in a population in France screened by a valid questionnaire [5]. Our lower results could exhibit that NP with minor symptoms or asymptomatic patients with NP do not attend medical consultation as shown by a study done on 69 autopsies on patients from either cardiopulmonary disease or malignant diseases, were

doi: 10.18176/jiaci.0679

NP was found in 32% of autopsies and none of the patients referred symptoms of NP on their medical records [6]. Another probable reason could be that they are being managed by general practitioners.

Blood eosinophils in this sample are relatively high (491.55±327) and 35% had >500/µL eosinophils, which means that most had a T2 phenotype [7] as previously observed. Concerning the age of diagnosis, male predominance, and comorbidities, such as association with atopy (29%), asthma (45.32%) and NSAIDs hypersensitivity (13.16%) found is according to that described in previous studies [1-3,5]. No NP was diagnosed in any pediatric patient.

Remarkably, about half of the patients have had Functional Endoscopic Endonasal Surgery (FEES), and 51.05% had more than one FEES. From the 190 subjects with 1 or more FEES, 125 (65.79%) had recurrence of NP at follow-up visits. Previous data show that about 40% of patients with surgical polypectomies have recurrences 18 months after surgery [8] or 22% on a Spanish study with 10 years follow-up [9]; population from our study had a mean of 3.62±5.79years of follow-up since last FEES, possibly the fact that 56% of subjects with FEES had eosinophilia (>500eos/µL) could explain the higher recurrence; specially since blood eosinophilia has been associated with nasal tissue infiltration of eosinophils [10].

As recommended, the nasal steroid was the first-line treatment in our patients. Surprisingly, many patients abandoned this treatment during the study, since a significant decrease in nasal steroids used ($p<0.05$) was found among visits. This finding is in line with the result of Guo et al. [11], who found that patients with single recurrences of polyps after surgery had poor adherence to topical steroids. This fact may reflect a failure of medical care but not a failure of the surgery. Interestingly, systemic steroids were used in 40.50% of patients with a mean of 1.82±1.39 pulses during the follow-up. Although a

doi: 10.18176/jiaci.0679

significant decrease in corticoid bursts ($p<0.05$) was observed, many patients are still exposed to the potential side effects of systemic steroids, as NP is a chronic disease. Despite all treatment used, no significant difference in the polyps scores between the first and last visit ($p=0.77$) was observed. The main weaknesses of this study are that it is retrospective and monocentric.

We highlight the fact that even though prevalence in general population is of approximate one and 20 per 1000; the majority of patients with NP would not need a specialized care; a probable cause could be that asymptomatic or NP with minor symptoms are not searching for medical care or are not been referred to specialized clinics.

Funding sources

This study did not receive any funding.

Conflicts of interest

J.S. reports having served as a consultant to Thermofisher, MEDA, Novartis, Sanofi, Leti, Faes Farma, Mundipharma, and GSK; having been paid lecture fees by Novartis, GSK, Stallergenes, Leti, and Faes Farma; as well as having received grant support for research from Thermofisher, Sanofi, and ALK. Other authors declare no conflicts of interest.

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(20):1-464.
2. Khan A, Vandeplas G, Huynh T, Joish VN, Mannent L, Tomassen P, et al. The global allergy and asthma European network (GALEN rhinosinusitis cohort: a large European cross-sectional study of chronic rhinosinusitis patients with and without nasal polyps. Rhinology. 2019;57(1):32-42.
3. 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
4. Johansson L, Akerlund A, Holmberg K, Melén I, Bende M. Prevalence of nasal polyps in adults: the Skövde population-based study. Ann Otol Rhinol Laryngol. 2003;112:625-9.
5. Larsen PL, Tos M. Origin of nasal polyps: an endoscopic autopsy study. Laryngoscope. 2004;114:710–9.
6. Klossek JM, Neukirch F, Pribil C, Jankowski R, Serrano E, Chanal I, et al. Prevalence of nasal polyposis in France: a cross-sectional, case-control study. Allergy. 2005;60(2):233-7.
7. Bachert C, Marple B, Hosemann W, Cavaliere C, Wen W, Zhang N. Endotypes of Chronic Rhinosinusitis with Nasal Polyps: Pathology and Possible Therapeutic Implications. J Allergy Clin Immunol Pract. 2020;8(5):1514-19.

doi: 10.18176/jiaci.0679

8. DeConde AS, Mace JC, Levy JM, Rudmik L, Alt JA, Smith TL. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. Laryngoscope. 2017;127:550-55.
9. Lobo DR, López-Cortijo C, Laguna D, Pinilla M, Górriz C. Endoscopic sinonasal surgery: Review of 1,093 cases. Acta Otorrinolaringológica Española. 2003;54(6), 435-40.
10. Brescia G, Sfriso P and Marioni G. Role of inflammatory cells in chronic rhinosinusitis with nasal polyps. Acta Oto-Laryngologica. 2019;139(1):48-51.
11. Guo M, Alasousi F , Okpaleke C , Habib AR, Javer A. Prognosis of Chronic Rhinosinusitis With Nasal Polyps Using Preoperative Eosinophil/Basophil Levels and Treatment Compliance. Am J Rhinol Allergy. 2018;Sep32(5):440-6.

doi: 10.18176/jiaci.0679

Table 1. Demographic, clinical and treatment characteristics of patients (N=395)

Epidemiologic data	
Age, mean (SD)	58.7 (14.9)
Gender, male, No. (%)	234 (59.24)
Smoking habit, active smoking No. (%)	52 (13.16)
Smoking habit, never smokers No. (%)	252 (63.8)
Asthma, No. (%)	179 (45.32)
Atopy[1], No. (%)	115 (29.11)
NSAIDs hypersensitivity, No. (%)	52 (13.16)
Characteristics of Nasal Polyposis	
Polyps score first visit, mean (SD)	2.55 (1)
Polyps score last visit, mean (SD)	1.45 (1.34)
Sinus CT scan, mean (SD)	0.91 (0.81)
Peripheral eosinophilia[2], No. (%) >500	138 (34.94)
Eosinophils/µL, mean (SD)	491.55 (327.19)
Polypectomy, No. (%)	190 (48.10)
Recurrent polypectomy, No. (%)	97 (51.05)
Number of polypectomies, mean (SD)	1.3 (0.88)
Treatments of Nasal Polyposis	
First visit:	
No previous treatment, No. (%)	9 (2.28)
Nasal steroids	**339 (85)***
FP nasal spray[3], No. (%)	141 (36.7)
FF nasal spray[4], No. (%)	54 (13.67)
MF nasal spray[5], No. (%)	144 (36.45)
AH[6] and FP[7] nasal spray, No. (%)	12 (3.04)
Corticoid bursts, No. (%)	**160 (40.50)***
Amount of corticoid bursts, mean (SD)	1.82 (1.39)
Antibiotic bursts, No. (%)	49 (12.41)
Amount of antibiotic bursts, mean (SD)	1.41 (0.84)
Last visit:	
No treatment, No. (%)	29 (7.34)
Nasal steroids	**130 (32)***
FP nasal spray[3], No. (%)	46 (11.65)
FF nasal spray[4], No. (%)	16 (4.05)
MF nasal spray[5], No. (%)	64 (16.20)
AH and FP nasal spray[6], No. (%)	4 (1.01)
Oral Corticoid bursts, No. (%)	**62 (15.70)***
Amount of corticoid bursts, mean (SD)	1.90 (2.83)
Antibiotic bursts, No. (%)	40 (10.13)
Amount of antibiotic bursts, mean (SD)	1.42 (1)

[1] Positive skin prick test to 1 or >1 to usual aeroallergens. [2] Eosinophilia is reported when eosinophils are equal or higher to 500 eos/µL. [3] FP: Fluticasone Propionate; [4] FF: Fluticasone Furoate; [5] MF: Mometasone Furoate; [6] AH: Azelastine hydrochloride and [7] FP: fluticasone propionate. * P<0.005 between first and last visit.

doi: 10.18176/jiaci.0679