

ORIGINAL ARTICLE

Influence of allergy on the symptoms and treatment of nasal polyposis

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Abstract

Conclusion. Allergy does not modify the symptoms of nasal polyposis, either initially or after a 1-year medical treatment. **Objectives.** To assess the role of allergy in the symptoms and treatment of patients presenting with the diagnosis of nasal polyposis. **Patients and methods.** Two simultaneous studies were carried out. In the first study, 180 consecutive patients with nasal polyposis (60% males, mean age = 48.4 years) were analyzed to detect whether the severity of their symptoms correlated with the presence of positive allergic tests. In the second study, 74 consecutive patients (57.5% males, mean age = 48.3 years) were analyzed to detect whether the results of a 1-year medical treatment of nasal polyposis were influenced by the presence of positive allergic tests (Phadiatop®). Five nasal criteria were scored: nasal obstruction, anterior and posterior rhinorrhea, facial pain, and the loss of sense of smell. The frequency of asthma was evaluated. Treatment of nasal polyposis consisted of washing of the nasal cavities, steroid spray, and oral steroid administration. The amount of steroid consumption (prednisolone and beclomethasone) was studied. **Results.** In the first study, mean scores of nasal symptoms did not differ between the two groups of patients with and without allergy. The prevalence of asthma ($p=0.03$) was higher in the group with than without allergy. In the second study, decrease of all nasal symptoms was not statistically different in the two groups. Cumulative consumption of prednisolone and beclomethasone between baseline and year 1 were similar in the two groups.

Keywords: Allergic rhinitis, nasal polyposis, asthma, prednisolone, beclomethasone

Introduction

Chronic rhinosinusitis is an increasingly common cause of patient visits to GP and represents nearly 2% of all visits seeking otolaryngologic care [1]. Over two decades, the introduction of computed tomography (CT) scanning and endoscopy of nasal cavities has led to a reappraisal of the main chronic rhinosinusitis pathologies. Nasal polyposis is one of the most common inflammatory pathologies of the nasal cavity and paranasal sinuses, and its prevalence is around 2.7% in Europe [2]. On the other hand, allergic rhinitis is a high prevalence disease in developed countries, affecting about 10–20% of the general population [3]. A variety of severe symptoms attached to these two conditions (i.e. nasal polyposis and allergic rhinitis) testify to the serious alteration of the nasosinusal function: airway

blockage, anterior and posterior rhinorrhea, stuffiness and facial pain, sneezing episodes, loss of the sense of smell, alteration of the sense of flavor.

The high prevalence of these two conditions explains why many patients with nasal polyposis have positive allergic tests. Nevertheless, the relationship between nasal polyposis and allergy is not clear in the literature. Is the presence or severity of nasal symptoms in patients with nasal polyposis correlated with the presence of positive allergic tests? Are the results of a medical treatment of nasal polyposis influenced by the presence of positive allergic tests? No obvious response appears in the literature. The design of this prospective study was aimed at assessing the role of allergy in symptoms and medical treatment of patients presenting with the diagnosis of nasal polyposis.

Patients and methods

Patients

Two simultaneous studies were carried out between 2001 and 2003. In the first study, 180 consecutive patients with nasal polyposis were prospectively analyzed to detect whether the presence and severity of their symptoms correlated with the presence of positive allergic tests. For all patients the diagnosis of nasal polyposis was based on the following criteria: (i) the visualization of bilateral polyps in the nasal cavities on endoscopic examination and (ii) the existence on computed tomography (CT) of bilateral opaque areas located in the ethmoidal sinuses, whether in the anterior and the posterior ethmoid portion [4]. This examination was performed without contrast medium (axial and coronal planes) [5].

Allergic investigation was carried out with specific IgE antibodies measured by the Phadiatop® test (Pharmacia Diagnostics AB, Uppsala, Sweden) [6]. No patient had Wegener's granulomatosis, Churg-Strauss syndrome, or cystic fibrosis. Patients who had already benefited either from ethmoidal surgery or from a previous medical treatment were not included. Patients with asthma did not receive concomitant asthma medication, such as montelukast sodium orally, that could reduce symptoms of nasal polyposis. The study sample (60% were male patients) had a mean age of 48.4 years (SD = 13 years).

In the second study, 74 consecutive patients with nasal polyposis were prospectively analyzed to detect whether the results of medical treatment of nasal polyposis were influenced by the presence of positive allergic tests. The diagnosis of nasal polyposis was based on the same criteria as in the first study. The study sample (57.5% male patients) had a mean age of 48.3 years (SD = 13.5 years). Three different therapeutic measures were applied [4]: washing of the nasal cavities, steroid spray, and oral steroid administration. Assessments were conducted at baseline and every 3 months over a 1-year period. Washing of the nasal cavities was carried out twice a day with a sterile physiological solution. Patients received intranasal steroid spray (beclomethasone) at a daily dose of 1000 µg (500 µg twice a day) in each nasal cavity. Systemic steroid treatment was systematically prescribed for all patients on entry to the study with the exception of patients for whom it was contraindicated (uncontrolled psychosis, evolutive viral infection, evolutive infectious disease, allergy to the used steroid). The regimen was prednisolone 1 mg/kg body weight per day for an initial 6-day period (one single dose during breakfast). At every consulting visit, the physician kept track of the

precise drug consumption over the preceding period. At every consultation, the regimen was tailored to the individual patient's need. Whenever possible (i.e. every time the symptoms had been reduced to a state compatible with near-normal life with little or no impairment of the patient's activities), the administration dosage of steroid spray was lowered [4]. Dosage reduction was achieved progressively by 250-µg steps. However, if deterioration of the patient's physical condition was clearly threatening, the prescribing physician resorted to a new course of systemic steroid administration (i.e. same dosage). Furthermore, if more than three systemic courses of prednisolone proved to be necessary, a surgical option was proposed.

Nasal function

All patients were examined and treated by the same physician for the duration of the two studies. In the two studies, the nasal function was checked on the basis of five criteria: nasal obstruction, anterior rhinorrhea, posterior rhinorrhea, facial pain, and the loss of sense of smell. The severity of each symptom was evaluated according to a three-point scale (0, no symptoms; 1, moderate symptoms that were frequently troublesome but not sufficiently to interfere with normal daily activities or sleep; 2, severe symptoms that interfered with normal activities or sleep). In regard to the particular case of disorders concerning the sense of smell, anosmia was noted as grade 2, hyposmia as 1, and normal function as 0. The grading was performed each time before any clinical, endoscopic, and CT scan examination [4]. The severity of each symptom was recorded for each patient at baseline (study 1 and 2), and at the end of every 3-month period (study 2). At baseline, the patient was asked to evaluate the mean symptom severity on the duration of the past year. In study 2, the patient was asked to evaluate the symptom severity on the mean duration since the past visit. At each visit, a clinical global severity index (GSI) was derived; it represented the mean score of the five symptoms under analysis: nasal obstruction, anterior and posterior rhinorrhea, facial pain, and hyposmia-anosmia. In the study 2, the amount of steroid consumption was separated into two subsets: oral treatment (prednisolone – in milligrams), and topical therapy (beclomethasone – in micrograms). The average quantity of each steroid subset was analyzed for the preceding period for every patient. Results are given after 1-year treatment.

Table I. Characteristics of the patients with nasal polyposis in the first study ($n=180$).

Characteristics	Patients with allergy	Patients without allergy	<i>p</i> value
<i>n</i>	35	145	
Age (years, SE)	44.7±2.1	49.3±1.2	NS
Number of males (<i>n</i>)	23	85	NS
Asthma (<i>n</i>)	17	41	0.03
Aspirin idiosyncrasy (<i>n</i>)	3	7	NS
Clinical score (mean±SE)			
Nasal obstruction	1.54±0.10	1.39±0.06	NS
Anterior rhinorrhea	0.71±0.14	0.65±0.06	NS
Posterior rhinorrhea	1.11±0.14	1.03±0.07	NS
Facial pain	0.40±0.12	0.31±0.05	NS
Loss of sense of smell	1.57±0.09	1.65±0.05	NS
Loss of flavor	0.71±0.13	0.93±0.07	NS
GSI	1.07±0.07	1.01±0.03	NS

SE, standard error; GSI, global severity index.

Pulmonary function

In study 1, bronchial provocation tests were performed according to the guidelines of the European Society for Clinical Respiratory Physiology [7]. Baseline forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were measured in all subjects. Subjects were advised to avoid smoking for 4 h and to avoid using β_2 -agonist or anticholinergic inhalers for 4 h or oral medication (β_2 -agonist, theophylline or antimuscarinic drugs) for 8 h before the test. Subjects who reported a respiratory tract and/or nasal infection in the previous 3 weeks were rescheduled. Patients were permitted 10 attempts to provide at least 2 technically acceptable maneuvers. All those whose FEV₁ was at least 70% of the predicted value and >1.5 litres were invited to undergo methacholine challenge unless they reported that they had epilepsy or heart disease, were pregnant or breastfeeding or taking a β -blocker [8,9]. Bronchial challenge started with inhalation of saline diluent, and the maximum post-diluent FEV₁ recorded 2 min later was used as the control value. Subjects whose control FEV₁ was <90% of the baseline value were not challenged further. The methacholine was made up from lyophilized methacholine chloride (Provocholine; Hoffman La Roche, Basle, Switzerland) and was delivered using a Mefar dosimeter (Bovezzo, Italy) set to deliver the aerosol over a period of 1 s. Patients were asked to expire to functional residual capacity, place their lips around the mouthpiece, inspire to total lung capacity, hold their breath for at least 3 s and then exhale. FEV₁ was recorded 2 min later, and in the absence of a 20% fall from baseline, the next dose was given. Non-specific bronchial hyperresponsiveness (BHR) to methacholine was measured using a maximum dose of 1.6 mg. The test was stopped if there was a >20% fall in FEV₁ from the control value or if the maximum cumulative dose had been reached.

Statistics

In study 1, the mean severity of symptoms (BHR, nasal obstruction, anterior and posterior rhinorrhea, facial pain, anosmia-hyposmia) was described according to the presence or absence of allergy. Differences, according to Student's *t* test, were judged significant when *p* was <0.05. In study 2, comparison of the mean drug consumption between the two groups of patients was based on the classic use of the Student *t* test for comparison of two means. Differences were judged significant when *p* was <0.05. In the second study, the reasonable assumption that the distribution of drug consumption was normal ensured the validity of the Student's *t* test despite the small size of the allergic group.

Results

Study 1 ($n=180$)

Thirty-five patients (19.5% of the patients) had positive allergic tests.

Prevalence of asthma. In the first group (allergy), 17 patients (48.6%) were suffering from asthma; eight patients without asthma (22.8%) had bronchial abnormal reactivity to methacholine, while 10 patients (28.6%) had normal respiratory function without any abnormal reactivity to methacholine (Table I). Three patients (8.5%) had typical hypersensitivity reactions to aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs), diagnosed on the basis of abnormal clinical manifestations (asthma, nasal symptoms, dyspnea, etc.) occurring after aspirin or NSAID consumption. In the second group (no allergy), 41 patients (28.3%) were suffering from asthma, 29 (20%) had bronchial abnormal reactivity to methacholine without any clinical symptom of asthma, and 75 patients (51.7%) were free of

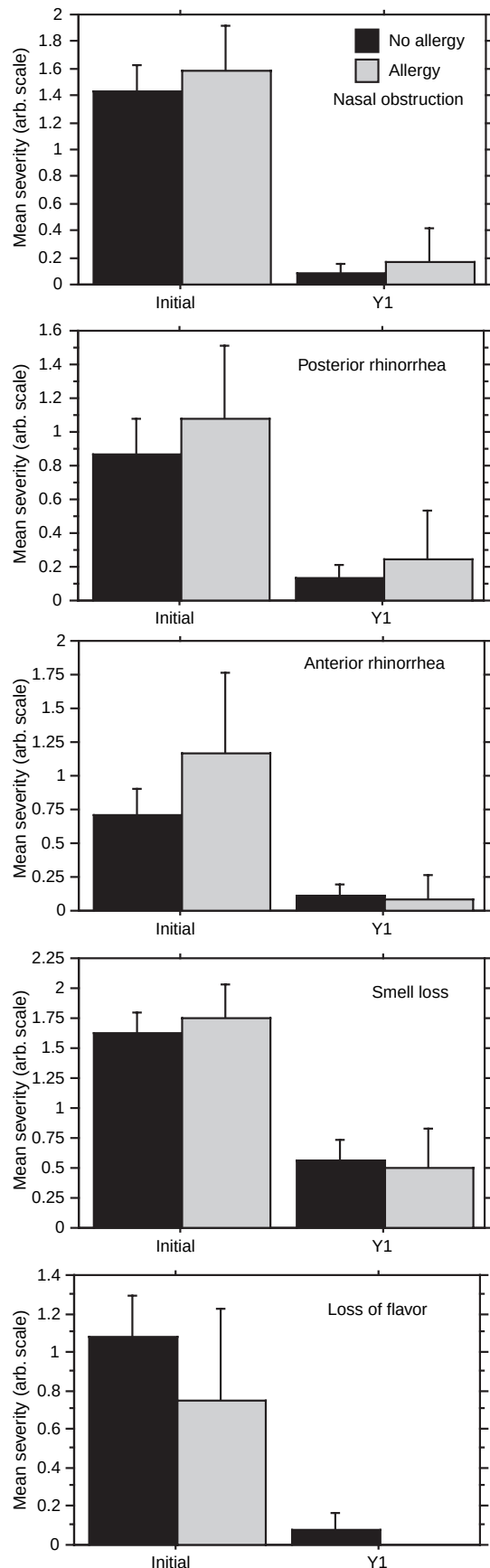


Figure 1 (Continued)

pulmonary disease. In this second group, seven patients (4.8%) had typical hypersensitivity reactions to aspirin or NSAIDs. The two groups did not differ with regard to age, sex ratio or prevalence of aspirin idiosyncrasy. The prevalence of asthma ($p=0.03$, χ^2 test) was higher in the group with than without allergy.

Symptoms. The two most disabling symptoms of nasal polyposis were anosmia and nasal obstruction (Table I). Mean scores of nasal symptoms did not differ between the two groups (with and without allergy). The clinical GSI (1.07 ± 0.07 versus 1.01 ± 0.03) was almost identical in the two groups.

Study 2 ($n=74$)

Twelve patients (16.2% of the patients) had positive allergic tests. The two groups did not differ with regard to age, sex ratio, prevalence of aspirin idiosyncrasy and asthma. The two most disabling symptoms of nasal polyposis also were anosmia and nasal obstruction (Table II). At baseline, mean scores of nasal symptoms did not differ between the two groups with and without allergy. The clinical GSI (1.30 ± 0.11 versus 1.00 ± 0.05) was almost identical in the two groups.

Modification of symptoms after a 1-year (Y1) treatment. A significant decrease ($p < 10^{-3}$) in the mean scores of nasal symptoms was observed in the two groups between baseline and Y1 (Figure 1). Decrease of all nasal symptoms was not statistically different in the two groups (i.e. allergy and nonallergy).

Steroid consumption data. The cumulative consumption of prednisolone tablets (mg) and beclomethasone spray (μ g) between baseline and Y1 is shown in Table III. The quantities of orally administered prednisolone and beclomethasone spray administration were similar between the two groups (i.e. allergy and nonallergy).

Discussion

Nasal polyposis is a chronic inflammatory disease of the paranasal sinus mucosa, leading to the protrusion of benign edematous polyps from the meatus into the nasal cavities [10]. This pathology is the most incapacitating illness of the nasal cavity and paranasal sinuses [11]. A variety of severe symptoms attached to this condition testify to the serious alteration of the nasal and paranasal function: nasal

Figure 1. Mean severity (and 95% confidence interval) of nasal symptoms at baseline (initial) and after a 1-year treatment (Y1) in patients with and without allergy.

Table II. Characteristics of the patients with nasal polyposis in the second study ($n=74$).

Characteristics	Patients with allergy	Patients without allergy	<i>p</i> value
<i>n</i>	12	62	
Positive RAST	12	62	
Age (years, SE)	46.7 ± 3.6	48.7 ± 1.7	NS
Number of males (<i>n</i>)	6	36	NS
Asthma (<i>n</i>)	4	17	NS
Aspirin idiosyncrasy (<i>n</i>)	2	2	NS
Initial clinical score (mean ± SE)			
Nasal obstruction	1.58 ± 0.15	1.43 ± 0.10	NS
Anterior rhinorrhea	1.16 ± 0.27	0.71 ± 0.10	NS
Posterior rhinorrhea	1.08 ± 0.19	0.87 ± 0.10	NS
Facial pain	0.58 ± 0.26	0.37 ± 0.08	NS
Loss of sense of smell	1.75 ± 0.26	1.63 ± 0.08	NS
Loss of flavor	0.75 ± 0.22	1.08 ± 0.11	NS
GSI	1.30 ± 0.11	1.00 ± 0.05	NS

SE, standard error; RAST, radioallergosorbent test; GSI, global severity index.

obstruction, anterior and posterior rhinorrhea, loss of smell and flavor, facial pain [12]. On the other hand, allergic rhinitis is a high-prevalence disease affecting about 10–20% of the general population [3]. Nasal itching, anterior and posterior watery rhinorrhea, facial pain, and nasal obstruction characterize allergic rhinitis. Impaired smell and headache can be associated. The aim of this paper was to analyze differences in term of symptoms and treatment in two series of patients with nasal polyposis with and without allergy (i.e. the interaction between nasal polyposis and allergic rhinitis).

The prevalence of allergy in our two studies (19.5% and 16.2%) is in agreement with prevalence of allergy in the general population [3]. The identification of atopic patients was carried out using a specific immunoglobulin E (IgE) antibody test: the Phadiatop® test. This test was shown to be highly sensitive and specific in differentiating individuals who are sensitized to common inhalants from those who are not [6]. On the other hand, the characteristics of our patients are close to those usually found in the nasal polyposis literature, with reference to age (mean age around 45–50 years), sex ratio (around 1.3), prevalence of asthma (around 30%), and sensitivity to aspirin (below 10%) [13,14].

Table III. Mean doses of prednisolone (in mg per year) and beclomethasone (in µg per day) administered in each nasal cavity during the year of treatment in group 1 (positive allergic tests) and group 2 (negative allergic tests).

	Prednisolone		Beclomethasone	
	Mean	SE	Mean	SE
Group 1 ($n=12$)	649	94	844	76
Group 2 ($n=62$)	653	44	879	32

SE, standard error.

The interaction of nasal polyposis and allergy had been mainly studied in order to determine if nasal polyps in allergic individuals are different from those in nonallergic individuals. Polyp histology typically shows chronic, eosinophilic inflammation. In most publications, there appears to be no difference between allergic and nonallergic polyps in terms of mast cells and eosinophilic numbers but there may be differences in cytokine expression by cells [15].

First, our results suggest that the presence of allergy does not change initial symptoms in patients with nasal polyposis (study 1). Previous papers have pointed to allergy as a possible exacerbating factor of various symptoms in patients with nasal polyposis. Nevertheless, there have been a very limited number of papers presenting this relationship [15]. To explore the association of nasal polyps with allergy, Keith et al. [16] studied four series of patients: 16 patients with polyps and ragweed allergy, 16 patients with polyps who were not allergic to ragweed, 16 patients allergic to ragweed without polyps, and 16 patients not allergic to ragweed without polyps. The level of ragweed allergy was comparable in patients with and without polyps. Symptom scores before the ragweed season for the nasal symptoms (nasal obstruction, anosmia-hyposmia, rhinorrhea) were high in patients with nasal polyps regardless of the presence or absence of allergy. These symptoms did not change during the ragweed season. Such results are in agreement with our conclusion. Our first study was conducted on a large series of patients ($n=180$). Patients were asked to evaluate the symptom severity over a 1-year duration. The mean degree of severity of all symptoms (nasal obstruction, anterior and posterior rhinorrhea, anosmia-hyposmia, facial pain, loss of flavor, GSI) did not significantly differ in patients with or without allergy. On the other hand, the percentage of patients

with asthma in this series was 32.2% ($n=58/180$). This percentage is in agreement with published reports in the literature [17]. The only difference ($p=0.03$) was a higher prevalence of asthma in patients with nasal polyposis and positive allergic tests (48.6%, $n=17/35$ versus 28.3%, $n=41/145$) (Table I). Such a difference was not found in our second study, probably because of the limited number of patients evaluated ($n=74$). Moreover, the total number of patients with asthma and asymptomatic BHR was higher in the allergic population than in the nonallergic population (71.4%, $n=35/45$ versus 48.3%, $n=70/145$). This difference cannot be explained only by the high prevalence of asthma in patients with aspirin idiosyncrasy, because the percentage of patients with aspirin idiosyncrasy did not statistically differ between the two populations. Thus, the main cause of high incidence of asthma in patients with nasal polyposis could be the presence of allergy.

Second, our results suggest that the presence of allergy does not change symptoms in patients with nasal polyposis after a 1-year medical treatment (study 2). Drake-Lee [18] and Settipane [19] found that the presence of a positive allergy skin test did not correlate with the number of polypectomies [15]. Nishioka et al. [20] published a study carried out on 283 consecutive patients who had undergone functional endoscopic sinus surgery, but only 140 had nasal polyps (49%). There was a greater recurrence of polyps in those having positive skin tests (36%) than those who had not (17%), but no statistical analysis was given. In conclusion, Keith and Dolovich suggest that the effectiveness of allergen avoidance or allergen immunotherapy is unknown but if concomitant allergic rhinitis or asthma is present, these treatments may be beneficial [15]. In contrast, in the second study, 74 allergic and nonallergic patients with nasal polyposis were compared in terms of medical treatment after a 1-year period despite the large size of the sample. No significant difference was found between the two groups in terms of symptoms, or in terms of doses of treatment. These results suggest that specific treatment of allergy in patients with nasal polyposis does not seem useful.

Conclusion

The relationship between nasal polyposis and allergy remains incompletely defined. Allergy was considered as an exacerbating factor despite an apparent lack of major effect of inhaled allergen in patients with nasal polyps. This work confirms that allergy does not modify the symptoms of nasal polyposis, neither initially nor after a 1-year medical treatment.

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