

ORIGINAL ARTICLE

Influence of allergy in patients with nasal polyposis after endoscopic sinus surgery

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Abstract

Conclusion. Allergy does not modify the symptoms and steroid consumption (oral and local) of nasal polyposis (NP) patients after functional endoscopic sinus surgery (FESS). **Objectives.** To assess the role of allergy in the evolution after FESS of patients presenting with the diagnosis of NP. **Patients and methods.** This was a prospective study of 63 consecutive patients with NP (57% males, mean age 45.8 years), who were analyzed to detect whether the results of a surgical treatment of NP were influenced by the presence of positive allergic tests (Phadiatop®). Three nasal criteria were scored: nasal obstruction, posterior rhinorrhea, and the loss of smell. The frequency of asthma was evaluated. Medical treatment of NP after FESS consisted of washing of the nasal cavities, steroid spray, and oral steroid administration. The amount of consumption of steroids (prednisolone and beclomethasone) was studied. **Results.** Decrease of all nasal symptoms was not statistically different in the two groups of patients with and without allergy. Cumulative consumption of prednisolone and beclomethasone after surgery was similar in the two groups.

Keywords: Nasal polyposis, allergy, FESS, ethmoidectomy, steroid, nasal obstruction, rhinorrhea, olfaction, smell loss, anosmia

Introduction

Chronic rhinosinusitis is one of the most common health care problems in Europe and United States, and there is evidence that it is increasing in prevalence and incidence [1]. It is an increasingly common cause of patient visits to general practitioners (GPs) and represents nearly 2% of all visits seeking otolaryngologic care [2]. Nasal polyposis (NP) is one of the most common inflammatory pathologies of the nasal and paranasal sinus cavities. Its pathogenesis is not yet fully understood and its prevalence is around 2.7% in Europe [3].

On the other hand, allergic rhinitis is a high prevalence disease in developed countries. Estimates of the prevalence of allergic rhinitis range from as low as 9% to as high as 42% [4]. A variety of severe symptoms attached to these two conditions (i.e. NP 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.

The high prevalence of these two conditions explains that many patients with nasal polyposis have positive allergic tests. Nevertheless, the relationship between NP 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 NP. A recent publication has shown that allergy does not modify the symptoms of NP, neither initially nor after a 1-year exclusive medical treatment [5]. The design of this prospective study aimed to assess the role of allergy in symptoms and medical treatment after functional endoscopic sinus surgery (FESS) of patients presenting with the diagnosis of NP.

Patients and methods

Patients

Sixty-three consecutive patients with nasal polyposis were prospectively analyzed to detect whether the presence and severity of their symptoms after FESS

correlated with the presence of positive allergic tests. The diagnosis of NP was based for all patients on two concomitant criteria: the visualization of bilateral polyps in the nasal cavities on endoscopic examination, and the existence on CT of bilateral opaque areas located in the ethmoidal sinuses, whether in the anterior or the posterior ethmoid portion [6]. This examination was performed without contrast medium (axial and coronal planes) [7]. Allergic investigation was carried out with specific IgE antibodies measured with the Phadiatop® test (Pharmacia Diagnostics AB, Uppsala, Sweden) [8]. No patient had Wegener's granulomatosis, Churg-Strauss syndrome, or cystic fibrosis. Patients with asthma did not receive concomitant asthma medication, such as montelukast sodium orally, that could reduce symptoms of NP. The study sample (57% were male patients) had a mean age (mean $\pm$ SE) of 45.8 ± 1.5 years.

Before FESS, three different therapeutic measures were applied [6]: washing of the nasal cavities, steroid spray, and oral steroid administration. Washing of the nasal cavities was carried out twice a day with a sterile physiologic solution. Patients received intranasal steroid spray (beclomethasone) at a daily dose of 1000 μ g (dosage = 500 μ g twice a day) in each nasal cavity. Systemic steroid treatment was systematically prescribed for all patients at the study entrance with the exception of patients for whom it was contraindicated (uncontrolled psychosis, evolving viral infection, evolving 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 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 [6]. 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. The minimum duration of medical treatment in this study was 6 months (i.e. the patient needed three courses of systemic steroid administration in 6 months). Only patients with a minimal follow-up after surgery of 2 years were included in this study.

Functional endoscopic sinus surgery (FESS)

All patients were examined and treated by the same physician for the duration of the study. FESS was performed between 1998 and 2004 by the same surgeon and under general anesthesia. The same surgical procedure was carried out for all patients [9]. FESS procedure began with the inferior resection of the middle turbinate. Fenestration of the maxillary antrum was carried out after resection of the uncinate process, identification and widening of the maxillary ostium. Then, posterior ethmoid cells were opened, and their party walls were totally removed as far as the white roof. The anterior ethmoid cells were exenterated and the nasofrontal duct was identified. Lasers and microdebriders were never used in these procedures. After surgery, all patients received a systematic medical treatment. The usual medical treatment began by the end of the first month. Three different therapeutic measures were systematically applied: washing of the nasal cavities, steroid spray, and oral steroid administration if needed. Washing of the nasal cavities was carried out twice a day with a sterile physiologic solution. Patients received intranasal steroid spray (beclomethasone) at a daily dose of 1000 μ g (dosage = 500 μ g twice a day) in each nasal cavity. No oral steroid administration was systematically given after surgery. At every visit, 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 [9]. Dosage reduction was achieved progressively by 250 μ g 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. prednisolone 1 mg/kg body weight per day for a 6-day period).

Clinical evaluation

Clinical evaluation was conducted at baseline (before any treatment), and two to four times a year after surgery. At baseline, the patient was asked to evaluate the mean symptom severity over the duration of the past year. At each visit after baseline, the patient was asked to evaluate the symptom severity on the mean duration since the past visit. At each visit, nasal function was checked on the basis of three criteria: nasal obstruction, posterior rhinorrhea, and the loss 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, or CT scanner examination [6].

At baseline, endoscopic examination for measurement of polyp size was performed on a four-point scale (0, normal mucosa; 1, mild polyps [small polyps not reaching the upper edge of the middle meatus antrostomy]; 2, moderate polyps [medium-sized polyps extending between the upper and the lower edges of the inferior turbinate]; 3, severe polyps [large polyps extending below the lower edge of the inferior turbinate]). After surgery, endoscopic examination for measurement of polyp size was performed at each visit on a five-point scale (0, normal mucosa; 0.5, absence of polyps but mucosal thickening; 1, mild polyps [small polyps not reaching the upper edge of the middle meatus antrostomy]; 2, moderate polyps [medium-sized polyps extending between the upper and the lower edges of the inferior turbinate]; 3, severe polyps [large polyps extending below the lower edge of the inferior turbinate]). Preoperative and postoperative polyp sizes 1, 2, and 3 were rated identically.

Bronchial provocation tests were performed according to the guidelines of the European Society for Clinical Respiratory Physiology [10]. Baseline forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were measured in all subjects. The methacholine was made up from lyophilized methacholine chloride (Provocholine; Hoffman La Roche, Basle, Switzerland) and was delivered using a dosimeter set (Mefar, Bovezzo, Italy) to deliver the aerosol over a period of 1 s. 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.

At every visit, the physician kept track of the precise drug consumption over the preceding period. The amount of steroid consumption was also separated into two subsets: oral treatment (prednisolone) and topical therapy (beclomethasone [in micrograms]). For oral steroid consumption, results are given for the entire year before surgery (−1y), during the first year (1y), during the second year (2y), during the third year (3y), during the fourth and fifth year (4–5y), and during the sixth and seventh year (6–7y). For local steroid consumption,

results are given for the entire year before surgery (−1y), for the 6 months period (6m), between 6 and 12 months (1y), at the end of the second year (2y), at the end of the third year (3y), at the end of the fifth year (5y), and at the end of the seventh year (7y).

Statistics

Patients were split into two groups. The first group included patients with allergy; the second group included patients without allergy. The statistical analysis was performed using Statview 5.0 software (Statview, Inc.). For all continuous variables, applicable data were expressed as mean ± SEM. Being a composite of several rather independent qualitative variables, global severity index (GSI) was taken to be a continuous variable, and sample size was large enough for GSI distribution to be unimportant. For all continuous variables entering comparisons, Student's unpaired *t* test was used to compare mean values between patients with and without allergy. Repeated-measures ANOVA was performed for the pooled data (baseline, 6m, 1y, 2y, 3y, 5y, 7y), with time as within factor, group (allergy +/allergy −) as between factor, and an interaction between time and group. Repeated-measures ANOVA was used for within-group comparisons (factor time).

An actuarial analysis using the Kaplan–Meier life table method was performed with regard to the 3- and 5-year symptoms control rates. Two 3-year and 5-year actuarial symptom control rates were studied for each symptom. The 3-year and 5-year actuarial symptom control rates were studied as a function of either the presence of the symptom or the presence of a severe symptom. Severe symptoms were symptoms that interfered with normal activities or sleep. In regard to the particular case of disorders concerning the sense of smell, severe loss of smell was rated as anosmia. Comparison was performed with a log rank test. Statistical significance was assumed when *p* value was <0.05.

Results

Twenty-two patients (34.9% of the patients) had positive allergic tests.

Prevalence of asthma and BHR

In the first group (allergy), 13 patients (59.1%) were suffering from asthma; 3 patients without asthma (13.6%) had bronchial abnormal reactivity to methacholine, while 6 patients (27.3%) had normal respiratory function without any abnormal reactivity to methacholine (Table I). Three patients (13.6%) had typical hypersensitivity reactions to aspirin or

Table I. Characteristics of the patients with nasal polyposis (NP) at baseline ($n=63$).

Characteristics	Patients with allergy	Patients without allergy	<i>p</i> value
<i>n</i>	22	41	
Age (years, SE)	43.3 $\pm$ 2.5	47.3 $\pm$ 1.9	NS
Number of males (<i>n</i>)	13	23	NS
Asthma (<i>n</i>)	13	18	NS
BHR (<i>n</i>)	16	30	NS
Aspirin idiosyncrasy (<i>n</i>)	3	9	NS
Clinical score (mean $\pm$ SE)			
Nasal obstruction	1.81 $\pm$ 0.11	1.63 $\pm$ 0.11	NS
Posterior rhinorrhea	1.41 $\pm$ 0.18	1.37 $\pm$ 0.12	NS
Smell loss	1.77 $\pm$ 0.13	1.85 $\pm$ 0.05	NS
GSI	1.66 $\pm$ 0.09	1.62 $\pm$ 0.06	NS

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), 18 patients (43.9%) were suffering from asthma, 12 (29.3%) had abnormal bronchial reactivity to methacholine without any clinical symptom of asthma, and 11 patients (26.8%) were free of pulmonary disease. In this second group, nine patients (21.9%) had typical hypersensitivity reactions to aspirin or NSAIDs. The two groups did not differ with regard to age, sex ratio, asthma, BHR, or prevalence of aspirin idiosyncrasy.

Baseline symptoms

The three most disabling symptoms of nasal polyposis were anosmia, posterior rhinorrhea, and nasal obstruction (Table I). Mean scores of nasal symptoms did not differ between the two groups (with and without allergy). The clinical GSI (1.66 $\pm$ 0.09 vs 1.62 $\pm$ 0.06) was almost identical in the two groups.

Improvement of symptoms after surgery in the two groups

The mean follow-up for the series was 5.8 $\pm$ 0.4 years ($n=63$). One patient died of cardiovascular disease, 3 years after FESS.

A significant decrease ($p<0.001$) in the mean GSI score and in the mean polyp grade was observed in allergic as well as non-allergic patients between baseline and 6 months after surgery ($p<0.001$) (Figure 1). In contrast, these parameters remained stable in allergic and nonallergic patients between 6 months and 7 years. No significant difference was found between the two groups in terms of mean GSI score or nasal polyp grade evolution.

The 3-year and 5-year actuarial symptom control rates were studied as a function of either the presence of the symptom or the presence of a severe

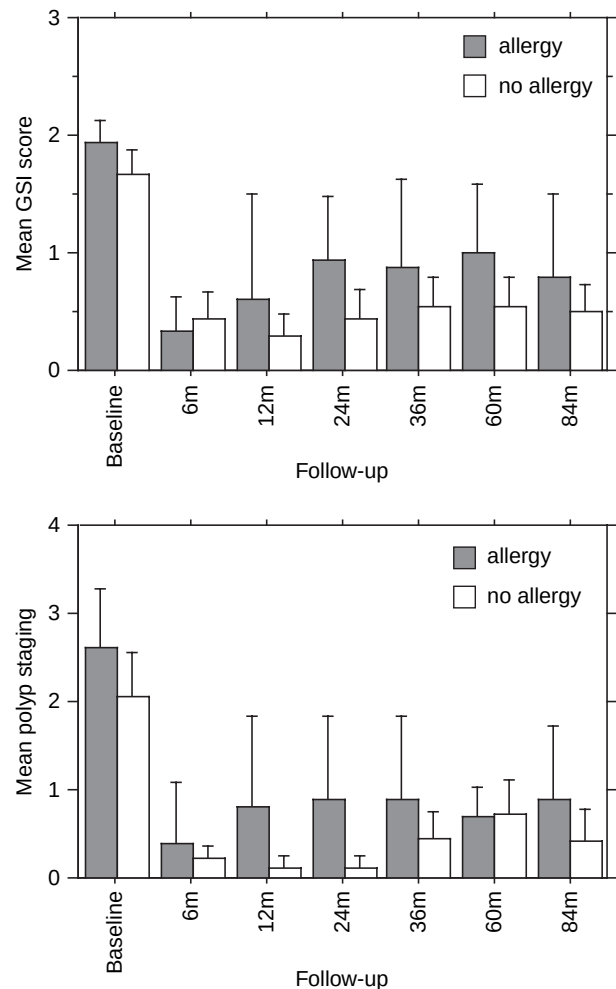


Figure 1. Top: mean (and 95% confidence interval, CI) global severity index (GSI) at baseline and its evolution during the 7 years after surgery (xm, x months), in patients with (shaded bars) and without (open bars) allergy. Bottom: mean (and 95% CI) polyp grade at baseline and after surgery in patients with (shaded bars) and without (open bars) allergy. No significant difference was found between the two groups in terms of mean GSI score and mean nasal polyp grade evolution after surgery.

symptom (i.e. symptoms that interfered with normal activities or sleep). The 3-year and 5-year actuarial nasal obstruction control rates varied from 74.4 and 65.6% in the nonallergy group to 72.3 and 65.1% in the allergy group, respectively ($p=0.65$, Figure 2). The 3-year and 5-year actuarial severe nasal obstruction control rates were 97.4% in the non-allergy group to 95.5% in the allergy group ($p=0.64$, Figure 2). The 3-year and 5-year actuarial posterior rhinorrhea control rates varied from 57.3 and 53.2% in the nonallergy group to 60.9 and 60.9% in the allergy group, respectively ($p=0.61$, Figure 3). The 3-year and 5-year actuarial severe posterior rhinorrhea control rates varied from 87.1 and 82.6% in the non-allergy group to 81.1 and 81.1% in the allergy group, respectively ($p=0.61$, Figure 3). The 3-year and 5-year actuarial hyposmia control rates varied from 29.0 and 29.0% in the nonallergy group to 30.0 and 30.0% in the allergy group, respectively ($p=0.71$, Figure 4). The 3-year and 5-year actuarial anosmia rates varied

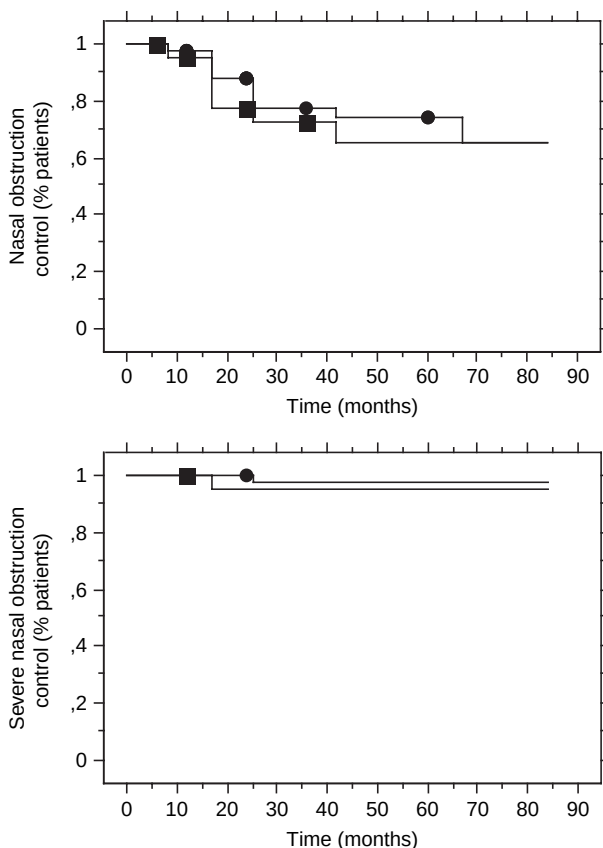


Figure 2. Nasal obstruction control in patients with (squares) and without (circles) allergy. On ordinate is the percentage of patients without moderate nasal obstruction (upper) or severe nasal obstruction (lower). Arbitrarily, the percentage of patients without the symptom is 100% at T0 (during FESS). This percentage decreases after surgery in patients with or without allergy. There was no significant difference between the two curves. Then, no significant difference was found between the two groups in terms of nasal obstruction control whatever the severity of the symptom.

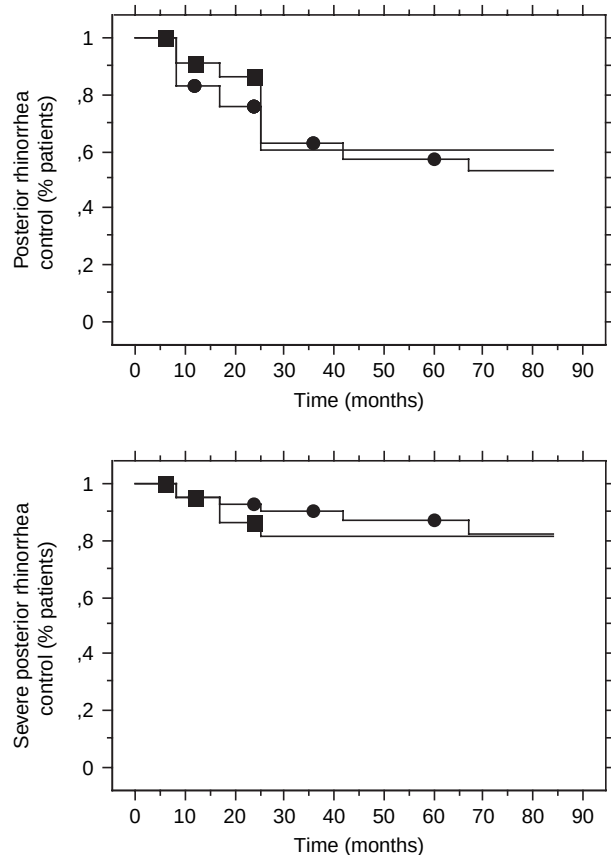


Figure 3. Posterior rhinorrhea control in patients with (squares) and without (circles) allergy. On ordinate is the percentage of patients without moderate posterior rhinorrhea (upper) or severe posterior rhinorrhea (lower). Arbitrarily, the percentage of patients without the symptom is 100% at T0 (during FESS). This percentage decreases after surgery in patients with or without allergy. There was no significant difference between the two curves. Then, no significant difference was found between the two groups in terms of nasal posterior rhinorrhea whatever the severity of the symptom.

from 72.0 and 67.7% in the nonallergy group to 85.9 and 71.5% in the allergy group ($p=0.44$, Figure 4). Thus, no significant difference was found between the two groups in terms of control of nasal obstruction, posterior rhinorrhea, and sense of smell.

Consumption data after surgery

Comparison of the mean drug consumption between patients with and without allergy was carried out after surgery (Figure 5). A significant decrease ($p<0.001$) in the mean quantity of orally administered prednisolone between baseline and after surgery was observed in allergic and nonallergic patients. In contrast, this parameter remained stable between the first year and the seventh year after surgery. Moreover, a significant decrease ($p<0.001$) in the mean quantity of daily administered beclomethasone between baseline and after surgery was observed in allergic

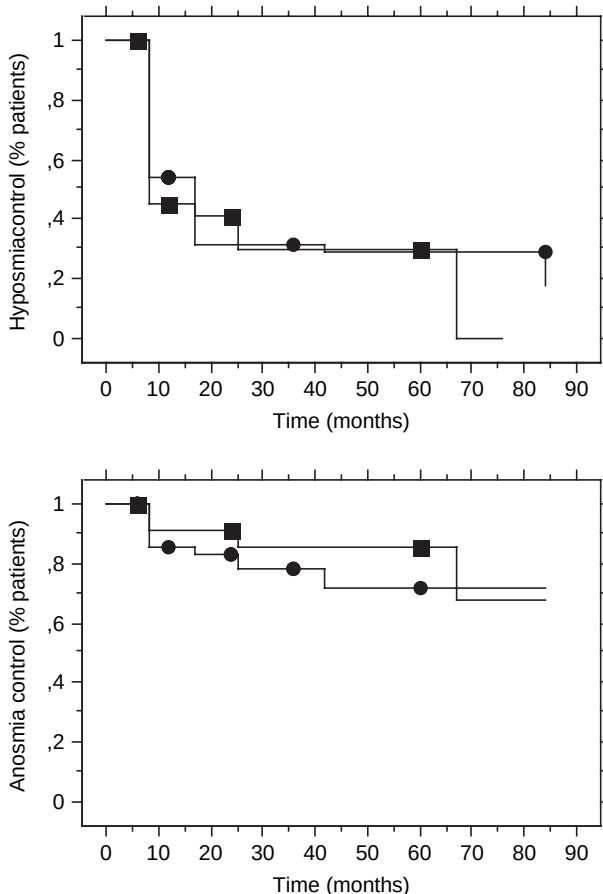


Figure 4. Smell loss control in patients with (squares) and without (circles) allergy. On ordinate is the percentage of patients without hyposmia (upper) or anosmia (lower). Arbitrarily, the percentage of patients without the symptom is 100% at T0 (during FESS). This percentage decreases after surgery either in patients with or without allergy. There was no significant difference between the two curves. Then, no significant difference was found between the two groups in terms of smell loss whatever the severity of the symptom.

and nonallergic patients. This parameter decreased between the first year and the seventh year after surgery. The quantities of orally administered prednisolone and beclomethasone spray administration were similar between the two groups.

Discussion

Nasal polyposis is the most incapacitating chronic inflammatory disease of the nasal and paranasal sinus mucosa, leading to the protrusion of benign edematous polyps into the nasal cavities [11]. Some severe symptoms are attached to this condition and testify to the serious alteration of the nasal physiology: nasal obstruction, posterior rhinorrhea, and loss of sense of smell and flavor [12]. On the other hand, allergic rhinitis is a high prevalence disease affecting about 9–42% of the general population [4]. Nasal itching, posterior rhinorrhea, facial pain, smell loss,

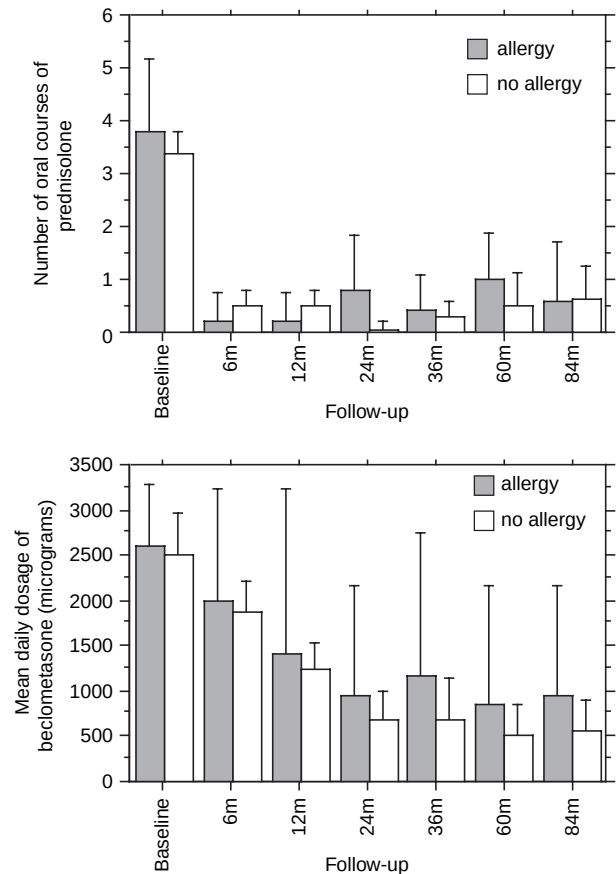


Figure 5. Mean (and 95% confidence interval) number of short courses of prednisolone (upper) and mean daily dosage of beclomethasone spray (lower) administered during the 7 years of treatment (xm, x months) after surgery in patients with (gray) and without (white) allergy. No significant difference was noted between the two groups in terms of oral or spray steroid consumption.

and nasal obstruction characterize allergic rhinitis. The aim of this paper was to analyze differences in term of symptoms and treatment after FESS in two series of patients with NP with and without allergy (i.e. the interaction between nasal polyposis and allergic rhinitis).

The prevalence of allergy in our study (34.9%) is in agreement with high estimates of prevalence of allergy in the general population [4]. The identification of atopic patients was achieved using a specific immunoglobulin E (IgE) antibody test (i.e. 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 [8]. On the other hand, the characteristics of our patients are close to those usually found in the nasal polyposis literature, as regards age (mean age around 45–50 years) and sex ratio (around 1.3) [13]. Prevalence of associated asthma (around 50% in our series) and hypersensitivity reactions to aspirin or

NSAIDs (19%) were higher than those usually found in the literature. This higher prevalence could be explained by the fact that BHR has been demonstrated as the risk factor for steroid insensitivity in nasal polyposis [14]. This fact could explain that the percentage of surgically treated patients must include a very high percentage of patients with asthma and/or BHR.

A very limited number of papers presenting the relationship between NP and allergy have been published in the literature [15]. Symptom scores before the ragweed season for the nasal symptoms (nasal obstruction, anosmia-hyposmia, rhinorrhea) were high in patients with NP regardless of the presence or absence of allergy. The symptoms did not change during the ragweed season [16]. In a large series of patients, a recent publication reported that the mean degree of severity of all symptoms (nasal obstruction, anterior and posterior rhinorrhea, anosmia-hyposmia, facial pain, loss of flavor) did not significantly differ in NP patients with or without allergy before any treatment. The only difference was a higher prevalence of asthma in NP patients with positive allergic tests [5]. The same study showed that the presence of allergy does not change symptoms in patients with NP treated with a pure medical treatment [5]. On the other hand, the presence of a positive allergy skin test did not correlate with the number of polypectomies [17,18].

The role of allergy in surgical results in NP patients is only documented in one paper [19]. This study was carried out on 283 consecutive patients who had undergone FESS, 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 the present study, 63 allergic and nonallergic patients with NP were compared in terms of symptoms and steroid consumption (oral and spray) after FESS with a long follow-up period. No significant difference in terms of either symptoms or doses of treatment was found between the two groups. This result suggests that specific treatment of allergy in patients with NP does not seem useful after surgery. This paper is the first in the literature to present such a conclusion.

Conclusion

The relationship between NP 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 and steroid consumption of patients with NP after surgery.

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