



The natural history of respiratory allergy: A follow-up study of 99 patients up to 10 years

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A strict relationship between allergic rhinitis and allergic asthma has been seen recently, and in many ways respiratory allergy could be seen as a single disorder of the airways. The link between rhinitis and asthma can be elucidated only by studying the natural history of the disease over long periods. We describe the follow-up of 99 allergic patients up to 10 years and the evolution of their disease. Ninety-nine patients (50 male, 49 female, mean age 31 years) out of 142, suffering from allergic rhinitis or allergic asthma, could be monitored up to 10 years after the initial diagnosis. Demographics, sensitizations and smoke habit were assumed as evaluation parameters. At baseline, 44 patients suffered from AR alone, 12 from AA alone and 43 from AR + AA. After 10 years, 31.8% of the AR patients developed AA and 50% of the patients with AA developed AR. Only the familial history for atopy significantly influenced the disease's evolution, whereas gender, age, smoking habit and skin sensitization did not. Sixty-five percent of patients with a single sensitization at the beginning developed new sensitizations. In conclusion, this long-term survey confirms that a relevant percentage of patients with AR alone or AA alone have a progression of the disease.

Key words: allergic rhinitis; allergic asthma; respiratory allergy; natural history.

RESPIR. MED. (2001) 95, 9–12

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Introduction

The overall pathogenic view of allergic respiratory diseases has significantly changed during the last 10 years. It has been realized that respiratory allergy cannot be considered as confined to a single target organ (i.e. nose or bronchi), but rather as a global disorder of the airways, which may show various clinical expressions. In fact, a strict relationship existing between upper and lower respiratory tract has been seen (1,2). In this regard, several aspects should be considered: the possible involvement of paranasal sinuses, the presence of bronchial hyperreactivity in patients suffering from allergic rhinitis alone (3) and the role of viral respiratory infections (4). All these facts, taken together, depict the concept of the 'allergic rhinobronchitis'. This aspect may have both pathophysiological and therapeutic implications.

Indeed, the most valuable information on the links existing between allergic rhinitis (AR) and allergic asthma (AA) can be obtained only from the natural history of the

disease itself. Several experimental data are so far available concerning the evolution of upper respiratory allergy into bronchial asthma and the association between AR and AA. The reliability of these clinical data is directly correlated to the length of the observation period considered (1). In the present clinical study we studied the natural history of respiratory allergy in a population of 99 allergic patients, which could be followed-up up to 10 years after the initial diagnosis. We also evaluated the possible influence of some clinical and demographic parameters on the disease evolution.

Methods

We studied a population of allergic outpatients up to 10 years after the first visit and initial diagnosis (from 1986–1987 to 1996–1997). During the period 1986–1987, more than 500 patients were seen at our clinic with respiratory complaints. A detailed diagnosis of respiratory allergy was established in 142 patients (76 men and 66 women, mean age 23.1 years). The remaining patients suffered from other respiratory conditions [chronic obstructive pulmonary disease (COPD), infectious diseases, vasomotor rhinitis] and had no clinical or diagnostic evidence of atopy. Patients underwent a detailed clinical history, examination and skin testing. Skin tests were performed during the whole period using commercial extracts (Lofarma SpA,

Received 28 March 2000 and accepted in revised form 1 August 2000. Published online 28 November 2000.

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Milan, Italy); the standard panel included: mites, grasses, *Parietaria*, olive, birch, hazelnut, ragweed, cat and dog dander and *Alternaria*, plus a negative control and histamine. The RAST assay was performed only in few cases (discrepancy between clinical history and skin test or negative histamine control). The diagnosis of AA was based on the criteria established in 1986 by the American Thoracic Society (5), which are essentially clinical 'episodic cough, wheezing and dyspnea' either reported or actual. The young age of patients virtually excluded the presence of COPD. A non-specific bronchial challenge (with ultrasonic fog) was performed in selected patients with normal pulmonary function test. The diagnosis of rhinitis was performed on a clinical basis: clinical history (at least 2 years) of perennial or seasonal itching, sneezing, rhinorrhea and nasal blockage, in the absence of anatomical alterations.

Each patient received an appropriate drug therapy for the disease(s): oral anti-histamines, inhaled and nasal corticosteroids, β_2 -agonists and oral theophylline were prescribed. The treatments given at the first visit are summarized in Table 1. Allergen avoidance measures were suggested, when applicable. None of the patients was given specific immunotherapy or leukotriene receptor antagonists.

TABLE 1. Drug therapy prescribed at the first visit

Rhinitis ($n=44$)	Oral antihistamine ($n=31$), nasal corticosteroid ($n=10$), oral antihistamine + nasal corticosteroid ($n=3$)
Asthma ($n=12$)	Inhaled albuterol ($n=4$), inhaled albuterol + cromolyn ($n=2$), theophylline ($n=3$), inhaled albuterol + beclometasone ($n=3$)
Asthma + rhinitis ($n=43$)	Oral antihistamine + inhaled albuterol ($n=28$), anti-histamine + albuterol + beclometasone ($n=9$), inhaled + nasal beclometasone + theophylline ($n=3$), all previous ($n=3$)

Results

Out of the initial 142 allergic patients, 43 dropped out within 3 years because of refusal to perform further visits or because they could not be found. Thus, we were able to evaluate the remaining 99 patients. The baseline demographic data of the patients are shown in Table 2.

At baseline, 44 patients suffered from AR alone and 12 from AA alone; the remaining patients suffered from AR+AA. The patients were homogeneously distributed for gender and age (Table 2).

After 10 years, 31.8% of the AR patients had also developed AA (mean onset time 5 years) and 50% of the patients with AA had also developed AR (mean onset time 7 years). In contrast, no clinical change was seen in the 43 patients initially suffering from AR+AA (Table 3). At the follow-up visit the severity of asthma was as follows: 5% severe, 32% moderate, 41% mild-persistent and 22% mild-intermittent. The most relevant factor influencing disease evolution, as assessed by the χ^2 -square test, seemed to be the positive familial atopy history (one or both relatives suffering from respiratory allergy). In fact 12 out of the 14 patients (86%) progressing to concomitant AA from AR alone, and five out of six patients (83%) who also developed AR from AA alone, had a positive family history for atopy (Table 4). Gender, age and smoking habit seemed not to play a relevant role. The number of skin sensitizations at baseline did not significantly influence the evolution of the disease, as shown in Table 4. The nature of the allergens (perennial, seasonal or both) also did not affect the natural history.

Noteworthy, 11 out of 17 (65%) patients with single sensitization at baseline developed new sensitizations within 10 years. Finally, there was no spontaneous remission of both asthma and rhinitis.

Discussion

The prevalence of AA and AR significantly varies among different countries. The recent epidemiological ISAAC study (2) conducted on about 500 000 adolescents reported

TABLE 2. Baseline (1986–87) demographics of the global population subdivided per disease

	Global population	Rhinitis	Asthma	Rhinitis + asthma
Patients	99	44	12	43
Sex (M/F)	50/49	20/24	6/6	24/19
Mean age	22.6	23.1	20.4	21.9
Age range	14–37	14–36	14–35	14–37
Positive family history*	63	29 (66%)	9 (75%)	25 (58%)
Smokers	27	9 (20%)	5 (42%)	13 (30%)
Single sensitization	17	8 (18%)	3 (25%)	6 (14%)
Two allergens	18	7 (16%)	3 (25%)	8 (19%)
> Two allergens	64	29 (66%)	6 (50%)	29 (67%)

*One or both relatives suffering from respiratory allergy.

TABLE 3. Evolution of the disease

At baseline		After 10 years		% Evolved
Disease	Patients	Disease	Patients	
Rhinitis and asthma	43	Rhinitis and asthma	43	0
Rhinitis alone	44	Rhinitis and asthma	14	31.8
		Rhinitis alone	30	
Asthma alone	12	Asthma and rhinitis	6	50
		Asthma alone	6	
Rhinitis or asthma	56	Rhinitis and asthma	20	36%

TABLE 4. Evolution depending on skin sensitizations and family history

1 or 2 skin positivities			> 2 skin positivities		P value χ -square
R to R + A	5/14	36%	9/14	64%	NS
A to A + R	3/6	50%	3/6	50%	NS

Negative family history for atopy			Positive family history for atopy		
R to R + A	2/14	14%	12/14	86%	0.01
A to A + R	1/6	17%	5/6	83%	0.01

R: rhinitis; A: asthma.

a prevalence ranging from 1.6 to 38% for asthma and from 1.4 to 39.7% for rhinitis. Noteworthy, a strict association between AR and AA has become evident (for review see 6). For instance, AR seems to precede or to accompany AA in 59–85% of allergic patients in all age groups (7), and AR is a risk factor for developing asthma (1,8). Moreover, in a recent work conducted with rigorous criteria it was shown that about 90% of allergic asthmatics also have rhinitis (9). The link existing between upper and lower respiratory allergy suggest the hypothesis of the *allergic rhinobronchitis* or *united airways disease*, meaning that respiratory allergy is an unique disorder varying its clinical expression from rhinitis to asthma. Indeed, the possible evolution from bronchial or nasal symptoms into each other can be observed only by means of long-term studies.

The results herein reported, obtained from a 10-year follow-up of selected patients, confirm the presently available data: a relevant part (31.8%) of patients with AR developed AA and 50% of patients with AA developed AR. The data come from a homogeneous population, since only patients with clinical evidence of atopy were included. Indeed, the long period of observation itself imposes some limitations to our study. For instance, the criteria for AA and AR have partly changed over the 10-year period considered herein. Moreover, the criteria used in 1986 did not include a severity staging. Nevertheless, the main

clinical criteria for diagnosing rhinitis and asthma have remained approximately the same, as has the skin test for ascertaining allergic sensitizations. Data on non-specific bronchial hyperresponsiveness are not provided because, at the time of the first diagnosis we used the ultrasonic fog test, which was subsequently abandoned in favour of the methacholine test. Finally, we have no information about the presence of non-specific bronchial hyperresponsiveness in rhinitics, since at the time of the first diagnosis, this was not considered relevant. The sample studied is relatively small, certainly because of the very long period of observation, therefore it is difficult to properly identify 'risk factors'; on the other hand, it is possible to state that positive familial history influences the evolution of the disease.

However, the high rate of progression of AR towards AA and *vice versa* is further confirmed on a merely clinical basis; this simple fact has potential important implications.

In fact, an appropriate diagnosis and survey of allergic patients may lead to a better treatment approach and to a significant socioeconomic saving, when costs of asthma are considered (10). Moreover, the epidemiological data taken together with the experimental evidence would envisage the realistic possibility of improving the treatment strategy of respiratory allergy: an optimal control of rhinitis may also improve asthma symptoms (11) or prevent their onset (12).

Acknowledgements

Partially supported by: ARMIA (Associazione Ricerca Malattie Immunologiche e Allergiche) and MURST (Ministry of University and Scientific-Technologic Research).

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