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Characteristics of patients with allergic polysensitization: the polismail study

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Key words

Rhinitis, asthma, polysensitization, quality of life

Summary

Background: *The natural history of respiratory allergy is commonly characterized by a worsening of symptom severity, frequent comorbidity of rhinitis and asthma, and polysensitization to aeroallergens. The polysensitization phenomenon starts since childhood and is rare to find monosensitized adult patients. However, there are few studies investigating the characteristics of polysensitized patients.* ***Methods:*** *This study was performed on a large cohort of patients with allergic rhinitis (assessed by ARIA criteria) and/or mild to moderate asthma (assessed by GINA). The kind and the number of sensitizations, their patterns, and the relation with quality of life (QoL) measured by the Juniper's RQLQ questionnaire, were evaluated.* ***Results:*** *Globally 418 patients*

(50.2% males, 49.8% females, mean age 26.4 years, range 3.5-65 years, 64 smokers, 371 non-smokers) were enrolled: 220 had allergic rhinitis alone, and 198 allergic rhinitis and asthma. The mean number of sensitizations was 2.6. Three hundred-five patients (73%) had persistent rhinitis (PER), 220 of them with moderate-severe form. There was no significant difference in rate of rhinitis and asthma in monosensitized or polysensitized patients. Most patients were sensitized to pollens, whereas only 24.2% of them were sensitized to perennial allergens. Polysensitization was significantly associated with some issues of QoL, confirming previous findings, but not with number of sensitizations. ***Conclusions:*** *This study provides data confirming for polysensitized patients the relevance of ARIA classification of AR. PER is the most common form of AR in this cohort, symptoms are frequently moderate-severe, and asthma is present in about the half of patients with AR.*

Introduction

Allergic rhinitis (AR) is very frequent as it affects up to 40% of people (1) and its prevalence is still increasing (2). Social and economic costs are substantial because of such high prevalence and daily activities, productivity, and quality of sleep are significantly affected (3). AR classification has been recently revised by the Allergic Rhinitis and its Impact on Asthma (ARIA) group (1). This classification includes a measurement of the frequency and duration of the symptoms. Thus, intermittent AR (IAR) is defined by symptoms occurring for <4 days/week or <4 consecutive weeks. Persistent AR (PER) is defined by symptoms occurring for >4 days/week and >4 consecutive weeks. Additionally, a severity scale of mild to moderate-severe was included in the revised classification. This new classification has been object of some studies that compared it with the old one that was based on the period around the year of symptom occurrence, such as seasonal or perennial.

Demoly et al. assessed the characteristics of patients presenting for AR during the spring season (SAR) and patients presenting during the fall-winter season (PAR) (4). Their results show that SAR was not synonymous of IAR as well as PAR is not equivalent to PER. More recently, Bauchau and Durham performed a similar study in a larger population (5). They concluded that the classic types of SAR/PAR cannot be used interchangeably with the new classification of IAR/PER, as they do not represent the same status of disease. In addition, they stated that PER constitutes a distinct disease.

Moreover, it is well known that AR is frequently associated with asthma as evidenced by several studies (6, 7). Asthma is classified on the basis of severity and duration of symptoms as intermittent or persistent that may include mild, moderate or severe type (8). In addition, AR is characterized by the phenomenon of polysensitization, i.e. allergic patients tend to become sensitized to more allergens over the time (9).

Quality of life (QoL) is impaired in patients with AR (10) and asthma (11). This issue has been assessed in a number of studies, but the global relationship among type of AR, association with type of asthma, number of sensitizations, and QoL has been not investigated still now.

Therefore, this study was aimed at evaluating these parameters in a large cohort of Italian patients suffering from AR.

Material and methods

Study Design

The study was conducted in 26 Allergy Centres homogeneously distributed in Italy. It was designed to include samples representative of the general population and to have the ability to identify the new diagnosed cases. The study was approved by the Review Board of each participating center and an informed consent was obtained from each patient. The first part of the study was performed during autumn-winter 2005.

Subjects

418 patients (50.2% males, 49.8% females, mean age 26.4 years, range 3.5-65 years, 64 smokers, 371 non-smokers) with allergic rhinitis were prospectively and consecutively

evaluated. A detailed clinical history was taken and a complete physical examination was performed. The patients were included in the study on the basis of a clinical history of allergic rhinitis and presence of nasal symptoms according to validated criteria (1).
The diagnosis of intermittent or persistent allergic rhinitis was made on the basis of a history of nasal symptoms and positive skin prick test (1).
Skin prick tests were performed as stated by the European Academy of Allergy and Clinical Immunology (12). The panel consisted of: house dust mites (*Dermatophagoides farinae* and *pteronyssinus*), cat, dog, grasses, *Compositae*, *Parietaria officinalis*, birch, hazel, olive tree, cypress, *Alternaria*, *Cladosporium*, *Aspergillus* (Stallergenes, Milan, Italy).
The diagnosis and severity classification of asthma were made according to GINA criteria (8). Moreover, patients gave a subjective judgment of the severity of their condition and the use of drugs in the past 12 months by a visual analogue scale (VAS).
Quality of Life was evaluated by the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ); it consists of 28 items distributed in seven dimensions: sleep problems (3 items), non-hay fever symptoms (7 items), practical problems (3 items), nasal problems (4 items), eye symptoms (4 items), activities (3 items), and emotions (4 items). Responses to the items are scored on a 7-point Likert scale, while dimensions and overall scores are scored on a 0-6 scale, the lower the score, the better the HRQL (10).

Statistical Analysis

Continuous and/or discrete parameters were reported as mean, SD, third quartile, and frequency. Categorical parameters were reported in contingency tables.
Homogeneity of data was evaluated by Fisher exact test. The significance of the values concerning the relationship coefficient was calculated by Student's t test. The analysis on factors determinant the polysensitization was performed by polycotomic logistic regression, considering as dependent variable: gender, age, severity of rhinitis, VAS values, and QoL. About these parameters, coefficient values, standard error, coefficient/standard error ratio, and Odds ratio were reported.
The p value concerning the statistical significance was set at 0.05. Statistical analysis was performed by statistical package BMDP Dynamic produced by BMDP Statistical software, Inc.

Results

The distribution of patients on the basis of their age shows that 55 (12.6%) had < 10 years, 113 (25.7%) 11-20 years, 112 (25.7%) 21-30 years, 101 (23.2%) 31-40 years, 37 (8.5%) 41-50 years, and 18 (4.1%) > 50 years. Of the 418 patients included in the study, 220 had AR alone, 198 (47.4%) had AR associated with asthma, as reported in table 1. One hundred-thirteen patients had IAR, corresponding to 29% of sample. Three hundred-five patients had PER (73%). Mild severity was present in 34 patients with IAR and 85 with PER. Moderate-severe form was in 79 patients with IAR and 220 with PER. Thus PER was the type more frequent as well as moderate-severe was the severity more relevant. The type and severity of AR did not affect the association with asthma (Fisher test = 0.7476, Prob. = 0.8620).
Concerning asthma severity, 102 patients had intermittent form, and 96 persistent form (46 mild, 44 moderate, and 6 severe). However, the type and severity of AR did

Table 1 - Type and severity of allergic rhinitis and asthma in 419 patients with allergic rhinitis

Rhinitis Classification	Rhinitis alone	Rhinitis and Asthma	Total
Mild Intermittent	7.3% (16/220)	9.1% (18/198)	8.1% (34/418)
Moderate-Severe Intermittent	20% (44/220)	17.7% (35/198)	18.9% (79/418)
Mild Persistent	20% (44/220)	20.7% (41/198)	20.3% (85/418)
Moderate-Severe Persistent	52.7% (116/220)	52.5% (104/198)	52.6% (220/418)
Asthma Classification			
Intermittent	51.5% (102/198)		
Mild Persistent	23.2% (46/198)		
Moderate Persistent	22.2% (44/198)		
Severe Persistent	3% (6/198)		

not affect the severity of associated asthma (Fisher test = 2.6320, Prob. = 0.4519).
Only 10% of patients were monosensitized, the number of sensitizations is reported in figure 1. The number of patients was progressively decreasing with the increase of number of sensitization, but it was not associated with possible presence of asthma (Fisher test = 0.6843, Prob. = 0.7102).

Figure 1 - Rhinitis and rhinitis plus asthma according to number of sensitizations

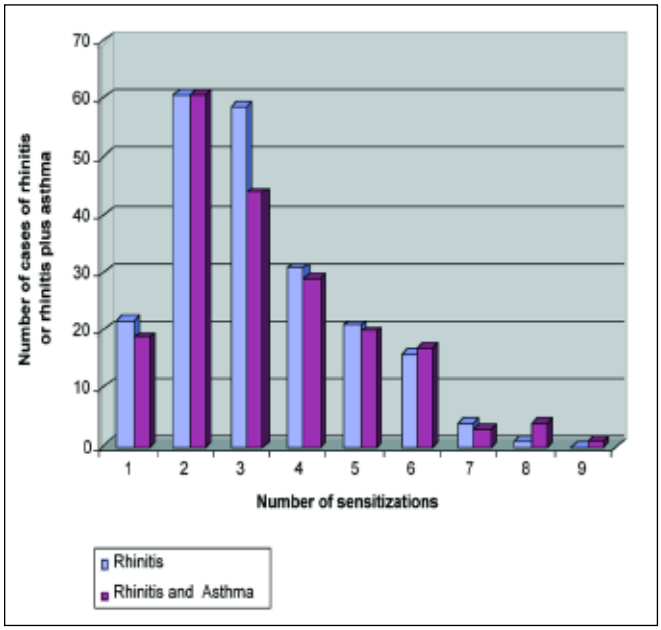


Figure 2 - Severity of rhinitis and kind of sensitization

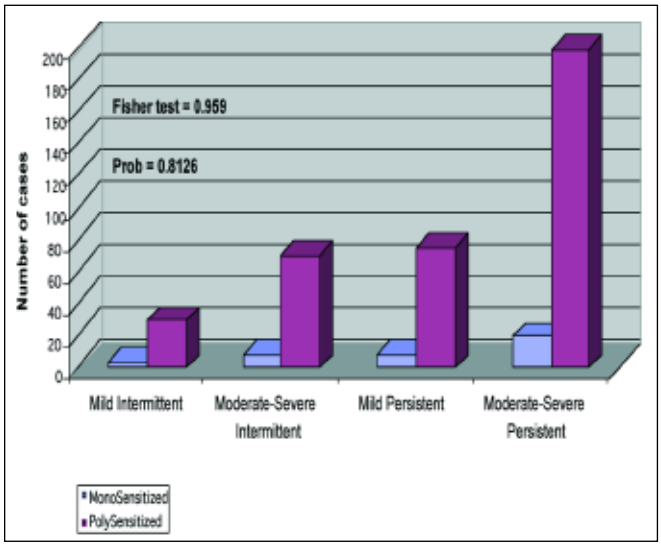
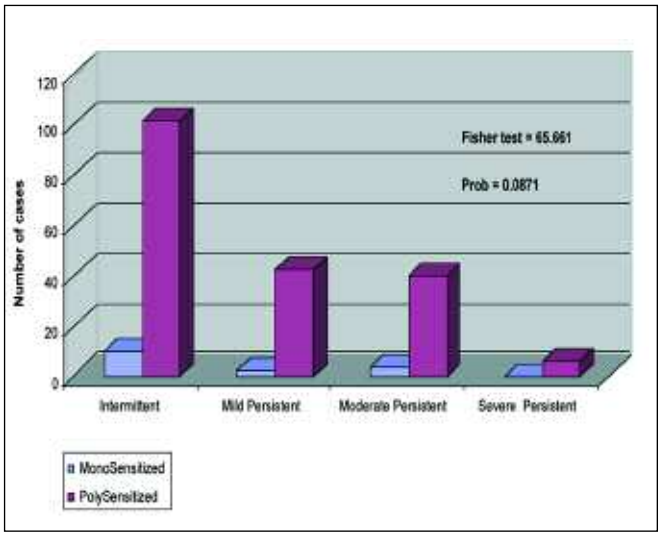


Figure 3 - Severity of asthma and kind of sensitization



Globally considering mono- or polysensitization as reported in figures 2 and 3, polysensitization did not affect the type and severity of AR (Fisher test = 0.9529, Prob. = 0.8126), whereas there was a trend for the association between polysensitization and asthma severity (Fisher test = 6.5661, Prob. = 0.0871), indeed only polysensitized patients had severe persistent asthma.
About specific sensitizations, grasses were the most relevant allergen, followed by house dust mites and several pollens, as reported in table 2. About the symptoms severity assessed by VAS, ocular symptoms had a mean value of 5.5 (S.D. 2.4), nasal symptoms 7.3 (S.D. 2.1), and bronchial symptoms 3.5 (S.D. 3.1).
Concerning the use of drugs assessed by VAS, oral antihistamines were the most consumed (5.9, S.D. 3.1), followed by topical nasal corticosteroids (4.0, S.D. 3.3), in-

Table 2 - Type of allergen sensitizations to SPT

Allergen	Number of positive SPT	%
Grasses	295	76.4
Dermatophagoides	183	47.4
Parietaria	150	38.9
Betulaceae	148	38.3
Olive	103	26.7
Ragweed	90	23.3
Cat	87	22.5
Dog	51	13.2
Alternaria	40	10.4
Cypress	37	9.6

Table 3 - Relationship among severity and diagnosis of rhinitis and asthma, symptoms score assessed by VAS, drugs use assessed by VAS, age, and sensitizations

Relationship coefficient	Severity	Prob.	Signif.
Age	0.0498	0.3672	N.S.
Diagnosis	-0.0233	0.6732	N.S.
Sensitizations	-0.0399	0.4701	N.S.
Symptoms by VAS			
Ocular	0.0184	0.7391	N.S.
Nasal	0.2335	0.0000	P<0.01
Bronchial	-0.0925	0.2143	N.S.
Drugs use by VAS			
Inhaled corticosteroids	0.0899	0.2032	N.S.
Beta2 long acting	0.0312	0.6594	N.S.
Beta2 short acting	0.1827	0.0093	P<0.01
Nasal corticosteroids	-0.0407	0.5652	N.S.
Antihistamines	-0.0123	0.8621	N.S.
Antileukotrienes	0.2201	0.0016	P<0.01

Table 4 - Polycotomic logistic regression model for relating QoL issue with polysensitization

						C.I. 95%	
Factor	Coefficient	E.S.	Coeff./E.S	Prob.	Odds ratio	Lower Limit	Higher Limit
Activity 1	0.208	0.075	2.79	P<0.01	1.2	1.1	1.4
Bad Sleep	0.245	0.098	2.5	P<0.05	1.3	1.1	1.5
Headache	0.164	0.065	2.52	P<0.05	1.2	1	1.3
Eye complaint	0.126	0.064	1.96	P=0.05	1.1	1	1.3
Irritability	0.168	0.072	2.33	P<0.05	1.2	1	1.4

haled corticosteroids (2.6, S.D. 3.4), long-acting Beta2 agonists (2.0, S.D. 3.1), short-acting Beta2 agonists (1.4, S.D. 2.3), and antileukotrienes (1.2, S.D. 2.8).

A significant relationship was found between severity of rhinitis and nasal symptoms score by VAS, moreover asthma severity was related with short acting Beta2 agonists use and antileukotrienes use, as reported in table 3.

However, the polycotomic logistic regression, considering as dependent variable the sensitizations number, does not single out significant prognostic factors.

As to QoL assessment by the specific questionnaire, the most impaired item was activities, followed by practical problems and nasal symptoms. A significant relationship between polysensitization and some issues of QoL was found, as reported in table 4.

Discussion

In this study, we addressed several questions about the characteristics of patients with AR assessing the new ARIA classification of AR (1) and the relationships with asthma co-morbidity and number of sensitisations.

Polysensitisation is an immunological phenomenon that is clinically relevant and seems to be increasing from an epidemiological point of view as recently reported in Italian surveys (7, 13, 14). Therefore, the increasing number of sensitisations seems to characterize the natural history of allergic patient and may represent an evolutionary aspect of allergic reaction. The problem concerns whether this phenomenon may cause an impairment of clinical picture. This study provides some informations about this issue.

Firstly, most patients (73%) have the PER form and the most frequent severity grade is moderate-severe (71.5%). This finding is relevant and appears to be different in comparison with previous studies conducted in general adult population: in Bauchau's study the percentage of patients with PER was 29%. This contrasting finding may be partially explained by the relevant number of sensitizations in our cohort and may depend on the type of studied populations. Indeed, two recent studies conducted on selected patients showed that the percentage distributions are inverse in comparison with Bauchau's study (13, 15). Moreover, the pollen seasons are very prolonged in Italy in comparison with other European countries, mainly concerning Northern ones. This fact may account the persistence of symptoms in our patients.

Secondly, about half patients with AR have also asthma. Thus, asthma represents an important co-morbidity for AR. This finding confirms the statements of ARIA document (1). About asthma severity, most patients had the intermittent form, whereas almost all patients with persistent asthma had mild-moderate severity of symptoms. This finding is partially conflicting with other surveys on asthma. Probably, it might be explained by the concomitant AR. Indeed, it is well known that AR represents a worsening factor for asthma (2).

Thirdly, most patients (90%) are polysensitized. This finding is not surprising as it was reported in previous studies (9,11). This finding outlines the clinical relevance of polysensitization as this phenomenon is very frequent and may influence the aptitude of physicians in managing allergic patients, mainly concerning the prescription of specific immunotherapy.

Fourthly, polysensitization does not appear to be relevant for asthma co-morbidity, and severity of both rhinitis and asthma. Also this finding is partially conflicting with a previous survey conducted in young AR patients (16), even though it seems singling out a trend for asthma co-morbidity and severity of both rhinitis and asthma in patients with polysensitisations. Probably these conflicting findings might depend on several confounding factor: age of patients, type of sensitisations, and overall duration of rhintis. In this regard, a very recent paper showed that the duration of allergic rhinitis and mite sensitisation are relevant risk factor for inducing spirometric impairment (17). Moreover, drug therapy partially could interfere the nose-bronchi relationship, even though it is well known that pharmacotherapy is not able of modifying the natural course of allergy.

Grasses are the most relevant allergen followed by house dust mites. This finding confirms previous studies conducted in Italy (16).

In addition, there is a significant relationship between degree of symptoms and severity of rhinitis as well as between use of both short acting bronchodilators and antileukotrienes and asthma severity. It is to consider that the studied population was essentially composed by patients with AR. However, this study was conducted during a season, i.e. autumn-winter, characterized by reduced severity of symptoms. This issue may constitute a limitation of this study.

Finally, polysensitisation was significantly associated with some issues of QoL, confirming previous findings (18). Therefore, polysenstization may represent an aggravating factor that contributes to impair clinical features in allergic patients.

In conclusion, this study provides new data confirming the relevance of ARIA classification of AR in polysensitized patients. PER is the most common form of AR in this cohort, symptoms are frequently moderate-severe, and asthma is present in about half patients with AR. Therefore, the new ARIA classification and its recommendations should be firmly considered mainly in patients with polysenstizations. Thus, polysenstitization has to be considered as a relevant aspect in allergic patients and has to be carefully evaluated, mainly if immunotherapy has to be prescribed. However, it is needed to address further studies to such issue to confirm these findings.

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