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Original article

A survey on features of allergic rhinitis in children

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Abstract

Objective:
A number of epidemiologic studies evaluated the prevalence of allergic rhinitis (AR), but few data are available on its different clinical presentations. We addressed this survey to assess the features of AR in children and adolescents.

Methods:
Thirty-five centers in Italy included 2623 pediatric patients with rhinitis, of whom 2319 suffered from AR, while 304 had other kinds of rhinitis. For each patient a standardized questionnaire was filled in, including ARIA classification, the duration of symptoms, the allergen identified as clinically relevant, the co-morbidities, the kind of treatment, the response to treatment, the satisfaction with the treatment, and the feasibility of allergen immunotherapy (AIT).

Results:
Of the 2319 patients, 597 (25.7%) had mild intermittent, 701 (30.2%) mild persistent, 174 (7.5%) moderate–severe intermittent, and 773 (33.3%) moderate–severe persistent AR. The allergens most relevant were grass pollen and dust mites. The most frequently used drugs were oral antihistamines (83.1%) and topical corticosteroids (63.5%). The response to treatment was judged as excellent in 13.5%, good in 45.1%, fair in 30.8%, poor in 10%, and very bad in 0.6% of cases. The satisfaction with treatment was judged as very satisfactory in 15.2%, satisfactory in 61.8%, unsatisfactory in 22.4%, and very unsatisfactory in 0.5% of cases. AIT was considered indicated in 53.1% of patients with mild intermittent, 79.2% of moderate–severe intermittent, 72.6% of mild persistent, and 82.7% of moderate–severe persistent AR.

Conclusions:
The limitation of this study is that the population was not unselected and this prevents epidemiological significance. These results offer confirmation of the adequacy of ARIA guidelines in classifying patients with AR and of the association of severe phenotype with lack of success of drug treatment.

Introduction

Allergic rhinitis (AR) is a very common disease with a high and still increasing world prevalence[1]. In Italy, the most recent data show a prevalence of AR of 18.9% in children and 35.1% in adolescents[2]. The burden of AR includes substantial social and economic costs related to such high prevalence, and to impairment of patients' daily activities, productivity, and quality of sleep[3–5]. AR may have different clinical presentations according to the kind of symptoms and their duration. The predominance of sneezing and nasal discharge or nasal blockage inspired the definition of two subtypes of AR patients as 'sneezers/runners' and 'blockers', respectively, and the period of occurrence of symptoms defined the two forms of 'seasonal' or 'perennial rhinitis'. A recent study found

that sneezers/runners prevailed in seasonal rhinitis and blockers prevailed in perennial rhinitis[6]. However, the Allergic Rhinitis and its Impact on Asthma (ARIA) document, endorsed by the World Health Organization, introduced a new classification of AR based on duration and severity of symptoms. Intermittent AR (IAR) was defined by symptoms occurring for <4 days/week or <4 consecutive weeks, while persistent AR (PER) was defined by symptoms occurring for >4 days/week and >4 consecutive weeks. According to the kind of symptoms, a severity scale of mild to moderate–severe (based on the AR impact on both daily activities and quality of life) was suggested[7]. The ARIA classification is currently widely used because it was validated in general[8] and also concerning the pediatric population[9].

We addressed this multicentric survey to assess the prevalence of the different ARIA stages and the features of the clinical presentations of AR in a large population of children and adolescents.

Patients and methods

Thirty-five Pediatric Allergy Centers throughout Italy included an overall number of 2623 patients presenting with rhinitis. The diagnostic flow-chart suggested by ARIA guidelines[7,9] was used, based on a detailed clinical history, to highlight the relationship between symptoms and exposure to the various aeroallergens, on the results of skin prick tests (SPT), and on the concordance between history and SPT results. In patients with negative SPT, nasal cytology was performed, as previously described[10], to assess the different types of non-allergic rhinitis. Patients who also had a negative result in nasal cytology were classified as having idiopathic rhinitis. For each patient with AR the attending physician must fill in a standardized questionnaire, which was previously validated by the Società Italiana di Allergologia e Immunologia Pediatrica (SIAIP). The items on the questionnaire were the ARIA classification of rhinitis, the duration of symptoms, the results of SPT, the allergen identified as clinically relevant, the co-morbidities, the kind of treatment, the response to treatment, the satisfaction with the treatment, and the feasibility of allergen immunotherapy (AIT). Concerning the response to treatment the outcome was assessed as excellent, good, fair, poor and bad. Regarding satisfaction with treatment the estimation was evaluated as very satisfied, satisfied, unsatisfied and very unsatisfied. Continuous parameters, such as age and duration of symptoms, were reported as mean, median, and standard deviation, while categorical parameters were reported as contingency tables. Data were statistically analyzed by the chi-squared test for two data tables and by log-linear models for more that two data tables. A p value lower than 0.05 was considered significant. Correlations were analyzed by linear regression.

Results

Out of the 2623 patients, 2319 (88.4%, 1388 children [range: 5–13 yrs] and 931 adolescents [range: 14–17]) were diagnosed as suffering from AR, while 304 had other kinds of rhinitis, the most common being infective rhinitis (127 cases), non-allergic rhinitis with eosinophilia (NARES, 59 cases), and idiopathic rhinitis (56 cases). Of the 2319 patients with AR, 597 (25.7%) had mild intermittent, 701 (30.2%) mild persistent, 174 (7.5%) moderate–severe intermittent, and 773 (33.3%) moderate–severe persistent AR; in 74 cases the data was missing. The mean duration of AR was 3.1 ± 2.4 years. Concerning sensitization, Table 1 shows all the allergens eliciting positive SPT and their clinical relevance as assessed by patients' history; 1092 patients were allergic to grass pollen, 395 with intermittent and 701 with persistent AR, 641 with mild and 456 with moderate–severe AR; 992 were allergic to dust mites, 280 with intermittent and 670 with persistent AR, 587 with mild and 409 with moderate–severe AR; 1018 patients had more than one sensitization. Table 2 reports the identified co-morbidities. Patients with no co-morbidities had a lower frequency of mild AR, while patients with two or more co-morbidities had a higher frequency of moderate–severe AR ($p \leq 0.01$).

Table 1. Allergens eliciting a positive skin prick test (SPT) and their clinical relevance.

Allergen	Number of positive SPT	% of total (according to clinical relevance)
Grass pollen	1092	47.1
House dust mites	992	42.8
Parietaria pollen	352	15.2
Olive pollen	249	19.7
Betulaceae pollen	135	5.8
Cypress pollen	105	4.5
Alternaria spores	61	2.6
Animal epithelia	58	2.5
Compositae pollen	56	2.4
Ragweed pollen	44	1.9
Other pollens	18	0.8
Foods	4	0.2
Other allergens	171	7.4

Table 2. Reported co-morbidities in patients with AR.

Co-morbidity	Number of cases (%)
Conjunctivitis	1200 (51.7)
Asthma	930 (40.1)
Sinusitis	240 (10.2)
Sleep disturbances	159 (6.9)
Adenoids/tonsils hypertrophy	153 (6.6)
Dermatitis	95 (4.1)
Cough	38 (1.6)
Nasal polyps	30 (1.3)
Urticaria	24 (1.0)
Oral allergy syndrome	10 (0.4)
Recurrent respiratory infections	9 (0.4)

The most frequently used drugs were oral antihistamines (1927 patients, 83.1%), and topical corticosteroids (1473 patients, 63.5%), followed by anti-leukotrienes (439, 18.9%), topical antihistamines (434, 18.7%), oral corticosteroids (119, 5.1%), nasal decongestant (91, 3.9%), chromones (65, 2.8%), and others (477, 20.6%). Table 3 reports the treatments and their rate of use in the two major causes of AR, grass pollen and dust mites. In 2208 questionnaires (95.2%) the response to treatment was available: it was judged as excellent in 298 cases (13.5%), good in 995 (45.1%), fair in 680 (30.8%), poor in 221 (10%), and very bad in 14 (0.6%). In 2191 questionnaires (94.6%) the satisfaction with treatment was available: the treatment was judged as very satisfactory in 334 cases (15.2%), satisfactory in 1354 (61.8%), unsatisfactory in 491 (22.4%), and very unsatisfactory in 12 (0.5%). Figure 1 shows the correlation between response to treatment and patients' satisfaction, which was significant ($p<0.01$). The rate of dissatisfaction was 15.8% in patients with mild AR and 32.4% in patients with moderate–severe AR, this difference being highly significant ($p<0.0001$). The data on the suitability of AIT were available in 2273 questionnaires: in 1618 cases (71.2%) the treatment was considered by the attending physician as indicated. This concerned 308 (53.1%) patients with mild intermittent, 137 (79.2%) moderate–severe intermittent, 502 (72.6%) mild persistent, and 626 (82.7%) moderate–severe persistent AR. Considering the two major causes of allergy, AIT was believed as suitable in 31.3% of patients allergic to mites and in 28.6% of patients allergic to grass pollen.

Table 3. Treatments prescribed in grass-pollen-induced and mite-induced allergic rhinitis (AR).

Treatment	Grass-pollen-induced AR	Mite-induced AR
Oral antihistamines	396 (86.8%)	364 (86.3%)
Topical corticosteroids	301 (66%)	309 (73.2%)
Antileukotrienes	96 (21.1%)	149 (35.3%)
Topical antihistamines	83 (18.2%)	55 (13%)
Bronchodilators	81 (17.8%)	86 (20.4%)
Oral corticosteroids	30 (6.6%)	36 (8.5%)
Nasal decongestants	18 (3.9%)	18 (4.3%)
Chromones	10 (2.2%)	12 (2.8%)
Others	115 (10.5%)	143 (11.8%)

Discussion

The ARIA classification introduced reliable criteria for identifying the clinical phenotype of patients with AR. A recent study showed that the ARIA severity classification in mild, moderate, and severe clearly discriminates the impact of AR in all domains of quality of life and categorized symptom score[11]. Of note, the adequacy of the ARIA classification was also confirmed by the correlation of the ARIA severity grade and nasal cytology, which showed different cell counts according to different severity; in particular, in moderate–severe AR significantly increased counts of mast cells and lymphocyte or plasma cells were found[10,12]. However, thus far the ARIA staging has been used very rarely in epidemiologic studies[13]. In particular, one study on 1275 children in Spain found that 7% of subjects had mild intermittent AR, 3.2% had mild persistent AR, 52% had moderate–severe intermittent, and 37.6% had moderate–severe persistent AR[9]. The present study was aimed at investigating the features of AR in a large population of children and adolescents. Concerning the ARIA stage, 25.7% of patients had mild intermittent, 30.2% had mild persistent, 7.5% had moderate–severe intermittent, and 33.3% had moderate–severe persistent AR. These data are different from those in the

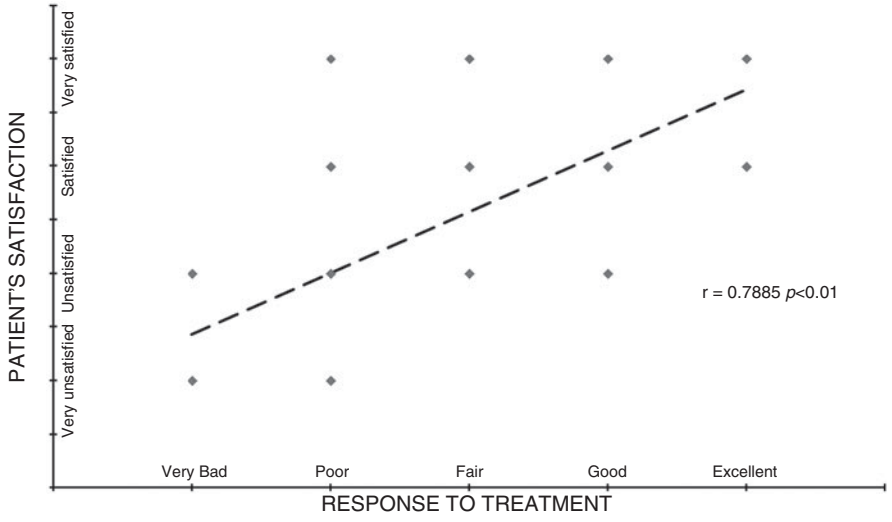

Figure 1. Correlation between patients' satisfaction and response to treatment. Linear regression analysis shows $r=0.7885$ ($p<0.01$).

Spanish study cited above, only the rate of moderate–severe persistent AR (36.7% vs. 33.3%) being comparable in the two studies, while the rates of mild intermittent and mild persistent AR were much higher in our study. It is difficult to argue about such difference. The factor possibly influencing the contrasting findings we may suppose is that in the Spanish studies not only allergy centers but also otorhinolaryngology centers (the number of which was not reported) participated, and one may speculate that children with mild AR are less likely to be referred to the otorhinolaryngologist.

We analyzed a number of aspects for their possible association with AR phenotype, including the results of SPT, the allergen identified as clinically relevant, the co-morbidities, the kind of treatment, the response to treatment, the satisfaction with treatment, and the feasibility of AIT, that is the only available treatment acting on the causes of allergy, being able to reduce the immunological and clinical reactivity to the responsible allergen[14]. The results highlighted interesting issues. Concerning the causative allergens, grass pollen and house dust mites were confirmed to be the two major actors in AR[15,16], with no difference in the distribution of mild and moderate–severe disease and also of intermittent and persistent form in grass-allergic or mite-allergic aspects. This further confirms the suitability of the ARIA classification, because the previous grouping in seasonal and perennial for grass pollen- and mite-induced AR would not assess clinical importance according to duration. Co-morbidities were more common in patients with moderate–severe AR, the commonest being conjunctivitis. The association of AR with allergic conjunctivitis defines the picture of rhinoconjunctivitis, which occurs very frequently[17] and was present in approximately 52% of the subjects we studied. The other two most common co-morbidities were asthma (40% of patients), and sinusitis (10% of patients)[7,18]. Of note, an oral allergy syndrome was present in only 0.4% of subjects. This seems to contrast with the available data, that show much higher figures[19], but the kind of population we studied, including children and adolescents, accounts for the difference, because sensitization to foods cross-reacting with pollens or mites is delayed and generally becomes clinically expressed in adults[20].

Considering treatment, the most frequently used drugs were oral antihistamines (83%) and topical corticosteroids (63%). This is in accordance with the suggestions from the ARIA guidelines, that reviewed the clinical efficacy of such therapeutic agents by evidence from controlled trials[7,18]. However, only a few studies explored patients' satisfaction with prescribed treatments, which is a crucial issue that may have a high clinical relevance by significantly affecting treatment compliance. A large survey of adult allergic patients has investigated patient and physician satisfaction with antihistamine treatment, showing that second-generation antihistamines were considered by both patients and physicians to be effective and well tolerated[21]. A similar study has been conducted in allergic children: a better risk–benefit ratio was reported with the second-generation antihistamine levocetirizine compared with first-generation antihistamines, leading the authors to conclude that levocetirizine seems to be a preferred and appropriate future treatment choice for allergic children[22]. However, the major limitation of these two studies is that they were sponsored by the company producing levocetirizine. A recent survey on 301 adult patients with AR, mostly treated with antihistamines and nasal corticosteroids, found that only 33.5% of them were satisfied with treatments. Factors significantly associated with treatment dissatisfaction were female gender, presence of co-morbidities, and severity of rhinitis[23]. In the present study, the response to treatment as assessed by the physician was analyzed: it was judged as excellent in 13.5%, good in 45.1%, fair in 30.8%, poor in 10%, and very bad in 0.6% of cases. Concerning satisfaction with treatment, the judgment was very satisfactory in 15.2%, satisfactory in 61.8%, unsatisfactory in 22.4%, and very unsatisfactory in 12 (0.5%) of cases. The data on response to treatment and satisfaction with treatment was significantly correlated. The judgment of poor and very bad concerning response to treatment, and of unsatisfactory and very unsatisfactory concerning satisfaction, warrant the highest attention from physicians. In particular, dissatisfaction was significantly more frequent in patients with moderate–severe AR than in those with mild AR. A recent advance in the improvement of therapeutic strategy in AR was achieved by the understanding that patients with more severe AR and resistance to drug treatment have, as demonstrated in a controlled trial on 410 patients, a good response to AIT[24]. Moreover, a recent post-hoc analysis of previously published studies showed that the higher clinical efficacy from immunotherapy is achieved in patients with more severe AR[25]. The data on the suitability of AIT in our survey showed that, with the exception of mild intermittent AR, there were no significant differences in the rate of indication for such treatment according to severity. This attitude is likely to be influenced by the fact that the study was performed in Pediatric Allergy Centers, where the physicians have good knowledge of the characteristics of AIT. In particular, the capacity to prevent asthma when applied in children with rhinitis offers a clear advantage for pediatricians[26]. Moreover, the indications in case of concomitant asthma[27] and recent data suggesting the feasibility of AIT in patients with allergic polysensitization[28] are other issues favoring AIT. Also, its cost-effectiveness compared with drug treatment, showed by a number of studies and mainly due to the maintenance of clinical benefit once AIT is discontinued[29], further reinforce the role of this treatment. The currently emerging data on the need for optimally targeting patients with severe AR not controlled by drugs needs to be acknowledged by pediatricians and

specialists involved in diagnosis and treatment of AR to provide these patients with an effective therapy.

Conclusions

This study confirms the adequacy of the ARIA guidelines in identifying the clinical forms of AR, particularly when the pediatric population is addressed. The phenotype of severe AR insufficiently responding to drug treatment is of special interest. Our findings show that in children and adolescents with moderate–severe AR caused by inhalant allergens both patients' satisfaction and clinical success of drug treatment, as judged by the physician, are scarce. This deserves a search for more effective therapies for severe AR, aimed at treating the cause of AR and not only its symptoms, such as AIT.

Transparency

Declaration of funding

No external funding was secured for this study. Contributorship of authors: A.M.Z. conceptualized and designed the study, contributed to analysis and interpretation of data, critically reviewed the manuscript and approved the final manuscript as submitted; L.I. conceptualized and designed the study, contributed to analysis and interpretation of data, critically reviewed the manuscript and approved the final manuscript as submitted; G.D.C. conceptualized and designed the study, critically reviewed the manuscript and approved the final manuscript as submitted; C.I.: contributed to analysis and interpretation of data, drafted the initial manuscript, critically reviewed the manuscript and approved the final manuscript as submitted; F.F. conceptualized and designed the study, contributed to analysis and interpretation of data, drafted the initial manuscript, critically reviewed the manuscript and approved the final manuscript as submitted; I.D.'A. contributed to analysis and interpretation of data, critically reviewed the manuscript and approved the final manuscript as submitted; M.S. contributed to analysis and interpretation of data, critically reviewed the manuscript and approved the final manuscript as submitted; P.P. contributed to analysis and interpretation of data, critically reviewed the manuscript and approved the final manuscript as submitted; M.D. conceptualized and designed the study, contributed to analysis and interpretation of data, critically reviewed the manuscript and approved the final manuscript as submitted.

Declaration of financial/other relationships

F.F., P.P., I.D.'A. and M.S. are employees of Stallergenes Italy. C.I. is a scientific consultant for Stallergenes Italy. A.M.Z., L.I., G.D.C. and M.D. have disclosed that they have no significant relationships with or financial interests in any commercial companies related to this study or article.

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