ORIGINAL ARTICLE

Rhinitis and its Association With Asthma in Patients Under 14 Years of Age Treated in Allergy Departments in Spain

MD Ibáñez,[1] A Navarro,[2] MC Sánchez,[3] C Rondón,[4] J Montoro,[5] V Matéu,[6] M Lluch-Bernal,[7] B Fernández-Parra,[8] MT Dordal,[9] I Dávila,[10] J Conde,[11] E Antón,[12] C Colás,[13] A Valero,[14,15] (SEAIC Rhinoconjunctivitis Committee)

[1]Department of Allergology, Hospital Infantil Universitario Niño Jesús, Madrid, Spain
[2]Department of Allergology, Hospital El Tomillar, AH de Valme, Sevilla, Spain
[3]Department of Allergology, CE Virgen de la Cinta, H. Juan Ramón Jiménez, Huelva, Spain
[4]Department of Allergology, Hospital Carlos Haya, Malaga, Spain
[5]Department of Allergology, Hospital La Plana, Villarreal, Castellón, Spain
[6]Department of Allergology Hospital Universitario N.S. Candelaria, Tenerife, Spain
[7]Department of Allergology, Complejo Hospitalario de Toledo, Toledo, Spain
[8]Department of Allergology, Hospital El Bierzo, Ponferrada, León, Spain
[9]Department of Allergology, Fundació Hospital Sant Pere Claver, Barcelona, Spain
[10]Department of Allergology, Hospital Universitario, Salamanca, Spain
[11]Department of Allergology, Hospital Virgen Macarena, Sevilla, Spain
[12]Department of Allergology, Hospital Universitario Marqués de Valdecilla, Santander, Spain
[13]Department of Allergology, Hospital Clínico Universitario, Zaragoza, Spain
[14]Allergy Unit, Department of Pneumology, Hospital Clínic i Universitari, Barcelona, Spain
[15]Centro de Investigación Biomédica en Red (CIBER) de Enfermedades Respiratorias, Barcelona, Spain

In memory of our colleague and friend, José Conde

Abstract

Background: Allergic rhinitis is the most frequent chronic allergic disease in children, and may be an important risk factor for the subsequent development of asthma.
Objective: To describe the characteristics of patients younger than 14 years of age presenting with rhinitis and the possible association with asthma.
Methods: We carried out a prospective, observational, descriptive, cross-sectional epidemiologic study (*Alergológica 2005*) of 917 patients under the age of 14 consulting for the first time in allergy departments in Spain.
Results: Rhinitis was diagnosed in 42.5% of the children. The association between asthma and rhinitis was significantly higher in children than in adults (44.9% vs 35.5%; $P<.05$). Time from onset of rhinitis was significantly associated with the development of asthma (2.97 vs 2.06 years; $P<.0001$). Allergy was the most frequent cause of rhinitis in children with and without asthma. Allergy to epithelia and fungi was more frequent in children with rhinitis and asthma than in children with rhinitis alone. We found no differences in the frequency of treatment with immunotherapy between children with and without asthma.
Conclusion: Rhinitis was frequently associated with asthma in children consulting for the first time at allergy departments. Time since onset of rhinitis and sensitivity to epithelia and fungi were associated with the development of asthma.

Key words: Allergic rhinitis in children. Rhinitis and asthma in pediatric patients.

Resumen

Antecedentes: La rinitis alérgica es la enfermedad alérgica crónica más frecuente en niños y puede constituir un importante factor de riesgo para el padecimiento de asma.
Objectivo: Presentar las características de los sujetos menores de 14 años con rinitis y su relación con el asma.
Métodos: Se realizó un estudio epidemiológico (*Alergológica 2005*) observacional descriptivo de tipo transversal con recogida prospectiva de la información, en 917 sujetos menores de 14 años atendidos por primera vez en consultas de alergología en España.
Resultados: Al 42.5% de los niños que acudieron por primera vez a consultas de Alergología se les diagnosticó de rinitis. En el 44.9 % se asoció asma, con una frecuencia significativamente superior a la de la población mayor de 14 años (35.5%) del mismo estudio (p<0.05). El tiempo de evolución de la rinitis se asoció de forma significativa con el desarrollo de asma (2,97 frente a 2.06 años; p< 0,0001). La etiología alérgica fue la causa más frecuente de la rinitis tanto en niños con asma como sin ella. La alergia a epitelios y hongos fue más frecuente en cuanto a la presentación clínica de rinitis-asma que de rinitis aislada. No hubo diferencia entre la frecuencia del tratamiento con inmunoterapia en los niños con y sin asma.
Conclusiones: La rinitis en la población infantil atendida en las consultas de Alergología españolas se asoció frecuentemente con asma. El tiempo de evolución de la rinitis y la sensibilización a epitelios y hongos se asoció al desarrollo de asma.

Palabras clave: rinitis alérgica en niños, rinitis y asma en población pediátrica

Introduction

The ARIA (Allergic Rhinitis and its Impact on Asthma) document [1] indicates that allergic rhinitis is the commonest chronic allergic disease in children and that it is frequently associated with other allergic disorders.

According to recently published data from phase III of the *International Study of Asthma and Allergies in Childhood* (ISAAC) [2] (data collected from adolescents and parents using a self-administered questionnaire), the prevalence of allergic rhinitis in Spain—15.5% in adolescents aged 13-14 years and 8.2% in children aged 6-7 years—is similar to that of the other countries included in the study. The different analyses performed in ISAAC revealed a trend toward increasing prevalence of allergic rhinitis in Spain and other countries [3-6].

With the aim of collecting data on the characteristics of patients consulting in allergy departments, the Spanish Society of Allergy and Clinical Immunology (SEIAC) designed an epidemiologic study (*Alergológica 92*) that was carried out in Spain in 1992 [7]. This study showed rhinitis to be the most frequently diagnosed disease in allergy departments. However, no specific analysis was made of data on the pediatric population included. In 2005, a second study, *Alergológica 2005*, was carried out using the same methodology. The study population included 4991 subjects, of whom 917 (18.37%) were under the age of 14. The present article analyzes the data obtained from patients aged under 14 years who were diagnosed with rhinitis and the association with subsequent development of asthma.

Methods

Alergológica 2005 was a descriptive, observational, cross-sectional study. The methodology has been described elsewhere [8]. Data were collected prospectively throughout Spain by 332 allergists of whom only 30 worked in pediatric allergology units. Both researchers in general allergology units and those in pediatric units included patients under the age of 14. Each researcher included 15 patients of any age consulting for the first time for allergy-related conditions. Consecutive cases were selected from patients occupying the first place on each researcher's list of daily consultations over a randomly assigned time period. Informed consent was obtained for all patients. Cases were included in 2 waves: March-June 2005 and September-December 2005.

Statistical Analysis

Prevalence and the remaining qualitative variables were analyzed by calculating the relative frequencies (%) and 95% confidence intervals (CI). Quantitative variables were described using the mean (SD), median, and other statistical measures. To compare differences between percentages of qualitative variables, 95% CIs of the difference in percentages were calculated or the Fisher exact test was used. Average values were compared using the *t* test or analysis of variance (Kruskal-Wallis test) [8].

The results for specific variables were compared with those obtained in the sample from patients with rhinitis over the age of 14 included in the *Alergologica 2005* study.

Results

Of the 917 patients under the age of 14 included in the study, rhinitis was diagnosed in 390 (42.5%). The characteristics of the study population and patients with rhinitis are shown in Table 1.

Skin tests were performed in 95% of the children with rhinitis and serum determination of specific immunoglobulin (Ig) E in 47%. Simple spirometry was performed in 31% of patients and a bronchodilator test in 9%. In 44.9% of cases (175 patients), rhinitis was associated with asthma. This association was significantly higher (P<.05) than the 35.5% found in patients aged over 14 years. A significant difference

in time since onset of rhinitis was found between children with and without asthma (2.97 vs 2.06 y, respectively) (*P*=.0001) irrespective of the age group analyzed (<6, 6-10, and 11-14 y). No significant association was found between presence of asthma in children with rhinitis and other variables such as gender (56.3% of males vs 57.6%, with and without asthma), mean age (9.27 vs 9.36 y, with and without asthma), or age group (<6 y, 13.7% vs 15.3%, with and without asthma; 6-10 y, 43.4% vs 38.6%, with and without asthma; 11-14 y, 42.9% vs 46%, with and without asthma).

Allergy was the most common cause of rhinitis (82%) both in children with and without asthma (85.7% and 79.1%, respectively). Sensitization to animal epithelia and fungi was more frequent in children presenting with rhinitis and asthma than in those presenting with rhinitis only (Table 2). All children (100%) sensitized to fungi were sensitized to *Alternaria*.

Immunotherapy was always prescribed subcutaneously and no differences were observed in frequency of treatment with immunotherapy between children with and children without asthma (23% vs 22%).

Table 1. Characteristics of the Total Population and Patients Aged Under 14 Years Diagnosed With Rhinitis

	Total Population <14 Years	Population <14 Years With Rhinitis
No. (%)	917 (100%)	390 (42.5%)
Sex (male)	504 (55%)	195 (57%)
Age, y (SD)	7.6 (3.9)	9.3 (3.4)
Distribution by age, %		
<6 y	34.8%	14.6%
6-10 y	36.6%	40.7%
11-14 y	28.6%	44.6%
Prevalence of rhinitis by age, %		
<6 y	–	17.9%
6-10 y	–	47.3%
11-14 y	–	66.4%

Table 2. Allergic Etiology of Rhinitis in Patients Without and With Asthma

	Rhinitis			
	Without asthma		With asthma	
Allergen	N	%	N	%
Pollens	98	56.0%	95	63.3%
Mites	85	48.6%	79	52.7%
Epithelia	28	16.0% [a]	40	26.7%[a]
Fungi	21	12.0%[b]	29	19.3%[b]

[a]P<.01
[b]P<.05

Discussion

In *Alergológica 2005*, rhinitis was the most frequently diagnosed condition in patients under the age of 14 (42.5%) and, in most cases (82%), it was caused by allergy. In a high percentage of cases, rhinitis was associated with asthma (44.9%). Time since onset and sensitization to epithelia and fungi were greater in patients with asthma.

The percentage of rhinitis among children is slightly lower than that detected in the total study population (52%) [9]. Most patients diagnosed with rhinitis were over the age of 6, and the prevalence of rhinitis by age group increased progressively with age: 18% (<6 years), 47% (6-10 years), and 66% (11-14 years). These findings are consistent with those of other studies [2,10].

Asthma can affect 21%-40% of patients with allergic rhinitis [11-13]. Rhinitis has been reported to be a risk factor for the development of asthma both in atopic and in nonatopic subjects [14-16]. Of note, almost half of the children with rhinitis in Alergológica 2005 had asthma (44.9%). Phase III of the ISAAC study [2] showed that 30% of 13 to 14-year-olds with rhinoconjunctivitis had asthma, as did 35% of 6 to 7-year-olds. This difference in the association between rhinitis and asthma in *Alergológica 2005* and the ISAAC study may be because the diagnosis was made by specialists in allergology and using specific tests, whereas in the ISAAC study, a survey was performed in the general population.

The association between asthma and rhinitis was significantly higher in children than in adults (44.9% vs 35.5%; *P*<.05), with no differences between age groups among the children. Children were more likely to develop asthma the longer the time since onset of rhinitis. The Spanish ONEAIR study [17], which analyzed the coexistence of rhinitis in adult asthmatic patients, found that most patients with asthma (89.5%) also had rhinitis and that they had been suffering from rhinitis significantly longer than from asthma. The 2008 ARIA guidelines [1] and those previously issued in 2001 [18] recommend performing spirometry in patients with allergic rhinitis, as asthma can be diagnosed in over 30% of patients with allergic rhinitis and no previous history of obstructive bronchial disease [19]. In *Alergológica 2005*, spirometry was performed in 31% and a bronchodilator test in 9% of patients under the age of 14 with rhinitis; therefore, in most cases, the diagnosis of asthma was based exclusively on symptoms suggestive of asthma with no use of respiratory function tests. We must remember that some children, because of their age, were not capable of performing spirometry adequately (14.6% of those with rhinitis were below 6 y).

If lung function tests—and even bronchial hyperreactivity tests—were routinely performed in children with allergic rhinitis, then patients with asthma and those at greatest risk of developing asthma could be detected early [20].

Sensitization to animal epithelia and fungi was significantly more frequent in patients who presented with rhinitis and asthma than in those presenting with rhinitis only. All children sensitized to fungi were sensitized to *Alternaria*.

In a previous study, sensitization to *Alternaria* was associated with coexistence of rhinitis and asthma [21].

According to the ARIA guidelines [1], subcutaneous and sublingual immunotherapy receives the highest recommendation (grade A), based on evidence or tests in the treatment of allergic rhinitis in children and adults. This category is shared with other treatments such as topical corticosteroids and antihistamines. As a result, it is surprising that subcutaneous specific immunotherapy was prescribed by allergists in so few children with allergic rhinitis and in the same proportion in those with and without associated asthma.

In conclusion, allergic rhinitis is the most frequently diagnosed allergic disease in patients under the age of 14 consulting for the first time at Spanish allergology departments. Almost half of the children with rhinitis (44.9%) suffer from asthma. The likelihood of developing asthma is related to the longer time since onset of rhinitis. Consequently, an asthma workup should be included in the periodic follow-up of patients with allergic rhinitis.

Acknowledgments

We thank Schering-Plough for sponsoring the epidemiologic study and their medical manager María José Rosales for the time she dedicated to the study. We are also grateful to the Clinical and Epidemiologic Research Unit Grupo Luzán 5 for performing the study and the data analysis, especially Dr. Fernando Caballero, all our fellow allergists involved in the project (Scientific Committee, Coordinators, and Researchers), and the Governing Board of SEAIC for promoting the project.

References

1. Bousquet J, Kaltaev N, Cruz AA, ARIA Workshop Group; World Health Organization. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen) Allergy. 2008;63 (Suppl. 86):8-160.
2. Aït-Khaled N, Pearce N, Anderson HR, Ellwood P, Monteford S, Shah J, and the ISAAC Phase Three Study Group. Global map of the prevalence of symptoms of rhinoconjunctivitis in children: The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. Allergy. 2009:64:123-48.
3. Arnedo-Pena A, García-Marcos L, García Hernández G, Aguinagua Ontoso I, González Díaz C, Morales Suárez-Varela M, Domínguez Aurrecoechea B, Busquets Monge R, Blanco Quiros A, Batlles Garrido J, Miner Kanflanka I, López-Silvarrey Varela A. Time trends in prevalence of symptoms of allergic rhinitis in 13-14 year-old schoolchildren in 8 areas of Spain between 1993-1994 and 2001-2002 according to the International Study of Asthma and Allergies in Childhood (ISAAC). Med Clin. 2004;123(13):490-5.
4. Arnedo-Pena A, García-Marcos L, García Hernández G, Aguinagua Ontoso I, González Díaz C, Morales Suárez-Varela M, Domínguez Aurrecoechea B, Busquets Monge R, Blanco Quiros A, Batlles Garrido J, Miner Kanflanka I, López-Silvarrey Varela A. Time trends and geographical variations in the prevalence of symptoms of allergic rhinitis in 6-7-year-old children from eight areas of Spain according to the ISAAC. An Pediatr. 2005;62(3):229-36.
5. Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, Williams H; ISAAC Phase Three Study Group. World time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet.2006;368:733-43.
6. Björkstén B, Clayton T, Ellwood P, Steward A, Strachan D, ISAAC phase III Study Group. World time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma and Allergies in Childhood. Pediatr Allergy Immunol. 2008;19:110-24.
7. Alergológica Factores Epidemiológicos Clínicos y Socioeconómicos de las enfermedades alérgicas en España. Sociedad Española de Alergología e Inmunología Clínica y Alergia e Inmunología Abelló SA (Eds). Madrid, NILO Industria Gráfica,1995.
8. Caballero F. Alergológica-2005. Methodological aspects and sample characteristics of the study. J Investig Allergol Clin Immunol. 2009;19 Suppl 2:2-6
9. Navarro A, Colás C, Antón E , Conde J , Dávila I, Dordal MT, Fernández-Parra B, Ibáñez MD, Lluch M, Matéu V, Montoro J, Rondón C, Sánchez MC, Valero A. Rhinoconjunctivitis Committee of the SEAIC. Epidemiology of Allergic Rhinitis in Allergy Consultations in Spain: Alergologica 2005. J Investig Allergol Clin Immunol. 2009;19 Suppl 2:7-13.
10. Strachan D, Sibbald B, Weiland S, Ait-Khaled N, Anabwani G, Anderson HR, Asher MI, Beasley R, Björkstén B, Burr M, Clayton T, Crane J, Ellwood P, Keil U, Lai C, Mallol J, Martinez F, Mitchell E, Montefort S, Pearce N, Robertson C, Shah J, steward A, von Mutius E, Williams H. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). Pediatr Allergy Immunol. 1997;8:161-76.
11. Linneberg A, Henrik Nielsen N, Frolund L, Madsen F, Dirksen A, Jorgensen T. The link between allergic rhinitis and allergic asthma: a prospective population-based Study. The Copenhagen Allergy Study. Allergy 2002;57:1048-1052.
12. Leynaert B, Neukirch C, Kony S, Guenegou A, Bousquet J, Aubier M, Neukirch F. Association between asthma and rhinitis according to atopic sensitization in a population-based study. J Allergy Clin Immunol 2004;113:86-93.
13. Downiw SR, Andersson M, Rimmer J, Leuppi JD, Xuan W, Akerlund A, Peat JK, Salome CM. Association between nasal and bronchial symptoms in subjects with persistent allergic rhinitis. Allergy. 2004;59:320-6.
14. Leynaert B, Bousquet J, Neukirch C, Liard R, Neukirch CF. Perennial rhinitis: an independent risk factor for asthma in nonatopic subjects. Results from the European Community Respiratory Health Survey. J Allergy Clin Immunol. 1999;104:301-4.
15. Settipane RJ, Settipane GA. IgE and the allergy-asthma conection in the 23-year follow-up of Brown University students. Allergy Asthma Proc. 2000;21:221-5.
16. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. J Allergy Clin Immunol. 2002;109:419-25.

17. Navarro A, Valero A, Juliá B, Quirce S. Coexistence of asthma and allergic rhinitis in adult patients attending allergy clinics: ONEAIR Study. J Investig Allergol Clin Immunol. 2008;18(4):233-8.
18. Bousquet J, Van Cauwenberge P, Khaltaev N, Aria Workshop Group, Eorld Health Organitation. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol. 2001;108 (Suppl.5):S146-S334.
19. Demoly P, Gauchoux R, Morera P, Touron D,Daures JP. The place of spirometry in the diagnosis of asthma in those suffering from allergic rhinitis : a pilot study. Allergy. 2005;60:1089-90.
20. Jacobsen L, Niggemann B, Dreborg S, Ferdousi HA, Halken S, Høst A, Koivikko A, Norberg LA, Valovirta E, Wahn U, Möller C; (The PAT investigator group). Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. Allergy. 2007;62:943-8.
21. Gergen PJ, Turkeltaub PC. The association of individual allergen reactivity with respiratory disease in a national sample: data from the second National Health and Nutrition Examination Survey, 1976-80 (NHANES II). J Allergy Clin Immunol. 1992;90:579-88.

Manuscript received May 7, 2009; accepted for publication December 9, 2009.

Dolores Paloma Ibáñez Sandín

Department of Allergology
Hospital Infantil Universitario Niño Jesús
Menéndez Pelayo, 65
28009 Madrid
Spain
E-mail: dibanezs@medynet.com