

Allergy in Patients Under Fourteen Years of Age in *Alergológica* 2005

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■ Abstract

Objective: To present the most significant data obtained on patients younger than 14 years from the Alergológica-2005 study.

Results: Nine hundred seventeen (18.3%) of the patients included in the study were under the age of 14 (average age 8 years with a similar distribution by gender) and were heavy users of healthcare resources. The most frequently diagnosed illnesses were rhinitis/conjunctivitis (44.7%), asthma (40.5%), food allergy (14.5%), and atopic dermatitis (11.6%). The prevalence of these diseases in children is notably higher than in the adult population in the study. However, urticaria (7%) and drug allergies (3%) were less frequent than in those aged over 14 years. Rhinitis and asthma are allergic in the majority of cases (> 80%). Egg (39%) and milk (32%) were the foods that most frequently caused allergies, especially in children under 7 years of age. Atopic dermatitis was mild in the majority of patients and the use of topical steroids for its treatment has become less widespread in comparison with Alergológica-92, probably as a result of the use of calcineurin inhibitors. Acute urticaria in children is more frequent than the chronic form and is usually caused by foods. Allergy to drugs is very infrequent although the agents responsible are the same as those for adults, beta-lactams and non-steroidal anti-inflammatories.

Conclusion: The study provides interesting and useful epidemiologic and clinical data on the child population consulting in Allergy services in Spain.

Key words: Childhood allergy. Epidemiology of childhood allergy. Rhinitis. Asthma. Allergy to foods. Atopic dermatitis. Allergy to drugs. Allergy to insects.

■ Resumen

Objetivo: Presentar los datos más significativos obtenidos en los pacientes menores de 14 años incluidos en el estudio Alergológica 2005.

Resultados: 917 (18,3%) de los pacientes incluidos en el estudio eran menores de 14 años (media 8 años y similar distribución por sexos) y grandes consumidores de recursos sanitarios. Las enfermedades más frecuentemente diagnosticadas fueron: rinitis/conjuntivitis (44,7%), asma (40,5%), alergia a alimentos (14,5%) y dermatitis atópica (11,6%). La prevalencia de estas enfermedades en niños es notablemente superior que en la población adulta del estudio. Sin embargo, la urticaria (7%) y la alergia a medicamentos (3%) son menos frecuentes que en los mayores de 14 años. La rinitis y el asma son de causa alérgica en la mayoría de los casos (> 80%). El huevo (39%) y la leche (32%) fueron los alimentos que con más frecuencia produjeron alergia, preferentemente en los menores de 7 años. La dermatitis atópica era leve en la mayoría de los pacientes y la utilización de esteroides tópicos para su tratamiento ha disminuido en relación a los utilizados en Alergológica 92, probablemente debido a utilización de inhibidores de la calcineurina. La urticaria aguda en niños es más frecuente que la crónica y suele estar causada por alimentos. La alergia a medicamentos es muy poco frecuente aunque los agentes responsables son los mismos que en edad adulta, betalactámicos y AINES.

Conclusión: El estudio aporta datos epidemiológicos y clínicos interesantes y útiles sobre la población infantil que acude a las consultas de alergología de España

Palabras clave: Alergia en la infancia, epidemiología de la alergia infantil, rinitis, asma, alergia a alimentos, dermatitis atópica, alergia a medicamentos, alergia a insectos.

Introduction

Few data exist on the epidemiologic and clinical aspects of the patients who consult Allergy services in Spain. More than 10 years ago, in the *Alergológica* study [1] important data were obtained on clinical practice in allergology. However, on that occasion, no specific analysis was made of the children who were included in the study. This article presents the most significant data obtained on patients younger than 14 years of age included in the *Alergológica-2005* study.

Methods

Alergológica-2005 is a descriptive, cross-sectional, observational epidemiologic study, with prospective collection of data. The selection criteria, data collection and methodological data are described elsewhere in this issue [2]. Three hundred thirty-two allergists participated in the study from all over Spain but only 30 of them worked in pediatric allergy services. Both researchers in general allergy services and those from pediatric allergy services included patients younger than 14 years of age.

Results

Characteristics of the Sample

Of the 4991 patients included in the study, 917 (18.3%) were younger than 14 years of age. Five hundred twenty-three had been referred to general allergy services and 394 to pediatric allergy services. Fifty-five percent were males. The average age of the patients was 7.58 years (SD 3.87 years). Pediatric allergy services more frequently treated children under 5 (42% vs. 29% in general allergy services) whereas in the general services there was a predominance of children over 10 (35% vs. 21% in pediatric allergy services).

Environmental Factors

Ninety-six percent of the children lived at the time the interview was carried out in the same region in which they had been born. Sixty-two percent of patients lived in urban areas, 20% in rural areas and 18% in semi-urban areas. Thirty-two percent of children lived with animals in their homes: dog (18%), bird (11%), cat (10%), rodent (3%) and horse (1%). Only 22 patients (4%) had contact with stables.

Sixty percent of children had been breastfed exclusively at least 3 months (57% for more than 3 months), in 15% breastfeeding had been supplemented with other foods and 25% had been given artificial milk from birth. Eight percent of children were considered passive smokers (being exposed more than 5 hours per day to tobacco smoke). Eighty-eight percent of patients attended school and the rest did not go to school or kindergarten due to their age. The socioeconomic level of the patients was considered low in 3%, medium/low in 47%, medium/high in 46% and high in 4% of cases.

Origin of Patients and Time on Waiting Lists

In 60% of cases, children were referred to the allergy service by other specialists (pediatricians 87%, ENT 7% and

others 7%), and in 27% of cases by family physicians. In 12% of cases patients consulted the allergology service on their own initiative. Average time on the waiting list was 65 days, with a median of 30 days and a standard deviation of 109 days.

Use of Healthcare Services

The patients had gone to their health center with symptoms suggestive of allergy an average of 2.9 times in the preceding 4 months, and during the previous 2 years they had made 2 visits to the emergency department and 2 visits to a specialist. 6.8% of children had required at least one hospital admission in the previous year.

Impact on School, Work and Quality of Life

Both children and their parents were forced to take a considerable number of days off school and work. The children lost on average 11.71 ± 15.9 days per year and had poor performance at school in 16% of cases. Twenty-four percent of parents had had to take time off work in the previous 12 months, losing on average 5 ± 4.5 days per year.

Presenting Complaint

Respiratory problems were the most common causes behind consultations to allergology services (figure 1). Table 1 shows the frequency of the different diseases diagnosed in those patients under 14 years of age.

Rhinitis/conjunctivitis

Nasal symptoms were the most common reasons for children consulting for allergy analyses (Figure 1) and rhinoconjunctivitis (R/C) the most common diagnosis (44.7%) (Table 1). The average age of children with R/C was 9 years. Conjunctivitis was present in 61% of 390 children diagnosed from rhinitis. Only 20 children (5%) presented with only conjunctivitis. In patients with R/C the most frequently associated allergic disorders were bronchial asthma in 190 patients (45%), atopic dermatitis (AD) in 38 patients (9%), food allergies (FA) in 30 patients (7%), urticaria/angioedema (U/AE) in 19 patients (4%) and drug allergies (DA) in 5 patients (1%). In 23 children (5.4%), rhinitis was associated with sinusitis. The study was set up in such a way that no firm conclusions can be drawn regarding the severity of the rhinitis suffered by the children.

Skin tests were performed in 95% of children and serum determination of specific immunoglobulin E (IgE) in 47%. Nasal or ocular challenge tests were performed in 3% of cases, a percentage similar to that in the overall sample of the study (4%). In 336 (86%) of children with rhinitis allergic sensitization was detected. Fourteen percent were diagnosed with infectious rhinitis (vs. 8% in the overall sample). The other types of rhinitis – vasomotor (1%), intrinsic/eosinophilic (3%), medicamentosa (0%) are very infrequent in pediatrics. Pollens (49%) were the allergens patients were most frequently sensitized to, followed by dust mites (42%), epithelia (13%) and fungi (12%). Of the 258 children presenting conjunctival symptoms, 79% were diagnosed with allergies, 12% with

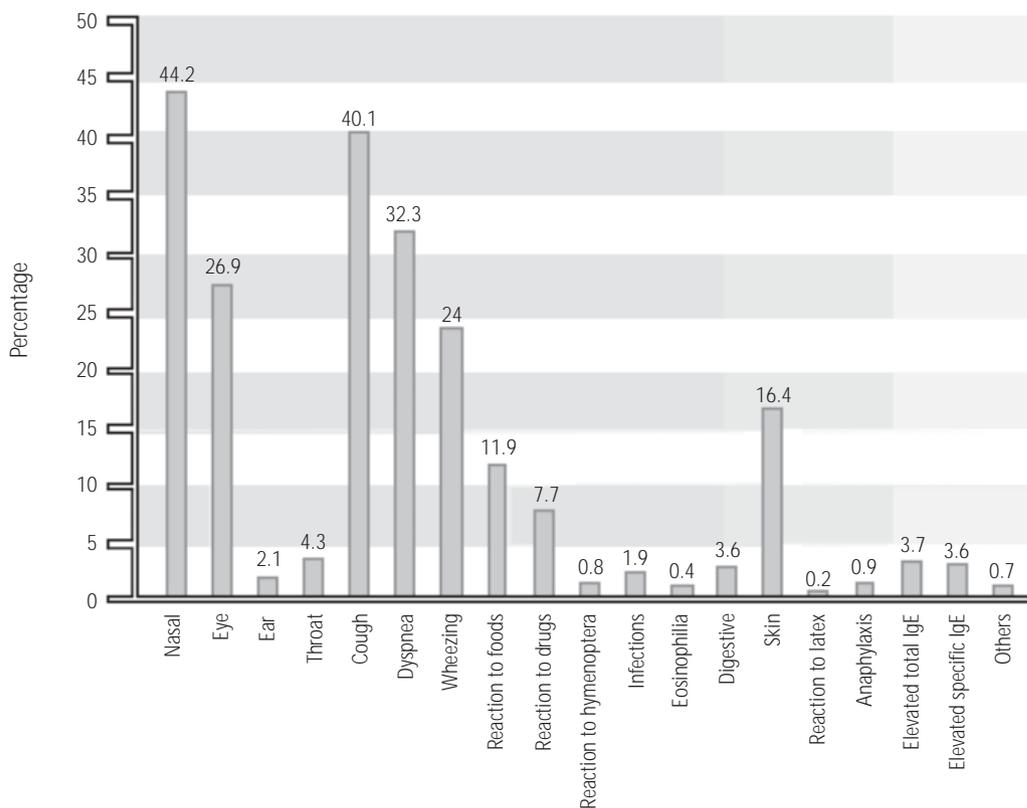


Figure 1. Reasons for the Consultation.

Table. Prevalence of the Different Disorders Diagnosed in Children Under the Age of Fourteen Years

Order by Frequency	Disorders	Total Number of Cases	Prevalence			
			Overall Sample	<5 years	5-10 years	>10 years
1	Rhinitis/conjunctivitis	410	44.7%	16.3%	45.4%	70.6%
2	Bronchial asthma	371	40.5%	22.6%	46.8%	43.9%
3	Allergy to foods	133	14.5%	37.6%	7.8%	3.8%
4	Atopic dermatitis	106	11.6%	17.2%	12.9%	3.4%
5	Other non-allergy related	77	8.4%	10%	9%	4.6%
6	Urticaria/angioedema	66	7.2%	10.4%	7.6%	5.3%
7	Allergy to drugs	28	3.0%	8.6%	7.8%	6.1%
8	Allergy to insects	8	0.9%	0.5%	1.2%	1.1%
9	Other allergic disorders	8	0.9%	1.4	0.7%	1.1%
10	Contact dermatitis	5	0.5%	1.8%	0.5%	0%

contact conjunctivitis, 2.4% with vernal conjunctivitis and 5% with other disorders of different etiologies.

Seventy-two percent of children were given written instructions on avoiding allergens and 76% received treatment with antihistamines. Topical nasal corticoids were prescribed in 49% of children and immunotherapy in 35% (always using the subcutaneous route of administration).

Bronchial Asthma

The prevalence of asthma in the children studied (40.5%) (Table) is notably higher than for the population over the age of 14 (25%). Fifty-five percent were males and only 30% of the children were younger than 6. In the 12 months prior to the consultation, the children had an average of 4.2 ± 3 asthma

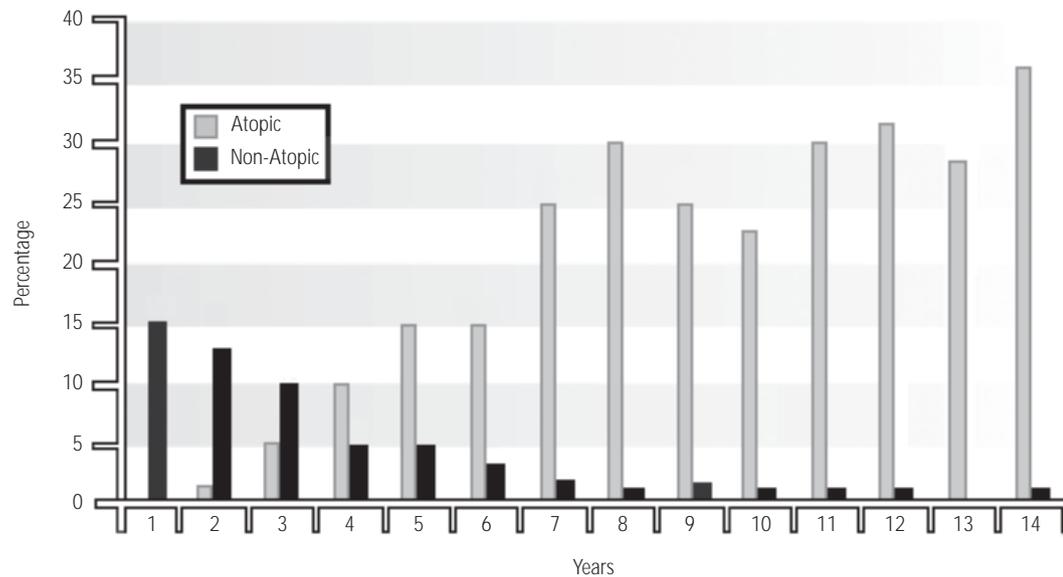


Figure 2. Type of Asthma and Age of the Children.

attacks. Three percent of children had nocturnal symptoms and 15% symptoms after exercise. Ten children (3%) required admission to hospital.

Skin tests were performed in 95% of cases, serum specific IgE tests in 50% and baseline forced spirometry in 46%. The bronchodilation test was performed in 77 patients (33% of those older than 6 years), non-specific bronchial challenge test in 16 patients (7% of those older than 6 years) and the specific bronchial challenge test was not used.

Asthma was considered episodic in 67% of cases, persistent in 33%; mild in 62%, moderate in 36% and severe in 1%. In 60% of patients it was perennial and in 40% seasonal. Eighty-two percent of the asthmatic children were sensitized to some type of allergen, 42% to dust mites, 34% to pollens, 14% to epithelia and 15% to fungi. The older the child, the greater the likelihood of suffering from atopic asthma (Figure 2).

In 190 (51%) children asthma was associated with R/C, in 45 (12%) AD, in 13 (3%) U/AE, in 28 (8%) FA and in 4 (1%) DA. In only one case gastroesophageal reflux was diagnosed and in no cases associated immunodeficiency. The first symptoms of asthma appeared most frequently in the autumn (38%), followed by the spring (33%) and winter (24%). Symptoms appeared in summer in only 5% of cases.

Inhaled bronchodilators were the drugs most frequently prescribed (80%), and in almost all cases by the inhaled route. The maintenance drugs most frequently used were the leukotriene inhibitors (44% vs. 24% in overall sample), followed by inhaled corticoids in 36% (vs. 32% in the overall sample). The combination of inhaled corticoids plus long-acting β -2 agonists was used in 16% of children (vs. 38.5% in the overall sample). Theophyllines and chromones were seldom used. Sixty-eight percent of children were offered written advice to avoid the allergen to which they were

sensitized and immunotherapy was prescribed in 44% (vs. 30% in the overall sample) (75% subcutaneous and 25% sublingual).

Food Allergy

Food allergy in patients under the age of 14 years occupied the third place in allergic disorders (Table). The prevalence was significantly higher than in patients over the age of 14 (14.5% vs. 5.8% $P=0.001$). In the age group of 0 – 2 years, the prevalence of food allergy was 47%, in the 3-6 years group 19%, in the 7-10 years group 4% and in the 11-14 years group 3%. Fifty-seven percent of all the children affected were male. The patients had an average age of 3 years and 83% of patients were under the age of 7. The majority of children with food allergy had been exclusively breastfed in the first years of life (63%), a figure similar to that for children in the study in general. Sixty-three percent had a relative with first grade atopy (FA 14%). Twenty-two percent of patients had simultaneously AD and in the same percentage asthma. The comorbidity with other allergic disorders was much lower.

Seventy-six percent went to their family physician or pediatrician and 25% to the specialist due to food allergy in the previous 4 months, with an average of 2 visits and 48% required attention in emergency departments. Thirteen patients (10%) had to be admitted to hospital in the previous year. Seventy-four percent consulted allergology services for an initial episode of an adverse reaction to foods.

Fifty-two children (39%) were allergic to egg, 43 (32%) to milk, 25 (19%) to nuts, 16 (12%) to fruit, 15 (11%) to fish 13 (10%) to legumes, 8 (6%) to shellfish, 4 (3%) to cereals and 1 (0.08%) to vegetables. Figure 3 shows the prevalence of allergy to each food by age group. Twenty-three percent

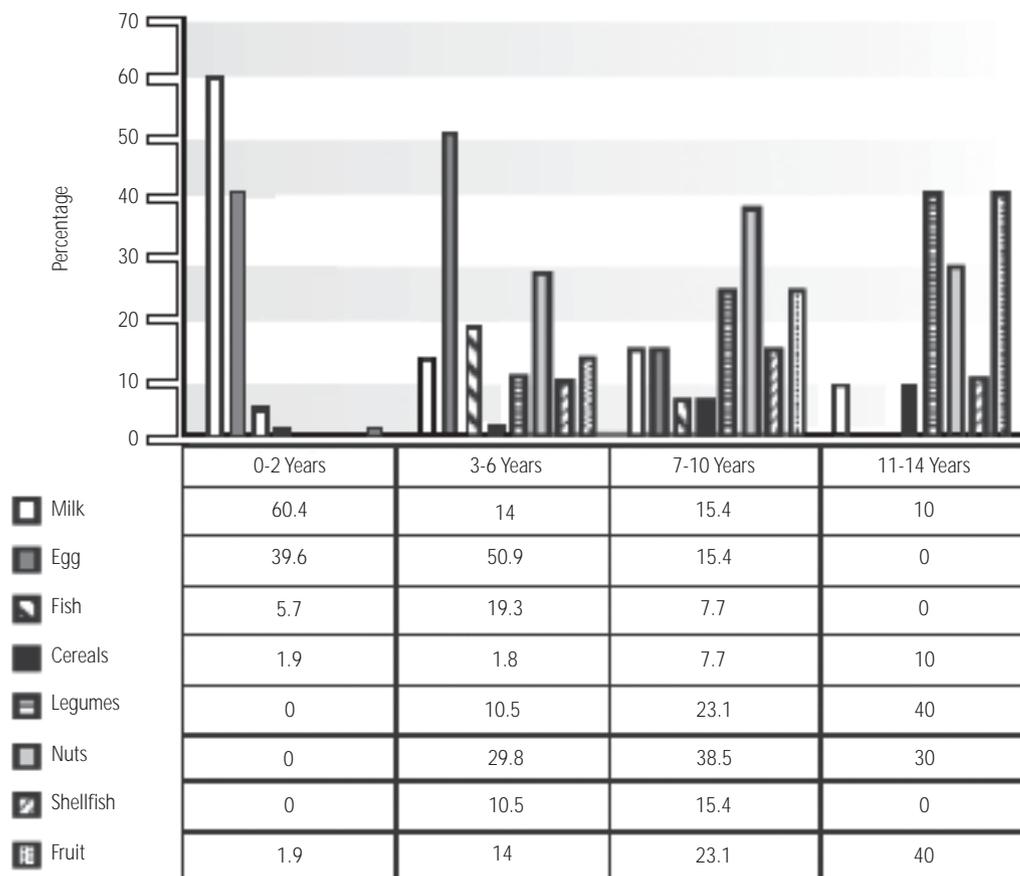


Figure 3. Frequency of Food Allergy by Age Group.

were allergic to more than one food. The most frequent type of clinical presentation was skin symptoms (88%), followed by digestive symptoms (41% vs. 16% in the overall sample, $P < .001$) and oral syndrome (26%). Seven percent of patients presented asthma with foods and 4% rhinitis. Interestingly, 10.5% of the children allergic to foods had had an anaphylactic reaction but none of anaphylaxis with exercise. The distribution of skin problems was as follows: 37% presented with contact urticaria, 36% with generalized urticaria and/or angioedema and 16% with AD. Fruits were the most common foods responsible for oral syndrome (75%).

In 93% of patients skin prick tests with foods were performed and in 72% tests of serum specific IgE. In 31 patients (23%) an oral challenge test was carried out. This test was more frequently used in children under the age of 3 than in the other age groups ($P = .048$). In 5 patients (4%) a simple blind challenge test was performed, in 27 (20%) an open test and in no cases a double-blind test.

Food avoidance was the therapy most frequently used by the specialists (90%). Treatment with antihistamines was recommended in 26% of patients. In no case was the administration of adrenaline recommended.

Atopic Dermatitis

Sixty-four percent of the cases diagnosed with AD in the *Alergológica*-2005 study were children with a prevalence of 11.6% (Table) in the child sample (vs. 1.5% in those over the age of 14, $P = .001$). Forty-seven percent of children with AD were male and 48% were aged between 3 and 6 years. The prevalence in the children aged from 0-3 years was 15%, in those aged from 3-6 years 17%, in those aged from 7-10 years 11% and in those aged from 11-14 years 3%.

Fifty-six percent of the children with AD had been exclusively breastfed, a figure similar to that for the general pediatric sample. AD began between one month and 82 months (mean 11 months, median 6 months). Patients had had an average of 4 episodes in the previous year. Seventy-three percent of patients with AD had a family history of atopy (29% of AD). Fifty-five percent of patients were referred by pediatricians and only 2 by dermatologists. Seventy-four percent of children had consulted their family physician or pediatrician in the preceding 4 months, with a median of 2 visits.

There were no severe cases of AD in the population studied and the disorder was slight in 26% of cases, moderate in 27%

and in almost half (46%) the skin was not or only minimally affected at the time of consultation. Seventy-one percent had another associated allergic disease (39% asthma, 34% R/C and 20% FA).

Tests for specific IgE were performed in 63 patients (59%), skin prick tests in 90 (85%), patch tests with pneumoallergens in 6 (6%) and in 8 (7%) with foods. Fifty-five children (60%) were diagnosed as having idiopathic AD and in 35 (40%) sensitization to allergens was detected. Twenty-two (21%) of these were sensitized to inhalants and 14 (13%) to foods. The most frequent were egg (52%) and milk (31%). No statistical differences were found between the ages of the patients with or without associated allergic sensitization.

In seventy-eight patients oral antihistamines were prescribed, in 47 (44%) topical steroids, in 2 systemic steroids and in 33 (34%) calcineurin inhibitors. Dietary measures were recommended to 13 of the 14 patients who had positive tests to foods.

Urticaria an Angioedema

Sixty-six children (7.2%) were diagnosed with urticaria (vs. 12% in those over the age of 14, $P=.01$). Fifty-two percent were male. Sixty-eight percent of patients had visited the emergency department in the previous year. Fifty-six percent had presented only with urticaria, 8% with angioedema and 36% both conditions. Urticaria was considered acute in 82% of cases (vs. 53% in the overall sample, $P<.0001$) and chronic in 18%. In 67% the urticaria was generalized, in 26% local and contact in 12%.

The urticaria was diagnosed on the basis of a clinical history and examination in 90% of cases. For reaching etiology, skin tests to foods were used in 64% of children, with pneumoallergens in 52% and serological tests of allergies in 53%. The cause of the urticaria was considered to be known in 64% of patients (vs. 20% in the overall sample, $P=.0001$). It is worth pointing out that foods were the most frequent cause of acute urticaria (60%) and physical factors in chronic urticaria (43%). The frequency of involvement of different foods was: egg (43%), nuts (38%), fruits (24%), milk (19%), fish and shellfish (both 14%), legumes (9%), and vegetables and cereals (both 5%). In 6 cases there was an association with infections, 3 viral and 3 bacterial. There was one case of family hereditary angioedema.

Twenty-nine patients were recommended to avoid the triggering agent, in 44 (67%) systemic antihistamines were prescribed and in 3 (4.5%) oral steroids.

Allergies to Drugs

A total of 69 patients younger than 14 years consulted due to possible allergy to drugs. This represents 7.5% of children consulting an allergology service for the first time. Twenty-eight patients (40%) were diagnosed with hypersensitivity to drugs (with a prevalence of 3% in children younger than 14 years of age as compared to 16.4% in those over 14 years). In 8 cases the diagnosis was reached by confirmation and in 20 it was suspected. Confirmation of the diagnosis was made using skin tests in 5 patients and by challenge in 3 patients. In the group where diagnosis of allergy to drugs was suspected, challenge

was performed in 60% of patients, probably with alternative drugs. Allergy to amoxicillin was diagnosed in 17 cases, to penicillin in 3 cases, to cephalosporins in 1, to macrolides in 1, nonsteroidal antiinflammatory drugs (NSAIDs) in 6, and to pyrazolones in 2. Only one patient had reactions to more than one NSAID. Information as to the type of reaction was obtained in 26 patients. In 18 (64%) the reaction was considered immediate, in 5 (18%) delayed, and in 3 (11%) late. As for clinical manifestations, 24 out of 26 patients had skin reactions (16 urticaria and 11 angioedema), anaphylaxis in one and in one other case asthma.

Allergy to Insects

The prevalence of allergy to insects in patients younger than 14 years was low (0.8% vs. 1.7% in those older than 14 years). In 5 cases the diagnosis was that of allergy to hymenoptera, all of them wasps (2 *vespula spp* and 3 *polistes spp*) and the 5 cases only had local reactions. The other 3 cases were reactions to mosquito bites (2 local and 1 generalized). Immunotherapy was not recommended in any case.

Contact Dermatitis

Three cases of contact dermatitis were diagnosed, thus giving a prevalence of 0.3% (vs. 5.1% in patients older than 14 years). Two cases were due to thiomersal and one to nickel sulfate.

Discussion

Allergic disorders are very frequent in the pediatric population. It has been calculated that the prevalence in children of AD is 15%-20%, of asthma 7%-10%, of rhinitis 15%-20% [3] and FA 6% [4] as a result of which it is of great interest to analyze the clinical and epidemiologic aspects of the children treated in Allergology services in Spain. The population younger than 14 years of age in the *Alergológica-2005* study represented 18% of the total sample included in the study and was practically equally distributed between the two sexes, both in the total sample of children and by disorders. These patients were heavy users of healthcare resources and their illness affected their school work. It must be highlighted that respiratory complaints were the most frequent causes for consultations and that R/C and asthma were the diseases most frequently diagnosed to a far greater extent than the other diseases. It is highly significant that the prevalence of asthma, FA and AD in children is notably higher than in the adult population in *Alergológica-2005*. However, the opposite is true for DA, U/AE and contact dermatitis.

R/C was the most frequent disease and allergic R/C the most common cause. This high comorbidity is consistent with other series and supports the concept of "one airway disease" [5]. The results of the study do not allow to draw clear conclusions on severity of rhinitis. But, on the basis of treatment received by patients, half of them should be mild.

In our study we see again the same asthma phenotypes previously described [6]. The older the child, the greater the likelihood that the asthma that he or she suffers from is allergic

asthma. Only 30% of children who consulted in *Alergológica*-2005 were younger than 6 years of age, which indicates that Spanish pediatricians do not refer to the specialist pre-school children with asthma unless, following established guidelines [6], the children have allergy risk factors or have asthma that is difficult to control.

The majority of children treated had mild or moderate asthma, and milder than the asthma suffered by the adults. Furthermore, the asthma was perennial, which corresponds to the greater frequency of sensitization to perennial allergens. Forced baseline spirometry was performed in 46% of cases. Bearing in mind that approximately 30% of the children who consulted were under the age of 7, spirometry was used in practically all those children in whom it was possible to perform it. The low percentage of children given the bronchodilator or non-specific challenge tests to confirm the diagnosis of asthma is striking. As could be expected given the severity and type of asthma and the age of the patients, the maintenance drugs most frequently prescribed to control the asthma, and in a higher proportion than in adults, were the leukotriene inhibitors, followed by inhaled corticoids. The combination of inhaled corticoids plus long-acting β -2 agonists was prescribed much less frequently than in adults, as has been described in other studies [7].

FA, the third most frequent disorder in our series, is one of the diseases which appear earliest in children. The frequency of FA progressively falls as age increases [4]. Egg, milk, fish, followed by nuts, are the foods which most commonly cause allergies in children under the age of 7. Allergies to these foods tend to disappear with age as allergies to plant foods increase, probably as a result of sensitization to pollen [8]. Digestive complaints were significantly more frequent in children than in the overall sample. This may be due to the fact that this population becomes sensitized to foods principally via the digestive route. Furthermore, the immaturity of the digestive tract may make these patients more vulnerable to suffering from this type of symptoms. No patient underwent double-blind challenge. Although this test is considered the gold standard, diagnosis based on open oral challenge in small children is recommended if they present compatible clinical symptoms, a clear cause-effect relationship and presence of specific IgE to the offending food [9,10]. Adrenaline was not recommended in any cases by allergists.

Alergológica-2005 shows that AD occurs predominantly in childhood and becomes less frequent and severe with age, which confirms the natural course of the disease [11]. In our series, the frequency of AD in children under 14 years of age is much higher than in older patients. The majority of patients suffered from only mild AD or were in remission which could be interpreted in that allergists, in general, evaluate less severe forms of the disease than do dermatologists [12]. The DERTA study [12] already showed that the allergist investigates into possible allergic sensitizations, mediated by IgE, as the etiology of the dermatitis or as a cause of worsening symptoms, but rarely uses patch tests with allergens as it is not a validated test and adds little to the normal allergy analyses [13]. More than 70% of patients with AD had another associated allergic disease which suggests that they are children with a large burden of atopy. Just under one half of patients were sensitized to allergens and 20% to foods. The frequent association

between sensitization to air-borne allergens and foods and AD is well known but their role as etiologic agent and trigger for dermatitis is controversial. Given the methodology used in this study, in which challenge tests were not performed, it is not possible to determine the influence of these sensitizations on the AD of the patients [14]. The treatment indicated for AD in allergology services is consistent with data from *Alergológica*-1992 [15] with regard to antihistamines (74% vs. 78%). However, the recommendation of topical steroids has become less frequent (44% vs. 68%) probably due to the use of calcineurin inhibitors.

Studies have reported that 3% of pre-school children and 2% of older children have had urticaria on some occasion [16]. In our population, the prevalence among children younger than 14 years of age is somewhat higher (7%) as they are patients referred to allergology services, but is still very much lower than in the adults in the study. In our study, associated urticaria and angioedema appear in a lower proportion than that described in other populations where they are associated in approximately 50% of cases [16]. Other studies have also confirmed the greater frequency of acute urticaria in children [17]. The most frequent cause of acute urticaria of known origin is foods, which is consistent with the high frequency of FA in children and the fact that urticaria is the main clinical manifestation of FA. In only 6 cases was the urticaria attributed to infections. This finding contrasts with that of a previous study [17] in which the most acute urticarias in children were associated with infections, especially of the viral type, with or without associated medication [17]. This may be because pediatricians do not refer to the specialist those urticarias they suspect of having an infectious cause. In pediatrics, urticaria is usually a benign disease but intense pruritus and the physical appearance may affect the quality of life of the child, which explains the higher frequency of visits to emergency departments for this reason.

Allergy to drugs in children is clearly less frequent than in adults. However, the agents responsible which most frequently produce allergic reactions are the same for adults and children: beta-lactam antibiotics and in particular amoxicillin, followed by NSAIDs. If we compare with the overall sample, it is clear that reactions to drugs in children are in general less severe (0.04% vs. 10% of anaphylaxis in the overall sample) as has also been shown in the review by Le et al. [18].

Allergy to insect venom in children is rare. In no case included in this study was immunotherapy recommended probably because the case of generalized reaction was due to allergy to mosquito, for which no commercial immunotherapy is available nor has its efficacy been established [19].

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