Increase in prevalence of rhinoconjunctivitis but not asthma and atopic eczema in teenagers

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Summary. *Objective.* We sought to assess changes in the prevalence of asthma and other allergic diseases in schoolchildren of Curitiba between 1995 and 2001. *Methods.* Schoolchildren (aged 13-14) were evaluated by a self-reported written questionnaire of ISAAC protocol for symptoms of asthma and allergic diseases. The diagnoses of asthma, rhinoconjunctivitis and atopic eczema were considered according to the ISAAC protocol. Probable asthma was considered: more than 4 attacks of wheezing in the last 12 months; 1 to 3 attacks of wheezing in the last 12 months with dry cough at night, and/or with sleep disturbance due to wheezing, and/or with wheezing after exercise. The data obtained in 2001 were compared with the data obtained in 1995 for the same age group. *Results:* We evaluated 2,946 schoolchildren in 1995 and 3,628 in 2001. The prevalence of symptoms of asthma, probable asthma, rhinoconjunctivitis and eczema in 1995 and 2001 was 18.4% and 18.7%, 11.6% and 12.4%, 14.2% and 17.2%, 3.8% and 3.7%, respectively. There was a 23.7% increase in the prevalence of rhinoconjunctivitis symptoms (p<0.05). *Conclusions.* the prevalence of symptoms of asthma, probable asthma and eczema did not change over the past 6 years but a significant increase of the rhinoconjunctivitis symptoms was detected.

Key words: asthma, prevalence, allergic diseases, ISAAC III.

Introduction

There is considerable concern that the prevalence of asthma and other allergic diseases is increasing in developed and in developing countries [1,2]. A number of surveys, first conducted in the 60's and 70's, and repeated on the same community in recent years with similar methodology, reported that asthma prevalence has increased with substancial magnitude in some cases [2-5]. The trend of prevalence increase among populations within countries of widely differing lifestyles and ethnic groups is a generally consistent observation independent of some methodological differences, which would make them difficult to compare [6]. However, the etiology of these conditions remains not completely understood, despite a large volume of clinical and epidemiological research within populations that has been directed to explain why some individuals develop asthma and allergies and others do not. To exemplify this point of view, we observe hundreds of asthma-prevalence studies, which have been made in various parts of the world. Nonetheless, they rarely have used standard approaches. Moreover, allergic rhinitis and atopic eczema population studies are more difficult to be found. An exception to this general rule is the

European Community Respiratory Health Survey (ECRHS) [7], which develops surveys of asthma prevalence in adults at 40 (forty) centres in 22 (twentytwo) countries. The largest standard study of asthma, allergic rhinitis and atopic eczema is the International Study of Asthma and Allergies in Childhood (ISAAC) Phase One [8-11]. ISAAC Phase three will obtain the first internationally comparable estimates of the directions and magnitude of changes in prevalence of asthma, allergic rhinoconjunctivitis and atopic eczema symptoms. There is a lack of publications describing what has been happening to asthma and hay fever prevalence over the last years. We intended to fulfill the need for this knowledge assessing time trends in the prevalence of asthma and allergic diseases at the city of Curitiba -Brazil with two surveys which were conducted in 1995 and in 2001 according to the protocol of the International Study of Asthma and Allergies in Childhood (ISAAC). The objective of this study was to evaluate the prevalence and time trends of allergic diseases among schoolchildren 13-14 years of age.

Methods

Population and data collection

The current report is a cross-sectional and observational study. It was conducted during the months of May and June 2001 according to the Phase Three protocol of the International Study of Asthma and Allergies in Childhood (ISAAC). Permission for the study was given by the school board. Ethical approval was obtained from the University Hospital Ethics Committee. Briefly, this study uses the information collected on two occasions, in the same period of the year with similarities of climate and pollen season, 6 years apart (Phase I 1995, Phase III 2001), using identical methods on symptoms of asthma and allergies in schoolchildren 13-14 years of age.

The standardized ISAAC written questionnaire was initially translated to Portuguese, translated back to English after being received, and validated for our population [12,13]. This study was carried out in a city

Table 1. Freque	ncy of symptom	s in ISAAC phases	I and III.
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	YEAR			
		1995	2001	
Number of subjects (Male/Female)	3008	(46/54)	3628	(47/53)
Wheezing in the past 12 mo	553	(18.4)	678	(18.7)
Number of wheezing attacks in the past 12 mo: 1 - 3 4 - 12 more than 12	430 81 21	(14.3) (2.7) (0.7)	459 73 24	(12.7) (2.0) (0.7)
Probable asthma	341	(11.6)	450	(12.4)
Have you ever had asthma	257	(8.5)	335	(9.2)
Wheezing during/after exercise	595	(19.8)	694	(19.1)
Coughing at night	905	(30.1)	1259	(35)#
Sneezing/runny/blocked nose when not having a cold/flu in the past 12 mo	869	(28.8)	1423	(39.2)#
Nose and eyes symptoms in the past 12 mo	417	(13.9)	625	(17.2)#
Intermittent itchy rash in skin creases in the past 12 mo	111	(3.7)	133	(3.7)
Itchy rash in the past 12 mo	188	(6.3)	224	(6.0)

Data are presented as numbers with percentages in parentheses p < 0.05



Figure 1. Inter-relation between reported current symptoms of allergic diseases in 3,628 children aged 13-14 evaluated in 2001.

with a population of 2 million (Curitiba) in South Brazil. Public and private high schools were chosen from the metropolitan area and we randomly selected 48 high schools with children aged 13 to 14. Schools with less than 100 students of this age were excluded and 16 actually participated in the survey. Permissions were obtained from the school directors to allow the students to self-complete the ISAAC written questionnaire that was applied in the classroom by trained interviewers. The recommended sample size was 3,000 to ensure good prevalence estimates for severe asthma [1].

The ISAAC protocol definitions of asthma [8,9], rhinitis [9,10], atopic eczema [9,11], and criteria for probable asthma [14] were followed throughout both studies. The results obtained were compared with the ones published in the ISAAC phase I performed in September 1995 [13].

Outcome measures

The main outcome measures used in this study were 12-month prevalence of symptoms of asthma, allergic rhinoconjunctivitis, eczema and probable asthma. These outcome measures were obtained from core questions. For asthma, about the presence of wheezing or whistling in the chest in the past 12 months; for allergic rhinoconjunctivitis, about a problem with sneezing, or a runny/blocked nose when not having a cold or flu in the past 12 months (if this has been so: Has this nose problem been accompanied by itchy-watery eyes?); for atopic eczema, about the presence of an itchy rash in the last 12 months that affected the skin creases and for probable asthma, about more than 4 attacks of wheezing in the last 12 months or about 1-3 attacks of wheezing in the last 12 months with a dry cough at night or/and with sleep disturbance due to wheezing and/or with wheezing after exercise.

Data analysis

The statistical package Statistica[®] was used to categorize and analyze the data. A gender/age stratified description of the study participants is found in Table 1. The response rate was calculated as the number of completed written questionnaires divided by the number of participants. Missing or inconsistent responses were included in the denominator for calculation of prevalence. Chi square analyses of contingency tables for trends assessed the differences in the prevalence rates. The significance level was 0.05 and all tests were two-tailed.

Results

In 2001, there were 53,857 schoolchildren aged 13-14 year-old registered at the Department of Education in Curitiba. From this total, 11,462 were enrolled in private schools. Four thousand and seven schoolchildren randomly selected were requested to complete the questionnaires. The response rate was 90.5% (n=3,628). The frequency of girls answering the questionnaire was greater (53%) than boys (47%). Regarding the studied diseases, the symptoms of asthma, wheezing in the last 12 months, had the same prevalence in both years of the study (18.4% in 1995 and 18.7% in 2001). Moreover, a change in the occurrence of probable asthma or symptoms of atopic eczema in both periods was not observed. The prevalence of probable asthma was 11.6% in 1995 and 12.4% in 2001. The symptoms of atopic eczema, an itchy rash in the last 12 months that had affected the skin creases, was as frequent as 3.7% in 1995 and 3.7% in 2001. On the other hand, the overall reported prevalence of symptoms of rhinitis and rhinoconjunctivitis increased from 28.8 and 13.6% in 1995 to 39.2 and 17.2% in 2001, respectively (p<0.05). Table 1 shows the frequency of self-reported symptoms in different time periods. In addition, there was a significant increase in the prevalence of coughing at night. This finding was associated with a higher prevalence of rhinoconjunctivitis symptoms ($\chi^2 = 10.56$; p=0.001).

At this point, it should be mentioned that dissimilarities in gender were not responsible for any observed differences in change of the prevalence trend overtime for any of the allergic conditions. However, the rates of asthma diagnosis, probable asthma, rhinoconjunctivitis, and atopic eczema in boys and girls were similar in 2001. Figure 1 illustrates the interrelation between reported current symptoms of wheezing, rhinoconjunctivitis and flexural rash. The presence of at least one or more of the three symptoms was 31.7%. The frequency of patients reporting only one symptom was 24.2%. For those patients, who were reporting current wheezing, 34.4% also had symptoms of other atopic diseases. Finally, there was a significant association between rhinoconjunctivitis and symptoms of wheezing (OR, 1.53) (CI 95%, 1.1-1.9); (p=0.004) in the present study.

Discussion

Repeated asthma surveys in the same communities using similar methods clearly have demonstrated an increase in asthma prevalence and atopic diseases [2-5,15,16]. However, the results from this report show unchanged prevalence of eczema, asthma and probable asthma in two surveys six years apart, but the prevalence of rhinoconjunctivitis has increased by 23.7% in the same time period. The results showed a high prevalence of allergic conditions, i.e. 24.2% considering schoolchildren currently affected by symptoms of asthma, rhinoconjunctivitis and eczema. This was similar to the results in European countries where allergic diseases are the most common chronic illnesses of childhood today, affecting more than one child in four in some countries [27]. Sixty-two percent of schoolchildren with symptoms of eczema also had symptoms of other allergic diseases. In addition, there is a higher prevalence of rhinoconjunctivitis symptoms than asthma symptoms, although the same observation was made in other centers [8].

The interpretation of reported symptoms from questionnaires should be cautious because of the general nature of the questions and because an objective test was not included to differentiate between allergic and other causes of rhinitis. However, the questionnaire has been validated, as well as the sensitivity of the combination of itchy eyes and nasal symptoms for the diagnosis of rhinoconjunctivitis [12]. The discrepant points towards differences in the development of asthma, and atopic eczema when compared to rhinitis symptoms cannot be understood at this point. It is interesting, however, that the factors, which act very early in life, are important for the development of asthma whereas rhinitis is affected by environmental exposure to allergen, which occurs beyond infancy and early life [17]. There are data indicating that the trend to increased asthma symptoms has slowed or ceased [17,18]. Ronchetti et al [19] assessed time trends in the prevalence of asthma in Roman schoolchildren (aged 6-14 years) in three different periods. The prevalence of asthma increased from 1974 to 1992 but remained stable from 1992 to 1998. It is possible that in Curitiba, as in Rome, some factors will continue to induce symptoms of asthma in genetically predisposed children until this self-limiting process comes to an end. Among such factors we can find environmental and current lifestyle changes. In addition, it is possible that a 6-year interval between the observations was not long enough to detect changes in the prevalence that might be occurring at a slower pace than before. Furthermore, recently Chatkin et al. published similar results about the prevalence of asthma in Pelotas, a city in southern Brazil, although these data were obtained with preschoolchildren [20].

The age of the study group might be a confounder. Change in the lifestyle of the population is changing the prevalence in different age groups in the recent years. Nowadays, attendance at day care centers early in life is more often and appears to be protective of wheezing. Moreover, the search of a more natural way of life has created stimuli for a more external contact. Recently, exposure to farm environment has been shown to have a protective effect against asthma and atopic sensitization [21]. Therefore, it is likely that allergy prevalence in older age groups will continue to increase, as more susceptible cohorts replace the generations apparently protected by a less affluent upbringing. Future trends among younger age groups are more difficult to predict, particularly as environment and patterns of child care continue to change. As living standards in different countries converge regional variations in the prevalence of allergies may become less marked among future generations [22].

This study also has shown that the prevalence of wheezing, rhinoconjunctivitis and atopic eczema is similar in boys and girls. Although previous studies showed a higher incidence of atopy in boys aged 12, other studies have reported that by 16 years of age this sex difference tends to disappear by a ratio reversion [23,24]. Our data suggest that this tendency to equilibrium in sex prevalence might occur as early as 13-14 years of age in our region. Recently Maziak et al. showed that there is a general tendency towards an increase in the symptoms of these disorders among children in Münster, Germany, remarkably more so among girls [16].

In the present study, there was a significant association between rhinoconjunctivitis and symptoms of wheezing. This demonstrates the inter-relation between wheezing and atopic diseases. Rhinitis and asthma are manifestations of the same allergic process. Pathogenic events are triggered by exposure to aeroallergens in both. The histology of tissues from these diseases shows chronic, eosinophilic inflammation along with an increase in lymphocytes, plasma cells, and mast cells. The stroma in the nose and bronchus is typically edematous. Rather than suggesting that the nose influences the lungs, rhinitis and asthma could represent global allergic involvement of the airways [25,26].

Within its established boundaries, this study has identified an increase in the prevalence of rhinoconjunctivitis but not in asthma, eczema and probable asthma in 13-14 year-old children in Curitiba over the past 6 years. The reason for the increase only in rhinoconjunctivitis symptoms is unclear, and beyond the objectives of this study. However, since both of them seem to have the same pathogenesis, we are stimulated to attain an elucidation. Whatever the reason, the implication of this stable trend is good news for people at risk of asthma and eczema but not rhinoconjunctivitis in this region of the world.

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References

1. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, Mitchell EA, Pearce N, Sibbald B, Stewart AW, Strachan D, Weiland SK, Williams HC. International study of asthma and allergies in childhood (ISAAC): rationale and methods. Eur Respir J, 8, 483-91, 1995.

- 2. Burr ML, Butland BK, King S, Vaughan-Williams E. Changes in asthma prevalence: two surveys 15 years apart. Arch Dis Child, 64, 1452-6, 1989.
- Shaw RA, Crane J, O'donnel TV, Porteous LE, Coleman ED. Increasing asthma prevalence in a rural New Zealand adolescent population: 1975-89. Arch Dis Child, 65, 1319-23, 1990.
- Ninan TK, Russell G. Respiratory symptoms and atopy in Aberdeen schoolchildren: evidence from two surveys 25 years apart. Br Med J, 304, 873-5, 1992.
- Robertson CF, Heycock E, Bishop J, Nolan T, Olinsky A, Phelan PD. Prevalence of asthma in Melbourne schoolchildren: changes over 26 years. Br Med J, 302, 1116-8, 1991.
- Beasley R, Crane J, Lai CKW, Pearce N. Prevalence and etiology of asthma. J Allergy Clin Immunol, 105 (suppl), 466-72, 2000.
- European Community Respiratory Health Survey. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). Eur Respir J, 9, 687-95, 1996.
- International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). Eur Resp J, 12, 315-35, 1998.
- International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. Lancet, 351, 1225-32, 1998.
- 10. Strachan D, Sibbald B, Weiland S, Ait-Khaled N, Anabwani G, Anderson HR, Asher MI, Beasley R, Bjorksten 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, Stewart 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.
- Williams H, Robertson C, Stewart A, Aït-Khaled N, Anabwani G, Anderson R, Asher I, Beasley R, Björkstén B, Burr M, Clayton T, Crane J, Ellwood F, Keil U, Lai C, Mallol J, Matinez F, Mitchell E, Montefort S, Pearce N, Shah J, Sibbald B, Strachan D, von Mutius E, Weiland SK. Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. J Allergy Clin Immunol, 103, 125-38, 1999.
- Esteves PC, Trippia SG, Rosário NA, Caleffe LG. Validaçao do questionário do ISAAC para rinite alérgica perene e sazonal (polinose). Rev Bras Alerg Imunopatol, 22, 106-13, 1999.
- Ferrari FP, Rosário NA, Ribas LFO, Callefe LG. Prevalência de asma em escolares de Curitiba – projeto ISAAC (International Study of Asthma and Allergies in Childhood). J Pediatr (Rio), 74, 299-305, 1998.
- 14. Rosário NA, Ferrari FP. Questionnaires in asthma epidemiology. Eur Respir J, 12, 1000, 1998.
- Onram M, Russell G. Continuing increase in respiratory symptoms and atopy in Aberdeen schoolchildren. Br Med J (Clin Res), 312, 34, 1996.
- 16. Maziak W, Behrens T, Brasky TM, Duhme H, Rzehak P, Weiland SK, Keil U. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I

and phase III surveys in Münster Germany. Allergy 2003;58:572-579.

- von Mutius E, Weiland SK, Fritzsch C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. Lancet, 1998; 351: 862-6.
- Fleming DM, Sunderland R, Cross KW, Ross AM. Declining incidence of episodes of asthma: a study of trends in new episodes presenting to general parctioners in the period 1989-98. Thorax 2000; 55: 657-61.
- Ronchetti R, Villa MP, Barreto M, Rota R, Pagani J, Martella S, Falasca C, Paggi B, Guglielmi F, Ciofetta G. Is the increase in childhood asthma coming to an end? Findings from three surveys of schoolchildren in Rome, Italy. Eur Respir J, 17, 881-6, 2001.
- Chatkin MN, Menezes AM, Victora CG, Barros FC. High prevalence of asthma in preschool children in southern Brazil. Pediatr Pulmonol 2003;35:296-301.
- von Mutius E. Environmental factor influencing the development and progression of pediatric asthma. J Allergy Clin Immunol 2002;109:525-32.
- 22. Strachan DP. Epidemiology of hay fever: towards a community diagnosis. Clin Exp Allergy 1995; 25: 296-303.
- 23. Anderson HR, Pottier AC, Strachan DP. Asthma from birth to age 23: incidence and relation to prior and concurrent atopic disease. Thorax 1992; 47: 537-42.
- 24. Austin JB, Kaur B, Anderson HR, Burr M, Harkins LS, Strachan DP, Warner JO. Hay fever, eczema, and wheeze: a

nationwide UK study of asthma and allergies in childhood. Arch Dis Child 1999; 81: 225-30.

- 25. Grossman J. One airway, one disease. Chest, 52, 20-8, 1997.
- Corren J. The link between allergic rhinitis and asthma, otitis media, sinusitis, and nasal polyps. Immunol Allergy Clin North Am 2000; 20: 445-60.
- 27. Wickman M, Lilja G. Today, one child in four has an ongoing allergic disease in Europe. What will the situation be tomorrow? Allergy 2003; 58: 570-71
- 28. Maziak W, Behrens T, Brasky TM, Duhme H, Rzehak, Weiland SK, Keil U. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Munster, Germany. Allergy. 2003 Jul;58: 572-9.

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