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Prevalence of asthma-related symptoms and bronchial responsiveness to exercise in children aged 13—14 yrs in Barcelona, Spain

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Prevalence of asthma-related symptoms and bronchial responsiveness in childen aged 13–14 yrs in Barcelona, Spain. R.M. Busquets, J.M. Antó, J. Sunyer, N. Sancho, O. Vall. ©ERS Journals Ltd 1996.

ABSTRACT: It is not clear whether asymptomatic bronchial responsiveness is a risk factor for development of asthma. A cross-sectional study was conducted to determine the prevalence of asthma among schoolchildren from Barcelona (Spain). The association between respiratory symptoms and bronchial responsiveness to exercise was examined.

For this study 3,033 schoolchildren aged 13–14 yrs were studied from the general population. Participants answered a respiratory questionnaire and a self-reporting video-questionnaire. A total of 2,842 children underwent bronchial responsiveness testing by exercise challenge. The study was part of the International Study of Asthma and Allergies in Childhood (ISAAC) project.

The prevalence of "current asthma" (recent wheezing and bronchial responsiveness to exercise) was 4% and the prevalence of "wheezing only" 10%. A fall in peak expiratory flow rate (PEFR) ≥15% after exercise testing was found in 324 (11%) children, 29 (9%) of whom presented clinical symptoms of asthma. Bronchial responsiveness to exercise was significantly associated with all items of the asthma questionnaire. The prevalence of asthma-related symptoms in this inner-city area was lower than frequently reported rates in other countries, although the prevalence of exercise-induced bronchoconstriction was relatively high, and threefold greater than in a geographical area in the vicinity of Barcelona.

These findings are consistent with the current view that asthma-related symptoms and bronchial responsiveness to exercise have different meanings in a community survey, and that local environmental factors could influence the prevalence of bronchial responsiveness.

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Asthma is the most frequently treated disease during childhood [1]. Although an increase in morbidity and mortality rates has been detected in some Western countries in recent years [2], there is a marked variability in the prevalence of asthma. This may be due, to some extent, to the definition of the illness itself [3], *i.e.* lack of consensus concerning the distinction between asthma and other disorders in which wheezing is present, such as bronchiolitis in infants, and in the methods used for the identification of asthma in epidemiological studies [4, 5]. Objective measures of variations in bronchial obstruction which are useful in the diagnosis of asthma [6] may be difficult to apply to the general population. Asthma is frequently defined as the concurrence of bronchial responsiveness and wheezing during the last 12 months [7]. This definition is not ideal, however, since the relationship between asthma and bronchial responsiveness is complex and controversial [5, 8–10].

It is currently accepted that, with few exceptions, the prevalence of asthma in children varies between 7 and 10% [11, 12], depending on local factors. In England, Williams *et al.* [13], using free running as the exercise test, reported a prevalence of exercise-induced asthma of 13%; whereas, in Denmark, Host *et al.* [14] found a prevalence of 7.2%. These geographical differences are obscured by the fact that in many areas the prevalence of asthma is increasing. In a study of children aged 12 yrs, Burr *et al.* [8] reported an increase in the occurrence of asthma from 6 to 12% between 1973 and 1988. In Spain, a few studies have been carried out to determine the prevalence of asthma in childhood. Recently, Bardagí *et al.* [15] reported a prevalence of exercise-induced bronchoconstriction and/or clinical asthma of 4.1 and 3.2% in children aged 13 and 14 years, respectively.

To provide a systematic assessment of variations in asthma prevalence in children, a multicentre International Study of Asthma and Allergies in Childhood (ISAAC) has been designed [16]. Barcelona and other Spanish areas are taking part in this study, together with other regional groups. The prevalence of asthma was determined in a population of schoolchildren in Barcelona and the association between respiratory symptoms and bronchial responsiveness, as measured by exercise testing, was assessed.

Materials and methods

Study subjects

For this cross-sectional study, all children aged 13–14 yrs (n=3,033) attending either private or state-owned primary schools along Barcelona's coastal fringe (Sant Marti and Ciutat Vella) were included in the study. Data were collected in two phases, the first from February to April and the second from October to December, in order to avoid periods of high pollinosis.

Measurements

The presence of respiratory symptoms was determined using a standardized, written questionnaire, which has been validated and shown to be reproducible in studies carried out in homogeneous study populations. This questionnaire, developed for ISAAC project [16], was based on the International Union Against Tuberculosis and Lung Disease (IUALTD) Questionnaire on bronchial symptoms [17]. The results were compared with a self-reporting video questionnaire [16].

Schoolchildren participating in the study completed a written, 49-item questionnaire based on the ISAAC protocol, that consisted of questions dealing with: respiratory symptoms (presence of wheezing during the previous 12 months, frequency of attacks, sleep disruption and wheezing severe enough to impair speech); nasal symptoms (sneezing, pruritus, runny or blocked nose and seasonal onset of symptoms); cutaneous symptoms; smoking habits (personal and family); treatment for respiratory problems and resulting visits to the doctor. In addition, a video-questionnaire, including sequences of asthma symptoms in young persons, was administered.

In conjunction with the questionnaire, an exercise-induced bronchial responsiveness test was carried out. Medication in known asthmatics was not discontinued. Children were asked to run as fast as they could (free running) for 6 min. The exercise test was performed outside under medical supervision (RMB). The method used was that reported by BARDAGÍ *et al.* [15], based on guidelines developed by the American Academy of Allergy [18]. The peak expiratory flow rate (PEFR) was measured by means of a mini-Wright device (Clement Clark International, UK). Children were instructed in the use of the device until they were able to perform the manoeuvre successfully. The highest of three satisfactory readings was kept as baseline. PEFR was measured 1 min after the end of the exercise and at 5, 10 and 15 min thereafter. At each time-point, at least three measurements were recorded with a variability of less than 10% each time. The highest value of the three readings was taken for calculation [19].

Heart rate was monitored at rest and after the exercise test by palpation of the carotid pulse. Results of the test were considered acceptable when there was an increase in heart rate of at least 85% of the expected maximum heart rate for the age range studied (160 beats·min^{-1}). A noseclip was not used during exercise. Temperature and relative humidity registered during the testing days were also recorded.

To calculate exercise-induced bronchoconstriction (EIB) the following formula was used: EIB = (baseline PEFR minus post-exercise PEFR/baseline PEFR) ×100. EIB was defined as a decrease in PEFR of at least 15% of the pre-exercise value. The selection of a 15% cut-off for EIB was based on a previous study [20], in which a value equal to 1.96 SD above the mean percentage fall in forced expiratory volume in one second (FEV_1) was around 15%. In all children with a decrease in PEFR of at least 15% of the pre-exercise value, the presence of cough, dyspnoea, cyanosis, prolonged expiration and wheezing was assessed by means of questioning and auscultation of the chest.

Informed consent was obtained from families for their children to complete the questionnaire and carry out the physical exercise test. Those children who were unable to participate in the exercise test because of illness, completed the questionnaire only. The study protocol was approved by the Ethics Committee of our institution.

Definitions

According to the presence of wheezing in the previous 12 months (recent wheezing) and/or EIB, the following groups were established: "current asthma" (children with recent wheezing and bronchial responsiveness to exercise); "wheezing only" (children with recent wheezing and no bronchial responsiveness to exercise); "bronchial responsiveness only" (children with bronchial responsiveness to exercise and no recent wheezing). Moreover, children with exercise-induced wheezing and bronchoconstriction but without recent wheezing, were classified as "exercise-induced asthma only". Children without current asthma but with "asthma ever" and bronchial responsiveness to exercise were classified as "past asthma". Those with recent wheezing associated with other respiratory symptoms (such as night cough), but without bronchial responsiveness to exercise, were classified as "probable asthma".

Statistical analysis

The EPI INFO [21] program (version 5.01) was used for the statistical analysis of data. The frequency of symptoms and bronchial responsiveness to exercise was determined by prevalence rates and their corresponding confidence intervals (CI). The association between respiratory symptoms and exercise-induced EIB was calculated by the odds ratio (OR) and 95% CI according to Cornfield, as described by FLEISS [22] and THOMAS [23].

Results

From a cohort of 3,431 schoolchildren registered in 76 schools, a total of 3,324 belonging to 74 schools (97% of schools) was included in the study. The questionnaire was completed by 3,033 (91%) children (1,497 boys and 1,536 girls). The exercise challenge test was carried out by 2,842 (94%) of those who had completed the questionnaire (1,420 boys and 1,422 girls). The remaining 191 schoolchildren were not authorized to take part in the study unknown reasons (n=124), current symptomatic asthma (n=14), and other diseases (n=53).

Table 1. – Prevalence of asthma-related symptoms by gender in 3,033 children aged 13–14 yrs

	All subjects			Boys			Girls		
Questionnaire item	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)
Wheezing									
Ever	800	26	(25–28)	382	26	(23–28)	418	27	(25–29)
In the past 12 months	434	14	(13–16)	194	13	(11–15)	240	16	(14–17)
Speech impairment	81	3	(2–3)	31	2	(1–3)	50	3	(2–4)
Asthma									
Ever	336	11	(10–12)	171	11	(10–13)	165	11	(9–12)
Exercise-induced*	564	19	(17–20)	254	17	(15–19)	310	20	(18–22)
Cough at night	622	21	(19–22)	266	18	(16–20)	356	23	(21–25)
Treatment for respiratory symptoms									
In the past 12 months	508	17	(15–18)	256	17	(15–19)	252	16	(15–18)
At present	173	6	(5–7)	89	6	(5–7)	84	5	(4–7)
Doctor's visits for wheezing	610	20	(19–22)	277	18	(17–20)	333	22	(20–24)

95% CI: 95% confidence interval. *: wheezing during or after exercise in the past 12 months.

Table 2. – Frequency of bronchial responsiveness to exercise (BRE) in 2,842 children aged 13–14 who underwent exercise testing

	All subjects			Boys			Girls		
BRE*	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)
After 1 min	48	1.7	(1.2–2.2)	18	1.3	(0.7–1.8)	30	2.1	(1.4–2.9)
After 5 min	103	3.6	(2.9–4.3)	41	2.9	(2.0–3.8)	62	4.4	(3.3–4.4)
After 10 min	94	3.3	(2.6–4.0)	36	2.5	(1.7–3.4)	58	4.1	(3.0–5.1)
After 15 min	79	2.8	(2.2–3.4)	39	2.8	(1.9–3.6)	40	2.8	(2.0–3.7)
Total	324	11.4	(10.2–12.6)	134	9.4	(7.9–11.0)	190	13.4	(11.6–15.1)

*: decrease in peak expiratory flow rate (PEFR) of at least 15% of the pre-exercise value; 95% CI: 95% confidence interval.

The results obtained in the questionnaire are presented in table 1. The prevalence of "wheezing ever" was 26%. This figure, however, decreased by 50% (to 14%) for the question referring to wheezing during the previous 12 months. Both genders had a similar prevalence. The prevalence of "wheezing severe enough to impair speech" over the past year was 3%. Nineteen percent reported wheezing during or after exercise over the 12 months prior to the study. Episodes of nocturnal cough had been experienced by 21% in the previous 12 months and showed the greatest difference between genders. Asthma ever was found in 11% of children. Seventeen percent of children had received treatment for respiratory symptoms in the last 12 months and 6% were receiving treatment "at present".

Table 3. – Association between bronchial responsiveness and results of the written questionnaire on asthma symptoms in 2,842 children aged 13–14 yrs who underwent the exercise test

Symptom	OR	(95% CI)
Wheezing		
Ever	2.41	(1.89–3.05)
In the past 12 months	3.37	(2.70–5.14)
Speech impairment	3.33	(2.00–5.54)
Asthma		
Ever	3.25	(2.44–4.32)
Exercise-induced	2.82	(2.20–3.63)
Cough at night	1.80	(1.39–2.33)
Treatment for respiratory symptoms		
In the past 12 months	2.22	(1.70–2.89)
At present	5.53	(3.90–7.82)
Doctor's visit for wheezing	2.73	(2.12–3.50)

OR: odds ratio; 95% CI: 95% confidence interval

Results of exercise testing are shown in table 2. A total of 2,842 children performed the exercise challenge test and reached their predicted rate. Of these 2,842 children, 324 (11%) showed a decrease in PEFR ≥15% after free running. Ninety three of the 324 children had received treatment for respiratory symptoms during the previous 12 months, although only 11 children were receiving treatment at the time of exercise testing. The prevalence of a positive response was higher in girls than in boys (13 *versus* 9%). The greatest decrease in PEFR occurred 5–10 min after the run. A total of 29 children had bronchial responsiveness to exercise and respiratory symptoms.

Mean (±SD) temperature and relative humidity during the testing days were 13.4±4.2°C and 67.3±15%, respectively.

In the 2,842 children who carried out the exercise challenge test, the prevalence of "current asthma" (wheezing in the previous 12 months and bronchial responsiveness to exercise) was 4% and the prevalence of "wheezing only" 10%.

From the 2,842 children who carried out the exercise challenge test, 2,452 had never experienced respiratory symptoms and 218 (9%) showed a decrease in PEFR ≥15% after free running. Of the 390 children who performed the exercise test and had experienced respiratory symptoms ever, 106 (27%) showed bronchoconstriction after exercise. Of the remaining 284 patients with negative exercise test, 126 (44%) had been taking treatment in the past 12 months and 64 of the 126 children were taking treatment at the time of the study. However, only 16 were given anti-asthma drugs (immunotherapy 5; nonsteroidal anti-inflammatory drug 4; $beta_2$-adrenoceptor agonist 4; inhaled steroids 2; antihistamine 1).

The relationships between bronchial responsiveness to exercise and results of the written questionnaire are shown in table 3. There were statistically significant associations for all symptoms. The weakest association was "cough at night", whereas the strongest corresponded to "current treatment for asthma".

Discussion

In this study, a prevalence of current asthma (recent wheezing and bronchial responsiveness to exercise) of 4% was found. In addition, the prevalence of exercise-induced airway narrowing was 11%. The prevalence of wheezing in the 12 months prior to the study was 14%. In a recent study in children aged 12–15 yrs, conducted in five regions of four different countries, the prevalence of wheezing during the previous 12 months varied from 20% in Bochum (Germany) to 30% in Sydney (Australia) [24]. Variations were also noted in the prevalence of self-reported severe attacks of wheezing impairing speech during the previous year, with 3% in Barcelona, and a range from 13% in Sydney to 6% in Bochum [24]. Given that these studies have used the same questionnaire and standardized procedures, these differences indicate a wide international variation in the prevalence of asthma-related symptoms and a relatively low prevalence in the city of Barcelona.

This geographical pattern is consistent with results of exercise-induced bronchoconstriction reported in the literature. Using a similar free running test in children, the prevalence of exercise-induced bronchoconstriction varies from 12% in children aged 12 yrs from New Zealand [25] to 6% in children aged between 7–16 years in Copenhagen [9]. However, an extremely low prevalence of 0.1% has been reported in a rural area of Zimbabwe [26]. Although the presence of such marked variations strongly suggests that the environment influences both asthma and bronchial responsiveness, the influence of genetic factors is also possible at this wide geographical scale.

Marked changes in the prevalence of asthma and bronchial responsiveness have also been found on a more restricted local scale. In a study of 2,114 children carried out in Mataró, an industrial Mediterranean city in the vicinity (30 km) of Barcelona, the prevalence of exercise-induced bronchoconstriction in 13 year old children was 4.1% and in 14 year old children was 3.2%, an almost threefold change as compared with the prevalence of 11% in the present study.

When planning this study, the protocol reported by Bardagí *et al.* [15] was followed and, consequently, the influence of methodological factors in the aforementioned differences should be small. In the present study, the high pollen season was exluded and, therefore, this factor cannot account for the reported difference. When assessing bronchial responsiveness by strenous exercise, fatigue may contribute to a reduction in peak flow rate. In this study, of the 48 patients who had a 15% fall 1 min after the run, 16 still had bronchoconstriction at 5 min. Of the remaining 32, one child presented asthma symptoms during the run and six were already known to be asthmatics. The exclusion of these 25 has a small influence on the prevalence of bronchial responsiveness (11.4 *versus* 10.5%). Since reduction in PEFR due to fatigue was not studied by Bardagí *et al.* [15], it is not known whether differences in the prevalence of bronchial responsiveness after running between the present study and that of Bardagí *et al.* [15] may be attributed to the previously mentioned fatigue effect. In Zimbabwean children, the prevalence of exercise-induced bronchoconstriction varied from 5.8% in an urban area with high living standards to 0.1% in a rural district [26]. Different prevalence rates in populations with a similar genetic background are illustrated by studies in Barcelona and Mataró [15]. In Zimbabwe, Keeley *et al.* [26] have also shown large differences in prevalence of reversible airway obstruction between populations living in close geographical proximities. By contrast, similar prevalence in different ethnic groups sharing a similar environment are illustrated by the Zimbabwe study [26]. These observations indicate that strong, as yet unidentified, environmental factors may be involved.

The fact that exercise-induced bronchoconstriction can be measured before symptoms, may simply relate to the fall in lung function and perception. Most people do not complain about "exercise-induced asthma" unless they have a ≥25% fall in lung function. The majority of studies on bronchial responsiveness measured by exercise in children and adolescents have used a cut-off value around 15% [20]. Given that, in this case, symptoms and measurements do not always come together, it is considered that a child has bronchial responsiveness despite the lack of exercise-induced asthma symptoms.

The relationship between asthma-related symptoms and bronchial responsiveness to exercise in the present study is consistent with previously published reports. Airways narrowing was documented in 27% of children who had respiratory symptoms ever and in 9% of asymptomatic children. However, only 6% of children who had experienced respiratory symptoms ever and had a negative bronchial challenge test were receiving antiasthma medication at the time of the study. It is also possible that a negative test would have been obtained in symptomatic asthma, in the first minute after running, because exercise can cause a marked bronchodilatation and mask airways narrowing. However, it is likely that the EIB would have been detected 5, 10 or 15 min later. Jones [27], in a study of 956 schoolchildren, reported a 35.8% prevalence of a positive free running test among children with known asthma. A clinically based sample of asthma cases recruited in an outpatient department, receiving treatment, showed a 79% prevalence of exercise-induced bronchoconstriction [28].

An important subgroup in the present population was the 8% with wheezing and other symptoms but without bronchial responsiveness. Ninan and Russell [29], however, have shown bronchial responsiveness, a fall of PEFR ≥10% after free running, in 15 of 128 (11.7%) symptomatic children and in one of 26 (3.8%) asymptomatic children. These authors concluded that exercise testing is not an adjunct in establishing the diagnosis of asthma in a survey. Martinez *et al.* [30] have recently shown, in a longitudinal study that the majority of infants with wheezing have transient conditions associated with diminished airway function at birth and have no increased risk for asthma or allergies in later life (at

6 yrs of age). Although the present study followed a cross-sectional design, the presence of a large group who reported wheezing in the last year but who did not respond to an exercise test is consistent with observations made by these authors [30]. Another implication of these findings is that estimates of asthma prevalence that are based on questionnaire definitions only and which include wheezing on their definition could substantially overestimate the true prevalence of asthma.

In summary, the results of this study suggest that the prevalence of asthma-related symptoms in the inner-city area of Barcelona is lower than the rates frequently reported in other countries. This is in agreement with recent evidence that most of the Spanish areas included in an international study of asthma had prevalence rates of asthma below the mean [31]. By contrast, the finding that prevalence of exercise-induced bronchoconstriction was relatively high and threefold greater than in a geographical area in the vicinity of Barcelona, is consistent with the current view that symptoms and bronchial responsiveness to exercise have different meanings in a community survey. It also suggests that local environmental factors could influence the prevalence of bronchial responsiveness.

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