

How accurate is the diagnosis of exercise induced asthma among Vancouver schoolchildren?

M Seear, D Wensley, N West



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See end of article for authors' affiliations

Correspondence to:
Dr M Seear, Children's & Women's Health Centre of BC, 4480 Oak Street, Room 1C42, Vancouver, British Columbia, V6H 3V4, Canada; mseear@cw.bc.ca

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Background: Limited access to exercise testing facilities means that the diagnosis of exercise induced asthma (EIA) is mainly based on self-reported respiratory symptoms. This is open to error since the correlation between exercise related symptoms and subsequent exercise testing has been shown to be poor.

Aim: To study the accuracy of clinically diagnosed EIA among Vancouver schoolchildren.

Methods: Fifty two children referred for investigation of poorly controlled EIA were studied. Following a careful history and physical examination, children performed pulmonary function tests before, then 5 and 15 minutes after a standardised treadmill exercise test. Based on overall assessment, a diagnostic explanation for each child's respiratory complaints was provided as far as possible.

Results: Only eight children (15.4%) fulfilled diagnostic criteria for EIA (fall in FEV₁ ≥10%). Of the remainder: 12 (23.1%) were unfit, 14 (26.9%) had vocal cord dysfunction/sigh dyspnoea, 7 (13.5%) had a habit cough, and 11 (21.1%) had no abnormalities on clinical or laboratory testing, so were given no diagnosis. Initial reported symptoms of wheeze or cough often changed significantly following a careful history, particularly among the eight elite athletes. The final complaint was sometimes not respiratory, and, in a few cases, was not even associated with exercise.

Conclusions: The clinical diagnosis of EIA is inaccurate among Vancouver schoolchildren, principally due to the unreliability of their initial exercise related complaints. Symptom exaggeration, familiarity with medical jargon, and psychogenic complaints are all common. A careful history is essential in this population before basing any diagnosis on self-reported respiratory symptoms.

In many asthmatic and some non-asthmatic children, strenuous exercise is followed by acute narrowing of the airways and consequent reduction in expiratory flow rates.¹ Abrupt changes in airway temperature and humidity during exercise are probably the initiating events. "Exercise induced bronchoconstriction" is a more accurate description, but the term "exercise induced asthma" (EIA) persists through common use.² Depending on the definitions and measurements used, exercise induced asthma is reported to affect 10–15% of the general population,³ but the prevalence is much higher among asthmatics (80–90%)⁴ and those with allergic rhinitis (30–40%).⁵

The condition is defined and quantified on the basis of changes in lung function measured before and after a standardised exercise test.⁶ Limited access to specific exercise testing facilities means that in general clinical practice, most diagnoses are based on exercise related respiratory symptoms reported by the child or parents. However, several authors have shown poor correlation between self-reported exercise symptoms and the results of specific exercise testing,^{7–9} with high frequencies of false positive and false negative results. Our own experience gained from a large referral paediatric clinic would also suggest that misdiagnosis (particularly over-diagnosis) of EIA is common.

In the absence of specific research, we investigated the diagnostic accuracy of EIA by prospectively studying a cohort of children referred to our clinic for investigation of poorly controlled EIA. In each case, the diagnosis of EIA made by the referring physician (and the apparent poor response to treatment) were entirely based on self-reported respiratory symptoms. Each child underwent a detailed history and clinical examination, followed by pulmonary function testing before and after a standardised treadmill exercise test.⁶ Since each case was primarily referred for a clinical opinion, we

also provided, as far as possible, a diagnostic explanation for each child's respiratory complaints based on the overall results of our assessment.

METHODS

Patients and preparation

Over an 18 month period, we prospectively studied 52 children referred to our clinic with a complaint of poorly controlled EIA (table 1).

In all cases, the diagnosis of EIA had been made prior to referral. The majority had already had previous consultations and investigations. All, except one, were taking regular inhaled medications. In the absence of reference data, a control group of eight healthy children was used to derive normal values for stable treadmill speed and maximum heart rate. Children were asked to withhold all drugs for 24 hours and to dress in light clothing with gym shoes. On the day of testing, they were instructed to take only a light meal and avoid vigorous exercise. Studies were conducted in an air conditioned exercise laboratory (relative humidity 30–50%, temperature 20–25°C). The study was approved by the Research Ethics Committee of the University of British Columbia. After explanation of the study, all parents gave written consent.

Clinical examination

All children initially had a thorough history and physical examination, including measurement of height, weight, and body mass index (BMI). Early in the study, it became clear that a careful history was particularly important, since many

Abbreviations: BMI, body mass index; EIA, exercise induced asthma; FEF_{25–75}, ; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; PEFR, peak expiratory flow rate; VCD, vocal cord dysfunction

Table 1 Demographic details of study group

| Demographic parameter | Results |
|---|------------------------------------|
| Gender | M 29/52 (55.8%) F 23/52 (44.2%) |
| Age | 11.5 ± 2.7 years |
| Competitive athlete | 8 (15.4%) |
| Past hospital admission | 1 (1.9%) |
| Past oral corticosteroids | 6 (11.5%) |
| Current medications | |
| Salbutamol | 50 (96.2%) |
| Inhaled corticosteroids | 21 (40.4%) |
| Combined inhaled corticosteroids/long acting β agonists | 8 (15.4%) |
| Leukotriene inhibitors | 4 (7.7%) |
| Past consultations | |
| General practitioner | 52 (100%) |
| Paediatrician | 29 (55.8%) |
| Allergist | 18 (34.6%) |
| Ear, nose, and throat | 5 (9.6%) |
| Cardiologist | 5 (9.6%) |
| Past investigations | |
| Allergy tests | 22 (42.3%) |
| Chest x ray | 18 (34.6%) |
| Electrocardiogram | 5 (9.6%) |
| Pulmonary function test (not including exercise test) | 3 (5.8%) |

children were familiar with asthma terminology. Initial complaints of wheeze, cough, or shortness of breath (and even their association with exercise) often changed significantly once care was taken to determine the exact nature of the child's symptoms. The same physician then observed the child throughout the subsequent pulmonary function and exercise tests. These observations often helped resolve the diagnosis in children whose exercise tests proved to be normal.

Pulmonary function tests

Pulmonary function tests were performed at baseline and again at 5 and 15 minutes after a standardised exercise protocol. Nebulised salbutamol was then given to all children and a final set of measurements made 10 minutes later. Testing procedure followed ATS guidelines⁶ using regularly maintained and calibrated equipment (Jaeger Masterlab, VIASYS Healthcare, Conshohocken, Pennsylvania, USA). Predicted values were based on published reference nomograms.¹⁰

Briefly, following suitable coaching, children performed maximal flow-volume loop manoeuvres while standing and wearing nose clips. The best of three reproducible loops was selected for study.¹¹ The principal endpoint was forced expiratory volume in one second (FEV₁), but forced vital capacity (FVC), peak expiratory flow (PEFR), and forced mid-expiratory flow (FEF₂₅₋₇₅) were also recorded. The percentage change in FEV₁ was calculated at 5 and 15 minutes post-exercise and also post-salbutamol. Behaviour during the tests and variability in the shapes of the flow-volume loops was also noted.

Unfortunately, the definition of a positive bronchoconstrictor response to exercise is not standardised. Adult^{2 6} and paediatric^{12 13} studies usually accept a fall in FEV₁ of 10% or 15% as significant, although other variables¹⁴ and composite scores¹⁵ have also been suggested. Based on past experience, we defined a positive response to exercise as a $\geq 10\%$ drop in FEV₁ measured at 5 or 15 minutes post-exercise.

Exercise testing

Published paediatric exercise protocols vary widely. In the absence of an accepted standard, our practice is to follow current guidelines of the American Thoracic Society.⁶ Briefly, after detailed explanation of the procedure, children were

exercised on a computer controlled treadmill (Q4500, Quinton, Bethel, Washington, USA). A technician and physician were in attendance with resuscitation equipment immediately available. Children ran wearing nose clips without touching the handrails. Heart rate and oxygen saturation were monitored continuously. During the first two minutes of exercise, treadmill grade was increased to 10% and speed adjusted to achieve a heart rate $\geq 90\%$ of predicted maximum (220 – age in years).¹⁶ The target for total exercise time was 10 minutes.

Diagnostic categories

Since study participants were primarily referred for a respiratory consultation, we provided, as far as possible, a clinical diagnosis and management plan for each child. Children were initially classified as EIA/non-EIA based on quantifiable exercise test results. Non-EIA cases were further classified using subjective but clearly definable observations. The following diagnostic groups (listed with their major clinical criteria) were used:

- Exercise induced asthma:^{6 13} Children whose FEV₁ fell $\geq 10\%$ following standardised exercise test.
- Habit cough:^{17 18} Long standing, explosive, barking, or hacking cough, often dating from a flu-like illness. Socially disruptive but absent during sleep or pleasurable activity. Invariably present when observed during testing; stops briefly when distracted. No response to therapy; inconsistent relation with exercise (e.g. present with soccer but not skateboarding); often present at rest. Normal exercise test.
- Vocal cord dysfunction^{19 20}/sigh dyspnoea:²¹ Abrupt onset of inspiratory stridor, dysphonia, and throat "tightness", usually at start of exercise. Inconsistent association with different sports; no response to therapy. Easily precipitated by treadmill test. Normal test results. Variable extrathoracic obstruction often noted on consecutive flow-volume loops. Often also associated with intermittent sighing respirations at rest and a sensation that the lungs could not be filled.
- Poor physical fitness:^{22 23} Complaints of tiredness rather than shortness of breath with exercise; no improvement with medication. Usually no interest or involvement in school sport; considerable encouragement needed during

treadmill test. Normal test results; low endurance and treadmill speed. Obesity common but not invariable.

- No diagnosis: Convincing history of exercise associated respiratory complaints but no measurable reduction in FEV₁ following exercise; often a past history of asthma. Since there is no clear consensus on the use of ancillary tests for diagnosing EIA,²⁴ we elected to use a trial of therapy in this group. Children were offered a monitored four week course of daily inhaled medication (salmeterol and fluticasone, GlaxoSmithKline, London, UK) followed by repeat exercise testing at the end of that four week period.

Statistics

All numbers are expressed as mean ± 1 SD. Fractional data are also expressed as a percentage. Measured pulmonary function variables are expressed as percentages of predicted values based on published nomograms.¹⁰ Means of continuous data were compared with the unpaired *t* test. Fractional data were compared with Fisher’s exact test; the significance level was 5% for all tests. Response to exercise was defined as greatest post-exercise drop in FEV₁ (expressed as a percentage of baseline FEV₁). Bronchodilator response was defined as FEV₁ change, 10 minutes post-salbutamol (expressed as a percentage of FEV₁ at 15 minutes post-exercise).

RESULTS

Fifty two children were enrolled in the study; all completed the test protocol successfully. Exercise induced asthma had been diagnosed prior to referral in each case. All, except one child (98.1%) were taking regular respiratory medications (1.4±0.2 prescription drugs/day). Thirty seven (71.2%) had been referred to other consultants and 22 (42.3%) had had at least one investigation, but none had undergone an exercise test. None of the 52 children had abnormalities on auscultation at any time before or after exercise. The child with past hospitalisation for asthma had a positive exercise test, but even a history of oral corticosteroid use was of weak predictive value (2 of 6 had EIA). Demographic details are summarised in table 1. Principal measured end-points are summarised by final diagnosis in table 2.

- EIA: Despite the universal referral diagnosis of EIA, only eight children (15.4%) had a significant drop in FEV₁ (≥10%)⁶ following standardised exercise testing. If a more rigorous cut-off of ≥15%² had been chosen, only two children (3.8%) would have met the laboratory criteria for EIA.

- Poor physical fitness: Twelve children (23.1%) were unfit. Compared to controls, they had significantly lower endurance time (7.8±2.0 min *v* 10.0±0, *p* < 0.01) and treadmill speed (6.2±0.8 kph *v* 7.4±0.3, *p* < 0.01). Obesity was also significantly more common (6/12 *v* 0/8, *p* < 0.05). Post-exercise FEV₁ was normal.
- VCD/sigh dyspnoea: Fourteen children (26.9%) had vocal cord dysfunction; competitive athletes were overrepresented. Complaints of throat tightness and inability to take a full breath were common. Dysphonia and inspiratory stridor were reproducibly induced during exercise and pulmonary function testing. Post-exercise FEV₁ was normal, but it was sometimes difficult to obtain reproducible flow volume loops because of varying degrees of laryngeal constriction.
- Habit cough: Seven children (13.5%) had a tic-like, dry cough that varied from frequent “throat clearing” to a loud staccato bark. It was invariably present at rest but usually improved as exercise progressed. Post-exercise FEV₁ was normal in all cases.
- No diagnosis: Eleven children (21.1%) had normal exercise tests despite giving a convincing symptom history. Seven of these accepted a monitored one month trial of inhaled drugs. Five completed the course; all reported symptomatic improvement. Their repeat exercise tests were all normal and unchanged.
- Competitive athletes: The eight children who gave a history of high level competitive sport were not listed as a separate diagnostic category but they emerged as a subgroup with surprisingly similar characteristics. Taken together, they had received extensive medical attention and often had a long history of medication. They had had twice as many consultations as the children with confirmed EIA (3.1±0.6 *v* 1.5±0.5, *p* < 0.001) and took significantly more daily medications (2.3±0.5 *v* 1.3±0.7, *p* < 0.01). Despite this, they all had a normal response to exercise (+10 min FEV₁, -0.25±2.3 *v* -13.4±4.8, *p* < 0.001). Six had vocal cord dysfunction, one had a very loud habit cough, and one had no diagnosis.

DISCUSSION

We prospectively studied 52 children who had been referred to our clinic for investigation of incompletely controlled exercise induced asthma. After careful clinical and laboratory testing, we found that only eight (15.4%) of these children met conventional diagnostic criteria for EIA. Exercise associated respiratory complaints in the majority of the

Table 2 Study results listed by diagnostic category

| Diagnosis | Exercise induced asthma | Poor physical fitness | Habit cough | Vocal cord dysfunction/sigh dyspnoea | No diagnosis | Normal exercise controls |
|--|-------------------------|-----------------------|--------------|--------------------------------------|---------------|--------------------------|
| Number | 8/52 (15.4%) | 12/52 (23.1%) | 7/52 (13.5%) | 14/52 (26.9%) | 11/52 (21.1%) | 8 |
| Exercise time, min | 9.7±0.7 | 7.8±2.0 | 10.0±0 | 9.7±0.7 | 9.7±0.6 | 10.0±0 |
| Treadmill speed, kph | 6.6±0.3 | 6.2±0.8 | 6.9±0.5 | 7.2±0.6 | 6.9±0.6 | 7.4±0.3 |
| FEV ₁ baseline, % predicted | 99.1±15.9 | 97.8±8.9 | 104.7±6.8 | 107.6±9.0 | 105.5±13.4 | 116.6±7.4 |
| % change FEV ₁ + 5 min | -6.9±2.7 | 0.2±2.8 | 0.4±1.3 | 0.6±1.2 | -0.4±1.7 | -2.6±4.0 |
| % change FEV ₁ + 15 min | -13.4±4.8 | 1.8±4.9 | 0.1±4.5 | 0.1±2.3 | -0.9±4.8 | 0.4±4.5 |
| % change post-salbutamol | 16.1±7.4 | 4.1±4.9 | 4.1±3.0 | 2.4±2.3 | 4.5±3.4 | 2.7±2.4 |
| Max pulse, bpm | 195.3±9.0 | 180.8±15.9 | 179.9±11.2 | 196.9±14.1 | 192.4±10.5 | 190.6±10.9 |
| BMI >95% | 2/8 (25%) | 6/12 (50%) | 0/7 (0%) | 0/14 (0%) | 0/11 (0%) | 0 |
| Consults/child | 1.5±0.5 | 1.8±0.5 | 2.4±0.8 | 2.7±0.8 | 1.8±1.0 | 0 |
| Drugs/child | 1.3±0.7 | 1.1±0.7 | 1.7±0.8 | 1.6±0.8 | 1.4±0.7 | 0 |
| Competitive athlete | 0/8 (0%) | 0/12 (0%) | 1/7 (14.3%) | 6/14 (42.9%) | 1/11 (9.1%) | 0 |
| Previous OCS | 2/8 (25%) | 0/12 (0%) | 1/7 (14.3%) | 1/14 (7.1%) | 2/11 (18.2%) | 0 |

No significant differences between males and females so values combined.

What is already known on this topic

- Studies of EIA are complicated by the absence of clearly defined diagnostic tests
- Self-reported respiratory symptoms remain the basis for diagnosing EIA

remainder were either due to functional disorders such as vocal cord dysfunction or were the result of poor physical conditioning. Misdiagnosis was principally due to the unreliability of the initial self-reported respiratory symptoms. In a study of 256 adolescents, Hallstrand and colleagues⁸ published very similar results. Of the 47 children they identified with previously diagnosed EIA, who reported persistent respiratory symptoms with exercise, only eight (17%) subsequently had a positive exercise test.

The biggest obstacle to any form of asthma research is diagnosis.²⁵ Asthma is an inhomogeneous condition for which there is no absolute diagnostic test combining acceptable sensitivity with specificity.²⁶ Unquantifiable diagnostic error is the unavoidable result but, surprisingly, the topic is often overlooked.²⁷ Clinical studies of diagnostic accuracy in asthma are rare, in both the adult²⁸ and paediatric²⁹ literature. Even the relatively well defined treadmill exercise test is still far from being a gold standard. Variations in the exercise load,³⁰ exercise time,³¹ or the temperature²⁴ and humidity⁶ of inspired air will all alter the fraction of children diagnosed with EIA. Simply changing the defined drop of FEV₁ from 10% to 15% (both widely used definitions)^{2, 6} would significantly reduce the number of children defined as having EIA (from 15.4% to 3.8% in our study).

Despite the problems of measurement error, we believe that our broad conclusions are reliable, particularly within the subgroups of poor physical fitness, VCD, and habit cough. These diagnoses were not made unless the clinical picture was unambiguous. None of these children had responded to conventional EIA therapy and all had normal exercise tests. Exaggeration of their symptoms during the test procedure was common and also helped to confirm the non-respiratory nature of their complaints.

While it is possible that some of the “no diagnosis” group were false negatives (due to insufficient exercise stimulus or the lingering effects of inhaled corticosteroid therapy), the lack of measured response to a month of therapy in five of them would suggest that the error rate was low. Equally, several of the children in the EIA group would become false positives just by changing the defined drop in FEV₁ from 10% to 15%. These diagnostic problems are not unique to our study and emphasise the fact that attention should be paid to measurement error when interpreting the results of any asthma study.

The weakest link in the diagnostic chain was the unreliability of the presenting respiratory symptoms. In keeping with others, we found that imprecise use of medical terms such as “wheeze” was particularly common.³² It was important to ask the child clear questions about their symptoms and the relation to exercise without parental prompting.⁷ With care and patience, it was usually possible to obtain a clear history. The primary complaint that eventually emerged was sometimes neither respiratory (headache, aphonia, or fainting) nor, in a few cases, even associated with exercise. For example, deep sighing or the sensation of being unable to take a full breath,²¹ although initially attributed to EIA, were often associated with watching

What this study adds

- EIA is greatly overdiagnosed among Vancouver children principally due to the unreliability of their initial respiratory history
- More emphasis should be placed on the possibility of diagnostic error when analysing paediatric asthma studies

television. Despite these problems, it should be emphasised that, in most cases, a careful history and physical examination would have revealed the possibility of alternative diagnoses.

Early puberty is a difficult time for many children, particularly when the stress of athletic competition is added.³³ Functional respiratory complaints such as habit cough¹⁸ or sigh dyspnoea²¹ are common at this age,³⁴ both in athletic³⁵ and non-athletic children.³⁶ In addition, obesity³⁷ and poor physical fitness²³ are growing problems among children across North America. Exercise related complaints are commonly associated with all of these conditions. Failure to appreciate the broad differential diagnosis of self-reported exercise symptoms in children will lead to over-diagnosis of EIA.¹⁹ The poor correlation between self-reported exercise symptoms and exercise testing in paediatric studies^{7, 8} is more likely due to unreliable symptoms rather than inaccurate test results.

Over-diagnosis of EIA among competitive athletes is a concern that has been raised by others, including the International Olympic Committee.³⁸ In our study, the athletic children all had normal exercise tests despite an extensive history of investigation and medication. There appeared to be almost a “culture” of asthma and allergies amongst the athletic children and their team-mates. For example, two of the hockey players believed they were allergic to diesel fumes from the ice cleaner, the competitive gymnast felt that her symptoms were due to chalk dust used on her hands, while both competitive swimmers believed they were allergic to chlorine. All of these children had normal exercise tests. There is clearly room for more research into medical beliefs among paediatric elite athletes.

Although our results suggest that symptom based diagnosis of EIA is unreliable among Vancouver schoolchildren, we would stress that as long as care is used in the initial assessment, the majority of exercise associated respiratory complaints can be diagnosed and managed without the need for exercise testing. In addition, careful questions concerning exercise symptoms should always be included in the investigation and management of any asthmatic child. We would also suggest a need for greater appreciation of the possibility of diagnostic error when interpreting any asthma study, particularly those relying primarily on self-reported respiratory symptoms.³⁹

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Authors' affiliations

M Seear, D Wensley, N West, Department of Respiratory Medicine, Children's & Women's Health Centre of British Columbia, Vancouver, British Columbia, Canada

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