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Poor perception of dyspnoea in children with undiagnosed asthma

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ABSTRACT: The aim of the present study was to establish the differences in dyspnoea perception between children with undiagnosed and diagnosed asthma.

A cross-sectional community-based study was performed, which included a parental questionnaire on the child's respiratory health and testing of airway reversibility and bronchial hyperresponsiveness (BHR). ''Diagnosed asthma'' was defined by a physician's diagnosis of asthma. ''Undiagnosed asthma'' was defined by the presence of asthma symptoms combined with either airway reversibility or BHR without a physician's diagnosis of asthma. Only children with a positive BHR test were selected for further analysis. Perception of dyspnoea was assessed using the Borg scale and the visual analogue scale (VAS), plotted against the percentage fall in forced expiratory volume in one second and expressed as the slope of the regression line.

Of the initial 1,758 participating children, 70 had undiagnosed asthma and 38 had diagnosed asthma. The Borg and VAS slopes in children with undiagnosed asthma were less steep than those of children with diagnosed asthma (Borg: 0.07 and 0.14, respectively; VAS: 0.06 and 0.11, respectively).

Among children with bronchial hyperresponsiveness, those without a parent's report of physician's diagnosis of asthma had a worse perception of dyspnoea than children with diagnosed asthma.

KEYWORDS: Asthma, children, dyspnoea, perception

In Western European and affluent countries, asthma is the most common chronic disease with up to 32% prevalence in childhood [1, 2]. Patients with asthma vary greatly in their ability to perceive spontaneous and acutely induced bronchoconstriction [3, 4]. JULIUS *et al.* [5] showed that children with life-threatening asthma were poor perceivers of dyspnoea during bronchoprovocation. Furthermore, a substantial proportion of children with asthma underestimate their bronchoconstriction, as measured by symptom scores, obstruction scores or breathing perception [6].

In recent decades it has been suggested that asthma in children is underdiagnosed and, subsequently, under-treated [7]. Recent data show that underdiagnosis is still a problem. For example, JOSEPH *et al.* [8] reported an 11.7% prevalence of undiagnosed asthma.

Although poor perception of dyspnoea seems to play a role in severe asthma, it is unclear whether poor perception is also a cause of under-recognition of asthma symptoms in the general population [9]. To date, no information is available on perception of dyspnoea in children with undiagnosed asthma. Therefore, the present study explored whether perception of dyspnoea differs between children with undiagnosed and diagnosed asthma. To address this question, the perception of dyspnoea was evaluated during a bronchial hyperresponsiveness (BHR) test in children aged 7–10 yrs with both undiagnosed and diagnosed asthma from an unselected population cohort.

METHODS

Population and study protocol

The study was conducted at the Máxima Medical Center (Veldhoven, the Netherlands) in 41 out of 44 primary schools in four cities in the south of the Netherlands. All children aged 7–10 yrs (groups 5 and 6) and their parents were asked to participate in the present study. All participating children were invited for lung function testing with assessment of reversibility after administration of salbutamol. Bronchial challenge testing was performed in all children with asthma symptoms, irrespective of a physician's diagnosis of asthma. A child was considered to have asthma symptoms if he/she had wheeze or dry cough in the previous 12 months. For the present study, a child was considered to have

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current ''diagnosed asthma'' if the parents confirmed that the child had current complaints and physician-diagnosed asthma in the previous 12 months. A child was considered to have ''undiagnosed asthma'' if the child had: 1) no parent report of physician-diagnosed asthma in the previous 12 months; 2) asthma symptoms (wheeze or dry cough) in the previous 12 months; and 3) either reversible airway obstruction or BHR.

Approval for the study was obtained from the Central Committee on Research involving Human Subjects (the Hague, the Netherlands), from the hospital ethics committee and from the principals of the schools involved. Informed written consent was obtained from the parents of all children.

Lung function testing

Maximal flow–volume curves were measured using a hand-held spirometer (Vitalograph Ltd, Maids Moreton, UK) according to European Respiratory Society guidelines [10]. Airway reversibility was defined as an increase in forced expiratory volume in one second (FEV_1) $\geqslant$10% of the predicted value 10 min after administration of 800 μg salbutamol using a Volumatic® spacer (GlaxoSmithKline, Uxbridge, UK) [11].

Hypertonic saline testing

BHR was assessed by an inhalation challenge with nebulised hypertonic (4.5%) saline using an ultrasound nebuliser (Klava 2000/4000; Klava Eltromed, Bielefeld, Germany) according to the International Study of Asthma and Allergies in Childhood (ISAAC) protocol [12]. All children were asked to withhold all asthma medications for $\geqslant$12 h beforehand. Children with a baseline FEV_1 $\leqslant$75% pred were excluded. Children with a respiratory tract infection $\leqslant$4 weeks before the BHR test received a new appointment. Children inhaled the saline for periods of increasing duration: 0.5, 1, 2, 4 and 8 min. FEV_1 was measured 1 min after each inhalation period and the next inhalation period started after 3 min. Bronchial challenge was stopped if FEV_1 had fallen $\geqslant$15% from the baseline value or if the total inhalation period of 15.5 min had been completed. A child was defined as having BHR if FEV_1 had dropped $\geqslant$15% from baseline during the inhalation challenge. The provocative dose of hypertonic saline causing a 15% fall in FEV_1 was calculated by linear interpolation between the last two points in the dose–response curves [13].

Assessment of perception of dyspnoea

The severity of dyspnoea during the challenge test was assessed by a Borg scale and a visual analogue scale (VAS) [14]. After each dose step children were asked: ''How severe is your breathlessness during and directly after this inhalation?'' The Borg scale consists of vertically labelled categories ranging 0–10, *i.e.* no dyspnoea to maximal dyspnoea. The VAS scale is a horizontal line (100 mm) labelled ''no breathlessness at all'' at one end (0 mm) and ''most extreme breathlessness ever experienced'' at the other (100 mm), whereby equal distances represent equal increments in the severity of breathlessness. During the tests, subjects were blinded to their lung function response.

Questionnaire

Parents completed a questionnaire that included the ISAAC core questions on symptoms of asthma, rhinitis and eczema. The questionnaire used has been reported elsewhere [15]. Additional data were collected on household characteristics, such as parental education, passive smoking and pet ownership. Asthma symptoms were defined as wheeze or a dry cough at night in the previous 12 months.

Statistical analysis

Chi-squared and unpaired t-tests were used to test whether the demographic, patient and clinical characteristics differed between children with diagnosed and undiagnosed asthma. Only children with a positive BHR test were selected for further analysis. Borg and VAS scores were plotted against percentage decrease in FEV_1 from baseline. These individual Borg/FEV_1 and VAS/FEV_1 slopes are known to represent an index of dyspnoea, *i.e.* each slope indicates the perception of airway obstruction: the steeper the slope the more sensitive the subject is to signals of bronchoconstriction [16]. The intercepts represent baseline Borg and VAS scores. Differences between the slopes and the corresponding intercepts were analysed by the Mann–Whitney U-test.

RESULTS

Participants

Of 44 eligible schools, 41 participated in the study. Reasons for nonparticipation were recent involvement in another study (n=2) and a school policy never to participate in medical studies (n=1). The parents of all 2,745 children were invited to participate in the study from September 2002 to April 2005. Of these, 1,758 (64%) parents gave informed consent to participate. A total of 144 children were excluded from further analysis due to missing questionnaire data (n=60) or refusal to participate in bronchial challenge testing (n=31). Additionally, 53 children were excluded from data analysis as they were unable to complete the bronchial challenge test due to nausea or coughing (n=3), or were unable to meet technical conditions (n=50).

Diagnosis and demographics

The study population comprised 1,614 children, of whom 130 (8%) had undiagnosed asthma and 81 (5%) had diagnosed asthma according to the present authors' criteria. Of these, 99 children had a positive BHR test: 70 children with undiagnosed asthma and 29 with diagnosed asthma. Table 1 presents the characteristics of the final study population. No differences were found between children with undiagnosed and diagnosed asthma with respect to age, parents with asthma and currently smoking parents. Demographic data of children with (un)diagnosed asthma without BHR did not differ from the demographic data in the group of children with diagnosed or undiagnosed asthma with a positive BHR (data not shown).

Table 2 presents the questionnaire and lung function data. Children with diagnosed asthma had more wheezing symptoms and less change in FEV_1 at the end of the BHR test than children with undiagnosed asthma. All children with a parent's report of asthma reported asthma symptoms (wheeze or dry cough at night) in the previous 12 months.

Figure 1 presents a representative example of the relationship between the Borg score and FEV_1. Each slope indicates the perception of airway obstruction of an individual patient: the steeper the slope the more sensitive the subject is to signals of

TABLE 1 Characteristics of the two study groups

	Undiagnosed asthma	Diagnosed asthma
Subjects n	70	29
Sex		
Male	30 (43)	19 (66)
Female	40 (57)	10 (35)
Age yrs	9.3±0.8	9.4±0.8
Mother asthma ever	10 (17)	3 (10)
Father asthma ever	3 (6)	3 (12)
Mother or father current smoker	19 (27)	8 (28)
Mother's education		
Low	7 (12)	6 (21)
Moderate	28 (46)	12 (45)
High	25 (42)	10 (34)
Father's education		
Low	7 (13)	5 (19)
Moderate	22 (42)	10 (38)
High	24 (45)	11 (41)

Data are presented as n (%) or mean±SD, unless otherwise stated.

bronchoconstriction. Table 3 gives the results of the slopes and intercepts of the Borg and VAS scores. The intercept, which represents baseline perception, did not differ between the groups. Children with undiagnosed asthma were significantly less sensitive to signals of bronchoconstriction than children with diagnosed asthma, as illustrated by the slopes for Borg/FEV1, which were twice as low in children with undiagnosed asthma compared with children with diagnosed asthma (0.07 and 0.14, respectively; p=0.04). A similar trend was found for the VAS/FEV1 slope (0.06 and 0.11, respectively; p=0.11). Analysis of children not receiving inhaled steroids showed similar results for the slopes of Borg/FEV1 (0.07 and 0.16 for children with undiagnosed asthma and diagnosed asthma, respectively; p=0.03). A significant result was found for the VAS/FEV1 slope (0.06 and 0.11 for children with undiagnosed asthma and diagnosed asthma, respectively; p=0.04).

DISCUSSION

The present results show that children whose parents do not report a physician's diagnosis of asthma appear to perceive bronchoconstriction less well than children with diagnosed asthma. Baseline perception did not differ between both groups.

It was also found that, in real life, undiagnosed asthmatics are more frequent than those correctly diagnosed (8 *versus* 5%). These results underline that underdiagnosis of asthma is still a problem and are in agreement with BRAUER *et al.* [17], who reported a similar result in a large cohort of children at the age of 4 yrs.

To the best of the current authors' knowledge, the present study is the first regarding the perception of dyspnoea in children whose parents do not report a physician's diagnosis of asthma. The current results are consistent with a previous study among Dutch adults [18], which showed that underpresentation of obstructive airway symptoms to the general practitioner is often caused by a decreased perception of dyspnoea. The results of VAS and Borg scores are identical, although analysis of the VAS slopes did not reach statistical significance. This can be explained by a better correlation of the Borg score with ventilation than the VAS score [14].

Children with undiagnosed asthma and a blunted sensation of dyspnoea are at increased risk for underestimation of their illness and a severe asthma attack [5]. Presumably, they will report fewer symptoms to their caregivers and physician. It has been suggested that the asthmatic inflammatory process could reduce perception of dyspnoea, possibly due to damage to the sensory receptors in the airways [16]. BOULET *et al.* [19] showed that adults with mild asthma not using anti-inflammatory agents perceive respiratory symptoms less acutely during metacholine-induced bronchoconstriction than those currently using anti-inflammatory agents. SALOME *et al.* [20] showed a better perception of dyspnoea in adults after treatment with inhaled corticosteroids. However, analysis of children not receiving inhaled corticosteroids showed the same results for the Borg/FEV1 slope as analysis of the whole group of children receiving or not receiving inhaled steroids. Furthermore, the results for the VAS slope showed a significantly lower perception in children with undiagnosed asthma. Therefore, the difference in perception of dyspnoea between the groups cannot be clarified by differences in the number of children using inhaled corticosteroids. Another explanation for the differences between children with undiagnosed and diagnosed asthma could be that children with undiagnosed asthma have an acquired degree of tolerance to bronchoconstriction due to adaptation related to frequent bronchoconstriction [21]. Furthermore, a low baseline FEV1 and severe bronchial responsiveness are associated with a low degree of perceptiveness for bronchoconstriction [22, 23]. In the present study, however, differences in perception of bronchoconstriction between children with undiagnosed and diagnosed asthma could not be explained by differences in BHR or a lower FEV1. Future research should focus on possible methods of improving the perception and awareness of children with symptoms of asthma. The Borg scale has been used in children to measure the severity of perceived wheeze or chest tightness during induced airway narrowing [24]. Furthermore, perception indices are repeatable if asthma control remains unchanged [25]. In addition, NUIJSINK *et al.* [26] found a slope of 0.14 for the Borg/FEV1 correlation in 93 children aged (mean±SD) 10.9±2.6 yrs with moderately severe diagnosed asthma (FEV1 98±15% pred). The Borg slope in children with diagnosed asthma in the present study was in the same range as in the study by NUIJSINK *et al.* [26], which can be seen as a confirmation of the reliability of the method used. Furthermore, the bronchial hyperreactivity tests were performed by experienced lung function assistants, who also had experience with Borg and VAS scores in children. In adults (median age 25 yrs), VEEN *et al.* [27] found a slope of 0.06 for the Borg/FEV1 correlation in adults with brittle asthma and a Borg slope of 0.11 in stable asthma. Thus, the same small differences observed in the present study are found in adult patients with a clinically different asthma presentation.

Abnormal dyspnoea perception in children may be a factor in the delay in diagnosing asthma. Due to the cross-sectional

TABLE 2 Clinical characteristics of the two study groups

	Undiagnosed asthma	Diagnosed asthma	p-value
Symptoms in previous 12 months			
Wheeze	38 (54)	25 (86)	0.002
Dry cough at night	52 (75)	18 (69)	0.36
Lung function parameters			
Mean baseline FEV_1 % pred	96	92	0.17
Mean baseline FVC % pred	91	92	0.75
Change in FEV_1 after BD %	6.9	6.1	0.48
Reversibility FEV_1 $\geqslant$10%	23 (33)	7 (31)	0.48
Median PD_{15} mL	4.3	3.7	0.87
Mean Borg scores per child	3.3	2.9	0.7
Mean VAS scores per child	3.3	2.9	0.7
Borg scores range	0–9	0–8	
VAS scores range	0–9.2	0–9	
Inhaled corticosteroids	4 (6)	23 (79)	<0.001

Data are presented as n (%), unless otherwise stated. FEV_1: forced expiratory volume in one second; % pred: % predicted; FVC: forced vital capacity; BD: bronchodilator; PD_{15}: provocative dose of hypertonic saline causing a 15% fall in FEV_1; VAS: visual analogue scale.

design of the present study, it is only possible to speculate about this. The child's poorer perception of dyspnoea might have contributed to the nondiagnosis, but there may be many other reasons to explain the fact that a medical label has not been attached. However, when children grow up they are much less under the direct attention of their parents. Subsequently, parents cannot take the child to the doctor if the children themselves did not notice and complain about their dyspnoea.

Some possible limitations should be mentioned. First, the ISAAC questionnaire used in the present study depended on the recall of asthma symptoms by parents. Recall by parents can be inaccurate. However, there is no reason to suppose that the inaccuracy influenced diagnosis differently in the different patient groups. Secondly, the results are only generalisable for children with undiagnosed asthma with a positive BHR. Thirdly, the challenge test does not reflect the real-life situation of bronchoconstriction episodes. Children will probably be more focused on their respiratory sensation during a provocation test in a laboratory setting than in daily life. Fourthly, the relatively rapid airway narrowing during induced bronchoconstriction probably makes it easier to assess the degree of bronchoconstriction [28]. Fifthly, the present study may have been biased due to selective nonparticipation. Information on the reasons for not participating in the study was not collected and thus the extent to which this may have biased the present results has not been analysed. It is possible that children with undiagnosed asthma more frequently refused to participate since they perceive fewer symptoms and, therefore, felt no urge to participate. These children could have poorer perception of dyspnoea than the participating children. Alternatively, it is possible that the participating children with undiagnosed asthma perceived more symptoms than the nonparticipating children and thus have a better perception of dyspnoea than

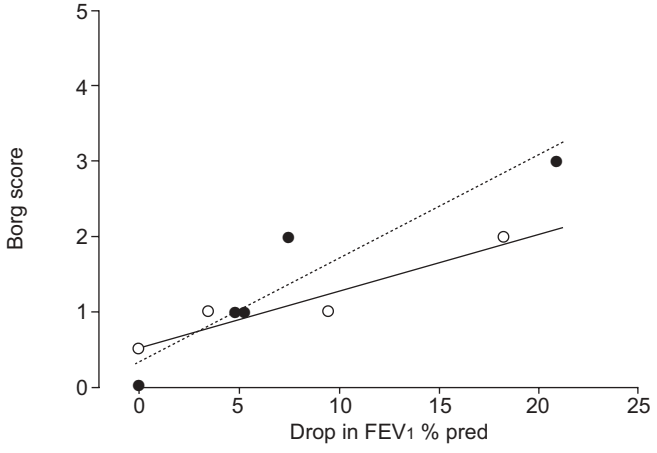

FIGURE 1. Representative example of the relationship between the Borg score and forced expiratory volume in one second (FEV_1). ·····: linear regression of a child with diagnosed asthma (●); ———: linear regression of a child with undiagnosed asthma (○). The correlation coefficient, slope and intercept are 0.89, 0.14 and 0.34 for the child with diagnosed asthma and 0.93, 0.07 and 0.54 for the child with diagnosed asthma. % pred: % predicted.

TABLE 3 Intercepts and slopes of the Borg and visual analogue scale (VAS) scores in children with positive bronchial hyperresponsiveness

	Undiagnosed asthma	Diagnosed asthma	p-value
Intercept			
Borg	0.65 (-0.16–5.6)	0.79 (-0.57–5.1)	0.43
VAS	0.96 (-0.09–6.4)	0.80 (-0.05–5.1)	0.99
Slope			
Borg/FEV_1	0.07 (-0.09–0.40)	0.14 (-0.03–0.46)	0.04
VAS/FEV_1	0.06 (-0.06–0.52)	0.11 (-0.07–0.49)	0.11

Data are presented as median (range), unless otherwise stated. FEV_1: forced expiratory volume in one second.

nonparticipants. If both conditions happened, the perception of dyspnoea in real life is even worse than revealed in the present study.

The major strengths of the present study are that, to the current authors' knowledge, it is the first population-based study that evaluates perception of dyspnoea in children whose parents do not report a physician's diagnosis of asthma with the well-known Borg scales. Furthermore, a clear definition of undiagnosed asthma was used involving the collection of objective measures.

In conclusion, children with bronchial hyperresponsiveness whose parents do not report a physician's diagnosis of asthma perceive their breathlessness less well during a provocation test than children with bronchial hyperresponsiveness and diagnosed asthma. For a number of children this might be an explanation for the delay in asthma diagnosis.

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