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Limitations of questioning asthma to assess asthma control in general practice

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Summary

Background: The monitoring of children with asthma in primary care is based on the occurrence and frequency of asthma symptoms. We questioned whether the current approach is adequate to identify all children in whom a sufficient level of asthma control is not achieved.

Aim: The aim of this study is to illustrate that in some children asthma was incorrectly considered controlled, because the children failed to report current symptoms of asthma.

Patients and methods: One hundred and nineteen children were identified with recent wheezing plus moderate or severe airway hyperresponsiveness. We analyzed whether these children reported current symptoms of asthma (as normally questioned during a routine visit).

Results: In 20 children (18%) current asthma symptoms were absent despite moderately or severe airway hyperresponsiveness and wheezing in the last year. In addition, the usage of controller medication was very poor.

Abbreviations: AHR, airway hyperresponsiveness; FEV₁, forced expiratory volume in 1 s; GP, general practitioner; ICS, inhalation corticosteroids; PD₂₀, provocative doses methacholine which gives a 20% fall in FEV₁ compared to baseline.

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Conclusion: We conclude that the general practitioner has insufficient tools to adequately assess asthma control in all children. The assessment of airway hyperresponsiveness as an additional guide to manage asthma in children in general practice is recommended. In this way, better asthma control can be achieved.

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Introduction

In asthma, disease control refers to control of the clinical manifestations. Therefore, it is current practice to use a symptom-based approach for the monitoring of patients with asthma in primary care settings. However, recent studies have shown that treatment based on symptoms alone is inferior to treatment also based on an additional (inflammatory) marker. Two studies demonstrated that treatment based on airway hyperresponsiveness (AHR) and sputum eosinophils, respectively, resulted in a decrease of asthma exacerbations compared to treatment based on symptoms alone.^{1,2} Two other studies, one in adults and one in children, showed beneficial effects when information about the patients exhaled nitric oxide was used in addition to treatment based on symptoms only.^{3,4} AHR is one of the hallmarks of asthma. It is an objective parameter of asthma reflecting the severity of airway disease.¹ In our opinion, children with moderate or severe AHR should be treated with controller medication if AHR is part of the clinical manifestation of asthma. In an earlier paper we reported on a large group of children treated for their asthma in general practice. We showed that in most children the severity of AHR in these children could not be suspected by their general practitioner (GP), based on symptoms alone.⁵ In the present study, children with borderline to severe AHR were followed for one year to study prospectively the relationship between symptoms and AHR. In addition to the previous report we also questioned parents whether children had symptoms of wheezing during the study year. We hypothesized that in a substantial number of asthmatic children presenting with less pronounced, atypical or trivialised symptoms of asthma, the severity of their disease could be easily underestimated.

Methods

Patients

All children described in this paper participated in an intervention study that compared different methods to improve disease control in childhood asthma in general practice. GPs were subject to one to three cumulative strategies to improve control in childhood asthma: (1) distribution of an asthma guideline, (2) a single educational session and (3), a onetime individualized treatment advice based on symptoms and lung function including the degree of AHR. Children were eligible to participate in the original study if at least two prescriptions of β_2 -mimetics and/or an inhaled corticosteroid (ICS) were prescribed in the year before invitation. The flow sheet of participation selection is shown in Fig. 1. The patient selection is described in more detail elsewhere.^{5,6}

Study design and patient selection

At the end of the original one-year study, 362 asthmatic children were re-evaluated on asthma symptoms, Peak Expiratory Flow (PEF) variability, degree of AHR, and medication usage. Parents were asked to fill in a standard questionnaire on asthma symptoms of their child in the past year. AHR was assessed by means of a methacholine inhalation challenge test when the FEV₁ was $\geq 75\%$ of predicted. The method used is validated in children and described elsewhere.⁷ The degree of AHR was expressed as a PD₂₀, a provocation dose that induces a 20% fall in FEV₁ from baseline. Severe AHR was defined as a PD₂₀ below 75 μg methacholine, moderately severe AHR as a PD₂₀ below 300 μg , mild AHR as a PD₂₀ below 1000 μg and borderline to normal AHR as a PD₂₀ above 1000 μg according to the classification used by Sont and colleagues.¹ Children were challenged to a maximal cumulative dose of 3600 μg methacholine. Children with a baseline FEV₁ value below 75% of predicted were not challenged. These children were classified as having severe AHR.

We analyzed whether children scored current symptoms of asthma in their diary. The diary was filled in during two weeks prior to the inhalation challenge test. In the diary the frequency of asthma related symptoms, cough, wheeze and shortness of breath was scored ('0' (no complaints), '1' (once a day), '2' (more than once a day), and '3' (whole day)). Total day as well as total night scores could range from 0 to 9. Moreover, we calculated: (1) a total symptom score and (2) a symptom-free days score, defined as the total number of symptom-free days (range 0–14).

PEF variability was also assessed in the two-week diary. Children were provided with a 'Personal Best' peak flow meter. The best of three PEF measurements was used and the percentage of predicted was calculated.^{8,9} PEF variability was calculated as: evening PEF value minus the morning PEF value divided by their mean value.

The number of prescribed inhalers for ICS and β_2 -adrenergic drugs was obtained from electronic medication lists of the GPs.

Statistical analysis

Data analysis was performed with the statistical package SPSS (version 12.2) (SPSS, Inc., Chicago, IL). To compare groups with regard to continuous normally distributed data, independent samples *t*-tests were performed.

Results

Of 404 children who were included on the basis of AHR at the start of the study, 362 participants (90%) completed

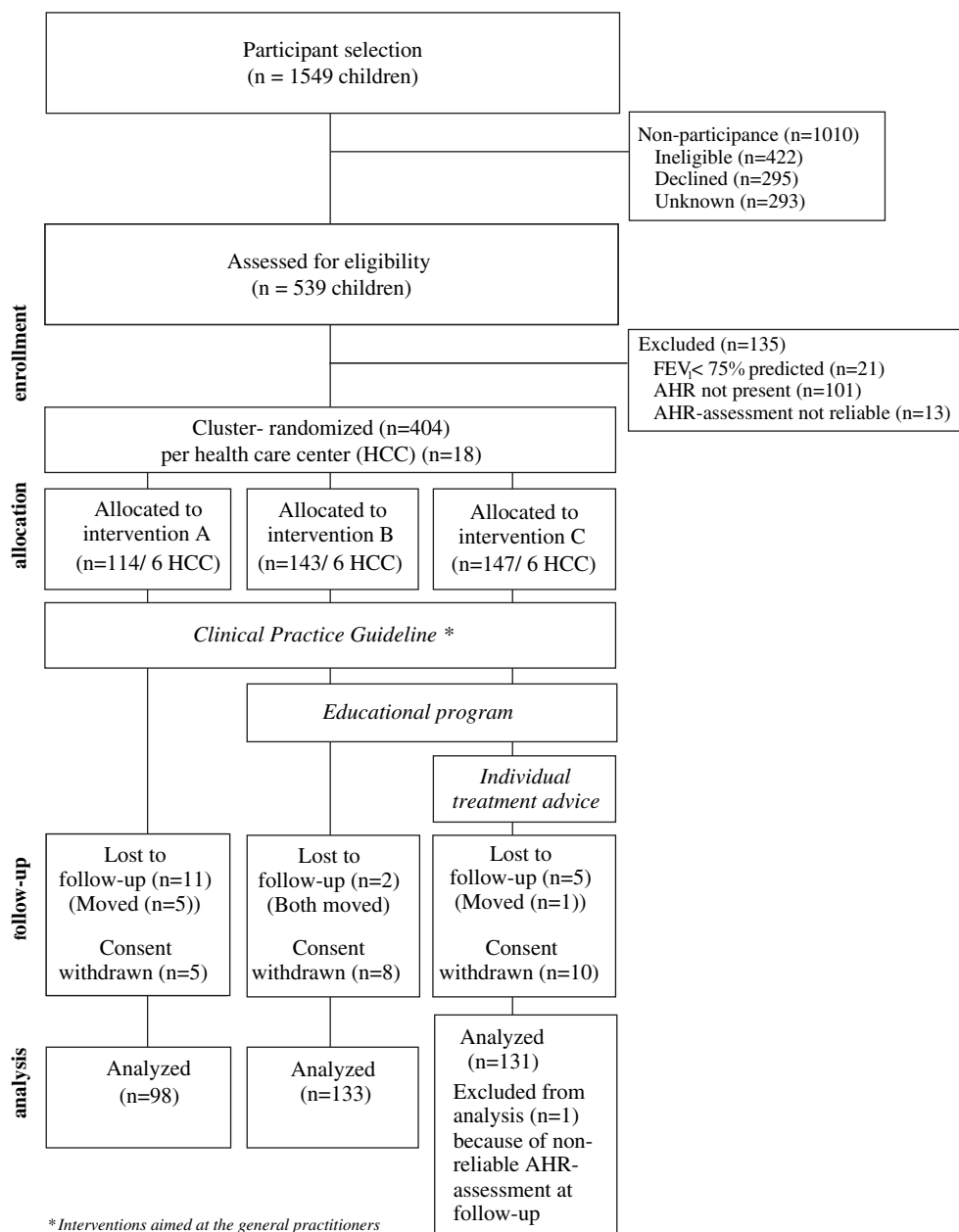


Figure 1 Design of the intervention study and flow diagram of participants in accordance with CONSORT (Consolidated Standards of Reporting Trials). HCC Health Care Centre.

follow-up for one year. From these children we got 328 completed diaries (91%), characteristics of these children are shown in Table 1. At evaluation at the end of the intervention study, 167 children (51%) had moderate or severe AHR (Table 1). Parents of 119 of these children (71%) reported wheezing in the last 12 months ('recent wheezing'). Fig. 2 shows the percentages of children with recent wheezing in subgroups of children with respect to lung function and degree of AHR. In contrast to the report of 'recent wheezing', 20 children (17%) with moderate to severe AHR did not report wheezing, cough or shortness of breath in the last two weeks, despite the fact that nine of these children showed severe AHR (PD₂₀ < 75 µg). The PEF variability of these 20 children

was significantly lower as compared to the children who reported symptoms in their diary (4.6% versus 7.8%, $p < 0.01$). Consistently with their lack of symptoms, these 20 children were prescribed fewer β_2 agonists (Table 1). The mean usage of inhaled corticosteroids was poor in both groups.

Children with moderate or severe AHR without 'recent wheezing' report less symptoms of asthma in their diary than those with 'recent wheezing' (median 0.1 versus 1.1; $p = 0.005$). Subsequently, they were prescribed less short acting reliever medication (median 16 versus 55 µg/day; $p = 0.04$). Except for these differences in symptoms and usage of reliever medication, no significant differences with respect to lung function were found.

Table 1 Characteristics of 328 children with asthma stratified to severity of airway hyperresponsiveness (AHR) and recent wheezing

	Moderate or severe AHR			Mild AHR or borderline to normal ^c	
	Wheezing last year			non-wheezing ^b	
	Present	Absent ^a	Missing data		
Number	92	20	7	48	161
Age	12.0 (2.6)	12.6 (2.5)	11.6 (1.3)	10.8 (2.4)	10.6 (2.5)
Gender, male	47 (51)	8 (40)	5 (71)	29 (60)	103 (58)
Symptom-free days	5.0 (0–13)	14**	–	13* (0–14)	12** (0–14)
Symptom score	1.4 (0–9)	0**	–	0.1* (0–5)	0.2* (0–8)
FEV ₁ , % predicted	93 (56–125)	93 (76–114)	91.0 (71–103)	96 (76–118)	100** (78–168)
PEF variability	7.8 (2–27)	4.6** (2–11)	–	6.8 (1.3–20.1)	5.3** (0.9–24.7)
Severe AHR (%)	44 (48)	9 (45)	2 (29)	16 (33)	–
ICS, µg/day	30 (0–410)	20 (0–140)	30 (0–150)	20 (0–200)	30 (0–300)
β ₂ -mimetic, µg/day	70 (0–660)	50* (0–230)	30 (0–60)	20* (0–590)	20** (0–400)

Data are presented as mean with \pm SD, as number of children with percentage of subgroup, or as median with range.

* $p < 0.05$, and ** $p < 0.01$.

^a Statistical comparison versus children with moderately or severe AHR and wheezing and present symptoms.

^b Statistical comparison versus children with moderately or severe AHR and wheezing.

^c Statistical comparison versus children with moderately or severe AHR.

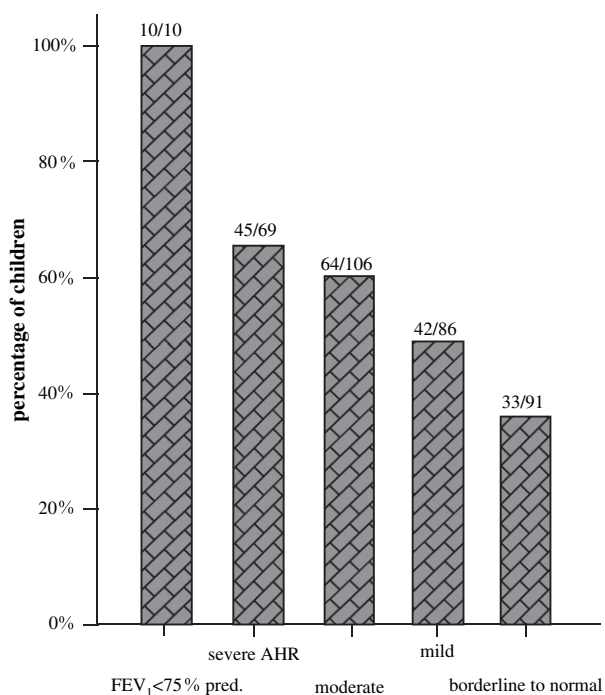


Figure 2 The percentage of 362 children who had wheezing in the last 12 months (as reported by the parents) is shown per subgroup. Children were stratified according to the degree of airway hyperresponsiveness (AHR).

Children with mild AHR or a normal response reported significantly less asthma symptoms, had more symptom-free days, had better lung function (PEF variability and FEV₁) and were prescribed less short acting reliever medication compared to children with moderate or severe AHR (Table 1). There was no difference in mean prescribed controller medication (ICS).

Discussion

In this study we showed that almost one-sixth of asthmatic children with 'recent wheezing' and moderate or severe AHR, were not identified as 'at risk' when questioning current asthma symptoms only. These children could be easily missed as 'not well controlled' by the GP at a routine visit. Eight of these children were not prescribed any controller medication in the previous year; the majority of the others (except four), probably did not use their medication regularly. These findings support our earlier conclusion that it is difficult if not impossible to assess the severity of asthma in a number of "at risk" children by means of only questioning asthma symptoms. Also lung function (PEF variability and FEV₁) is often not very helpful because of relative minor abnormalities.

All children in this study were treated for their asthma in general practice. A priori, participants of our study were likely to have (a diagnosis of) asthma because they were selected on the basis of prescribed asthma medication, which they were prescribed in the year prior to the start of the original study. Furthermore, all children were included

for follow-up because of the presence of AHR. AHR could be mild or even borderline normal, but in 212 children out of 362 (59%), AHR was moderate or severe at inclusion in the study.⁶

Furthermore, our data suggest that it is relevant to question wheezing during the last year. Of all children with severe AHR, 65% were identified on the basis of the prevalence of recent wheezing and all children with an FEV₁ below 75% of predicted were selected. However, questioning wheezing is not very specific to assess the severity of asthma.

The severity of AHR reflects the severity of asthma,¹ it is a tool to monitor asthma treatment¹⁰ and it predicts the outcome of asthma.¹¹ Furthermore, it is an objective characteristic of asthma. AHR is considered to be one of the major consequences of airway inflammation and remodeling. The degree of AHR has been shown to correlate both with an increase in airway inflammatory cells and with altered structural components in the airway wall, such as a deposition of subepithelial collagen or proteoglycans.^{12,13} The frequently observed lack of association between AHR and airway inflammation supports the assertion that other factors such as remodeling may be involved.¹⁴ Airway hyperresponsiveness is a key feature in asthma, but also occurs during other conditions, such as active smoking, respiratory infections, specific allergens and vigorous exercise.¹⁵ We hypothesize that this group of children (occasional presentation with symptoms at the GP and moderate to severe AHR) is under treated. However, we are not aware of intervention studies with ICS in this specific group, and can only guess what the benefits of such treatment would be.

There are several possible explanations for the apparent absence of symptoms in children. It maybe that children trivialize their asthma, or that children and parents do not recognize asthma symptoms as relevant enough to report. Because the perception of symptoms associated with airway obstruction follows a normal unimodal distribution in patients with asthma, patients with marked reductions in expiratory flow can sometimes be asymptomatic or have minimal symptoms.¹⁶ Perceptual accuracy may be affected by physiological, psychological, cognitive and parent-child factors.¹⁷ The absence of symptoms may be due to insufficient triggers, such as lack of exercise or absence of exposure to relevant allergens or respiratory irritants. Or it simply may be the natural course of the disease, which is known for its intermittent character. This is demonstrated in two studies who found large variations in morning PEF, asthma symptoms, and use of rescue medication, with the result that individual patients moved frequently across different severity categories over time.^{18,19}

In conclusion, a group of children with asthma in general practice is difficult to manage because reporting of current asthma related symptoms is absent. The children described in this study were found to have moderate or severe AHR. The assessment of AHR in these children is considered to be an additional and necessary tool to estimate the severity and control of the disease. Based on current guidelines these children would be incorrectly considered well controlled. At present, no consensus exists on how to monitor these children. We recommend monitoring of AHR or other

validated inflammatory markers in children who have had airway symptoms in the past year but do not report current asthma related complaints. They might be poorly controlled and in need of controller medication.

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Statement of interest

There are no competing interests by neither of the authors.

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