Preschool spirometry in clinical practice

Espirometria em idade pré-escolar na prática clínica

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ABSTRACT

Introduction: Spirometry is essential for evaluating asthmatic patients, and it is possible to perform it in preschool age children. However, there are no studies that demonstrate spirometry and bronchodilator test (BD) differences in asthmatic children and those with other clinical conditions, such as nonatopic recurrent wheezing (NRW) and chronic cough. **Aim:** To compare spirometry parameters in preschoolers diagnosed with asthma, NRW or chronic cough. To assess the recently published positive BD criteria on children in this study. **Methods:** During 2010, preschoolers with asthma, cough or NRW underwent spirometry on an outpatient basis. Bronchodilator response was evaluated, with BD considered positive (+) with a documented forced expiratory volume $(FEV)_{0.75}$ increase > 14%. Additionally we studied children with $FEV_{0.75}$ variation > 12% but <14%, to document how many would have been included in the BD+ group if the BD > 12% criterion (used in school children and adults) was chosen. **Results:** We studied 88 children with asthma and 99 with other diagnoses. In the majority it was possible to report FEV_1. Most children with other diagnoses (n=60; 61%) had normal spirometry with negative BD, a statistically significant difference in relation to asthmatics (n=36; 41%) (p=0.014). Of the asthmatics, 21% had obstruction with BD+, *versus* 4% of the cough/wheezing group, the differences being statistically significant (p=0.001). 20% (n=20) of children with cough/NRW had BD+ with normal spirometry and 11% had FEV variation between 12 and 14%. The BD differentiates asthmatic children from the remaining, since 40% of the asthmatics had BD+, regardless of any obstruction. **Conclusions:** Assessing lung function is now a reality in daily practice in preschool children, differentiating asthmatic children from other groups with chronic cough or wheezing. This is useful for clarification and eventual diagnosis of asthma in cases of atypical presentation. It is essential to use appropriate BD cut-offs to avoid overdiagnosing asthma.

Keywords: Asthma, bronchodilator, chronic cough, lung function evaluation, preschool, recurrent wheezing.

RESUMO

Introdução: *A espirometria é essencial para avaliação do doente asmático, sendo exequível em idade pré-escolar. Porém não existem estudos que demonstrem as diferenças entre crianças asmáticas e outras entidades clínicas, como sibilância recorrente não atópica (SRNA) e tosse crónica, quer na espirometria quer na prova de broncodilatação (BD).* ***Objectivos:*** *Comparar os parâmetros espirométricos em crianças em idade pré-escolar com diagnóstico de asma, SRNA ou tosse crónica. Aferir os critérios recentemente publicados para a positividade da BD nas crianças em estudo.* ***Métodos:*** *Durante o ano de 2010, realizaram-se espirometrias às crianças em idade pré-escolar com diagnóstico de asma, tosse ou SRNA, seguidas em ambulatório especializado. Foi avaliada a resposta ao broncodilatador, considerando uma BD positiva (+) se variação do volume expiratório forçado ($FEV_{0.75}$ > 14%. Adicionalmente foram estudadas crianças com variação $FEV_{0.75}$ > 12% mas < 14%, para documentar quantas teriam sido incluídas no grupo BD+ caso tivesse sido utilizado o critério BD > 12% (utilizado em idade escolar e adultos).* ***Resultados:*** *Incluíram-se 88 crianças com asma e 99 com outros diagnósticos. Na maioria foi possível reportar FEV_1. A maioria das crianças com outros diagnósticos (n=60; 61%) apresentou espirometria normal com BD negativa, diferença estatisticamente significativa em relação aos asmáticos (n=36; 41%) (p=0,014). No grupo dos asmáticos, 21% tinha obstrução com BD+, contra 4% dos restantes, diferença estatisticamente significativa (p=0,001). 20% (n=20) das crianças com tosse e/ou SRNA apresentava espirometria normal com BD+; 11% apresentavam variação do $FEV_{0.75}$ entre 12 e 14%. A BD permitiu distinguir crianças asmáticas das restantes; 40% dos asmáticos tinha BD+ independentemente da presença de obstrução.* ***Conclusões:*** *A avaliação funcional respiratória é actualmente uma realidade na prática desde a idade pré-escolar, permitindo distinguir precocemente crianças asmáticas de doentes com SR ou tosse crónica. É útil para esclarecimento e eventual diagnóstico de asma em casos de apresentação atípica. É fundamental utilizar* cut-offs *de BD adaptados, evitando sobrediagnosticar asma.*

Palavras-chave: *Asma, avaliação funcional respiratória, broncodilatação, pré-escolar, sibilância recorrente, tosse crónica.*

INTRODUCTION

Lung function tests are a vital tool for assessing and monitoring the asthmatic patient. Evidence of a marked prevalence of bronchial asthma in preschool children and the possible impact early treatment has on the disease's course justifies the need for a reliable measurement of the degree of pulmonary obstruction[1,2].

Recent years have shown it is possible to perform this measurement in preschoolers, particularly by using an interactive, computer-animated system[3-5]. It has been shown that it is possible to assess performance of this test[6]. There are reference measurements available solely for use with this age group[7,8].

Lung function testing in preschoolers is becoming used in the assessment of asthmatics. There are no studies proving its importance in daily clinical practice as an ancillary means of diagnosis in differentiating asthma from recurrent wheezing as part of an infection, or chronic cough[9]. A positive bronchial challenge test is important in diagnosing bronchial asthma, and is well defined in older children and adults (increased FEV_1 over 12% and 200mL[10-12]), but there is no assessment of its accuracy in preschool children[9,13]. This is particularly so for the setting of a positive cut-off for the bronchodilator test in asthmatic children in relation to response to the bronchial challenge test in healthy children[14-17]. Borrego *et al.*'s recent study proposed a limit of 14% for $FEV_{0.75}$ as positive criterion for this test

when comparing asthmatics to healthy subjects[18]. Studies proving the importance of this cut-off in daily clinical practice to differentiate asthmatics from children with nonatopic recurrent wheezing and chronic cough are needed.

AIMS

To compare spirometry parameters in preschool children diagnosed with asthma, NRW or chronic cough. To assess the recently published positive bronchodilator response criteria on children in this study and the real feasibility of using lung function evaluation in clinical practice.

METHODS

Between January and December 2010 all preschoolers aged 3-6 clinically diagnosed with bronchial asthma, chronic cough or NRW who attended outpatient Allergology and Clinical Immunology consultations and whose allergologist had requested a lung function study were included in the study.

All children with a history of prior hospital stay, particularly for asthma, or who had had breathing difficulty crisis in the two weeks prior to the study were excluded. Also excluded were children born before 37 weeks of gestation, with birth weight under the tenth percentile or with cardiac, metabolic, neurological or gastrointestinal pathologies. Children's parents or guardians gave their informed written consent and were present during the measurements.

No child in the study had presented any concurrent infection in the two weeks prior to the lung function test. Asthmatic children suspended their use of bronchodilator medication in the 48 hours prior to the test.

Weight and length/height were measured with a calibrated stadiometer with a digital scale and the measurements expressed in Z-scores adjusted for age and sex[19].

Spirometry was performed before and after administration of salbutamol (400 µg) using a holding chamber.

Spirometry was performed with Jaeger MasterScope spirometer (v.4.65, CareFusion Ltd) equipment. The measurements were taken with the child seated, using a mouth piece and nose clip. Incentive programmes were used to encourage the children to perform maximum expiratory manoeuvers. All curves obtained were scrutinised by two separate investigators. The children were not identified in this process. Results were only accepted if at least two acceptable and repeatable curves had been gleaned, in line with international recommendations[4,7,9,20]. The measurements were expressed in Z-scores, adjusted for sex, height and age[8,21]. All *Z*-scores under -2 were considered abnormal and an obstructive pattern was considered when FEVt (forced expiratory volume-time) and FEF_{25-75} scored were below -2.

Curves obtained after bronchodilation were subjected to the same criteria of acceptability and repeatability as the baseline curves.

Response to bronchodilation was assessed, with a bronchial challenge test considered positive when there was a variation in FEV_t over 14% following salbutamol administration. In addition, children whose variation in FEV_t following salbutamol administration was over 12% but under 14% were studied. This was to record the number of children who would have been included in the positive bronchial challenge test groupif the criterion of bronchodilation over 12%, used in adults and school-age children, has been used here.

Data analysis

Statistical data analysis was performed using SPSS version 18.0 for Windows (SPSS, Chicago, IL, USA). A median was used as a measurement of the central trend, and the interval as measurement of dispersal as the sample had an uneven distribution. The categorical variables were compared using the chi-squared test and continuous variables using the Mann-Whitney test. A 0.05 level of significance was set.

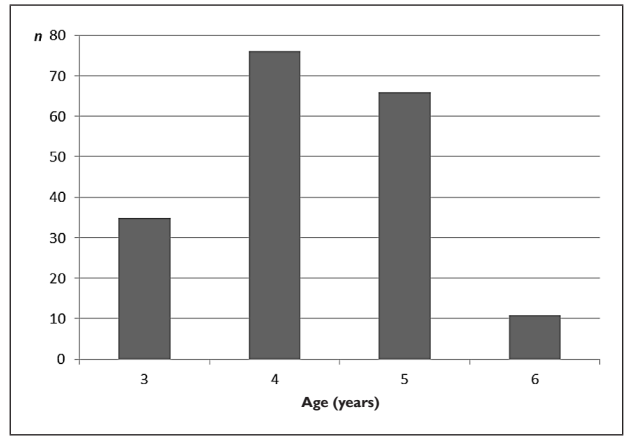

Figure 1. Sample distribution by ages

RESULTS

From January to December 2010 333 preschool children underwent lung function tests, with 146 cases excluded as they did not meet the inclusion / exclusion criteria, tests failed to meet baseline and bronchodilator test acceptability / repeatability criteria, or children being unable to perform expiration for over 0.5 seconds.

The final sample was composed of 187 children, whose characteristics are given in Table I. Of these, 88 were diagnosed with asthma and 99 had other diagnoses (56 chronic cough and 43 nonatopic recurrent wheeze). There were no significant differences seen between the sample of asthmatic children and the sample of children with other diagnoses in terms of sex, age and spirometry success relative to the duration of expiratory manoeuver, that is, the FEV_t reported (Table I). Figure 1 shows the distribution by age and shows the majority of children in the study were aged 4-5, with a median of 4.

In terms of the length of each manoeuvre in the volume-time curve, it was possible to report the FEV_1 in the majority of children (Table II). In 3% of the sample it was only possible to obtain expiratory manoeuvres with a duration of 0.5 seconds, here in children of 3-4 years of age.

Table I. Sample characteristics: diagnosis of asthma relative to other diagnoses (chronic cough or recurrent wheeze)

	Asthma ***n* = 88**	**Others** ***n* = 99**	**p**
Male sex	56 (64)	59 (69)	0.571*
Age, median (min-max)	4 (3 – 6)	4 (3 – 6)	0.599†
FEVt reported in the spirometry			
FEV_1	69 (78)	72 (73)	0.801*
$FEV_{0.75}$	17 (19)	23 (23)	0.343*
$FEV_{0.5}$	2 (2)	4 (4)	0.414*

Data shown as n (%), except when stated otherwise.
* Chi-squared test. †Mann-Whitney test; FEVt: Forced expiratory volume-time.

Table II. Collaboration and feasibility of the lung function study by age

	3 years n=34	4 years n=76	5 years n=66	6 years n=11	Global sample n=187
FEV_t reported					
FEV_1	22 (65)	56 (74)	55 (83)	8 (73)	141 (76)
$FEV_{0.75}$	11 (32)	15 (20)	11 (17)	3 (27)	40 (21)
$FEV_{0.5}$	1 (3)	5 (6)	0	0	6 (3)

Data shown as *n* (%). FEV: Forced expiratory volume.

It was seen that independent of age, 21% of children could only perform expiratory manoeuvres with a duration of 0.75 seconds. Reporting $FEV_{0.75}$ made for an effectively important gain in that it was possible to increase the obtaining of valid lung function parameters in the 3-year-old children from 67% to 97%, from 74% to 94% in the 4-year-old children, from 83% to 100% in the 5-year-old children and from 73% to 100% in the 6-year-old children. Overall, using $FEV_{0.5}$ and $FEV_{0.75}$ allowed for assessment of 46 (24%) of the children in the study.

The results of the lung function study gleaned for asthmatic and children with other diagnoses are given in Table III. The majority of children with other diagnoses (n=60; 61%) had normal lung function with negative bronchodilation, with this difference statistically significant in relation to asthmatics (n=36; 41%) (p=0.014). The majority of asthmatics (n=52; 59%) had an abnormal lung function (obstructive pattern and/or positive bronchodilation).

Comparing children with normal lung function and positive bronchial challenge test result with children with obstructive pattern and negative bronchial challenge test result, there were no differences found between asthmatics and children with other diagnoses. However, 20% (n=20) of the children with chronic cough and/or recurrent wheeze had a baseline lung function test with positive bronchial challenge test result.

Of the asthmatics, 21% had obstructive pattern and positive bronchial challenge test *versus* only 4% of the

Table III. Results of the lung function study in children with asthma compared to children with different diagnoses (chronic cough or recurrent wheeze)

	Asthma	Others	p
LFS normal, BD negative, *n* (%)	36 (41)	60 (61)	0.014
LFS normal, BD positive, *n* (%)	17 (19)	20 (20)	0.696
LFS normal, BD 12-14%, *n* (%)	11 (13)	11 (11)	0.827
Obstructive pattern with positive BD, *n* (%)	18 (21)	4 (4)	0.001
Obstructive pattern with BD 12-14%, *n* (%)	5 (6)	1 (1)	0.102
Obstructive pattern with negative BD, *n* (%)	1 (1)	3 (3)	0.317

BD: bronchodilation test; LFS: lung function study.

Table IV. Evaluation of the bronchodilation test in asthmatic children compared with children with other diagnoses (chronic cough or recurrent wheeze)

	Asthma (n=88)	Chronic cough (n=56)	Recurrent wheeze (n=43)	p
Postitive BD n (%)	35 (40)	12 (22)	12 (28)	<0.001

BD: bronchodilation test.

group of children with chronic cough or wheeze induced by infections who had this pattern. These differences between groups were statistically significant (p=0.001).

It is highlighted that 11% of the children with chronic cough or recurrent wheeze had a post-bronchodilation FEV variation between 12% and 14%.

Analysing just the bronchial challenge test result, independent of the presence of obstruction (Table IV), shows that bronchodilation can differentiate asthmatic children from children with other pathologies, in that 40% of the asthmatics had a positive bronchial challenge test.

Twenty-four of the group of children with chronic cough or recurrent wheeze had a positive bronchial challenge test result (Table III), 12 children in each category (Table IV).

DISCUSSION

This study showed that it is very feasible to perform lung function evaluations in preschoolers. It also demonstrated the usefulness of ancillary spirometry in this age group as a means of diagnosis and in assessing severity, and as a tool which also makes it possible to differentiate the asthmatics from the other groups of children in the parameters evaluated.

It is a pilot study as it evaluates the usefulness of spirometry in preschool children in daily clinical practice, and included asthmatic children and children with recurrent wheeze or chronic cough, this way allowing comparisons between the measurements obtained in these groups.

There were no statistically significant differences seen in sex and age in the study groups, meaning intra-group comparisons could be made due to the similarity. There were also no differences seen in FEV_t rates reported between asthmatic children and those with other diagnoses, suggesting it was feasible to perform, independent of clinical diagnosis.

The results' great impact in terms of the success achieved is also highlighted. Studies in this field have always reported encouraging results, with rates for the feasibility of performing spirometry of around 85%[1,6,23,24]. Even though the majority of our sample was made up of 4-5-year-old children, we showed that there is a benefit in reporting FEV_t below 1 second. and that even older children cannot often perform manoeuvers of over 1 second. Here it was possible to increase by 24% the number of preschoolers in whom it was possible to obtain lung function parameters.

All children with severe asthma – meaning prior hospital stay for the condition – were excluded, as were those with crises in the two weeks prior to the tests. This is reflected in a lesser number of asthmatics, but allowed for a more homogenous group to compare with the others.

Exclusion criteria for all children were premature birth and delayed intra-uterine growth, as both things are known to have a negative impact on lung function[25-26].

We found statistically significant differences between children with lung function within a normal range in the children with recurrent wheeze or chronic cough when compared to the asthmatics. We further highlight that 60 (61%) of the asthmatics had a normal evaluation. In addition 52 (59%) of the asthmatics had an abnormal lung function, corroborating their clinical diagnosis.

Twenty (20%) children with recurrent wheeze or chronic cough had normal baseline spirometry with positive bronchial challenge test and 4 (4%) had obstructive pattern with positive bronchial challenge test. In these cases nondiagnosed asthma can be suspected, meaning close monitoring of these patients is vital. Lung function evaluation can become fundamental in ancillary diagnosis and clarification in cases of bronchial asthma with nontypical presentation.

Asthma is a chronic disease which is common in childhood in almost all industrialised countries. While it is more commonly found in this age groups than in adults, there is only a limited amount of information available on specific aspects of asthma in children, in particular children aged under 5 years old[27]. There is consensus as to the need to treat, with specific guidelines published[27,28], and the importance of early diagnosis is recognised[27-29]. Here, where all semiological data overlap and there is ample heterogeneous presentation of different phenotypes, the usefulness of lung function testing is paramount.

In addition, 11 (11%) children with wheeze or chronic cough had baseline lung function within normal parameters but with a bronchodilation challenge test result between 12 and 14% (in line with the criteria for adults and older children). This could suggest that using the cut-off of 12% implies classifying the bronchodilation challenge test result as positive, bringing with it growing doubts for the clinician who may wrongly start treatment based on this isolated presupposition, which may then be seen in nonasthmatic children.

Borrego *et al.* and Dundas *et al.*[17,18] effectively showed that the cut-off usually used in adults and school age children is too low for this age group, postulating that there is a greater amount of bronchomotor tone. Borrego *et al.* inclusively showed that as around 15% of healthy children may present an increase in FEV_t >12% after salbutamol administration, this cut-off should not be used in this age group because of the risk of overdiagnosis.

Further, considering the very few lung function tests carried out in pre-school age children with asthma, we highlight that 21% of these asthmatic children had obstructive pattern of the airway with positive bronchodilation challenge test and with significant differences in relation to the group of children with cough or recurrent wheeze. This fact inclusively allows asthmatic children to be categorised as to disease severity and also permits monitoring of the course of the disease over time, namely after treatment.

There were no significant differences seen comparing between the groups studied as to normal lung function study and positive bronchodilation challenge test. This may have been the result of the small sample size, seeing as when the bronchodilation challenge test result is analysed on its own, independent of the result of the lung function test, it makes it possible to differentiate the different groups, with 40% of the asthmatics having a positive bronchodilation challenge test.

CONCLUSIONS

Lung function evaluation is currently a normal part of clinical practice for preschool children as it is for other older age groups. It differentiates asthmatic children from other groups of patients with recurrent wheeze or chronic cough, very frequently seen in daily clinical practice.

This study further highlights the use of lung function evaluation for clarification and eventual diagnosis of asthma in cases of more atypical presentation. This is extremely important since asthma is one of the more prevalent chronic diseases seen in preschool children, and one whose late detection and inadequate treatment can lead to irreversible abnormalities.

In addition, we stress the importance of using bronchodilation challenge test cut-offs appropriate for this age group. Using the criteria set for school-age children and adults will lead to overdiagnosis of asthma in children with recurrent wheeze or chronic cough.

A future analysis of the impact of lung function evaluation on the clinical decision and its role in monitoring preschool age asthmatic patients is vital.

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