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Home spirometry and asthma severity in children

Alwin FJ Brouwer

Ruurd Jan Roorda

Paul LP Brand

Princess Amalia Children's Clinic

Isala klinieken

Zwolle, the Netherlands

Address for correspondence and reprint requests:

AFJ Brouwer

Princess Amalia Children's Clinic

Isala klinieken

PO Box 10500, 8000 GM Zwolle

The Netherlands

Tel: +31 38 424 2234

Fax: +31 38 424 2734

E-mail: a.f.j.brouwer@isala.nl

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Abstract

Background: The usefulness of peak expiratory flow monitoring is disputed because of the unreliability of written peak flow diaries. The aim of this study was to examine the relationship of peak flow and forced expiratory volume in one second (FEV_1) variation to other estimates of asthma severity in children, using an *electronic* home spirometer with automatic data storage.

Methods: Over a 3-month period, thirty-six children with mild to moderate persistent asthma recorded peak flow and FEV_1 electronically twice daily and an asthma severity score in a written diary. Bronchial responsiveness was assessed at the beginning and bronchodilator response and asthma specific quality of life at the end of the study.

Results: Peak flow variation correlated significantly, but weakly to bronchial responsiveness and bronchodilator response, but not to the asthma severity score or quality of life scores. Within individual correlations between asthma severity scores and home spirometry indices and between peak flow and FEV_1 were highly variable.

Conclusions: Peak flow and FEV_1 variation obtained by home spirometry show poor concordance with other indices of disease activity and with each other. This limits the usefulness of home spirometry in childhood asthma.

Abstract Word Count: 189

Keywords:

Childhood asthma; asthma severity; self management; peak expiratory flow; home monitoring

Background

International guidelines on the management of asthma stress the importance of pulmonary function tests to monitor the clinical course of asthma and to achieve optimal control.[1][2][3] Measurements of bronchial responsiveness (BR) provide an estimate of asthmatic airway inflammatory activity and can be used in monitoring childhood asthma.[1][3][4] A study in adults has shown that adjusting maintenance therapy based on BR measurements improves asthma control and reduces asthmatic airway inflammation.[4] However, the downside of BR measurements – and of pulmonary function tests in general – is that they have to be performed in hospital and that they only provide a snapshot impression of asthma status, rather than that they reflect the inherent variability of the disease.[1][2][3][5] This variation of pulmonary function is considered to be one of the key characteristics of asthma.[1][2] Day-to-day home monitoring of peak expiratory flow (PEF) is thought to reflect this variability and is, therefore, recommended in guidelines as a monitoring tool.[6] Early studies have found a strong correlation between PEF variation and BR in adult asthmatics.[7][8] However, more recent studies have found a weaker relationship between PEF variation and BR in patients treated with inhaled corticosteroids.[9][10][11][12] In all studies on the relationship between PEF variation and other indices of asthma severity,[13][14][15] mechanical PEF meters and written PEF diaries were used. Several studies have shown that written PEF diaries are unreliable [16][17] and it has been suggested that using electronic home spirometers could overcome this drawback.[18] Before being able to use electronic home spirometers in a asthma self-management, the usefulness of these instruments in accurately reflecting asthma severity should be investigated. Therefore, this study was designed to examine the relationship of home measured PEF and FEV_1 and their variation, using an electronic home spirometer, to other parameters of asthma severity in children with chronic persistent asthma.

Patients and methods

Patients aged 6 to 16 years with mild to moderate persistent asthma [1][2] were recruited at our outpatient clinic. All had been using maintenance therapy with inhaled corticosteroids in daily dosages up to 400µg/day (budesonide, beclomethasone) or up to 200µg/day (fluticasone) for at least 6 months and were able to perform pulmonary function measurements reproducibly.[3][5] Children who had used systemic corticosteroids less than 4 weeks before the start of the study were excluded. Written informed consent was obtained from all participants and their parents. The study was approved by the hospital ethics review board.

For characterization purposes, different lung function measurements were completed by these patients. Flow-volume-loops were performed on a Jaeger Masterlab pneumotachograph (Erich Jaeger, Würzburg, Germany), following ATS/ERS guidelines.[3][5] Short-acting bronchodilators were withdrawn for 8 hours and long-acting bronchodilators for 24 hours prior to each session. At the start of the 3-month study period, the degree of bronchial responsiveness was assessed using a methacholine provocation test with the dosimeter method and results were expressed as the provocative dose of methacholine causing a 20% fall in FEV_1 (PD_{20}).[3][19] At the end of the 3-month period the patients performed flow-volume loops before and after inhalation of 800µg salbutamol to assess bronchodilator response.[5] Children seven years of age or older and one parent of each patient completed the validated Dutch versions of the disease specific Pediatric Asthma (Caregiver's) Quality of Life Questionnaire (PA(C)QLQ). Responses to these quality of life questionnaires were expressed on a 7-point Likert scale, higher scores reflecting better quality of life.[20][21]

At the first visit patients were instructed how to use the electronic portable spirometer (Koko Peak Pro, Ferraris, Louisville, Colorado, USA).[5][6][22] This home spirometer has been

validated using a precision waveform generator[23] demonstrating its agreement with performance standards as recommended by international guidelines.[5]

Patients were instructed to perform three forced expiratory flow manoeuvres twice daily between 6AM and 10AM and between 6PM and 10PM throughout the 3-month study period. All instructions were given by the same skilled assistant, encouraging the children to obtain optimal lung function values. Patients were instructed to expire for at least 2 seconds and measurements were only accepted if forced vital capacity exceeded FEV_1. The device automatically stored the highest of the three correctly performed PEFs on a microchip, along with the accompanying FEV_1.

Throughout the 3-month period, patients also recorded a validated asthma severity score on a continuous visual analogue scale twice daily in a written diary.[24] Score 0 represented the "worst possible state of their asthma" and score 10 the "sensation of having no asthma at all". Children were instructed to first score their perception of asthma severity, then perform the forced expiratory flow manoeuvres on their home spirometer and finally take their medication. Patients also recorded use of rescue bronchodilators in the diary, both as a measure of asthma stability at home and to identify and exclude lung function values influenced by bronchodilator medication. In order to identify exacerbations of asthma, patients were instructed to return to the clinic if they felt their asthma symptoms could not be controled with rescue bronchodilators. Such exacerbations and use of systemic corticosteroids were recorded in the diary. Monthly, data from the home spirometer were downloaded to a personal computer. After careful inspection following a predefined algorithm [25], recordings due to technical errors and unexplained outliers were excluded.[22] Adherence to the home recordings was calculated by comparing the expected recordings in 13 weeks (180 recordings minus the technical errors) with the actually obtained recordings. The PEF and the asthma severity score were expressed as percentage of the personal best value (%PB) and the FEV_1 as

percentage of the predicted value (%pred).[26] Variation of PEF (and of FEV_1) was expressed as the amplitude (maximum-minimum) as a percentage of the day's mean (ampl%mean).[13] These calculations of diurnal variation were only performed in children with an overall adherence with home spirometry of at least 80%, in order to obtain reliable variation calculations.

All data were analyzed using PRISM™ (GraphPad Software, San Diego, USA) for Windows™ version 3.00 applying Spearman rank correlation coefficient (ρ) as appropriate.[27]

Results

A total of forty-two children completed the study. The median overall adherence with home spirometry and with symptom diary keeping was 91.5% and 98.7%, respectively. Six children were excluded because of an adherence with home spirometry of less than 80%. Technical errors accounted for less than 10% of the missing data. Clinical characteristics of the remaining 36 children are presented in table 1 and results of home spirometry and asthma severity scores in table 2.

The mean PEF variation (expressed as amplitude%mean) over the 3-month period correlated significantly to bronchial responsiveness (Spearman's ρ=-0.43, p=0.009) and to bronchodilator response (expressed as a % of pre-bronchodilator FEV_1; Spearman's ρ=0.34, p=0.04), but the scatter was wide (fig. 1). Mean PEF and FEV_1 variation did not show significant correlations to the asthma severity score, or the patient's quality of life (table 3).

The correlations between the asthma severity score and home spirometry indices were highly variable in individual patients (fig. 2). For example, the individual correlation coefficients (Spearman's ρ) between asthma severity scores and corresponding FEV_1 values in individual patients ranged from -0.28 to 0.51, with a mean of 0.10.

Several examples of individual recordings of home spirometer indices and the asthma severity score are presented in figure 3. The most striking finding was the large variation between and within subjects in the relationships between PEF, FEV_1 and asthma severity scores. Increases in asthma severity scores were accompanied by decreases in PEF and FEV_1 values in some patients, but by increases in others. Based on the association patterns between home spirometry results and asthma severity scores, the study group could be divided into four distinguishable patterns; reasonable concordance (n=7 ,19.5%), dissociation or chaos (n=9 ,25%), poor perceivers (n=13 ,36%) and excessive symptoms (n=7 ,19.5%). (fig. 3) To our surpise, the concordance of PEF and FEV_1 values was highly variable between patients with only 67% of the patients showing an acceptable concordance (Spearman's $\rho > 0.5$). (fig. 4)

Falls of PEF below 80% or below 60% of personal best values were accompanied by highly variable FEV_1 values (fig. 5). For example, although the mean FEV_1 associated with a PEF falling below 60% of the personal best value was 65.8%pred (95%CI 63.9 to 67.8 %pred), the spread of FEV_1 values associated with this drop in PEF ranged from 18% to 120% of predicted.

Discussion

This study shows that in asthmatic children, the correlation of ellectronically recorded PEF variation to other asthma parameters is too inconsistent to be clinically usefull. This is not only true for PEF variation expressed as the amplitude as a percentage of the day's mean, but also for PEF expressed as a percentage of the personal best value and for the variation of FEV_1 (table 3). Although the unreliability of written PEF diaries is overcome by using an electronic home spirometer, this does not improve the poor concordance of PEF variation to other parameters of asthma severity.[11][12][28] We propose that this poor concordance, both between and within patients, limits the usefulness of home spirometers in the monitoring and management of childhood asthma.

It is commonly stated that variation in pulmonary function is one of the key characteristics of asthma,[1][2] and that PEF variation reflects this variability.[6] In this study, the variability of the subjective severity of disease was recorded on a daily basis using an asthma severity score which has been validated as accurate and reproducible.[24] Although PEF variation mirrored the variability of the asthma severity score in some patients, in most cases there appeared to be no relationship at all. In fact, 80% of the children displayed a (complete) dissociation between indices of home spirometry and the asthma severity score (fig. 3). These findings concur with earlier studies using mechanical PEF meters.[28] Some of these patients may be regarded as "poor perceivers" with little symptoms despite considerable variation of PEF and FEV_1 and others as patients with excessive symptoms without any variation of PEF and FEV_1.[29] It would be interesting to see if poor perceivers, identified by home recordings, could benefit from stepping up therapy, but this study was not designed to answer that question.

Another striking finding of our study was the poor concordance of changes in PEF with changes in FEV_1, the gold standard of peripheral airways obstruction. Although overall correlation between PEF and FEV_1 is present and can be expected with properly performed manoeuvres, there are some individual patients who show complete dissociation between PEF and FEV_1. (fig 4) With the low use of rescue bronchodilators in this study, it is highly unlikely that these findings were influenced by bronchodilators used during the day and before measurements.[30]

Similarly, falls of PEF below 80% or even below 60% of personal best values, which are commonly used as cut-off values for stepping up asthma therapy in self-management plans,[13] were accompanied by a wide range of drops in FEV_1 (fig. 5). This illustrates that PEF and FEV_1 are not interchangeable parameters of assessing airway obstruction.[6] FEV_1 is less dependent than PEF of the patient's effort and, consequently, is a better estimate of smaller airways obstruction.[5] Theoretically, therefore, monitoring FEV_1 could provide a more reliable assessment of airways obstruction than PEF. Possibly, the discordance between PEF and FEV_1 could, to some extent, be explained by FEV_1 being a better measure of smaller airways obstruction than PEF. In this study, however, the relationship of FEV_1 variation to other parameters of disease activity was as variable as that of PEF variation (table 3).

Our findings can probably not be explained by poor accuracy or measurement characteristics of home spirometers, which concord with performance standards as recommended by international guidelines, both for PEF and for FEV_1.[5][23]. Although it can be argued that measurements at home are not performed under supervision of a skilled assistant, who can encourage the children to obtain optimal recordings and who can provide visual feedback of correct performance by examining flow-volume loops or by using computer incentives or animations, it has been shown that the technical quality of home spirometry recordings in

children is usually acceptable.[31] It is therefore, even more striking that very low FEV_1 levels may be encountered occasionally in children with chronic persistent, but clinically stable asthma. (fig. 5) It can not be ruled out that some of these very low PEF and FEV_1 values were caused by poor lung function performance and lack of quality control at home. Lung function was, on average, normal in these patients (table 1). Even though there were no exacerbations requiring oral corticosteroids in this study group throughout the 3-month period, PEF and FEV_1 values were highly variable in a number of patients. (fig. 3) In such patients, FEV_1 values can drop as low as 18% of predicted, without being considered as technical errors or unexpected outliers according to predefined criteria. [25] Because, in the context of this study, the data, recorded on the home spirometer, were not used in a self-management setting as a basis for adjustment of therapy and were only analysed after completion of the 3-month study period, these low FEV_1 values did not prompt changes in asthma management immediately. If they *had* been used in such a setting, the poor concordance of FEV_1 and PEF (fig.5) would have complicated self-management considerably. If a drop of PEF below 60% of personal best can be accompanied by FEV_1 levels ranging from 18 to 120% of predicted, it is quite unclear what the best approach to asthma management should be. At such a point in time, current self-management strategies suggest commencing oral steroids. Although this is logical with accompanying low FEV_1 levels, giving oral prednisolon to children with an accompanying FEV of 120%pred is clearly inappropriate. Thus monitoring both FEV1 and PEF can be confusing when the changes in these two parameters are discordant. Similar findings have been previously described in adults with intermittent or mild persistent asthma [32], but not in children. Our study shows that such discordance occurs in as much as 33% of children with mild to moderate persistent asthma.

Asthma is a variable disease and although home spirometry appears to be a reliable and intuitively appealing method to monitor pulmonary function in children on a daily basis, this study demonstrates that home spirometry in children with asthma shows highly variable relationships with several distinct measures of asthma severity as bronchial responsiveness, bronchodilator response, asthma severity scores and quality of life. In addition, PEF values, obtained by home spirometry, show highly variable concordance to accompanying FEV_1 measurements. These results may help to explain why using an electronic home spirometer in self-management of childhood asthma does not appear to be useful in improving asthma control.[33] It is unlikely, therefore, that home spirometry is going to be useful in the long-term monitoring and management of childhood asthma.

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Legends

Figure 1 Correlation of PEF variation (ampl%mean) to PD_{20} methacholine and to bronchodilator response. Although the correlation is significant (Spearman's ρ= -0.43; p=0.009 and Spearman's ρ= 0.34; p=0.04) respectively), the scatter is wide.

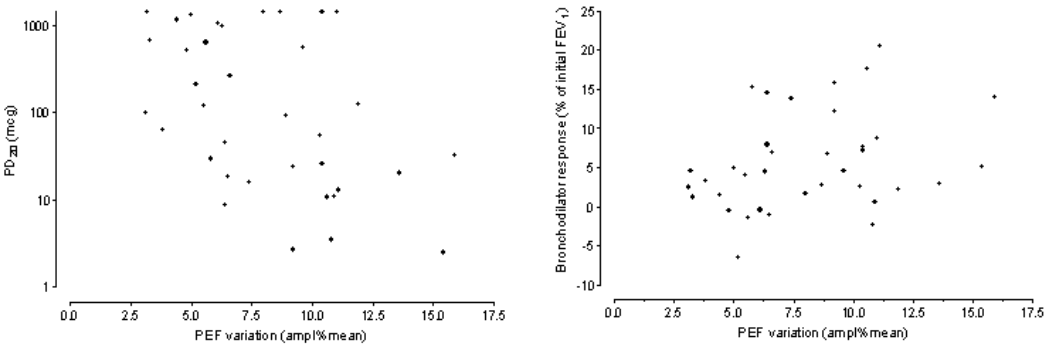

Figure 2 Distribution plots of individual Spearman's ρ correlations (one dot for each patient) of asthma severity score to PEF variation (ampl%mean; solid circles), FEV_1 (%pred; open circles), PEF (%personal best; solid triangles) and FEV_1 variation (ampl%mean;open triangles). Horizontal lines represent median values.

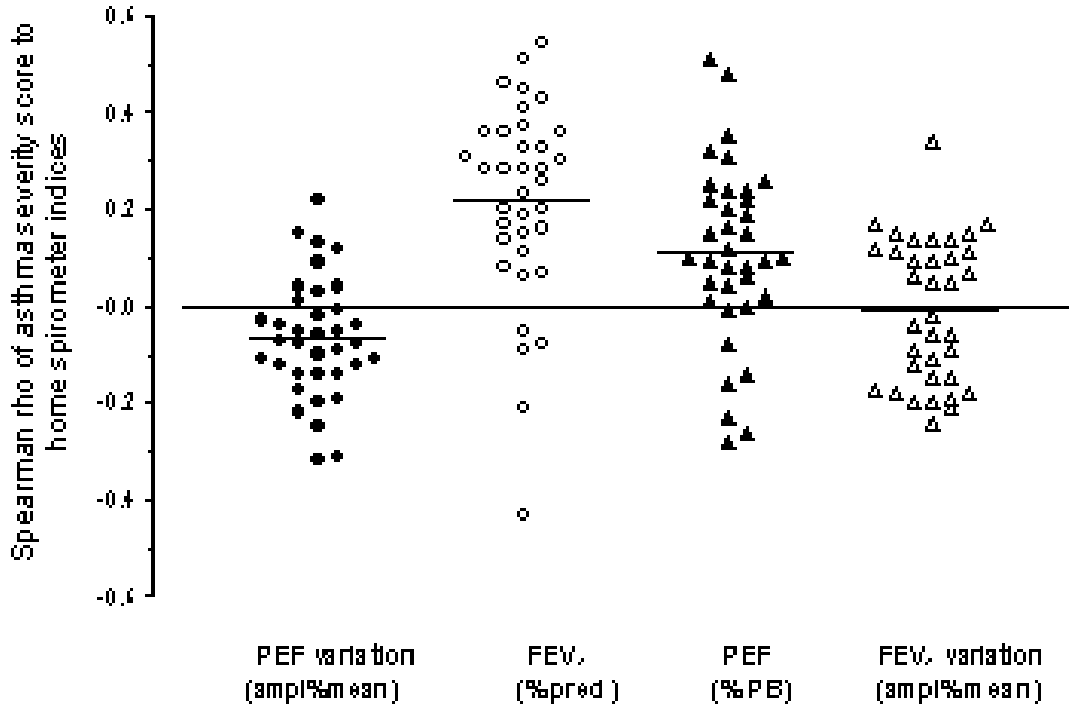

Figure 3 Samples of individual monitoring data showing four different patterns of relationships between asthma severity score, FEV_1 and PEF variation. patients with: a): concordance; b): dissociation or chaos; c): poor perceiver; d): excessive symptoms.

Solid line: asthma severity score (%personal best); open triangles: PEF variation (ampl%mean); closed triangles: FEV_1 variation (ampl%mean).

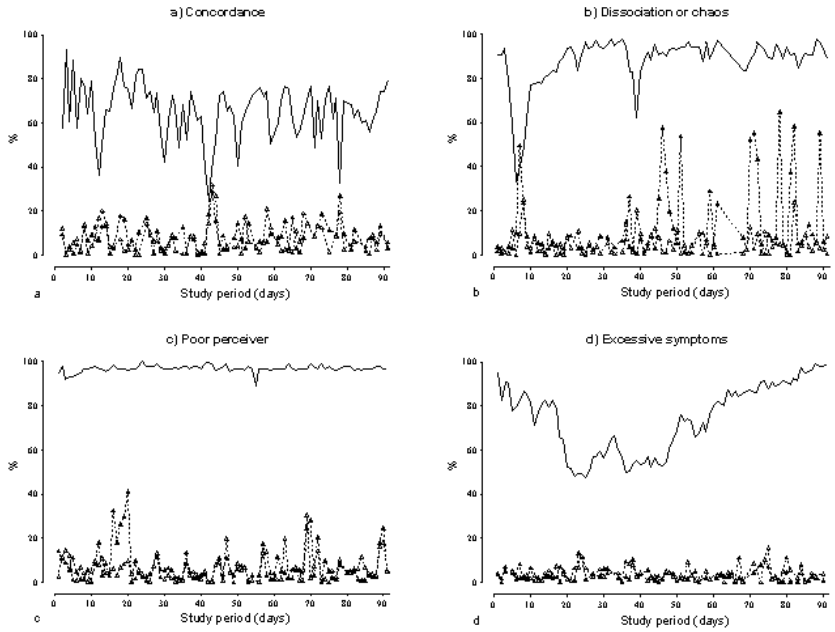

Figure 4 Examples of concordance (a) and discordance (b) between measured PEF and accompanying FEV_1 in two individual patients.

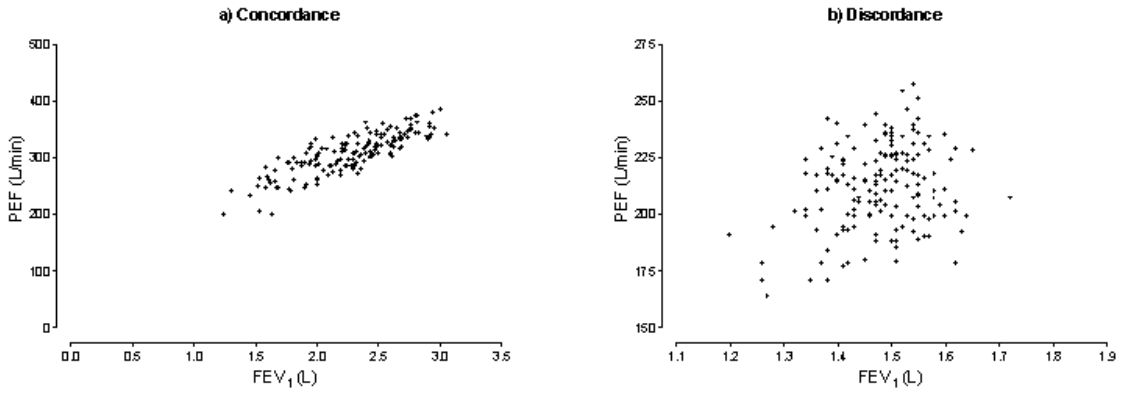

Figure 5 Box-and-whisker plots representing distributions of FEV_1 accompanying PEF values between 80 and 100-80% of personal best (n=4060), between 60 and 80% of personal best (n=2162) and <60% personal best (n=371). Values are presented as medians (horizontal lines) with inter-quartile ranges (boxes) and 90% ranges (error bars). Asterisks represent the minimal and maximal outliers outside the 90% range.

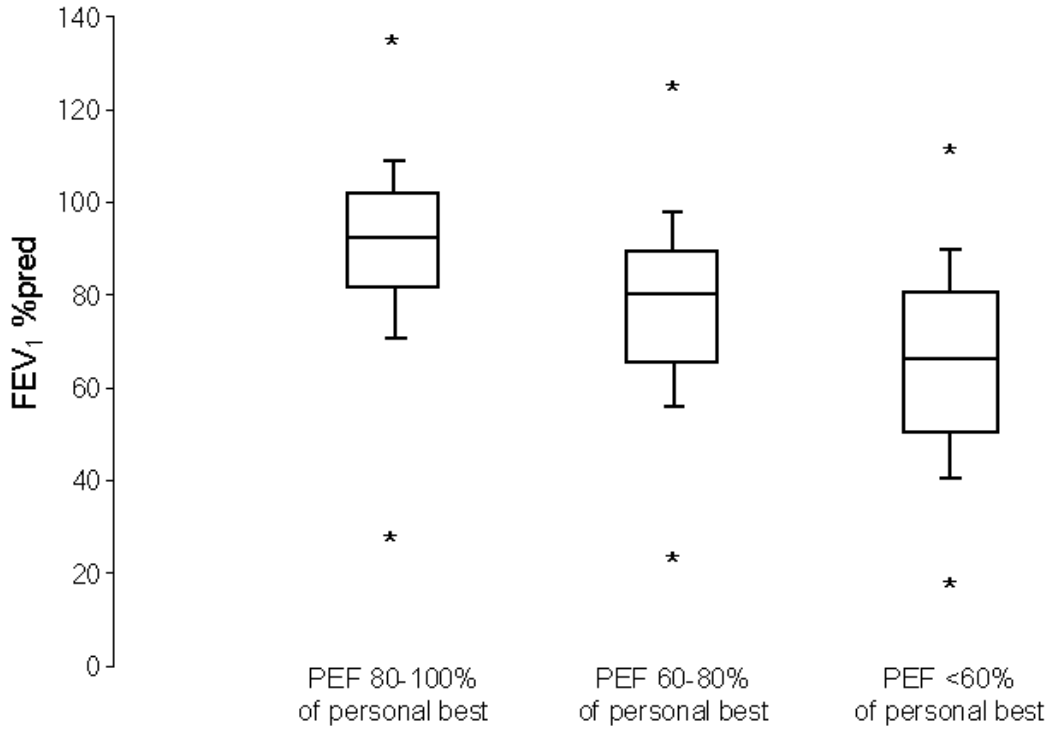
140
120
100
80
60
40
20
0
FEV1 %pred
PEF 80-100%
of personal best
PEF 60-80%
of personal best
PEF <60%
of personal best

Table 1. Characteristics of 36 asthmatic children completing the study with > 80% adherence with home spirometry

Sex (M/F)	25/11
Age (yrs)	10.4 ± 2.5
Age of onset of asthma (yrs)	2.8 ± 2.1
Maintenance medication:	
- Inhaled corticosteroids	100%
- Short-acting bronchodilators on demand	100%
- Long-acting bronchodilators	44%
- LTRA	none
Exacerbations requiring systemic corticosteroids	none
Smoking parent(s)	31%
Positive skin prick test or specific IgE to common inhalant allergens	89%
History of asthma in parent(s) or sibling(s)	78%
$logPD_{20}$-methacholine (μg)	1.98 (1.28-2.91)
FEV_1 (% pred FEV_1)	99.1 ± 12.6
QOL (children)* (n=34; 0-7)	6.0 ± 0.81
QOL (caregiver)† (0-7)	6.4 ± 0.48

Values are presented as mean ± SD, or as median and inter-quartile range for PD_{20}. M: male; F: female; LTRA: leukotriene receptor antagonists; FEV_1: forced expiratory volume in one

second; PD_{20}-methacholine: provocative dose of methacholine causing a 20% fall in FEV_1; QOL: quality of life. *Disease specific quality of life of children ≥ 7 years of age; †Disease specific quality of life of caregivers.

Table 2. Home spirometry and diary results

Home spirometry	
PEF (%PB)	81.4 ± 6.3
FEV_1 (%pred)	85.5 ± 15.5
vPEF (ampl%mean)	7.9 ± 3.4
$vFEV_1$ (ampl%mean)	9.5 ± 4.3
Symptom diary	
Use of rescue Salbutamol (puffs of 100μg/day)	0.5 ± 0.7
Asthma severity score (%PB)	83.4 ± 12.9

Values are presented as mean ± SD. PEF: peak expiratory flow; %PB: percentage of personal best value; FEV_1: forced expiratory volume in one second; vPEF: variation of PEF; %pred: percentage of predicted value; $vFEV_1$: variation of FEV_1; ampl%mean: day's amplitude (maximum-minimum) as a percentage of the day's mean.

Table 3.	PD_{20}-methacholine (µg)	Bronchodilator response (%initial FEV_1)	Pediatric asthma quality of life score	Asthma severity score (%PB)
PEF (%PB)	0.35; p=0.04 (0.01 to 0.61)	-0.38; p=0.02 (-0.64 to -0.06)	-0.10; p=0.58 (-0.43 to 0.26)	0.08; p=0.64 (-0.26 to 0.41)
FEV_1 (%pred)	0.36; p=0.03 (0.02 to 0.61)	-0.42; p=0.01 (-0.66 to -0.09)	0.15; p=0.39 (-0.20 to 0.47)	0.06; p=0.76 (-0.28 to 0.39)
vPEF (ampl%mean)	-0.43; p=0.009 (-0.67 to -0.11)	0.34; p=0.04 (0.00 to 0.61)	-0.05; p=0.79 (-0.39 to 0.31)	-0.15; p=0.39 (-0.46 to 0.20)
$vFEV_1$ (ampl%mean)	-0.43; p=0.008 (-0.67 to -0.11)	0.14; p=0.41 (-0.20 to 0.46)	-0.15; p=0.41 (-0.47 to 0.21)	-0.32; p=0.06 (-0.59 to 0.02)

Correlation matrix: values are presented as Spearman ρ with p-value and 95% confidence interval. FEV_1: forced expiratory volume in one second; %pred: percentage of predicted value; PEF: peak expiratory flow; %PB: percentage of personal best value; vPEF: PEF variation; ampl%mean: day's amplitude (maximum-minimum) as a percentage of the day's mean; $vFEV_1$: FEV_1 variation; VAS: visual analogue score.