Variability in Peak Expiratory Flow Does Not Classify Asthma According to Severity

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OBJECTIVE: The aim of this study was to determine whether variability in peak expiratory flow (PEF) could be used to classify the level of severity of asthma in children.

PATIENTS AND METHODS: We studied 387 boys and girls diagnosed with asthma and classified severity according to clinical criteria (Spanish Society of Pediatric Pneumology). PEF variability was determined using a portable mini-Wright peak flow meter (Clement Clarke International, London, UK; range, 50 L/min–800 L/min) over a 14-day period, with no changes in normal treatment. The following indices were used to calculate PEF variability: *1)* difference between morning PEF and nighttime PEF, expressed as a percentage of the mean value of the PEF measurements taken on that day; *2)* minimum PEF rate during a week, expressed as a percentage of the highest value recorded during that week; *3)* difference between the highest and the lowest PEF values, expressed as a percentage of the highest value; and *4)* the 10th percentile of PEF values recorded during a week, expressed as a percentage of the highest value recorded during that week. We assessed agreement between clinical classification and PEF variability using the weighted κ coefficient. We also analyzed the sensitivity and specificity of PEF variability indices for episodic and persistent asthma.

RESULTS: The analysis of levels of agreement between clinical classification of asthma and formulas 1, 2, 3, and 4 gave quadratic weighted κ coefficients of 0.494, 0, 0.488, and 0.346, respectively. The results were similar when patients were grouped and analyzed by type of asthma (episodic or persistent asthma).

CONCLUSIONS: The monitoring of PEF variability, a recommendation common in national and international guidelines on the management of asthma in children, is not valid for classifying severity of asthma in children.

Key words: *Asthma. Classification. Severity. Peak expiratory flow. Variability. Children.*

La variabilidad del flujo espiratorio máximo no clasifica el asma por niveles de gravedad

OBJETIVO: El objetivo de este estudio ha sido estudiar si la variabilidad del flujo espiratorio máximo (FEM) permite clasificar el asma en niños por niveles de gravedad.

PACIENTES Y MÉTODOS: Se ha estudiado a 387 niños y niñas diagnosticados de asma, cuya gravedad se clasificó atendiendo a criterios clínicos (Sociedad Española de Neumología Pediátrica). Se determinó la variabilidad del FEM con un medidor portátil (Mini Wright Peak Flow Meter Clement, Clarke International Ltd., Londres, Reino Unido; escala 50-800 l/min) en los 14 días siguientes, sin modificar los tratamientos habituales, según los índices de variabilidad del FEM: *1)* diferencia entre el FEM de la mañana y el de la noche, expresado como porcentaje del valor medio de las medidas del FEM durante el día; *2)* mínimo valor del FEM durante una semana, expresado como porcentaje del mejor FEM durante esa semana; *3)* diferencia del mejor sobre el peor FEM, como porcentaje sobre el mejor, y *4)* percentil 10 de los valores del FEM durante una semana, expresado como porcentaje del mejor FEM durante esa semana. Se analizó el grado de acuerdo entre la clasificación clínica y la variabilidad del FEM mediante el estudio de la concordancia (índice kappa ponderado). También se efectuó un análisis de sensibilidad y especificidad para el asma episódica y el asma persistente en relación con la variabilidad del FEM.

RESULTADOS: Los niveles de acuerdo entre la clasificación clínica del asma y las fórmulas 1, 2, 3 y 4 mostraron índices kappa ponderados bicuadrados de 0,494, 0, 0,488 y 0,346, respectivamente. Los resultados fueron similares cuando los pacientes se agruparon en asma episódica y asma persistente.

CONCLUSIONES: La medida de la variabilidad del FEM, recomendación común de las guías nacionales e internacionales para el manejo del asma en niños, no es válida para clasificar el asma en niños por niveles de gravedad.

Palabras clave: *Asma. Clasificación. Gravedad. Flujo espiratorio máximo. Variabilidad. Niños.*

Introduction

The National Asthma Education and Prevention Program[1] classifies asthma into 4 levels of severity: mild intermittent, mild persistent, moderate persistent, and severe persistent. In 2003 the Spanish Society of Pediatric Pneumology (SENP)[2] revised and modified this classification, mainly in regard to the frequency of asthma

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symptoms, and categorized the levels as occasional episodic, frequent episodic, moderate persistent, and severe persistent.

In children over age 5, the 3 main variables recommended for the classification of asthma are frequency of daytime symptoms, frequency of nighttime symptoms, and lung function measurements. Lung function measurements include percentage of predicted forced expiratory volume in 1 second (FEV_1), peak expiratory flow (PEF), and PEF variability. Most national[3] and international[1,4-7] protocols, consensus statements,[8] and clinical practice guidelines[9,10] include PEF variability, for which 3 levels are established: mild intermittent (<20%), mild persistent (20%-30%), and moderate or severe persistent (>30%) asthma.[11]

However, guidelines seldom mention how to calculate variability between 2 PEF measurements and there is some degree of confusion regarding how the measurement should be expressed.[12-14] Variability is sometimes determined by comparing measurements over a 24-hour period and sometimes by comparing 1 day with another. Thus, in order to obtain an intrapulmonary airflow measurement sufficiently sensitive to classify asthma according to severity and in order to allow measurement with easy-to-handle and inexpensive devices, several indices have been developed. These include daily variability, minimum compared to maximum PEF over a 7-day period, difference between maximum and minimum PEF expressed as a percentage of maximum, or minimum morning PEF before bronchodilator use expressed as a percentage of the 7-day maximum or of predicted.[5,6,15]

The aim of the present study was to determine whether PEF variability as defined in asthma management guidelines can indeed be used to classify asthma in children according to severity. To this end, we studied boys and girls diagnosed with asthma and, with no changes in normal treatment, classified asthma according to clinical criteria. We also determined PEF variability over the 14 days following classification in order to observe the level of agreement between clinical classification and classification by lung function, specifically PEF variability.

Patients and Methods

We carried out a prospective national multicenter observational study in boys and girls between the ages of 6 and 14 years diagnosed with asthma, comparing the clinical classification of asthma severity with PEF variability in order to assess the level of agreement between them. With this objective we classified asthma according to severity and measured PEF variability over the following 14 days, with no change in treatment. The study was carried out in the outpatient clinics of the participating researchers, all of whom were members of SENP.

The study was approved by the ethics committee of the Hospital Donostia in San Sebastián, Spain; that committee informed the hospitals of the participating researchers of approval. Informed consent and authorization for the use of data were obtained in all cases.

Sample Size

For the purpose of determining sample size, only the categories of episodic and persistent asthma were considered. According to the formula proposed by Fleiss,[16] for a predicted sensitivity of 90% and specificity of 80%, with a 95% confidence level and 90% power that would predict a 30% prevalence of persistent asthma, the minimum sample size required was 380 patients. Estimating that about 10% of the sample would be lost to follow-up, we calculated that we would need to collect data on 418 patients.

A consecutive sample of patients was established for each researcher until frequencies of levels of severity similar to those normally found clinically (episodic asthma, 70%; moderate asthma, 25%; severe asthma, 5%) were obtained.

Inclusion Criteria

Boys and girls between the ages of 6 and 14 years who had been diagnosed with asthma were included in the study. To meet inclusion criteria, medical histories had to show the following: *a)* signs and symptoms indicative of asthma; *b)* at least 3 asthma attacks in the previous 2 years, treated with bronchodilators and corticosteroids, with good response to treatment; and *c)* a positive bronchodilator test (increase in $FEV_1 \geq 12\%$ from baseline) or a positive stress test (decrease in PEF or $FEV_1 \geq 15\%$ from baseline). The diagnosis was considered to be asthma when conditions *a) + b)*; *a + c)*, or *a) + b) + c)* were met.

Exclusion Criteria

Exclusion criteria were age under 6 years or over 14 years, failure to meet criteria for diagnosis of asthma, inability to perform PEF maneuver, or a moderate or severe asthma attack during the first visit.

Measurements

1. Principal measurement. PEF was measured twice a day (between 8 AM and 10 AM and between 8 PM and 10 PM) for a period of 14 days, using a portable mini-Wright peak flow meter (Clement Clarke International, London, UK; range, 50-800 L/min). Results were expressed as absolute values and percentage of predicted: PEF = –425.5714 + (5.2428 × height), where PEF is expressed in liters per minute and height in centimeters.[17]

The PEF maneuver was performed after forced expiration (from residual volume) to maximum inspiration (total lung capacity) with the patient either standing or sitting with his or her back resting against the back of the chair. The mouthpiece was held between the teeth and over the tongue, with lips sealed around it. The patient was then instructed to blow as hard and as quickly as possible. The highest morning and nighttime values of 3 maneuvers were recorded.

Variability was calculated according to 4 indices:

– *Formula 1:* difference between morning and nighttime PEF expressed as a percentage of the mean value of PEF measurements taken on that day:

$$\frac{\text{Morning PEF} - \text{Nighttime PEF}}{(\text{Morning PEF} + \text{Nighttime PEF})/2} \times 100$$

– *Formula 2:* minimum PEF rate over the course of a week, expressed as a percentage of the highest value recorded during that week:

$$\frac{\text{Minimum PEF}}{\text{Maximum PEF}} \times 100$$

– *Formula 3:* difference between the highest and the lowest PEF values, expressed as a percentage of the highest value:

$$\frac{\text{Highest PEF} - \text{Lowest PEF}}{\text{Highest PEF}} \times 100$$

– *Formula 4:* The tenth percentile of PEF values recorded over the course of a week, expressed as a percentage of the highest PEF during that week:

$$\frac{P_{10}\ \text{PEF}}{\text{Highest PEF}} \times 100$$

2. Forced Spirometry. Forced spirometry was performed according to the guidelines of the American Thoracic Society and European Respiratory Society,[18] with FEV_1 expressed in absolute values in liters and as a percentage of the predicted value.[19]

Asthma Severity Classification

In accordance with SENP criteria, asthma was classified according to 4 levels of severity[2]:

– Occasional episodic asthma: episodes lasting a few hours or days, less than once every 10 to 12 weeks (maximum, 4-5 attacks/y); no symptoms between attacks and good tolerance of exercise. Functional characteristics: normal lung function tests between attacks: PEF or FEV_1 more than 80% of predicted; less than 20% variability in PEF

– *Frequent episodic asthma*: less than 1 episode every 5-6 weeks (maximum, 6-8 attacks/y), wheezing on heavy exertion, no symptoms between attacks. Lung function characteristics: normal spirometry results between attacks: PEF or FEV_1 more than 80% of predicted and less than 20% variability in PEF

– *Moderate persistent asthma:* more than 1 episode every 4-6 weeks, mild symptoms between asthma attacks, wheezing on moderate exertion, nighttime symptoms fewer than twice a week, and need for β_2-adrenergic agonists fewer than 3 times a week. Lung function characteristics: PEF or FEV_1 more than 70% of predicted and variability in PEF between 20% and 30%

– *Severe persistent asthma:* frequent episodes, symptoms between asthma attacks, need for β_2-adrenergic agonists more than 3 times a week, nighttime symptoms more than twice a week, and wheezing on slight exertion. Lung function characteristics: PEF or FEV_1 less than 70% of predicted between asthma attacks and variability in PEF more than 30%

Interventions and Timing of Visits

The only interventions were those required for asthma control. Two visits were scheduled:

1. During the first visit, the researcher *a)* reviewed inclusion criteria; *b)* filled in the data collection sheet; *c)* performed lung function tests (PEF and/or FEV_1); *d)* instructed patient in the use of the PEF meter and the patient diary (PEF value, consumption of β_2-adrenergic agonists, consumption of other drugs, clinical signs and symptoms); *e)* classified asthma according to severity; and *f)* made no change in previously prescribed treatment (until second visit).

2. During the second visit (day 15), the researcher *a)* reviewed the data collection sheet and collected and reviewed the patient's diary, in which the patient had recorded his or her nighttime asthma situation (no symptoms, discomfort on awakening, awakening once because of asthma symptoms, remaining awake most of the night because of asthma symptoms) and his or her daytime situation (no symptoms, short episode of asthma, short and mild episodes, asthma symptoms throughout most of the day, severe asthma) and *b)* established asthma control treatment in accordance with the clinical classification of severity determined during the first visit.

Statistical Analysis

For qualitative variables relative frequencies expressed as percentages were used as descriptive statistics for both PEF and FEV_1. In the quantitative expression of these variables, a goodness-of-fit test for normal distribution (Kolmogorov-Smirnov test) was applied; the results in both cases approximated to a normal distribution and we thus used the mean (SD) as descriptive statistics.

For the analysis of agreement, the 4-level SENP[2] classification was taken as the reference and compared with the various classification indices for PEF variability. As a first step, as the categories established were ordinal variables, we calculated the quadratic weighted κ coefficient, which improves the level of agreement established by the unweighted κ coefficient for ordinal variables, as it takes the magnitude of disagreement into account. Altman's[20] classification was used for levels of agreement, with weighted κ values of 0.20 or less considered poor agreement, values between 0.21 and 0.40 considered fair agreement, values between 0.41 and 0.60 considered good agreement, and values more than 0.81 considered very good agreement.

As a second step, the levels of asthma severity were grouped together and classified as either episodic or persistent and the sensitivity and specificity of the indices, and their 95% confidence intervals, were calculated. As there were only 2 groups, the unweighted κ coefficient was calculated in this case.

Results

Of the 405 patients enrolled, complete data were available for 387 (93.3% of the sample), of whom 37% were boys and 67% girls. As determined by body mass index, 1% of the patients were obese (>30 kg/m^2) and 7.2% overweight (25-30 kg/m^2). Weight was normal in the remaining 91.8% (<25 kg/m^2). Maintenance treatment consisted of inhaled corticosteroids as monotherapy in 118 (28.4%) patients, inhaled corticosteroids combined with long-acting β_2-adrenergic agonists in 118 (45.3%) patients, and other treatments in 27 (6.5%) patients. No maintenance treatment was being received by 33.5% of patients. Short-acting β_2-adrenergic agonists delivered from a dry powder inhaler (56.67%) or pressurized inhaler (42.84%) were used as rescue treatment.

Patients reported the following signs and symptoms in the previous 12 months: cough on minimal exertion, 18.2%; cough on moderate exertion, 47.8%; cough on heavy exertion, 7.5%; symptoms between attacks, 62.3%; nighttime symptoms, 41.2%; need for rescue bronchodilators, 83%; visits to the emergency department, 41.5%; and hospital admissions due to asthma exacerbations, 12.3%. The number of asthma exacerbations in the previous 12 months was less than 4 in 52.8% of patients, between 4 and 8 in 37.8% of patients, and more than 8 in 9.4% of patients.

PEF was measured in 392 patients, with a total of 5707 morning measurements and 5714 evening measurements. The mean (SD) value was 271.90 (81.51) L/min, with a median value of 260 L/min. Expressed as a percentage of predicted, the values were 85.86% (25.74%) (median, 82.11%). Forced spirometry was performed in 345 patients, and the mean FEV_1 was 2.3 (0.57) L (median, 1.97 L). Expressed as a percentage of predicted, the

TABLE 1
Agreement Between Clinical Classification of Asthma Severity and the First PEF Variability Index (Formula 1)*

Index	Severity				Total
	OEA	FEA	MPA	SPA	
OEA	117 (90.7%)	11	1	0	129
FEA	61	66 (49.3%)	5	2	134
MPA	24	60	16 (15.8%)	1	101
SPA	1	7	15	0 (0%)	23
Total	203	144	37	3	387

*PEF indicates peak expiratory flow; OEA, occasional episodic asthma; FEA, frequent episodic asthma; MPA, moderate persistent asthma; SPA, severe persistent asthma.

TABLE 2
Agreement Between Clinical Classification of Asthma Severity and the Second PEF Variability Index (Formula 2)*

Index	Severity				Total
	OEA	FEA	MPA	SPA	
OEA	0 (0%)	0	0	129	129
FEA	0	0 (0%)	0	134	134
MPA	0	0	0 (0%)	101	101
SPA	0	0	0	23 (100%)	23
Total	0	0	0	387	387

*PEF indicates peak expiratory flow; AEO, occasional episodic asthma; FEA, frequent episodic asthma; MPA, moderate persistent asthma; SPA, severe persistent asthma.

TABLE 3
Agreement Between Clinical Classification of Asthma Severity and the Third PEF Variability Index (Formula 3)*

Index	Severity				Total
	OEA	FEA	MPA	SPA	
OEA	117 (90.7%)	10	1	1	129
FEA	61	63 (40.0%)	7	3	134
MPA	24	58	18 (17.8%)	1	101
SPA	1	7	14	1 (4.3%)	23
Total	203	138	40	6	387

*PEF indicates peak expiratory flow; OEA, occasional episodic asthma; FEA, frequent episodic asthma; MPA, moderate persistent asthma; SPA, severe persistent asthma.

TABLE 4
Agreement Between Clinical Classification of Asthma Severity and the Fourth PEF Variability Index (Formula 4)*

Index	Severity				Total
	OEA	FEA	MPA	SPA	
OEA	43 (33.3%)	29	30	27	129
FEA	12	51 (38.1%)	35	36	134
MPA	2	9	40 (39.6%)	50	101
SPA	0	0	1	22 (95.7%)	23
Total	57	89	106	135	387

*PEF indicates peak expiratory flow; FEA, frequent episodic asthma; OEA, occasional episodic asthma; SPA, severe persistent asthma; MPA, moderate persistent asthma.

mean value was 87.3% (24.5%), with a median value of 84.7%.

Classification according to clinical severity on the first visit (and thus before PEF variability during the 14 consecutive days of the study was known) was as follows: occasional episodic asthma in 129 (33.33%) patients, frequent episodic asthma in 134 (34.65%) patients, moderate persistent asthma in 101 (26.09%) patients, and severe persistent asthma in 23 (5.94%) patients.

Patients' diaries for the 14 days showed the following:

– *Nighttime situation:* no symptoms, 84.81%; symptoms upon awakening,7.68%; awakened once because of asthma symptoms, 4.23%; awakened several times because of asthma symptoms, 2.25%; remained awake most of the night because of asthma symptoms, 0.16%; cough during the night and awakened once because of asthma symptoms, 0.46%; cough during the night and awakened several times because of asthma symptoms, 0.30%; cough and remained awake most of the night because of asthma symptoms, 0.02%. The mean number of inhalations of short acting β_2-adrenergic agonists was 0.22 (0.70) (minimum, 0; maximum, 12)

– *Daytime situation:* no symptoms, 85.00%; short asthma episode, 9.75%; 2 or 3 short mild episodes, 3.74%; asthma symptoms most of the day, 1.38%; severe asthma symptoms, 0.07%. The mean number of inhalations of short acting β_2-adrenergic agonists was 0.43 (1.10) (minimum, 0; maximum, 10)

Once data on morning and nighttime PEF had been collected for the 14 consecutive days after a physician's clinical classification of asthma severity, we carried out agreement analyses between the various indices of PEF variability and the clinical classification of asthma severity (Tables 1-4)

– Agreement between the clinical classification of asthma severity and PEF variability using formula 1 (Table 1) gave a quadratic weighted κ coefficient of 0.494 (moderate agreement). Agreement decreased as severity increased: it was high in occasional episodic asthma and nil in severe persistent asthma

– With formula 2 (Table 2), all values fell within the classification of severe persistent asthma and the level of agreement for each clinical classification was thus nil, with the exception of that of severe persistent asthma, for which it was 100%. In this case, the quadratic weighted κ coefficient was 0 (no agreement)

– The results with formula 3 (Table 3) showed levels of agreement similar to those obtained with formula 1, with a quadratic weighted κ coefficient of 0.488 (moderate agreement)

– Formula 4 (Table 4) gave results opposite to those of formulas 1 and 3: agreement increased as severity increased. However, in no case did it reach even 50%, except in severe persistent asthma, where agreement was very high. This formula gave a quadratic weighted κ coefficient of 0.346 (weak agreement)

To complete the study, patients with episodic asthma (occasional plus frequent) were grouped together and compared to those with persistent asthma (moderate plus severe) according to formulas 1 and 3 (Tables 5 and 6).

We carried out a sensitivity analysis and determined sensitivity, specificity, positive predictive value, and negative predictive value for persistent asthma (Table 7). These values were not determined for formulas 2 and 4, as they failed to attain even a moderate level of agreement.

Discussion

PEF is the maximum flow generated at any time during a forced exhalation, and usually occurs in the first 150 milliseconds of a forced expiratory maneuver.[21] It is related to the strength of the thoracic and abdominal muscles and is effort dependent. It can be measured either with a pneumotachometer equipped with a transducer that converts the input flow into an electrical output signal during forced spirometry or with a portable flow meter. In either case, both intersubject and intrasubject variability levels are great and reproducibility limited.[22] There is also considerable variability between the various peak flow meters. PEF obtained with a portable meter should be correlated with PEF obtained by forced spirometry.

Numerous studies of intrapulmonary airflow obstruction in asthmatic children have shown PEF to be a weak predictor of airway obstruction in bronchial challenge tests[23] and correlation with FEV_1 and with forced midexpiratory flow rates to be very limited.[24-26] The same results have been observed in both mild[27] and moderate or severe asthma in children with nonstandardized treatment. It must be borne in mind, however, that maintenance treatment with inhaled corticosteroids reduces PEF variability considerably.[28,29]

It is sometimes claimed that PEF variability is an expression of bronchial hyperresponsiveness, especially when variability is calculated as the difference between maximum PEF after bronchodilation and minimum PEF before bronchodilation,[30] even though correlation coefficients are low.[31] When bronchial hyperresponsiveness, defined as a PD_{20} (the provocation dose needed to produce a 20% decrease in FEV_1) of 8 mg/mL or less of histamine, has been compared with a PEF variability of 15% or more, no association has been observed.[32] Goldstein et al[33] found no association between PEF variability and bronchodilator response (FEV_1) to methacholine challenge.

Similar results have been reported in children, in whom bronchial hyperresponsiveness (histamine PD_{20}) is weakly associated with PEF variability.[34] PEF variability can therefore not replace bronchial challenge tests to determine the presence of bronchial hyperresponsiveness, as it does not measure the same aspects as the bronchial challenge test.[30]

Asthma management guidelines suggest that for the classification of asthma severity there is parity between FEV_1 and PEF expressed as a percentage of predicted and that asthma can be classified as mild (FEV_1 or PEF>80%), moderate (FEV_1 or PEF 80%-60%), or severe (FEV_1 or PEF <60%). However, numerous studies have shown that FEV_1 and PEF expressed as a percentage of predicted are not equivalent and thus recommend that guidelines do not assume parity between the 2 measurements for the classification of asthma severity.[35]

TABLE 5
Episodic and Persistent Asthma According to Formula 1*

	O/FEA	M/SPA	Total
O/FEA	256	8	264
M/SPA	91	32	123
Total	347	40	387

*O/FEA indicates episodic asthma (occasional plus frequent); M/SPA, persistent asthma (moderate plus severe).

TABLE 6
Episodic and Persistent Asthma According to Formula 3*

	O/FEA	M/SPA	Total
O/FEA	251	12	263
M/SPA	90	34	124
Total	341	46	387

*O/FEA indicates episodic asthma (occasional plus frequent); M/SPA, persistent asthma (moderate plus severe).

TABLE 7
Sensitivity, Specificity, and Predictive Value of Formulas 1 and 3 With Respect to Episodic and Persistent Asthma*

	Formula 1	Formula 3
Sensitivity	0.738	0.736
95% CI	(0.691-0.784)	(0.689-0.783)
Specificity	0.800	0.739
95% CI	(0.676-0.924)	(0.612-0.866)
Positive predictive value	0.970	0.954
95% CI	(0.949-0.990)	(0.929-0.980)
Negative predictive value	0.260	0.274
95% CI	(0.183-0.338)	(0.196-0.353)
κ coefficient	0.280	0.274
	(0.201-0.360)	(0.191-0.357))

*CI indicates confidence interval.

Furthermore, in many instances guidelines fail to specify how PEF variability is to be calculated. The various indices used give different results, as pointed out by Vargas et al,[36] who studied agreement of correlation coefficients using various formulas, as we did in our study.

It appears clear that FEV_1 is the most suitable lung function variable for the classification of asthma severity in children, especially when expressed as a percentage of predicted value. According to Fuhlbrigge et al,[37] this independent variable has been associated in longitudinal studies with risk of future exacerbations and with use of health care resources due to asthma. However, as our results show, isolated FEV_1 measurements are of little value in determining asthma severity,[38] especially when patients are receiving inhaled corticosteroid therapy, as was the case in our cohort. If, as our results indicate, PEF variability also fails to classify asthma severity, it would be reasonable to consider revising this parameter in guideline recommendations.

In conclusion, our results showed that measuring PEF variability, a common recommendation in national and international asthma management guidelines, is not valid for classifying severity of asthma in children. Monitoring

PEF in children may by useful in isolated cases, for example in cases in which diagnosis is uncertain, in difficult-to-control asthma, in identifying asthma triggers, and in the exceptional case of failure to perceive bronchial obstruction, with frequent and severe exacerbations.[29] As Brand and Roorda[39] stated, clinical evaluation and the analysis of expiratory flow-volume loops remain the cornerstones for the classification of asthma severity in children.

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