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Area under the Maximum Expiratory Flow-Volume Curve – A Sensitive Parameter in the Evaluation of Airway Patency

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Key Words
Airway patency · Bronchoconstriction · Bronchodilation · Children · Expiratory flow-volume curve · FEV_1

Abstract
Background: The most frequently used parameters for assessing bronchoconstriction and bronchodilation are forced expiratory volume in 1 s (FEV_1) and peak expiratory flow (PEF). ***Objectives:*** To assess the sensitivity of other parameters after induced bronchoconstriction and bronchodilation. ***Methods:*** From maximum expiratory flow-volume (MEFV) curves, forced vital capacity, FEV_1, PEF, maximum expiratory flows (MEF) at 25, 50 and 75% of vital capacity and the area under the MEFV curve (A_{ex}) were measured in two groups of asthmatic children after induced bronchoconstriction and bronchodilation, and in children with cystic fibrosis (CF) after bronchodilation. ***Results:*** In 142 asthmatics without airway obstruction, bronchoconstriction was induced by inhalation of 1% histamine aerosol. The 20% fall in A_{ex} compared to baseline was found in all asthmatics, while the 20 and 15% falls in FEV_1 were noted in 36 and 65% of the patients, respectively. Other parameters were less sensitive or interpretation was problematic. Another 110 asthmatics with mild-moderate airway obstruction were treated with various bronchodilators. The 20% increase in A_{ex} was observed in all asthmatics, while the 20% increase in FEV_1 was found in only 33% of the patients and the 15% increase in FEV_1 in 51%. In 9 CF children, the pattern of changes in A_{ex} and FEV_1 after bronchodilation was similar to that in asthmatics. ***Conclusions:*** A_{ex} was a sensitive and less problematic parameter in the evaluation of airway patency in comparison with FEV_1 and other parameters measured from the MEFV curve in our study patients.

Introduction

Changes in airway patency after inhalation of nonspecific bronchoconstrictors and bronchodilators provide significant information on the airway reactivity in both pediatric as well as adult patients with respiratory diseases. The evaluation of bronchial hyperresponsiveness (BHR) and the reversibility of airway obstruction can be assessed on the basis of selected functional parameters. Currently, forced expiratory volume in 1 s (FEV_1) and peak expiratory flow (PEF) represent the most frequently measured parameters to assess airway response after inhalation of bronchoconstrictors as well as bronchodilators. A large number of reports published in the literature evaluated FEV_1 and PEF in the assessment of BHR and bronchodilation in asthmatics [1–8]. FEV_1 is also the most frequently used parameter in the evaluation of air-

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way function in chronic obstructive pulmonary disease (COPD) [9].

The 20% fall in the absolute value of FEV_1 after inhalation of bronchoconstrictors compared to baseline is generally accepted to evidence BHR in both adults and children, and it is the most frequently used parameter in this respect [1–4, 8]. The dose of a bronchoconstrictor inducing a 20% fall in FEV_1 compared to baseline is called a provocation dose ($PD20_{FEV_1}$) and the concentration of a constrictor causing the latter change is a provocation concentration ($PC20_{FEV_1}$). FEV_1 and PEF are also frequently used in the evaluation of bronchodilation. We observed FEV_1 and PEF to be less sensitive indices of bronchoconstriction and bronchodilation in asthmatics than some other parameters [10–12].

Consequently, we searched for more sensitive lung function parameters after inhalation of a selected bronchoconstrictor to reveal BHR as well as to assess bronchodilation after inhalation of selected bronchodilators. Therefore, we measured functional parameters from maximum expiratory flow-volume (MEFV) curves in asthmatic children after inhalation of a bronchoconstrictor or some bronchodilators, and in patients with cystic fibrosis (CF) after inhalation of a bronchodilator. The present study is the only one dealing with this topic in children.

Patients and Methods

Bronchoconstriction

Bronchoconstriction was induced by inhalation of aerosol of 1% histamine solution during tidal breathing in 142 asthmatics attending our clinic (75 males and 67 females) aged 4–19 years (mean: 9.7 years) with body height ranging from 83 to 187 cm (mean: 138.0 cm). The patients were clinically in a stable period of asthma which was classified as persistent mild or moderate at the time of the study. They had characteristic clinical symptoms with periods of deterioration and improvement in airway obstruction, typical immunological findings and positive allergic skin tests. They were treated with various antiasthmatics, but treatment was not further specified since the purpose of our study was to evaluate the changes in airway patency with respect to some functional parameters. Our primary aim was to determine the decline in some functional parameters after the same bronchoconstricting stimulus. Patients with a 20% decline in the area under the MEFV curve (A_{ex}) after induced bronchoconstriction were included in the study. The study was approved by the local ethics committee.

In each patient, a series of 3–5 MEFV curves was obtained with a spirometer (ZAN 100; ZAN) before and after aerosol inhalation of 1% histamine solution. The best curve was automatically selected by a spirometry program according to the American Thoracic Society (the largest sum of forced vital capacity, FVC, and FEV_1) [13] and our own criteria, with details being described elsewhere [14, 15], and analyzed. The reproducibility of the MEFV curve was primarily based on the reproducible descendent portion of the curve and FVC. At the start of each measurement, the personnel explained how to perform a forced expiratory maneuver to each child. During the measurement, children were in the standing position while wearing a nose clip. From the best curve, the values of FVC, FEV_1, PEF, MEF at 25, 50 and 75% of vital capacity (MEF_{25}, MEF_{50} and MEF_{75}) and A_{ex} were calculated. In our previous studies in healthy children, the variability (1 SD from the mean) in FVC was 8%, FEV_1 9%, PEF 14%, MEF_{75} 14%, MEF_{50} 15%, MEF_{25} 16% and in A_{ex} 13% [14, 15].

Histamine inhalation was carried out with an inhalator (Pariboy; Pari) during quiet tidal breathing. A cumulative dosage was used to induce a 20% fall in A_{ex} compared to baseline to evidence a positive test (i.e. BHR) but not that of FEV_1. The initial dose of histamine was 0.3 mg in the majority of patients, and in some patients it was 0.15 mg. After a negative response, the next cumulative dose was 0.3 or 0.7 mg of histamine. The next doses were 1.2 and 2.2 mg, until the final cumulative dose of 3 mg of histamine was achieved. Assumably, some losses in histamine occurred during the expiratory phase of tidal breathing, which was not assessed. Therefore, a dose-response curve was obtained and PD_{20} was calculated for the functional parameters measured. After completion of the test, each patient inhaled 2 puffs of a bronchodilator (Berodual, ipratropium bromide/fenoterol; Boehringer) to abolish the induced bronchoconstriction. The dose of histamine varied from 0.15 to 3 mg of histamine (mean dose: 1.56 mg, median: 1.5 mg) in the patients. No side effects were observed. The major task of the test was to induce a 20% decrease in A_{ex}.

Bronchodilation

Bronchodilation was studied after inhalation of different bronchodilators in asthmatics and CF patients.

Asthmatics. The group comprised 110 asthmatics (68 males and 42 females) aged 4–19 years (mean: 11.0 years) with body height ranging from 103 to 190 cm (mean: 147.0 cm). Bronchodilation was evaluated 30 min after inhalation of the following bronchodilators, i.e. 2 puffs of Berodual, 4 puffs of Ventolin (salbutamol; GlaxoSmithKline), 4 puffs of Ecosal (salbutamol; Ivax) and 2 puffs of the Symbicort-Turbuhaler (formoterol/budesonide; AstraSeneca) according to the manufacturers' instructions. Each patient inhaled only one bronchodilator. The patients had characteristic clinical features of asthma and various degrees of airway obstruction. They were treated with different antiasthmatic drugs. Patients with a 20% increase in A_{ex} were included into the study. Our major aim was to determine the largest increase in the functional parameters after bronchodilator administration.

CF Patients. The CF group comprised 9 children with CF (4 males and 5 females) aged 3–18 years (mean: 10.3 years) with body height ranging from 94 to 175 cm (mean: 140.0 cm). Bronchodilation was also evaluated 30 min after 2 puffs of Berodual. We aimed to determine whether or not the changes in functional parameters in CF patients are similar to those in asthmatics, and thus specific or nonspecific for asthmatics. The CF patients had chronic airway obstruction with viscous mucus secretion and a positive sweat test with increased chloride levels. CF patients were treated with mucolytics, antibiotics and physical therapy, and in some of the patients the efficacy of bronchodilators on airway obstruction has been proven [16, 17].

Table 1. Mean absolute and predicted [14, 15] values of lung function parameters before and after induced bronchoconstriction in 142 asthmatics (age: 4–19 years, mean: 9.7 years, body height: 83–187 cm, mean: 138 cm)

Parameter	Means ± SD (% of predicted)		Decrease, % (mean ± SD)	z-score
	before	after		
FVC, liters	2.16 ± 1.04 (97.8)	1.93 ± 0.97 (87.4)	–10.6 ± 7.6[a]	–1.32
FEV_1, liters	1.95 ± 0.87 (104.1)	1.59 ± 0.73 (84.7)	–18.5 ± 7.0[c]	–2.05
PEF, $l \cdot s^{-1}$	4.11 ± 1.87 (94.1)	3.46 ± 1.66 (79.4)	–15.8 ± 9.5[b]	–1.13
MEF_{75}, $l \cdot s^{-1}$	3.73 ± 1.51 (94.1)	2.84 ± 1.74 (72.6)	–23.5 ± 11.6[c]	–1.68
MEF_{50}, $l \cdot s^{-1}$	2.57 ± 0.97 (93.4)	1.70 ± 0.71 (61.6)*	–33.8 ± 12.2[d]	–2.25
MEF_{25}, $l \cdot s^{-1}$	1.32 ± 0.52 (93.8)	0.82 ± 0.37 (58.1)*	–37.6 ± 14.5[d]	–2.35
A_{ex}, $l^2 \cdot s^{-1}$	5.86 ± 5.37 (104.1)	3.89 ± 3.69 (66.4)*	–34.0 ± 10.2[d]	–2.62

Asterisks denote a significant reduction (<2 SD) from the predicted value [14, 15], paired t test: [a] $p < 0.03$–0.05, [b] $p < 0.002$, [c] $p < 0.0001$–0.0004, [d] $p < 0.00001$. z-score = Number of SD below the predicted value.

A series of MEFV curves was carried out before and after inhalation of bronchodilators. Similar to the group of asthmatics after bronchoconstriction, the best curves before and after bronchodilation were selected according to the criteria of the American Thoracic Society and our own criteria, and analyzed [13–15]. The functional parameters required for the assessment of bronchodilation were derived from the curves (see bronchoconstriction test).

Statistical Analysis

All parameters before and after induced bronchoconstriction and bronchodilation in the patients were compared with the reference values for children and adolescents matched for body height, age and sex [14, 15]. The absolute values of the data in the tables are given as means ± SD and as percentages of predicted values. The changes in values before versus after inhalation of histamine and bronchodilators were tested by paired t test; $p < 0.05$ were considered significant. Percent decreases, increases and z-scores (number of SD from the predicted value) of parameters after inhalation versus before inhalation of bronchomotoric agents were also calculated. We focused our analysis primarily on the parameters A_{ex} and FEV_1. The incidence rates of asthmatics with 15 and 20% declines in FEV_1, and 20 and 30% declines in A_{ex} after inhalation of histamine were then calculated as well as the incidence rates of asthmatics and CF patients with 20% increases in A_{ex} and FEV_1, and a 15% increase in FEV_1 after inhalation of bronchodilators. A further McNemar test (χ^2 test for the same subject) was performed in order to compare the proportions of patients with positive responses in A_{ex} and FEV_1.

Results

Lung Function Parameters after Induced Bronchoconstriction

In all studied asthmatics, all parameters measured before induced bronchoconstriction were within normal limits (table 1). After bronchoconstriction, all functional parameters significantly ($p < 0.03$–0.00001) decreased in all of them. However, the mean percent decline was different for each parameter (table 1). The fall in MEF_{25} was about 37% on average, A_{ex} dropped by 34% and MEF_{50} also decreased by about 34% on average. The fall in FEV_1 was 18.5% and that of PEF only 15.8% on average after induced bronchoconstriction. The value of the z-score for A_{ex} showed the largest decline after bronchoconstriction (table 1).

Further, the incidence of positive bronchoconstriction tests, i.e. BHR, was assessed individually according to decreases ≥20% in FEV_1 and A_{ex} from baseline (table 2). Based on a 20% decrease in A_{ex}, BHR was detected in all (100%) patients. The 30% decrease in A_{ex}, another criterion of BHR, showed BHR in 66% of the patients. Based on the 20% fall in FEV_1, BHR was found in 36% of the patients, which implies BHR remained undetected in almost two thirds of our asthmatics. Based on the 15% decline in FEV_1, BHR was disclosed in 65% of the asthmatics. McNemar test showed the significantly higher proportions of subjects with a positive response in A_{ex} than FEV_1 (table 2). We did not evaluate the individual incidence of BHR based on the fall in MEF values because these parameters were not measured at the same lung volume levels before and after histamine inhalation due to decreases in FVC.

Lung Function Parameters after Induced Bronchodilation

In all studied asthmatics, before inhalation of bronchodilators airway obstruction was established by signif-

Table 2. Incidence of positive induced bronchoconstriction (BHR) in 142 asthmatics (age: 4–19 years, mean: 9.7 years, body height: 83–187 cm, mean: 138 cm)

Based on a fall in A_{ex} vs. baseline		Based on a fall in FEV_1 vs. baseline	
<20%	<30%	<15%	20%
142 patients 100% of patients	94 patients 66% of patients	92 patients 65% patients	51 patients 36% patients

McNemar test: A_{ex} <20% or <30% vs. FEV_1 <20% was highly significant, $p < 0.000005$. A_{ex} <30% vs. FEV_1 <15% was not significant.

Table 3. Mean absolute and predicted [14, 15] values of lung function parameters before and after induced bronchodilation in 110 asthmatics (age: 4–19 years, mean: 11 years, body height: 103–190 cm, mean: 147 cm)

Parameter	Mean ± SD (% of predicted)		Increase, % (mean ± SD)	z-score
	before	after		
FVC, liters	2.60 ± 1.05 (97.7)	2.73 ± 1.08 (102.6)	5.0 ± 5.5[a]	0.63
FEV_1, liters	1.98 ± 0.69 (88.4)	2.33 ± 0.85 (104.2)	17.3 ± 7.7[c]	1.92
PEF, $l·s^{-1}$	4.30 ± 1.52 (85.0)	4.89 ± 1.79 (96.5)	13.6 ± 10.4[b]	0.97
MEF_{75}, $l·s^{-1}$	3.22 ± 1.05 (71.9)*	4.26 ± 1.40 (95.1)	32.2 ± 18.0[c]	2.3
MEF_{50}, $l·s^{-1}$	1.86 ± 0.61 (58.7)*	2.74 ± 0.89 (86.5)	47.3 ± 21.0[d]	3.15
MEF_{25}, $l·s^{-1}$	0.86 ± 0.31 (52.0)*	1.33 ± 0.50 (81.7)	54.0 ± 27.0 [d]	3.37
A_{ex}, $l^2·s^{-1}$	5.59 ± 3.82 (83.5)	7.81 ± 5.63 (116.0)	40.0 ± 17.8[d]	3.08

For further information, see table 1.

icantly reduced MEF_{75}, MEF_{50} and MEF_{25}values (table 3). Airway obstruction was classified into mild, moderate and severe. FEV_1 <80% of the predicted value showed airway obstruction in only 25% of our asthmatics [14, 15].

In the whole group of patients, all parameters significantly ($p < 0.05–0.00001$) increased after inhalation of bronchodilators (table 3), particularly in MEF_{25}, MEF_{50} and A_{ex}. FEV_1 increased by about 17% and PEF by 14%. The z-score showed a pattern similar to the latter parameters (table 3).

According to the individual increases in the parameters after induced bronchodilation, the increase in A_{ex} was ≥20% compared to baseline in all our asthmatics. However, the positive bronchodilation based on an increase in FEV_1 ≥20% was revealed in only 33% of our asthmatics and based on a 15% increase in FEV_1 it was found in 51% of them (table 4). Using McNemar test, the proportion of patients with a positive response in A_{ex} was higher compared to FEV_1 (table 4).

Before inhalation of Berodual, all lung function parameters in all CF patients were significantly reduced suggesting moderate/severe airway obstruction (table 5). Following Berodual inhalation, these parameters significantly increased ($p < 0.05–0.0001$) and normalized except for MEF_{25}. Major increases were noted in A_{ex}, MEF_{25} and MEF_{50}. FEV_1 increased by 14% and PEF by 18% on average. The largest z-score was observed for A_{ex} (table 5).

A positive bronchodilation test defined as an increase in A_{ex} ≥20% was observed in all patients. The 15% increase in FEV_1 was revealed in 56% of the patients and the 20% increase in FEV_1 was found in none of them (table 4). McNemar test also showed higher numbers of patients with a positive response in A_{ex} compared with FEV_1 (table 4).

We assessed induced bronchodilation in patients based primarily on the increase in absolute values of A_{ex} and FEV_1 compared to baseline and not on the increase in MEF values. Nevertheless, MEF values also increased

Table 4. Incidence of a positive bronchodilation test 30 min after inhalation of Berodual in 9 CF patients (age: 3–18 years, mean: 10.3 years, body height: 94–175 cm, mean: 140 cm) and after inhalation of bronchodilators in 110 asthmatics (age: 4–19 years, mean: 11 years, body height: 103–190 cm, mean: 147 cm)

Based on an increase in A_{ex} vs. baseline	Based on an increase in FEV_1 vs. baseline	
>20%	>15%	>20%
CF Patients (n = 9)		
9 patients	5 patients	0 patients[a]
100% of patients	55% of patients	0% of patients[a]
Asthmatics (n =110)		
110 patients	56 patients[b]	36 patients[b]
100% of patients	51% of patients[b]	33% of patients[b]

Mc Nemar test: [a] $p < 0.01$, [b] $p < 0.00005$, vs. A_{ex} >20%.

Table 5. Mean absolute and predicted [14, 15] values of lung function parameters before and after induced bronchodilation in 9 CF patients (age: 3–18 years, mean: 10.3 years, body height: 94–175 cm, mean: 140 cm)

Parameter	Mean ± SD (% of predicted)		Increase, % (mean ± SD)	z-score
	before	after		
FVC, liters	1.83 ± 0.94 (79.5)*	2.04 ± 1.01 (88.6)	11.4 ± 4.3[a]	1.42
FEV_1, liters	1.47 ± 0.70 (75.4)*	1.68 ± 0.76 (86.2)	14.3 ± 3.6[b]	1.58
PEF, $l \cdot s^{-1}$	3.67 ± 1.62 (81.2)*	4.36 ± 1.94 (96.5)	18.8 ± 6.9[b]	1.34
MEF_{75}, $l \cdot s^{-1}$	3.22 ± 1.48 (79.7)*	3.90 ± 1.72 (96.5)	21.1 ± 10.9[c]	1.51
MEF_{50}, $l \cdot s^{-1}$	1.68 ± 0.69 (58.9)*	2.20 ± 0.91 (77.2)	30.9 ± 21.3[c]	2.06
MEF_{25}, $l \cdot s^{-1}$	0.56 ± 0.21 (38.3)*	0.74 ± 0.30 (51.0)*	33.0 ± 22.2[c]	2.06
A_{ex}, $l^2 \cdot s^{-1}$	3.72 ± 3.18 (71.8)*	5.01 ± 4.11 (96.7)	34.7 ± 8.7[c]	2.67

For further information, see table 1.

substantially after bronchodilation, which may be explained by the different lung volume levels for MEF before and after bronchodilation due to FVC increases after bronchodilation (tables 3, 5).

Discussion

In our asthmatic children and patients with CF, the lung function parameters derived from MEFV curves after induced bronchoconstriction and bronchodilation showed rather different results concerning the positivity of bronchoconstriction and bronchodilation (tables 1–5). The largest decline in the z-score of the mean A_{ex} value suggested A_{ex} to be the most sensitive parameter in the detection of BHR in our asthmatics (table 1).

The positivity of BHR in our asthmatics, based on a ≥20% decrease in the absolute A_{ex} value after versus before inhalation of histamine, showed BHR in all of them (table 2). Based on the 20% fall in the absolute FEV_1 value compared to baseline, BHR remained undiscovered in almost two thirds of our asthmatics. The 20% fall in A_{ex} was chosen as the cutoff value because the lower limit of A_{ex} was close to 20% in our healthy preschool and school children as well as adolescents studied [14, 15]. Another reason for selecting a 20% fall in A_{ex} as a criterion indicating a positive BHR was an already generally accepted 20% fall in FEV_1 ($PD20_{FEV_1}$) compared to baseline in the past [1–4]. The 30% fall in A_{ex} as another criterion of BHR still proved BHR in a large number of asthmatics, i.e. in 66% of our patients. We do not consider the 10–15% fall in FEV_1 (PD10 or PC10, PD15 or PC15) to be a correct cutoff of BHR, as quoted previously [18, 19], since the lower confidence limit (i.e. –2SD) from the mean FEV_1 was 18% in our healthy children [14, 15]. The 10–15% change in FEV_1 is still within the physiological range for this parameter. The 15% decline in FEV_1 as a measure of BHR did not show BHR in about one third of our asthmatics (table 2). Therefore, we suggest $PD20_{A_{ex}}$ as a parameter determining BHR.

The histamine dose in our asthmatics was probably lower due to a certain loss of histamine during the expiratory phase of tidal breathing. Such an error occurred similarly in all patients. We aimed to induce bronchoconstriction by the same manner in all patients and to evaluate the various declines in functional parameters.

In asthmatics, the incidence rates of BHR based primarily on the fall in FEV_1 and A_{ex} compared to baseline obviously differed depending on the therapeutic regimen employed. In the long-term management of asthmatics, using BHR as an additional guide is considered indispensable because BHR significantly correlates with chronic airway inflammation in asthma [3, 4]. Therefore, to assess BHR, sensitive lung function parameters are mandatory. First of all, we compared the sensitivity of A_{ex} with the most frequently and routinely used parameter FEV_1, and then with other parameters derived from the MEFV curve.

We considered the parameters MEF_{25}, MEF_{50} and MEF_{75} to be less suitable in the evaluation of BHR in our asthmatics, because they were measured at different absolute lung volume levels before and after induced bronchoconstriction due to a decrease in FVC resulting in a change in lung volume levels at which MEF values were measured. MEF values obtained after induced bronchoconstriction were actually falsely higher.

In spite of the problematic lung volume level, MEF values showed a larger increase after inhalation of histamine and bronchodilators than FEV_1 in our asthmatics, which was in agreement with previous studies [7]. Nevertheless, they might be used as a measure of bronchoconstriction and bronchodilation responses assuming that lung volume might be a source of error. If FVC remains constant, the measurement of MEF values is accurate. MEF values reflect primarily the obstruction of peripheral airways which are the predominant site of airway obstruction in patients with obstructive lung disease [20].

In our asthmatics, the bronchodilation test assessed by FEV_1 was less often positive than with A_{ex}. The 20% increase in the parameter A_{ex} revealed a positive bronchodilation response in all our asthmatics while the 20% increase in FEV_1 indicated a positive bronchodilation in only one third of them. Based on the 15% increase in FEV_1, about half of the patients had a positive test (table 4). A similar increase in z-scores for MEF_{25}, MEF_{50} and A_{ex} suggested a similar degree of bronchodilation (table 3).

In patients with CF, the positive bronchodilation test resembled that found in asthmatics. Based on a 20% increase in A_{ex}, bronchodilation was revealed in all patients (table 4), based on a 15% increase in FEV_1 in 56%, and on a 20% increase in none of them. The largest z-score for A_{ex} also proved A_{ex} to be the most sensitive parameter indicating bronchodilation.

The number of patients with a 12% increase in FEV_1 after bronchodilation was not included, similar to a previous study [18], due to the physiological variability in FEV_1.

Our results suggest that the parameter A_{ex} can be considered as a sensitive, simple and reliable index in the evaluation of airway patency, and is thus suitable for routine use. A_{ex} reflects both lung volume and airflow changes during the whole forced expiratory maneuver. It provides thus information on both central and peripheral airway obstruction. A_{ex} is expressed as l^2/s because the area under the MEFV curve is calculated as a product of volume × volume per second (l^2/s).

The greater sensitivity of A_{ex} in the evaluation of induced bronchoconstriction and bronchodilation can be attributed to both airflow and FVC changes as a result of residual volume increase or decrease during forced expiration. A_{ex} was not a specific feature of asthmatics because the pattern and magnitude of changes for FEV_1, PEF, MEF values and A_{ex} after bronchodilation were similar in both asthmatics and CF patients (tables 2–5).

The parameter A_{ex} was advantageous in the evaluation of airway patency in both asthmatics and patients with CF because A_{ex} includes both lung volume and flow changes over the whole range of FVC. It thus reflects airway obstruction during the complete forced expiratory maneuver. In contrast, FEV_1 reflects changes in airway patency at about 80–90% of FVC in the majority of healthy children [14, 15]. In patients with obstructive diseases, FEV_1 reflects airway obstruction even in patients with a smaller lung volume range than 80% of FVC and primarily a central airway obstruction.

The PEF parameter showed low sensitivity in the evaluation of airway patency in all of our patients (tables 1–5). It represents the highest expiratory flow derived from the MEFV curve and reflects primarily central airway obstruction. Both FEV_1 and PEF thus provide limited information mainly on the caliber of smaller airways. Nevertheless, both parameters (FEV_1 and PEF) are recommended in the guidelines of the *Global Initiative for Asthma* for the evaluation of airway obstruction in asthmatics [3]. It might result in unrecognized airway obstruction or BHR and consequently in inappropriate treatment in patients with mild/moderate asthma, for example.

Similarly, in patients with COPD the most commonly used spirometry parameter FEV_1 also showed only a weak correlation with the characteristic symptoms of COPD, such as dyspnea, reduced activity and poor health status, and did not reflect the severity of the disease [9, 21, 22] or frequency of exacerbations in COPD patients [23].

In the literature, there are few relevant studies on using the parameter A_{ex} in the evaluation of bronchoconstriction and bronchodilation. No study on this topic exists in children. Vermaak et al. [24] first introduced the parameter A_{ex} as a very sensitive indicator of lung function impairment and developed the equation for calculating A_{ex}. He assumed A_{ex} is a triangle with FVC as a base, PEF as a perpendicular and straight descendent portion of the MEFV curve as a hypotenuse. However, the MEFV curve is not a triangle in patients with obstructive disease. Sovijarvi [25] tested the sensitivity and reliability of A_{ex} after methacholine challenges in patients with BHR. A_{ex} showed the greatest decrease compared to baseline among the parameters derived from the MEFV curve. Struthers and Addis [26] measured A_{ex} before and after aminophylline in patients with COPD. A_{ex} was the most sensitive index assessing bronchodilation in the patients studied. Seppala [27] used A_{ex} to express the reproducibility of methacholine-induced bronchoconstriction in healthy subjects and established a higher sensitivity for A_{ex} than for FEV_1 and MEFs. Currently, studies using A_{ex} in the evaluation of airway patency in asthmatics or patients with other obstructive diseases are rare. Further studies are required to determine the significance of the parameter A_{ex} in the evaluation of BHR and bronchodilation as well as airway function in all patients with abnormalities of airway patency.

In conclusion, among the functional parameters derived from the MEFV curve following inhalation of a bronchoconstrictor and several bronchodilators in two groups of asthmatic children and one group of CF patients, the parameter A_{ex} was more suitable in the evaluation of BHR and bronchodilation than FEV_1 or PEF, and other parameters measured. The introduction of A_{ex} in the evaluation of airway function in patients with initial forms of asthma and CF patients as well as the routine use of A_{ex} to follow-up asthmatics and CF patients (probably also patients with COPD) might provide better information on their health status than the currently used parameter FEV_1.

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