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Comparison of peak expiratory flows and FEV₁ in assessing immediate asthmatic reactions due to occupational agents

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Key words: bronchial provocation tests; FEV₁; occupational diseases; peak expiratory flow (PEF).

Background: FEV₁ is more sensitive than PEF in assessing late asthmatic responses (LAR) after specific inhalation challenges (SIC) with occupational agents. As immediate asthmatic reactions (IAR) mainly involve proximal airways, PEF may, however, be as valid as FEV₁.

Methods: Thirty-seven subjects who experienced an immediate fall in FEV₁ of $\geq 20\%$ during SIC with occupational agents and 20 subjects with fall of $\leq 10\%$ in FEV₁ were included. Both FEV₁ and PEF were measured in a random order every 10 min for 1 h after exposure. We corrected PEF (PEFc) for inaccuracies of the mini-Wright meters by the Miller equation.

Results: Maximum changes in PEFc ($30 \pm 11\%$) were not significantly different from changes in FEV₁ ($27 \pm 5\%$) ($P=0.13$). Their timings after exposure were 14 ± 11 min and 17 ± 17 min, respectively ($P=0.4$). High sensitivity (92%), specificity (95%), accuracy (93%), and positive predictive value (97%) were found for a 20% fall in PEFc to detect a significant IAR. Results were better and not influenced by meter inaccuracies with a cutoff point of 15% change in noncorrected PEF (PEFnc). An absolute decrease in PEF of 70 l/min gave a good discrimination between reactions with and without an asthmatic response.

Conclusions: PEF is as satisfactory as FEV₁ for detecting a significant IAR after exposure to an occupational agent if one considers a cutoff point of

- 1) 15% fall in PEF
- 2) 20% fall in PEFc
- 3) 20% fall and/or 70 l/min decrease in PEFnc.

Because simple and inexpensive devices for measuring peak expiratory flow (PEF) are available, this method is used more and more to assess airway calibre (1). Although a good

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correlation is found between PEF and FEV₁ (2–4), the latter remains the “gold standard” from a physiological point of view; it is less effort-dependent, has a lower variability (5), and reflects the calibre of both central and peripheral airways. Furthermore, PEF monitoring may lead to underestimation or overestimation of changes in FEV₁. This may be partly due to meter inaccuracy (6, 7); a mathematic correction of the error has recently been proposed (8).

Moscato et al. found a significant correlation between FEV₁ and PEF during specific bronchial challenges; data presented by these authors included different temporal patterns of bronchoconstriction after exposure to an allergen (9). We demonstrated in a previous study that PEF is less sensitive than FEV₁ in assessing the late asthmatic response (LAR) after challenges with occupational agents (10). As it has been suggested that immediate asthmatic reactions (IAR) principally involve proximal airways, PEF may be as valid as FEV₁ in determining changes in airway calibre that occur during these responses.

We studied a group of 57 patients (37 patients with an IAR and 20 controls without an asthmatic reaction), exposed to different occupational agents, to determine the sensitivity and specificity of PEF in detecting an IAR with FEV₁ as the reference standard.

Material and methods

Subjects

The subjects were consecutive patients who had been referred to Mont-Godinne Hospital in Yvoir, Belgium ($n=34$), or the Department of Chest Medicine at Sacré-Cœur Hospital in Montreal, Canada ($n=23$), for the investigation of occupational asthma (OA). A clinical and occupational history was recorded. Skin prick tests with a battery of 22 common inhalant allergens and relevant occupational agents, as well as spirometry and nonspecific bronchial provocation test with methacholine (Montreal) or histamine (Yvoir) were performed.

Methods

Specific inhalation challenge (SIC) tests were performed using a standardized protocol (11). Inhaled β_2 -adrenergic agents were stopped before the challenge (8 h for short-acting and 72 h for long-acting agents). Subjects were exposed to a control product on the first day to confirm stability of asthma (variation in FEV₁ within 10% of

baseline). On the second day, exposure to the sensitizing agent was carried out using a closed-circuit apparatus (12) or by mimicking working conditions in a challenge room (13); one subject exposed to coniferous wood dusts was tested in the workplace. Duration of exposure was progressively prolonged on the same or subsequent days until a 20% fall in FEV₁ occurred. In a random order, both FEV₁ and PEF were measured every 10 min for the first hour, every 30 min for the second hour, and then hourly until 6–8 h after the end of exposure. The best of three satisfactory measurements of FEV₁ and PEF was kept for analysis. FEV₁ was assessed according to the criteria of the American Thoracic Society (1) with a Collins spirometer (W.E. Collins, Braintree, MA, USA) in Montreal and a pneumotachograph (Medisoft, Dinant, Belgium) in Yvoir. Reference values for FEV₁ were taken from Knudson et al. (14) for the Montreal patients or Quanjer for the Belgian patients (15). PEF was measured with a mini-Wright portable peak flow meter and supervised by a technician (1). A histamine or methacholine PC₂₀ (16) was obtained at the end of the control day and 6–8 or 24 h after the exposure to the sensitizing agent for all subjects in Montreal and for those patients who did not demonstrate significant changes in FEV₁ at Mont-Godinne Hospital.

Analysis of results

Maximum changes in FEV₁ and PEF from baseline value were kept for analysis (mean $\pm$ SD). We examined corresponding percentage changes of PEF and FEV₁ at the time of the maximum percentage change of FEV₁ and PEF, respectively. Measured PEF values were corrected by the following formula: $0.0009 \cdot \text{PEF}^2 + 0.37306 \cdot \text{PEF} + 47.4$ (8). Corrected PEF (PEFc) values were compared to noncorrected (PEFnc) values. Statistical analysis was done with a paired comparison test, and the alpha level of significance was set at a value of ≤ 0.05 . Sensitivity, specificity, accuracy, and predictive values of PEF in detecting a 20% change in FEV₁ were calculated at generally accepted cutoff points of PEF decrease (15%, 20%, 70 l/min). An absolute decrease in PEF of 70 l/min was shown to give optimal discrimination between challenges with and without an IAR (9).

Results

Anthropometric, clinical, and functional features of the subjects are presented in Table 1. Results of SICs are summarized in Table 2.

Negative challenges

Changes in PEFc were marginally greater than changes in FEV₁ ($P=0.05$): one patient had a maximum fall in PEFc of >20% 20 min after exposure when the maximum fall in FEV₁ was only 8%; in the same subject, at 10 min and 30 min after exposure, there was only a 4% fall in PEF. The other 19 subjects had decreases in PEFnc between 0 and

Table 1. Anthropometric, clinical, and functional characteristics of 37 subjects with IAR and 20 controls without asthmatic reaction during SIC

	Positive challenge n=37	Negative challenge n=20
Sex (M/F)	22/15	15/5
Age (years, mean $\pm$ SD)	37 $\pm$ 10	40 $\pm$ 12
Smokers/ex-smokers/nonsmokers	4/14/19	8/5/7
Atopy ($\pm$ /dermo)	23/11/2	10/10/0
Medication		
Nil	3	5
β_2 alone	10	5
β_2 +ICS	22	10
β_2 +ICS+LAA	2	–
Duration of exposure without symptoms		
months, mean $\pm$ SD	109 $\pm$ 85	111 $\pm$ 143
Duration of exposure with symptoms		
months, mean $\pm$ SD	49 $\pm$ 58	30 $\pm$ 25
Baseline FEV ₁		
Litre, mean $\pm$ SD	3.2 $\pm$ 1	3.4 $\pm$ 0.8
%pred, mean $\pm$ SD	91 $\pm$ 17	98 $\pm$ 17
FEV ₁ /FVC <70%	9	4
Baseline PC ₂₀		
<2 mg/ml	25	7
2–8 mg/ml	7	8
$\leq$ 16 mg/ml	1	4
>16 mg/ml	4	1
Agents		
Latex	13	–
Flour	9	7
Wood dust	2	2
Isocyanates	2	3
Glutaraldehyde/formaldehyde	–	3
Enzymes	2	–
Others	9	5

dermo: dermatographism; β_2 : short-acting inhaled β_2 -adrenergic agents; ICS: inhaled corticosteroids; LAA: long-acting β_2 -adrenergic agents; other agents: psyllium, cobalt, sunflower seeds, insecticide, plaster, grass seeds, barley, cement, cement adhesive, benzalkonium chloride, amines, varnish, cleaner, acrylic paint. There were no significant differences in frequency of atopy ($P=0.3$), and FEV₁ ($P=0.8$) and PC₂₀ ($P=0.4$) values in two groups.

8.5% and in PEFc between 0 and 11.4%. Maximum absolute changes in PEFc were below 70 l/min in all subjects.

Positive challenges

Mean changes in PEFc were not different from changes in FEV₁ at any time ($P=0.13$) or at the time of maximum change ($P=0.35$), while PEFnc changes were significantly smaller in all instances. However, for a fall in FEV₁ between 20 and 38.8%, PEFc changes varied from 3.6 to 60.7% of baseline

Table 2. Results of FEV₁ and PEF during the first hour of specific inhalation challenges

	Positive challenges (n=37)	Negative challenges (n=20)
Maximum % changes in FEV ₁ any time		
Mean $\pm$ SD	27 $\pm$ 5	3 $\pm$ 3
Range	20–38.8	0–8
Maximum % changes in PEFnc any time		
Mean $\pm$ SD	24 $\pm$ 9	4 $\pm$ 5
Range	2.6–50.8	0–22
Maximum % changes in PEFc any time		
Mean $\pm$ SD	30 $\pm$ 11	5 $\pm$ 6
Range	3.6–60.7	0–22.9
% Changes in PEFnc at time of maximum		
% changes in FEV ₁		
Mean $\pm$ SD	20 $\pm$ 9	2 $\pm$ 2
Range	1.4–38.6	0–8.5
% Changes in PEFc at time of maximum		
% changes in FEV ₁		
Mean $\pm$ SD	30 $\pm$ 11	Not done
Range	3.6–60.7	
% Changes in FEV ₁ at time of maximum		
% changes in PEF		
Mean $\pm$ SD	23 $\pm$ 6	1 $\pm$ 2
Range	12–38	0–8
Time of maximum changes in FEV ₁ (min)		
Mean $\pm$ SD	14 $\pm$ 11	Not relevant
Time of maximum changes in PEF (min)		
Mean $\pm$ SD	17 $\pm$ 17	Not relevant
Maximum absolute changes in PEFnc (l/min)		
Mean $\pm$ SD	116 $\pm$ 58	18 $\pm$ 16
Range	15–310	0–60
Maximum absolute changes in PEFc (l/min)		
Mean $\pm$ SD	137 $\pm$ 73	21 $\pm$ 18
Range	15–370	0–51

PEFc: corrected PEF values; PEFnc: noncorrected PEF values; positive challenge defined as $\geq 20\%$ change in FEV₁ from baseline; negative challenge defined as $\leq 10\%$ change in FEV₁ from baseline.

value; in eight subjects, the difference in maximum percentage fall in FEV₁ and PEFc was more than 10%. The time of maximum changes in FEV₁ and PEF was not different (*P*=0.3); the mean difference in time of occurrence of the maximum change was 11 min (range 0–40 min). There were nine subjects in whom the percentage changes in PEFnc were <20% and three in whom the percentage changes in PEFc were <20%, which could be considered false negative tests. However, 6/9 subjects with PEFnc fall of <20% had an absolute decrease in PEFnc of ≥70 l/min. At a cutoff point of 15% decrease in PEFnc, there would have been only two false negative SICs; both of these also had a <70 l/min absolute decrease in PEFc. Mean baseline PEFc was 494 l/min, and it fell to a mean value of 363 l/min after exposure.

Table 3 shows results of sensitivity, specificity, accuracy, and predictive values of PEFc in detecting significant changes in FEV₁. Specificity and positive predictive value were high at all cutoff points (100% for the 70 l/min cutoff point). Better results were obtained for a 15 % change in PEFc than for a 20% change in detecting a ≥20% fall in FEV₁.

Discussion

This study shows that PEF, corrected for inaccuracies of the mini-Wright meters, is a satisfactory tool for detecting an immediate ≥20% fall in FEV₁ after exposure to occupational allergens. If PEF values are not corrected, the presence of a 20% fall or a 70 l/min decrease in PEFnc is as sensitive as a 20% fall in PEFc (8% false negative). Results were better and not confounded by meter inaccuracies when a cutoff point for PEF of 15 % change was considered. Moscato et al. also

found a good correlation between PEF and FEV₁ during SIC with different patterns of asthmatic reactions (39 IAR, 24 LAR, 12 dual), and an even better correlation when absolute values of PEF and FEV₁ were considered (9). These authors concluded that an absolute decrease in PEF of 70 l/min is a good detector of an IAR defined by a 15 % change in FEV₁ (sensitivity=70.6%, specificity=92% vs 86% and 100%, respectively, in our study). On the other hand, the negative predictive value was low in their study (39.5%) compared with ours (80%); we defined a significant bronchospastic reaction as a 20% fall in FEV₁ (11). This might be explained by the larger number of subjects in their study who had an FEV₁ fall less than 20%, particularly 15–20%.

The validity of PEF assessment by comparison with FEV₁, taken as the reference standard, has been examined in the case of IAR induced by several types of nonspecific agents with conflicting results. For nonspecific challenges with histamine, PEF was shown to be as valid as FEV₁ for detecting an immediate ≥20% fall in FEV₁ (17). Giannini and coworkers found a poor relationship between PEF and FEV₁ during bronchoconstriction induced by different stimuli (4, 18); maximum percentage changes in PEF were lower than FEV₁ changes in all challenges. In allergen challenge, a ≥15 % change in PEF could detect a ≥20% fall in FEV₁ (39 immediate and 19 late asthmatic reactions) with a sensitivity of 61 % (vs 95 % in our study) and a specificity of 92 % (vs 95 % in our study). In the study by Giannini, PEF was always measured after FEV₁; therefore, values could be lower due to inspiratory and expiratory manoeuvres, which may have an effect on airway tone (18).

In none of the above published studies did the investigators correct PEF values for inaccuracies of the meters in challenge tests. Mini-Wright meters are known to overread by up to 70 l/min in the mid-flow range (300–500 l/min) and to underread by about 50 l/min in the high range (6). Baseline PEF values in our patients were in the higher range, while the maximum decrease in PEF was in the mid-flow range; this explains the greater percentage change in PEF to baseline value after correction, changes that were of the same magnitude as the changes in FEV₁.

The reference standard for a positive reaction that we selected was a change of ≥20% in FEV₁. Obviously, if a change of at least 20% in PEF, and not in FEV₁, had been selected, it would have been necessary to increase the dose of occupational agent to elicit a positive reaction, and this would have resulted in elimination of false negative reactions but in probably greater symptomatology.

One problem with PEF measuring is within-subject variability. This could explain the only false positive case

Table 3. Results of sensitivity, specificity, accuracy, and predictive values of three different cutoff points of PEF in detecting immediate 20% fall in FEV₁ during SIC

	Maximum change in PEF (corrected)		
	≥20%	≥15%	≥70 l/min
Maximum % change in FEV ₁			
≥20	27 (34)	35 (34)	32 (31)
<20	1 (1)	1 (1)	0 (0)
Sensitivity (%)	73 (92)	95 (92)	86 (84)
Specificity (%)	95 (95)	95 (95)	100 (100)
Accuracy (%)	81 (93)	95 (93)	91 (89)
Positive pred. value (%)	96 (97)	97 (97)	100 (100)
Negative pred. value (%)	66 (86)	90 (86)	80 (77)
Results in parenthesis are those for corrected PEF values.			

in our study. Training subjects how to perform the measurement, as well as supervising them when they do so, is indicated (1).

We conclude that PEF may be sufficiently sensitive to detect an IAR in SIC with occupational sensitizers in considering a cutoff point of

- 1) a 15% fall in PEF_{nc}
- 2) a 20% fall and/or an absolute decrease of 70 l/min in PEF_{nc}

- 3) a 20% fall in PEF_c.

The situation, however, is different for late asthmatic reactions; for these and in consideration of the practical issue of having to choose only one functional parameter for assessing immediate and late reactions, the FEV₁ should still be preferred to the PEF (10).

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