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Can peak expiratory flow measurements reliably identify the presence of airway obstruction and bronchodilator response as assessed by FEV₁ in primary care patients presenting with a persistent cough?

H A Thiadens, G H De Bock, J C Van Houwelingen, F W Dekker, M W M De Waal, M P Springer, D S Postma

Abstract
Background—In general practice airway obstruction and the bronchodilator response are usually assessed using peak expiratory flow (PEF) measurements. A study was carried out in patients presenting with persistent cough to investigate to what extent PEF measurements are reliable when compared with tests using forced expiratory volume in one second (FEV₁) as the measure of response.

Methods—Data (questionnaire, physical examination, spirometry, PEF) were collected from 240 patients aged 18–75 years, not previously diagnosed with asthma or chronic obstructive pulmonary disease (COPD), who consulted their general practitioner with cough of at least two weeks duration. The relationship between low PEF (PEF < PEFpred − 1.64RSD) and low FEV₁ (FEV₁ < FEV₁pred − 1.64RSD) was tested. A positive bronchodilator response after inhaling 400 µg salbutamol was defined as an increase in FEV₁ of ≥9% predicted and was compared with an absolute increase in PEF with cut off values of 40, 60, and 80 l/min and APEF % baseline with cut off values of 10%, 15%, and 20%.

Results—Forty eight patients (20%) had low FEV₁; 86 (35.8%) had low PEF, and 32 (13.3%) had a positive bronchodilator response. Low PEF had a positive predictive value (PPV) for low FEV₁ of 46.5% and a negative predictive value (NPV) of 95%. APEF of ≥10%, ≥15%, or ≥20% baseline had PPVs of 36%, 52%, and 67%, respectively, and APEF of ≥40, ≥60, and ≥80 l/min in absolute terms had PPVs of 39%, 45%, and 57%, respectively, for APEF, ≥9% predicted; NPVs were high (88–93%).

Conclusions—Although PEF measurements can reliably exclude airway obstruction and bronchodilator response, they are not suitable for use in the assessment of the bronchodilator response in the diagnostic work up of primary care patients with persistent cough. The clinical value of PEF measurements in the diagnosis of reversible obstructive airway disease should therefore be re-evaluated.

Keywords: peak expiratory flow; asthma; chronic obstructive pulmonary disease; airflow obstruction; general practice; diagnosis

Many reports have emphasised the importance of measuring peak expiratory flow (PEF) in general practice. It has been reported to be useful in establishing a diagnosis of asthma and has been widely adopted for monitoring patients with asthma. In the consulting room PEF is used for diagnostic purposes to identify reversible airflow limitation and it is applied at home to assess peak flow variability. PEF measurements might reliably replace forced expiratory volume in one second (FEV₁) in general practice since the correlation of PEF values with FEV₁ values has been found to be high. However, restrictions must be applied because PEF measurements are more effort dependent than FEV₁, and may therefore underestimate the degree of airway obstruction.

Up to the present time almost all studies on the bronchodilator response have been performed using FEV₁ measurements. The use of PEF meters has also been recommended for the same purpose in general practice but has only been investigated in one study. This study, performed in adults with asthma and chronic obstructive pulmonary disease (COPD), showed that an increase in PEF of 60 l/min indicated a clinically significant improvement. The global consensus and the international consensus consider an increase of 15% in PEF from baseline as indicative of asthma, whereas others state that an improvement in PEF of ≥20% of the initial value should establish a diagnosis of asthma.

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However, none of these statements has been validated. The aim of this study was to investigate to what extent PEF measurements reliably identify the presence of airway obstruction and a positive bronchodilator response as assessed by FEV₁. It is obvious that, in general practice where spirometers are generally unavailable, PEF measurements would be particularly useful. We therefore investigated patients presenting in general practice with persistent cough who had no previous diagnosis of pulmonary disease. This study is part of a larger project, the results of which have been published elsewhere.9–10

Methods

Patients

The study took place between November 1993 and January 1995 in a primary health care centre manned by six general practitioners (GPs) serving a catchment area of 12 000; 8450 subjects aged 18–75 years were registered and their mean age and sex distribution matched that of the rest of the country.

We studied consecutive consultations of patients who presented with a troublesome cough that had lasted for at least two weeks, but who had no known pre-existing pulmonary disease. Patients with a previous diagnosis of asthma or COPD were excluded, as were pregnant patients and those with cardiovascular disease or concomitant pulmonary disease.9 To ensure that all subjects with a cough of at least two weeks duration had been included, records of every patient in the practice were checked using the GP’s computerised register. Subjects were seen by the investigator on the same day as they attended their GP. Once a patient had been admitted to the study any subsequent episode of coughing for two weeks or more was not investigated.

Informed consent was obtained from all the participants and the study was approved by the medical ethics committee of Leiden University.

Measurements

Ventilatory function was measured using a turbine spirometer (Microlab 3300, Sensormedics Ltd Rochester, UK). Forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), and peak expiratory flow (PEF) were measured until three reproducible recordings (with a difference of less than 5%) were obtained, of which the highest was used in the analysis. Reference values of FEV₁, FVC, and PEF were those of the European Respiratory Society.11 The bronchodilator response was assessed 15 minutes after inhaling 400 µg salbutamol.11–13 Airway obstruction was defined as FEV₁ < FEV₁pred – 1.64RSD (low FEV₁).9 Obstruction as assessed by PEF was defined as PEF < PEFpred – 1.64RSD (low PEF).9

Statistical analysis

Data for this study were analysed using SPSS 4.0 (SPSS Inc, Chicago, Illinois, USA). Normal distributions of FEV₁ and PEF were inspected visually by probability plots. Correlations between PEF and FEV₁, were calculated for their absolute values before and after inhaling 400 µg salbutamol. The relationship between “low” PEF (test) and “low” FEV₁ (reference) was studied using χ² tests.

Pearson correlation coefficients between bronchodilator response in PEF (for different expressions) and bronchodilator response in FEV₁ as % predicted FEV₁ after inhaling a bronchodilator (400 µg salbutamol) were calculated. The relationship between ΔFEV₁ and ΔPEF was investigated by calculating sensitivity, specificity, and predictive values for several cut off values. Absolute increases in PEF of 40, 60, and 80 l/min after 400 µg salbutamol were compared with ΔFEV₁ of 9% predicted, the “reference”. The same procedures were performed taking different cut off values (10%, 15%, and 20%) of ΔPEF % baseline in relation to the “reference” ΔFEV₁ of 9% predicted. In the Netherlands this cut off value is recommended to indicate a positive bronchodilator response both by the Dutch College of General Practitioners and the Dutch Society of Pulmonologists. Since there is no universal agreement for the cut off value of significant ΔFEV₁, we also studied the ΔPEF measures against the following recommended ΔFEV₁ measurements: (1) ΔFEV₁ absolute (FEV₁post-BD − FEV₁pre-BD) > 200 ml;14 (2) ΔFEV₁ ≥12% predicted and 200 ml;14 and (3) ΔFEV₁ ≥15% to baseline and 200 ml.15 Finally, receiver operating characteristic (ROC) curves were generated against ΔPEF % baseline and ΔPEF absolute using the above mentioned cut off values for ΔFEV₁, as the gold standard.

Table 1 Characteristics of patients (n=240)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (%)</td>
<td>40.4</td>
</tr>
<tr>
<td>Age (years)</td>
<td>44.9 (15.9)</td>
</tr>
<tr>
<td>Median (range) pack years</td>
<td>2.1 (0–65.0)</td>
</tr>
<tr>
<td>FEV₁ (% predicted)</td>
<td>91.3 (17.9)</td>
</tr>
<tr>
<td>PEF (l/min)</td>
<td>394.8 (122.9)</td>
</tr>
<tr>
<td>PEF (% pred)</td>
<td>84.8 (19.0)</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>78.8 (8.9)</td>
</tr>
<tr>
<td>ΔFEV₁ (% predicted)</td>
<td>3.7 (4.7)</td>
</tr>
<tr>
<td>ΔFEV₁ ≥9% predicted (n, %)</td>
<td>32, 13.3</td>
</tr>
<tr>
<td>ΔFEV₁ &gt; 200 ml absolute (n, %)</td>
<td>63, 26.3</td>
</tr>
<tr>
<td>ΔFEV₁ ≥12% predicted and 200 ml (n, %)</td>
<td>11, 4.6</td>
</tr>
<tr>
<td>ΔFEV₁ ≥15% baseline and 200 ml (n, %)</td>
<td>15, 6.3</td>
</tr>
<tr>
<td>FEV₁pre-BD &gt; 1.64RSD (n, %)</td>
<td>48, 20</td>
</tr>
<tr>
<td>PEF &lt; PEFpred - 1.64RSD (n, %)</td>
<td>86, 35.8</td>
</tr>
</tbody>
</table>

*All values are expressed as mean (SD) unless stated otherwise. FEV₁ = forced expiratory volume in one second; PEF = peak expiratory flow; FVC = forced vital capacity; RSD: residual standard deviation.
Diagnosis of airway obstruction

Figure 1 Relationship between predicted values of PEF and FEV₁ in the population.

Table 2 Relationship between airway obstruction as assessed by FEV₁ and PEF

<table>
<thead>
<tr>
<th>PEF &lt; PEFpred – 1.64RSD</th>
<th>PEF ≥ PEFpred – 1.64RSD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ &lt; FEV₁, pred</td>
<td>40</td>
<td>46</td>
</tr>
<tr>
<td>FEV₁ ≥ FEV₁, pred</td>
<td>8</td>
<td>146</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>192</td>
</tr>
</tbody>
</table>

p = 0.0001 (χ² test).

Results

During the study period 256 subjects had a cough lasting for at least two weeks and met the inclusion criteria. Sixteen subjects refused to enter the study. Those participating in the study (n = 240) did not differ in age and sex from the rest of the study group (n = 16). Table 1 shows the characteristics of the patients. Men were under-represented in the study. There was no significant difference in ventilatory function and age between sexes. Airway obstruction as assessed by FEV₁ (low FEV₁) was found in 48 subjects (20%) and a positive bronchodilator response as assessed by FEV₁, ranged from 11 subjects (4.6%) when a cut off value of ΔFEV₁ of ≥12% predicted and 200 ml absolute increase was used to 63 subjects (26.3 %) when the cut off value used was ΔFEV₁ absolute ≥200 ml.

The correlation between absolute values of FEV₁ and PEF was high (r = 0.82, p<0.001 before bronchodilation, r = 0.80, p<0.0001 after bronchodilation). Figure 1 shows the relationship between the predicted values of FEV₁ and PEF before bronchodilation and table 2 shows the relationship between low PEF and low FEV₁. More patients had a low PEF (n = 86, 35.8%) than a low FEV₁ (n = 48, 20%). Forty six of the 86 patients with a low PEF value (53.5%) did not have a low FEV₁. Eight patients with low FEV₁ did not have obstructive disease according to their PEF values. The sensitivity of a low PEF in relation to a low FEV₁, was 83.3%, the specificity was 76%, positive predictive value (PPV) 46.5%, and negative predictive value (NPV) 94.4%.

BRONCHODILATOR RESPONSIVENESS

Correlations between ΔPEF % baseline and absolute ΔPEF with ΔFEV₁ % predicted were r = 0.43 and r = 0.32, respectively (p<0.001). Figure 2 shows the scatter between ΔFEV₁ % predicted and ΔPEF % baseline.

Figure 3 shows ROC curves using different expressions of ΔFEV₁ cut off at different levels against ΔPEF % baseline and ΔPEF absolute. Table 3 shows the test qualities of both ΔPEF absolute with increases of 40, 60, and 80 l/min as cut off values and ΔPEF % baseline with improvements of 10%, 15%, and 20% as cut off values after 400 µg salbutamol in relation to (1) ΔFEV₁ % predicted with a cut off value of 9%, (2) ΔFEV₁ absolute with a cut off value of 200 ml, (3) ΔFEV₁, cut off at an increase of 12% predicted and 200 ml absolute, and (4) ΔFEV₁ cut off at an increase of ≥15% to baseline and 200 ml. Specificities and NPVs were high but sensitivities and PPVs were low. The highest PPV (83%) was found for ΔPEF % baseline with a cut off value of 20% in relation to ΔFEV₁, absolute with a cut off value of 200 ml.

Discussion

The study shows that, in patients who attend their GP with persistent cough, there is a considerable lack of agreement between PEF and FEV₁, values in assessing airway obstruction and bronchodilator response. Although most patients with a “normal” PEF did not have airway obstruction, there were far more patients with airway obstruction as assessed by PEF than by FEV₁, in this study population. There was a lack of agreement between the bronchodilator response as assessed by ΔFEV₁, and different expressions of bronchodilator response as assessed by PEF. For example, ΔPEF absolute with a cut off value of 60 l/min and ΔPEF % baseline with cut off values of 15% and 20%, as recommended in the literature, had low sensitivities and PPVs but high specificities and NPVs in relation to ΔFEV₁ ≥9% predicted.
Also, when using different expressions and cut-off values for $\Delta FEV_1$, PPVs remained low while NPVs remained high.

Thus, in the diagnostic work up of primary care patients presenting with persistent cough, PEF can reliably exclude airway obstruction when normal PEF values are present. Otherwise it is an unreliable tool, especially for assessment of the bronchodilator response.

More patients had low PEF values than low FEV$_1$ values in this study population. We measured PEF and FEV$_1$ with a turbine meter which might provide a systematic underestimation of PEF by mass inertness. However, this is not very likely because PEF and FEV$_1$ values assessed by the Micro Medical turbine spirometer used in this study are in agreement with the values obtained with pneumotachometers. Besides, the advantage of assessing ventilatory function with a turbine spirometer is that it measures both PEF and FEV$_1$ during the same forced exhalation. Another explanation might be that the reference values of PEF are less reliable than those of FEV$_1$. We feel that the most likely explanation is that PEF and FEV$_1$ were assessed during an unstable phase of the patient—that is, during a coughing period. Since PEF is more effort dependent than FEV$_1$, this may have resulted in more subjects having a low PEF value.

A single PEF measurement is of limited value in assessing airflow limitation but it may sometimes suffice to exclude the presence of airway obstruction at the time of measurement. Our study confirms this statement: the presence of low PEF had a low PPV for airway obstruction (low FEV$_1$) whereas the absence of low PEF made airway obstruction unlikely. In other words, PEF testing to assess airway obstruction has the properties to be a good screening test (high specificities and NPVs) but it was of less clinical value as a diagnostic test (requiring high sensitivity and high PPVs) because of the low PPV.

The correlations between changes in PEF and FEV$_1$ after inhaling 400 µg salbutamol were only weak to moderate. This is in accordance with studies showing a weak correlation between changes in FEV$_1$ and PEF after bronchodilation and after bronchoconstriction. It seems likely that PEF and FEV$_1$ respond in a different way to changes in the mechanical
qualities of the airways as caused by a bronchodilator.

The presence of a positive reversibility test in addition to respiratory symptoms is considered to be a key factor in diagnosing airway obstruction (asthma)\textsuperscript{17,18} so general practitioners are interested in the precision of the PPV (rarely false positives) of the different recommended measurements of APEF.

The European Respiratory Society (ERS) states that an increase in PEF of 60 l/min is a clinically significant improvement.\textsuperscript{3} This statement was based on one study of 73 adults known to have asthma or COPD\textsuperscript{5} in which an absolute increase in PEF measured with a mini-Wright spirometer was compared with an increase in FEV\textsubscript{1}, % predicted with a cut off value of 9%. In contrast, we have found that, using the same dose and bronchodilating agent (salbutamol 400 μg) but in a different population, this cut off value has a low PPV. We therefore conclude that this cut off value is not suitable for use in assessing a significant bronchodilator response during a coughing episode in patients not previously known to have asthma or COPD.

In recent guidelines it is stated that an increase in PEF of 15% or 20% from baseline after bronchodilation is a clinically significant improvement.\textsuperscript{2–4} These statements are not based on studies but are probably derived from FEV\textsubscript{1} measurements. In the current study none of these proposed expressions corresponded sufficiently with an increase in FEV\textsubscript{1}, % predicted which is considered to be a clinically significant response and is recommended in several papers.\textsuperscript{12–15} The use of ≥9% FEV\textsubscript{1}, % predicted as the reference value with which to compare other tests for bronchodilator response may be open to question. Every cut off value is arbitrary because acute reversibility of airway obstruction to a bronchodilator is a continuous variable rather than a dichotomous trait.\textsuperscript{16} However, a cut off value for APEF of 9% predicted has been found to be useful and valid for measuring the bronchodilator response, both in separating asthma from COPD and because it is not dependent on the initial FEV\textsubscript{1}, and it is now the accepted cut off value in The Netherlands.\textsuperscript{12,13} Furthermore, PPVs to assess the bronchodilator response were also low with other cut off values recommended by the ERS and BTS (APEF ≥12% predicted or 15% baseline in combination with 200 ml\textsuperscript{17} or an absolute increase in FEV\textsubscript{1}, of 200 ml\textsuperscript{18}).

One may argue that the use of any cut off value might result in a loss of power and precision. However, it is commonly used by doctors since most medical action is dichotomous—to operate or not to operate, to initiate treatment or not.\textsuperscript{19}

The findings of this study might have implications in general practice for the assessment of airway obstruction and the bronchodilator response in the diagnostic work up of asthma and COPD. If a patient has a low PEF, conclusions about the presence or absence of airway obstruction cannot be made. Further investigation such as spirometric testing is necessary before the general practitioner can decide which treatment is the most appropriate. In the absence of a low PEF further investigation is not necessary. In this analysis all the expressions of bronchodilator response by PEF study showed high NPVs and high specificities in relation to a positive bronchodilator response (good screening test) but the diagnostic properties were poor (low sensitivity, low PPV). Thus, testing of the bronchodilator response by PEF should be replaced by FEV\textsubscript{1} measurements in the diagnosis of reversible airway disease. As a consequence, general practitioners should be better trained in spirometric testing than at present to ensure that quality controls are performed according to international guidelines.

In conclusion, general practitioners should be cautious in interpreting low PEF values and bronchodilator response assessed by PEF in patients presenting with a troublesome cough. The lack of agreement with FEV\textsubscript{1} values raises the question whether PEF measurements are of sufficient clinical value in assessing airway obstruction and bronchodilator responsiveness.


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