Evaluation of asymptomatic subjects with low forced expiratory ratios (FEV₁/VC)

S Kivity, A Solomon, Y Schwarz, I Trajber, M Topilsky

Abstract

Background — Heightened bronchial hyperreactivity is frequently associated with airflow limitation, atopy, or cigarette smoking. The purpose of this study was to evaluate healthy subjects with significantly low values of forced expiratory volume in one second/vital capacity % (FEV₁/VC%) by measuring their airway response to exercise and methacholine challenge, compared with a control group with normal spirometric values.

Methods — Eighty four healthy subjects with significantly low flow rates (group A, FEV₁/VC% < 2 SD% predicted) were evaluated and compared with 37 subjects with normal flow rates (group B). Static lung volumes, spirometric tests, exercise, and methacholine challenges were performed.

Results — Lung volumes were normal for both groups. Mean FEV₁/VC% was 69% for group A and 82% for the control group. Salbutamol improved baseline FEV₁ in eight subjects in group A (mean 15%), while methacholine induced a drop in FEV₁ in 12 subjects. The dose–response curve to methacholine reached a plateau in all the responders. None of the subjects in the control group improved their baseline FEV₁/VC% to salbutamol, but three showed bronchial hyperreactivity similar to those in group A.

Conclusions — Bronchial hyperreactivity does not occur more often in asymptomatic subjects with mildly low FEV₁/VC% so these subjects do not require special investigations for airway disease.

(Thorax 1994;49:554–556)

Bronchial hyperreactivity to histamine and methacholine is a fundamental feature in both patients with bronchial asthma and those with chronic obstructive pulmonary disease (COPD). In patients with COPD the level of bronchial hyperreactivity is partially determined by the initial extent of airway obstruction. Ramsdale et al found a correlation between the initial forced expiratory volume in one second (FEV₁) and the degree of bronchial hyperreactivity in these patients.

Most studies performed on asthmatic subjects report no correlation between the extent of bronchial hyperreactivity and the baseline airway calibre. Ryan et al showed that asthmatic patients may have a moderate or severe increase in bronchial hyperreactivity (PC₂₀ < 2 mg/ml to histamine) when their FEV₁ is within 10% of maximum. In subjects with symptomatic airflow limitation bronchial hyperreactivity is a concomitant finding. We occasionally encounter young asymptomatic subjects with a low ratio of FEV₁ to vital capacity (FEV₁/VC%), the significance of which is not entirely clear. We therefore measured the airway response to exercise and methacholine of healthy subjects with a low FEV₁/VC% and compared the results with a control group.

Methods

Eighty four subjects aged 17–39 (mean 24) years (group A) were included on the basis of two spirometric studies (including one in our laboratory) showing FEV₁/VC% of less than two standard deviations of their predicted mean. The subjects were examined at the Chest and Allergy Institute, Tel Aviv Medical Center, based on previous routine spirometric measurements performed elsewhere.

Initial screening excluded subjects with obvious causes for bronchial hyperreactivity including smoking, atopy, or recent viral respiratory infection. The remaining 84 subjects underwent the following measurements: (1) physical examination; (2) spirometric testing and measurement of static lung volumes using a Jaeger Masterlab and slow vital capacity measured by an expiratory manoeuvre with the best of three reproducible measurements being recorded; (3) measurement of the effect of exercise challenge on the spirometric data as previously described. Each patient underwent spirometric tests followed by 10 minutes running on a treadmill (Quinton) reaching 90(5)% of maximal predicted heart rate. Spirometric testing was repeated 15 minutes later and a drop of ≥ 15% in FEV₁ was considered significant; (4) methacholine challenge performed according to a modification of Chai’s method, not using a dosimeter. A Devilbis (645) nebuliser delivering compressed air at a rate of 6 1/min was used for inhalation challenge. Each patient inhaled increasing concentrations of methacholine (0·07, 0·15, 0·3, 0·6, 1·5, 3, 6, 12, 25 mg/ml), each of which was inhaled by five inspirations from FRC to TLC. Spirometric parameters were measured at baseline and repeated 1·5 minutes after each dose of methacholine until at least two technically correct manoeuvres were obtained; the better value was recorded. The concentration inducing a 20% drop in FEV₁ was calculated from the semilogarithmic dose–response curve. The provocation was continued until the last dose in all subjects.

Each subject participated in three study
Flow rates, FEV₁/VC in asymptomatic subjects

days at the same time of the day within a two week period. On day 1 baseline pulmonary function tests and response to salbutamol were measured, on day 2 exercise challenge was performed, and on day 3 a methacholine challenge was performed. Subjects who demonstrated bronchial hyperreactivity underwent skin tests (prick) with environmental allergens (dust, mite, cockroach, mixed moulds, mixed grasses, mixed trees, dog, cat, with histamine and saline as control). These subjects also had an additional bronchial hyperreactivity evaluation by measuring peak expiratory flow rates (mini Wright) twice a day for a week.

As a control group 37 young healthy men were included in the study (group B). All were employed by the hospital and had volunteered for the study. None were smokers, and none had atopy nor recent viral respiratory infections. They all underwent the same evaluations as those in group A.

The study was approved by our local Helsinki Ethical Committee.

STATISTICAL ANALYSIS
The data obtained from both groups (static lung volumes, flow rates, and the rates of bronchial hyperreactivity) were analysed using the Student’s paired t test.

Results
The subjects in group A fulfilled the criteria of having FEV₁/VC% < 2 SD% predicted, while those in group B had normal spirometric values (FEV₁/VC% > 2SD). The difference between the two groups was significant for FEV₁/VC% (p < 0.05). All were healthy men with no history of airways disease and most participated in strenuous physical activity. Simple anthropometric data of the groups are summarised in table 1.

A summary of their baseline pulmonary function is given in table 2. Although the mean values for lung volumes (VC, FVC, TGV, and TLC) were high in group A, all were within the normal range and no significant differences were found. Salbutamol inhalation (1 ml of 5 mg/ml normal saline) significantly improved the baseline FEV₁ (by more than 10%) in eight of the subjects in group A (table 3) and in none of the control group. Treadmill running did not have any effect on spirometric parameters in either group. Methacholine induced a significant drop in FEV₁ in 12 subjects from group A and in three from group B. An interesting feature of the airway responses in both groups was the fact that at certain points all the subjects reached a plateau, after which no further drop in FEV₁ was observed (figure). The rates of bronchial hyperreactivity in both groups and the shape of the dose-response curve were not significantly different. Two of the subjects in group A and one in group B had positive skin tests (> 5 mm weal diameter), two to mite, and one to grass mix; they denied atopic symptoms.

Table 1 Subject characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A Mean</th>
<th>Group A Range</th>
<th>Group B Mean</th>
<th>Group B Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24</td>
<td>17-44</td>
<td>27</td>
<td>22-48</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>178</td>
<td>170-185</td>
<td>174</td>
<td>169-182</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75</td>
<td>60-100</td>
<td>76</td>
<td>62-92</td>
</tr>
</tbody>
</table>

Table 2 Baseline pulmonary function parameters expressed as percentage predicted

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A Mean</th>
<th>Group A Range</th>
<th>Group B Mean</th>
<th>Group B Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC</td>
<td>108</td>
<td>82-125</td>
<td>102</td>
<td>83-110</td>
</tr>
<tr>
<td>FVC</td>
<td>109</td>
<td>86-130</td>
<td>103</td>
<td>84-108</td>
</tr>
<tr>
<td>TGV</td>
<td>121</td>
<td>80-145</td>
<td>109</td>
<td>80-110</td>
</tr>
<tr>
<td>TLC</td>
<td>107</td>
<td>81-126</td>
<td>103</td>
<td>83-109</td>
</tr>
<tr>
<td>RV/TLC</td>
<td>115</td>
<td>91-155</td>
<td>106</td>
<td>92-112</td>
</tr>
<tr>
<td>TGV/TLC</td>
<td>111</td>
<td>93-164</td>
<td>105</td>
<td>90-110</td>
</tr>
<tr>
<td>FEV₁</td>
<td>86</td>
<td>66-118</td>
<td>91</td>
<td>77-110</td>
</tr>
<tr>
<td>FEV₁/VC%</td>
<td>69*</td>
<td>64-73</td>
<td>82*</td>
<td>76-92</td>
</tr>
<tr>
<td>MEF₁₅₀</td>
<td>62</td>
<td>25-84%</td>
<td>74</td>
<td>64-89</td>
</tr>
<tr>
<td>MEF₂₀₀</td>
<td>64</td>
<td>28-83%</td>
<td>73</td>
<td>62-91</td>
</tr>
</tbody>
</table>

VC = vital capacity (slow); FVC = forced vital capacity; TGV = thoracic gas volume; TLC = total lung capacity; RV = residual volume; FEV₁ = forced expiratory volume in one second; MEF₁₅₀, MEF₂₀₀ = maximal expiratory flow at 25% and 50% of VC.

* p < 0.05.

Table 3 Effect of salbutamol inhalation on pulmonary function in responders (percentage)

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>VC%</th>
<th>FEV₁ %</th>
<th>FEV₁/VC%</th>
<th>MEF₁₅₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>-1</td>
<td>14</td>
<td>14</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td>-2</td>
<td>13</td>
<td>14</td>
<td>43</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>12</td>
<td>12</td>
<td>28</td>
</tr>
<tr>
<td>25</td>
<td>-2</td>
<td>17</td>
<td>20</td>
<td>53</td>
</tr>
<tr>
<td>40</td>
<td>-2</td>
<td>15</td>
<td>17</td>
<td>35</td>
</tr>
<tr>
<td>51</td>
<td>2</td>
<td>17</td>
<td>15</td>
<td>25</td>
</tr>
<tr>
<td>60</td>
<td>3</td>
<td>18</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>72</td>
<td>-2</td>
<td>13</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>Mean</td>
<td>15</td>
<td>15</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>2</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Individual methacholine dose-response curves in 12 asymptomatic subjects with low flow rates (FEV₁/VC%) (group A) and in three subjects with normal flow rates (group B).
The mean change in peak expiratory flow rate (ΔPEF%) was expressed by:

\[
\text{PEF morning} - \text{PEF evening} \\
\text{PEF morning}
\]

For the nine subjects in group A who completed the test for the whole week ΔPEF was 12 (3)% for the six subjects who had PC_{20} < 8 mg% (asthmatic range) the mean ΔPEF was 17 (2)%, and for the three who had PC_{20} > 8 mg% it was 9 (3)%. There was a good correlation between the PC_{20} of the six hyper-reactive subjects to the ΔPEF (p<0.05). The mean ΔPEF for the control group was 11%.

Discussion

Asymptomatic subjects found on routine screening to have significantly low FEV_{1}/VC% (<2 SD% predicted) were evaluated for airway disease. None of the subjects had any common risk factors for developing airway disease or viral respiratory tract infection, and none had a first degree relative with bronchial asthma. Two who had bronchial hyperreactivity were also atopic upon skin testing.

In spite of the significantly low FEV_{1}/VC% in group A the other pulmonary function tests were found to be in the normal range. Following heavy exercise there was no change in FEV, and the rate of bronchial hyperreactivity was not significantly different between the two groups. It also appears that high lung volume, as seen in a few of the subjects, did not affect the rate or the degree of bronchial hyperreactivity. As expected, the subjects with bronchial hyperreactivity also had significant fluctuation in their PEF during the day.

There are relatively few reports on the relationship between non-specific bronchial hyperreactivity and pulmonary function. In these reports increased responsiveness was associated with a decreased level of pulmonary function. However, little insight was provided of this relation in healthy subjects as most studies have concentrated on selected populations such as smokers, asthmatics, bronchitics or other groups of subjects with disease. Possible selection bias and the occurrence of disease itself on other factors may therefore have affected the association between bronchial hyperreactivity and pulmonary function.

Malo et al. examined 100 non-smoking volunteers who were completely free of respiratory symptoms in a cross sectional study and found that PC_{20} methacholine was related to the baseline FEV, Welty et al. studied a random population of 171 adults and found no statistically significant association between bronchial hyperreactivity (assessed by cold air challenge test) and pulmonary function after adjusting for smoking habits.

The small decrease of FEV_{1}/VC% in our symptomatic subjects had no effect on bronchial hyperreactivity. Interestingly, our subjects showed a particular dose–response pattern following methacholine, with a relatively small drop in FEV_{1}, previously shown by Woolcock et al to occur in healthy subjects. We conclude that the low FEV_{1}/VC% ratios of our group of otherwise normal subjects was not associated with any evidence of disease. Bronchial hyperreactivity does not occur more frequently in this group of subjects than in healthy controls, but when it is found a plateau of FEV_{1} is seen that is similar to the normal bronchoconstrictor response to methacholine and unlike that of asthmatics. Low FEV_{1}/VC% with normal values of VC in asymptomatic subjects does not merit special investigation for airway disorders.

Evaluation of asymptomatic subjects with low forced expiratory ratios (FEV1/VC).

S Kivity, A Solomon, Y Schwarz, I Trajber and M Topilsky

Thorax 1994 49: 554-556
doi: 10.1136/thx.49.6.554

Updated information and services can be found at:
http://thorax.bmj.com/content/49/6/554

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/