Effect of short and long term antibiotic response on lung function in bronchiectasis

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ABSTRACT In a study designed to show whether purulent bronchial secretions damage the lung irreversibly, 18 patients with bronchiectasis underwent lung function tests before and after two weeks' antibiotic treatment to convert their sputum from purulent to mucoid, and 10 of them also after four months' treatment. After two weeks FEV₁, forced vital capacity, vital capacity, functional residual capacity, and total lung capacity showed small but statistically significant (though not clinically useful) improvements. In the 10 patients studied after four months only FVC (of the four indices with significant improvements at two weeks in this group) was still higher than before treatment. These results contrast with those of an earlier study, in which large acute changes were found, perhaps because of differences in the patients studied. It is concluded that the absence of major changes in lung function points to physiological abnormality that is largely irreversible in these patients with chronic bronchial sepsis.

Patients with bronchiectasis who usually produce purulent, elastase positive secretions have worse lung function than those who produce mucoid secretions. This raised the possibility that the type of secretion could determine the degree of lung damage. Cole and his colleagues, however, suggested that major changes in forced expiratory volumes could occur after one week of successful antibiotic treatment. This point was emphasised in a recent leading article in the British Medical Journal and suggests that the abnormality previously observed by us could be reversible.

A preliminary study of our own patients suggested that major changes in lung function did not occur after short term antibiotic treatment. In view of this apparent discrepancy we have carried out formal lung function tests before and after successful antibiotic treatment for two weeks and four months.

Methods

We studied 18 patients (13 female) with radiologically proved bronchiectasis (nine with cystic bronchiectasis demonstrable by plain radiograph and nine by bronchography). Their ages ranged from 19 to 67 years.

Fourteen patients were lifelong non-smokers and four had ceased smoking at least two years earlier. Three had previously undergone lobectomy for the disease.

All were producing purulent secretions and received a two week course of either amoxycillin or, in two cases, intravenous gentamicin, resulting in macroscopic clearance of their secretions, which changed from purulent to mucoid as assessed by SLH. Lung function tests were performed before and at the end of treatment. Ten patients continued treatment for a total of four months, during which time their sputum remained mucoid, and they were retested at the end of the treatment period.

Dynamic lung volumes, FEV₁, and forced vital capacity (FVC) were measured with a Wedge bellows spirometer (Vitalograph). Values for static lung volumes, vital capacity (VC), residual volume (RV), and total lung capacity (TLC) were obtained during and from the determination of functional residual capacity (FRC), for which the helium dilution method was used. Transfer factor for carbon monoxide (TLCO) and the transfer coefficient (Kco) were determined by the single breath method. All measurements were corrected to BTPS.

Bronchodilator treatment was stopped for at least 12 hours before lung function testing on every occasion and the measurements were performed in the morning at about the same time (to within one hour) by SLH. All patients carried out their usual morning postural drainage routine before attending for tests.

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Accepted 25 March 1986
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Table 1  Effect of two weeks' antibiotic treatment on lung function in 18 patients (means with standard deviations in parentheses)

<table>
<thead>
<tr>
<th>Test</th>
<th>Before</th>
<th>After</th>
<th>Significance (p)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ (l)</td>
<td>1.53 (0.84)</td>
<td>1.61 (0.85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.76 (0.84)</td>
<td>2.94 (0.83)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>52.35 (15.07)</td>
<td>52.35 (15.07)</td>
<td>NS</td>
</tr>
<tr>
<td>VC (l)</td>
<td>2.83 (0.81)</td>
<td>3.00 (0.78)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FRC (l)</td>
<td>3.24 (0.75)</td>
<td>3.40 (0.82)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>RV (l)</td>
<td>2.37 (0.74)</td>
<td>2.43 (0.84)</td>
<td>NS</td>
</tr>
<tr>
<td>TLC (l)</td>
<td>5.21 (0.86)</td>
<td>5.44 (0.98)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>45.75 (12.05)</td>
<td>44.54 (11.62)</td>
<td>NS</td>
</tr>
<tr>
<td>TLC (mmol min⁻¹ kPa⁻¹⁻¹)</td>
<td>6.67 (1.81)</td>
<td>6.54 (1.65)</td>
<td>NS</td>
</tr>
<tr>
<td>Kco (mmol min⁻¹ kPa⁻¹⁻¹)</td>
<td>1.81 (0.40)</td>
<td>1.72 (0.27)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Student's t test for paired data.

FVC—forced vital capacity; VC—vital capacity; FRC—functional residual capacity; RV—residual volume; TLC—total lung capacity; TLco—transfer factor for carbon monoxide; Kco—transfer coefficient.

Table 2  Effect of two weeks and four months' antibiotic treatment on lung function in 10 patients (means with standard deviations in parentheses)

<table>
<thead>
<tr>
<th>Test</th>
<th>Before</th>
<th>After 2 weeks</th>
<th>After 4 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ (l)</td>
<td>1.58 (0.81)</td>
<td>1.68 (0.80)**</td>
<td>1.61 (0.83)</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.85 (0.89)</td>
<td>3.08 (0.84)**</td>
<td>3.00 (0.86)*</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>53.3 (15.0)</td>
<td>53.3 (15.0)</td>
<td>52.8 (14.6)</td>
</tr>
<tr>
<td>VC (l)</td>
<td>2.98 (0.83)</td>
<td>3.15 (0.99)</td>
<td>3.12 (0.81)</td>
</tr>
<tr>
<td>FRC (l)</td>
<td>3.26 (0.91)</td>
<td>3.51 (0.95)**</td>
<td>3.29 (0.80)</td>
</tr>
<tr>
<td>RV (l)</td>
<td>2.42 (0.84)</td>
<td>2.58 (0.93)</td>
<td>2.40 (0.73)</td>
</tr>
<tr>
<td>TLC (l)</td>
<td>5.40 (1.06)</td>
<td>5.74 (1.17)*</td>
<td>5.52 (1.07)</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>44.9 (12.3)</td>
<td>44.7 (11.5)</td>
<td>43.5 (10.5)</td>
</tr>
<tr>
<td>TLco (mmol min⁻¹ kPa⁻¹⁻¹)</td>
<td>7.03 (1.89)</td>
<td>6.83 (1.60)</td>
<td>6.86 (1.67)</td>
</tr>
<tr>
<td>Kco (mmol min⁻¹ kPa⁻¹⁻¹)</td>
<td>1.81 (0.49)</td>
<td>1.73 (0.27)</td>
<td>1.74 (0.26)</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.02 in the comparison with results obtained before treatment (Student's t test for paired data).

Abbreviations as in table 1.

At the first visit we did a bronchodilator challenge with a β₂ agonist delivered from a metered dose inhaler (Rimiterol, 4 × 200 μg).

The significance of any difference after treatment was determined by means of Student's t test for paired data.

Results

Only one patient showed clear reversibility of FEV₁ after formal bronchodilator challenge of more than 15%, which represented an actual change of 0.88–1.04 litres. The remainder showed little or no response, with a mean increase in FEV₁ of 4.3% (SD 4.97%).

The average changes in lung function indices over two weeks for the 18 patients are summarised in table 1. Small but significant increases were seen in FEV₁, FVC, VC, FRC, and TLC.

The results for the 10 patients studied over four months are summarised in table 2. Similar changes in FEV₁, FVC, FRC, and TLC were seen in this group.

By four months, however, only the FVC remained better than the pretreatment results.

Discussion

The present results show that after a two week course of successful antibiotic treatment only small increases (about 5%) were observed for FEV₁, FVC, VC, FRC, and TLC. This change could be the effect of reduction in sputum volume, which we have shown to be associated with the response to antibiotics in these patients. In support of this is the similarity to the 8% increase in FEV₁ reported by Cochrane et al after chest physiotherapy in a similar group of patients. Another possibility is a small degree of bronchodilation as a result of antibiotic treatment. This would be consistent with the small increase in FEV₁ observed after bronchodilator challenge (see “Results”). All patients were assessed after β₂ agonist treatment had been withdrawn and hence the antibiotic effect is not due to this other treatment.

The changes we observed in lung function are at
variance with the acute changes found by Cole et al.\textsuperscript{2}
after antibiotic treatment. These workers found
increases in FEV\textsubscript{1}, FVC and peak flow of 50\%, 32\%,
and 36\% respectively in a group of 17 patients after
seven days of treatment. These increases were even
more dramatic when their group was further divided
and subjective responders were examined; increases of
91\%, 50\%, and 64\% were seen for the same indices of
lung function. No information was provided by these
workers on the degree of formal bronchodilator
reversibility. The presence of a significant "asthmatic" element could explain the difference between
the current study results and those of Cole and his
colleagues. Only one of the patients who underwent
repeated lung function tests in our study showed a
significant degree of reversibility after inhaling bronchial dilators, and the absolute changes were small.
This suggests that our patients may differ from those
of Cole et al.\textsuperscript{2} Thus the large acute changes seen
previously\textsuperscript{2} and quoted in the recent British Medical
Journal leader\textsuperscript{3} are not universal in patients with
chronic bronchial sepsis.

The lack of major changes in lung function over
two weeks suggests that most of the physiological
abnormality is permanent. In support of this is the
fact that no further change was seen even after four
months' treatment. This suggests that any effect of
large sputum volumes and airways oedema on lung
function can be reversed within two weeks of the start
of successful treatment. These results, however, again
raise the possibility that purulent elastase positive
secretions may be the cause of lung damage rather
than being an associated phenomenon. Whether deter-
mination in lung function would have occurred without antibiotic treatment is uncertain. Further long
term follow up of patients in a controlled study of
antibiotic treatment is required to resolve this ques-
tion.

We thank Bencard for financial support and Miss
Roberts for typing the manuscript. RAS is a Wolfson
research fellow of the Royal College of Physicians of
London.

References

1 Stockley RA, Hill SL, Morrison HM, Starkie CM. Elas-
tolytic activity of sputum and its relation to purulence
and to lung function in patients with bronchiectasis.

2 Cole PJ, Roberts DE, Davies SF, Knight RK. A simpli-
ified antimicrobial regimen effective in severe chronic
bronchial suppuration associated with culturable

3 Cochrane GM. Chronic bronchial sepsis and progres-

4 Hill SL, Burnett D, Stockley RA. Bronchiectasis: dosage
of Amoxil required to clear purulent secretions and its
effect on lung function [abstract]. Am Rev Respir Dis
1985;131(No 4 part 2):A112.

5 Hill SL, Morrison HM, Burnett D, Stockley RA. The
short term response of patients with bronchiectasis to
treatment with amoxycillin given in standard or high
doses orally or by inhalation. Thorax 1986;41:559–66.

6 Cochrane GM, Webber BA, Clarke SW. Effects of spi-