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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 reversibly or 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 FEV_1, 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, elatase positive secretions have worse lung function than those who produce mucoid secretions.[1] This raised the possibility that the type of secretion could determine the degree of lung damage. Cole and his colleagues,[2] 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*[3] 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.[4] 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, FEV_1, 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 (T_{LCO}), and the transfer coefficient (K_{CO}) 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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Table 1 *Effect of two weeks' antibiotic treatment on lung function in 18 patients (means with standard deviations in parentheses)*

Test	*Before*	*After*	*Significance (p)**
FEV_1 (l)	1·53 (0·84)	1·61 (0·85)	<0·001
FVC (l)	2·76 (0·84)	2·94 (0·83)	<0·001
FEV_1/FVC (%)	52·53 (14·76)	52·35 (15·07)	NS
VC (l)	2·83 (0·81)	3·00 (0·78)	<0·01
FRC (l)	3·24 (0·75)	3·40 (0·82)	<0·05
RV (l)	2·37 (0·74)	2·43 (0·84)	NS
TLC (l)	5·21 (0·86)	5·44 (0·98)	<0·02
RV/TLC (%)	45·75 (12·05)	44·54 (11·62)	NS
TLCO (mmol min^{-1} kPa^{-1})	6·67 (1·81)	6·54 (1·65)	NS
KCO (mmol min^{-1} kPa^{-1} l^{-1})	1·81 (0·40)	1·72 (0·27)	NS

*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)*

Test	*Before*	*After 2 weeks*	*After 4 months*
FEV_1 (l)	1·58 (0·81)	1·68 (0·80)**	1·61 (0·83)
FVC (l)	2·85 (0·89)	3·08 (0·84)**	3·00 (0·86)*
FEV_1/FVC (%)	53·5 (13·8)	53·3 (15·0)	52·8 (14·6)
VC (l)	2·98 (0·83)	3·15 (0·99)	3·12 (0·81)
FRC (l)	3·26 (0·91)	3·51 (0·95)**	3·29 (0·80)
RV (l)	2·42 (0·84)	2·58 (0·93)	2·40 (0·73)
TLC (l)	5·40 (1·06)	5·74 (1·17)*	5·52 (1·07)
RV/TLC (%)	44·9 (12·3)	44·7 (11·5)	43·5 (10·5)
TLCO (mmol min^{-1} kPa^{-1})	7·03 (1·89)	6·83 (1·60)	6·86 (1·67)
KCO (mmol min^{-1} kPa^{-1} l^{-1})	1·83 (0·49)	1·73 (0·27)	1·74 (0·26)

*$p < 0·05$, **$p < 0·02$ 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 β_2 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 FEV_1 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 FEV_1 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 FEV_1, FVC, VC, FRC, and TLC.

The results for the 10 patients studied over four months are summarised in table 2. Similar changes in FEV_1, 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 FEV_1, 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.[5] In support of this is the similarity to the 8% increase in FEV_1 reported by Cochrane *et al*[6] 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 FEV_1 observed after bronchodilator challenge (see "Results"). All patients were assessed after β_2 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*[2] after antibiotic treatment. These workers found increases in FEV_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 bronchodilators, and the absolute changes were small. This suggests that our patients may differ from those of Cole *et al.*[2] Thus the large acute changes seen previously[2] and quoted in the recent *British Medical Journal* leader[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 deterioration 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 question.

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