Nocturnal oxygen desaturation and spirometric parameters in adults with cystic fibrosis

M N Pond, S P Conway

Abstract

Background – Correction of nocturnal hypoxaemia in patients with cystic fibrosis may delay the development of pulmonary hypertension. Descriptive statistics used for nocturnal arterial oxygen saturation (Spo2) lack uniformity. The relationship between Spo2 and spirometric parameters has not previously been explored in a large number of exacerbations in adult patients with cystic fibrosis.

Methods – Over a 21 month period overnight Spo2, forced expiratory volume in one second (FEVf), and forced vital capacity (FVC) were recorded on admission and discharge in 120 treatments of pulmonary exacerbations in 47 patients with cystic fibrosis who did not receive supplemental oxygen during recording. Nocturnal Spo2 was related to spirometric parameters for the whole group and individually in 11 patients, each of whom had at least five treatments.

Results – There was a close linear relationship between the percentage of the recording spent with Spo2 <90% and mean overnight Spo2. Mean Spo2 correlated moderately with percentage predicted FEVf (%FEVf), r = 0.6, and more poorly with percentage predicted FVC (%FVC), r = 0.34. The relationship between mean Spo2 and % FEVf was non-linear at mean Spo2 <89%, but approximately to linearity above this value. After exclusion of treatments with mean Spo2 <89% the regression relationship between mean Spo2 and % FEVf was the same on admission and discharge. Individual correlation coefficients of mean Spo2 versus % FEVf in the 11 patients with repeated treatments ranged from 0.57 to 0.77. The slopes of the regression lines did not differ, with a pooled slope of 0.116, but the intercepts varied widely.

Conclusions – In patients with cystic fibrosis mean overnight Spo2 can be substituted for percentage of recording <90%. The relationship between mean Spo2 and percentage predicted FEVf is non-linear at low values of Spo2 and is not influenced by treatment of pulmonary exacerbations. Patients with cystic fibrosis desaturate at a uniform rate compared with percentage predicted FEVf, but the value of FEVf, at which desaturation first occurs varies between patients. The spirometric values do not accurately predict nocturnal desaturation in a cystic fibrosis population, but FEVf is a useful guide in individual patients with moderate desaturation.

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Keywords: cystic fibrosis, nocturnal oxygen desaturation, spirometry.

The value of oxygen therapy in cystic fibrosis is uncertain. In acute pulmonary exacerbations the mainstay of treatment are intravenous antibiotics, physiotherapy, and increased calorie intake. There are no published studies concerning the effects of oxygen therapy in this setting. Nocturnal hypoxaemia is common in cystic fibrosis and is likely to precede daytime hypoxaemia. The mechanism is probably a combination of hypoventilation and reduced functional residual capacity. Pulmonary artery pressure (PAP) is inversely correlated with Spo2 in cystic fibrosis, and decreases with supplemental oxygen. The development of pulmonary hypertension might be delayed by correction of nocturnal hypoxaemia. A variety of descriptive statistics has been used for nocturnal Spo2 in cystic fibrosis – for example, 10% of an overnight recording with Spo2 <90% is usually taken to represent significant desaturation. The first aim of our study was to determine whether simple mean Spo2 or lowest recorded Spo2 could substitute for time spent with Spo2 <90%. It is unclear from previous work whether nocturnal desaturation can be predicted by FEVf. The second aim was to clarify the relationship between routinely measured spirometric parameters and nocturnal desaturation in a large number of acute pulmonary exacerbations in a cystic fibrosis population, and in a smaller number of individual patients with repeated admissions for treatments of exacerbations.

Methods

From February 1992 to November 1993 all patients with cystic fibrosis admitted for intravenous antibiotic treatment of pulmonary exacerbations underwent overnight Spo2 recording on the night of admission and on the night prior to discharge. The second recording was performed only after the decision to discharge was taken. The decision to treat with intravenous antibiotics was made on the basis of an increase in respiratory symptoms and/or a decline in FEVf, or FVC of 10% or more compared with the patient's previous values. All patients were treated with two intravenous antipseudomonal antibiotics,
Table 1  Admission and discharge values of analysed exacerbations (120 exacerbations in 47 patients)

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>Discharge</th>
<th>ANOVA (admission vs discharge)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) % predicted FEV₁</td>
<td>49·9 (21·0)</td>
<td>62·4 (24·0)</td>
<td>p&lt;0·0001</td>
</tr>
<tr>
<td>Mean (SD) % predicted FVC</td>
<td>76·8 (22·6)</td>
<td>95·7 (23·9)</td>
<td>p&lt;0·0001</td>
</tr>
<tr>
<td>Mean (SD) mean Spo₂ (%)</td>
<td>93·96 (3·59)</td>
<td>93·77 (2·46)</td>
<td>p&lt;0·0001</td>
</tr>
<tr>
<td>Mean (SD) lowest Spo₂ (%)</td>
<td>83·17 (7·67)</td>
<td>85·71 (5·62)</td>
<td>p&lt;0·005</td>
</tr>
<tr>
<td>Median (IQ range) percentage recording with Spo₂ &lt;90%</td>
<td>3 (0·0·2·5)</td>
<td>0 (0·0·5)</td>
<td>p&lt;0·0001</td>
</tr>
<tr>
<td>Median (IQ range) recording duration (hours)</td>
<td>7·37 (6·7·7·9)</td>
<td>7·54 (6·7·7·9)</td>
<td>p=NS</td>
</tr>
</tbody>
</table>

based on their most recent sputum pseudomonal sensitivities. Oxygen therapy was continued in those considered to be oxygen-dependent, but only newly commenced after demonstrating that >10% of the admission Spo₂ recording was below 90%.

Spo₂ was recorded using four Biox 3740 and one Biox 3700 oximeters (Ohmeda), with a probe carefully attached to one finger. These oximeters have previously been validated. The presence of finger clubbing does not affect pulse oximetry results. Spo₂ was monitored only for the period when the patients were asleep. Where the duration of sleep exceeded eight hours only the last eight hours of the recording were analysed. On the day after recording oximeter data were analysed using in-house software which automatically excluded artefactual desaturation. Each oximeter recording was also examined by an experienced observer (MNP) on a compressed time base to confirm the exclusion of artefact and to ensure that only the data pertaining to the previous night’s recording were included for analysis (in cases with a record duration of less than eight hours). The following summary statistics were then calculated by the software: mean Spo₂, lowest Spo₂, duration of record, and time spent with Spo₂ <90%.

On the day of admission and the day of discharge FEV₁ and FVC were recorded using one Vitolograph Compact spirometer. Patients were asked to repeat forced manoeuvres until the highest two readings differed by no more than 5%. FEV₁ and FVC were obtained from the expiratory effort with the greatest FEV₁ were then recorded and expressed as percentage predicted based on the patient’s sex, age, and height.

Data were included for analysis only from those exacerbations which met the following criteria: treatment solely in hospital (no element of home therapy); duration of treatment at least 10 days; and no supplemental oxygen used during either admission or discharge recordings.

**Figure 1  Percentage recording with Spo₂ <90% versus mean in all recordings (n=240).**

**Figure 2  Mean Spo₂ versus percentage predicted FEV₁. Each point represents mean of admission values in individual patients (n=47). Significant desaturation = mean Spo₂ <92%.**

**STATISTICAL ANALYSIS**

Because we aimed to identify patients with repeated qualifying exacerbations, variable numbers of exacerbations were included for each patient. Consequently, in the group analysis ANOVA was performed with patients as a nested factor to determine improvement with treatment, mean values were calculated for each patient for correlation and regression, and regression analyses (including general linear modelling) were then weighted for number of exacerbations. Statistical calculations were performed with the Minitab programme.

**Results**

One hundred and twenty exacerbations in 47 patients fulfilled the criteria for inclusion in the analysis. Details of the exacerbations analysed
Table 2 Predicted FEV$_1$ and FVC and correlation of % predicted FEV$_1$ with mean Spo$_2$ in 11 individuals with ≥5 repeated exacerbations. Both admission and discharge values are included yielding a minimum of 10 observations per patient.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>n</th>
<th>Mean % predicted FEV$_1$</th>
<th>Mean % predicted FVC</th>
<th>Mean (mean Spo$_2$)</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>70.2</td>
<td>106.4</td>
<td>92.52</td>
<td>0.61</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>33.4</td>
<td>73.8</td>
<td>90.43</td>
<td>0.65</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>40.0</td>
<td>56.8</td>
<td>92.93</td>
<td>0.64</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>42.4</td>
<td>63.7</td>
<td>92.85</td>
<td>0.63</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>54.1</td>
<td>73.2</td>
<td>92.35</td>
<td>0.77</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>95.6</td>
<td>14.5</td>
<td>95.36</td>
<td>0.73</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>86.7</td>
<td>116.9</td>
<td>95.77</td>
<td>0.68</td>
</tr>
<tr>
<td>8</td>
<td>12</td>
<td>40.9</td>
<td>94.9</td>
<td>90.58</td>
<td>0.77</td>
</tr>
<tr>
<td>9</td>
<td>12</td>
<td>36.2</td>
<td>82.4</td>
<td>93.20</td>
<td>0.57</td>
</tr>
<tr>
<td>10</td>
<td>18</td>
<td>44.9</td>
<td>85.9</td>
<td>92.30</td>
<td>0.72</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>65.7</td>
<td>93.1</td>
<td>94.25</td>
<td>0.69</td>
</tr>
</tbody>
</table>

The relation between mean Spo$_2$ and % FEV$_1$ appeared to be linear until very low mean Spo$_2$ values were recorded. Regression analysis with the exploratory lack of fit model confirmed that this was the case. For both the admission and discharge plots exclusion of patients with mean (mean Spo$_2$) <89% (n=8) resulted in a regression relationship that did not significantly differ from linearity. This resulted in a greater correlation coefficient of 0.61 on discharge, but the admission value was unchanged. Both regression equations were statistically significant and not significantly different from each other (p=NS using the general linear model):

\[
\text{mean Spo}_2 \text{ (admission)} = 90.3 + 0.0471 \times \text{FEV}_1 \text{ (admission)} (p<0.0001)
\]

\[
\text{mean Spo}_2 \text{ (discharge)} = 91.6 + 0.0377 \times \text{FEV}_1 \text{ (discharge)} (p<0.0001)
\]

The relationship between mean Spo$_2$ and FEV$_1$ was explored further for the individual case in 11 patients who had had at least five eligible exacerbations during the period of the study. Since the same relationship between mean Spo$_2$ and % FEV$_1$ holds on both admission and discharge, both of these data points were included, yielding a minimum of 10 observations per patient. Individual correlations between mean Spo$_2$ and percentage predicted FEV$_1$ are shown for these patients with the clinical characteristics in table 2. The regression lines of these 11 patients are shown in fig 3. General linear modelling showed the differences between the slopes of the individual lines to be non-significant, and hence parallel, but the intercepts were significantly different (p<0.005). The pooled slope was 0.116.

Discussion

Spo$_2$ during sleep remains at a steady level in patients with cystic fibrosis, with slightly lower values recorded during periods of REM sleep. Because of this lack of variation from baseline there is a close linear relationship between mean Spo$_2$ and the percentage of recording time with Spo$_2$ <90% (Pearson r = -0.95, fig 1). Mean Spo$_2$ can therefore substitute for the cumbersome percentage of recording with Spo$_2$ <90% as a descriptive statistic. It is generally accepted that significant desaturation occurs when Spo$_2$ is <90% (corresponding to a Po$_2$ of 8 kPa at pH 7.4) for more than 10% of the overnight recording. The corresponding mean Spo$_2$ is 92%.

We observed a closer relationship between mean Spo$_2$ and FEV$_1$ than between mean Spo$_2$ and FVC. Further analysis of our data was confined to mean Spo$_2$ and FEV$_1$. Exploratory regression of mean Spo$_2$ on % FEV$_1$ revealed definite curvature at low values of Spo$_2$ for both the admission and discharge cases (fig 2) which has not previously been described. This is not due to inaccuracy of the oximeters since they tend to overread in this range and the true relationship is therefore likely to be even more curvilinear. Given that the oxygen dis-
sociation curve is sigmoid, it is likely that this relationship is non-linear over the whole range of SpO2, but for both the admission and discharge cases exclusion of patients with admission mean SpO2 <89% (n = 8) resulted in a regression that did not differ significantly from linearity. This allowed comparison of the admission and discharge plots with simple linear statistics. The relationship between mean SpO2 and FEV1 might be different on admission and discharge as the various therapeutic interventions employed in treating pulmonary exacerbations might have differential effects on FEV1 and nocturnal SpO2, and some subjects may require a night to acclimatise to hospital surroundings.14 However, both regression equations were very similar and not significantly different. This result may not apply to the very low mean SpO2 values that had to be excluded to allow the comparison. When patients are in a stable phase routinely measured clinical parameters usually fall between the admission and discharge values. The relationship between mean SpO2 and FEV1 is thus the same at the extremes of the variation in short term pulmonary function and it is likely that this relationship also applies when patients are in a stable phase.

It has been suggested that clinically significant desaturation does not occur in cystic fibrosis patients with predicted FEV1 >65%.3 In our study significant desaturation occurred in three patients (12% of the total who desaturated) with predicted FEV1 >65%. It is probably not possible to identify a value of FEV1 above which desaturation will not occur in a cystic fibrosis population. Correlation between mean SpO2 and % FEV1 for the group as a whole was modest, as found by previous authors,17 but in the 11 patients with more than five treatments stronger individual correlations were found. All 11 patients desaturated at a similar rate relative to % FEV1 (fig 3) with a pooled slope of 0.116 — that is, for each 10% decrease in % FEV1 mean SpO2 decreased 1.16%. However, the value of % FEV1 at which desaturation first occurred varied widely between patients.

Spirometric parameters do not predict nocturnal desaturation during pulmonary exacerbations in a cystic fibrosis population, and desaturation must initially be specifically sought with overnight oximetry. However, since individual patients desaturate predictably in relation to FEV1, the FEV1 at which desaturation first occurs can subsequently serve as a marker of the presence of desaturation in that individual, reducing the need for subsequent overnight recordings during exacerbations. In the outpatient setting FEV1 can then guide whether pulmonary exacerbations are treated at home or in hospital where nocturnal desaturation would be more easily corrected, and FEV1 can also guide the timing of assessment of suitability for continuous home overnight oxygen.

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