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 (Spo_2) lack uniformity. The relationship between Spo_2 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 Spo_2, forced expiratory volume in one second (FEV_1), 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 Spo_2 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 Spo_2 <90% and mean overnight Spo_2. Mean Spo_2 correlated moderately with percentage predicted FEV_1 (% FEV_1), $r = 0{\cdot}6$, and poorly with percentage predicted FVC (% FVC), $r = 0{\cdot}34$. The relationship between mean Spo_2 and % FEV_1 was non-linear at mean Spo_2 <89%, but approximated to linearity above this value. After exclusion of treatments with mean Spo_2 <89% the regression relationship between mean Spo_2 and % FEV_1 was the same on admission and discharge. Individual correlation coefficients of mean Spo_2 versus % FEV_1 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 Spo_2 can be substituted for percentage of recording <90%. The relationship between mean Spo_2 and percentage predicted FEV_1 is non-linear at low values of Spo_2 and is not influenced by treatment of pulmonary exacerbations. Patients with cystic fibrosis desaturate at a uniform rate compared with percentage predicted FEV_1, but the value of FEV_1 at which desaturation first occurs varies between patients. The spirometric values do not accurately predict nocturnal desaturation in a cystic fibrosis population, but FEV_1 is a useful guide in individual patients with moderate desaturation.**

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Keywords: cystic fibrosis, nocturnal oxygen desaturation, spirometry.

Adult Cystic Fibrosis Centre, Seacroft Hospital, York Road, Leeds LS14 6UH, UK
M N Pond
S P Conway

Reprint requests to:
Dr S P Conway.

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The value of oxygen therapy in cystic fibrosis is uncertain. In acute pulmonary exacerbations the mainstays 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[1–6] and is likely to precede daytime hypoxaemia.[4 6 7] The mechanism is probably a combination of hypoventilation and reduced functional residual capacity.[3 8] Pulmonary artery pressure (PAP) is inversely correlated with Spo_2 in cystic fibrosis, and decreases with supplemental oxygen.[1 9] The development of pulmonary hypertension might be delayed by correction of nocturnal hypoxaemia.

A variety of descriptive statistics has been used for nocturnal Spo_2 in cystic fibrosis – for example, 10% of an overnight recording with Spo_2 <90% is usually taken to represent significant desaturation.[4–6 10] The first aim of our study was to determine whether simple mean Spo_2 or lowest recorded Spo_2 could substitute for time spent with Spo_2 <90%. It is unclear from previous work whether nocturnal desaturation can be predicted by FEV_1.[5 7 11] 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 Spo_2 recording on the night of admission and on the night prior to discharge. The second recording was performed only after the decision to discharge had been taken. The decision to treat with intravenous antibiotics was made on the basis of an increase in respiratory symptoms and/or a decline in FEV_1 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)

	Admission	*Discharge*	*ANOVA (admission v discharge)*
Mean (SD) % predicted FEV_1	49·9 (21·0)	62·4 (24·0)	p<0·0001
Mean (SD) % predicted FVC	76·8 (22·6)	95·7 (23·9)	p<0·0001
Mean (SD) mean Spo_2 (%)	91·86 (3.59)	93·77 (2·46)	p<0·0001
Mean (SD) lowest Spo_2 (%)	83·17 (7·67)	85·71 (5·62)	p=0·005
Median (IQ range) percentage recording with Spo_2 <90%	3 (0–20·5)	0 (0–2·5)	p<0·0001
Median (IQ range) recording duration (hours)	7·37 (6·7–7·9)	7·54 (6·7–7·9)	p=NS

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 Spo_2 recording was below 90%.

Spo_2 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.[12] The presence of finger clubbing does not affect pulse oximetry results.[13] Spo_2 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 Spo_2, lowest Spo_2, duration of record, and time spent with Spo_2 <90%.

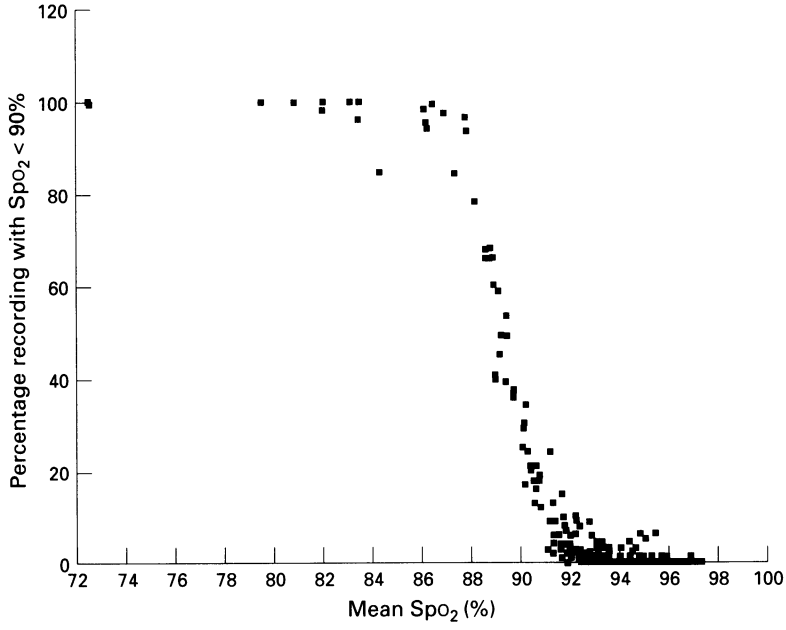

Figure 1 Percentage recording with Spo_2 <90% versus mean in all recordings (n=240).

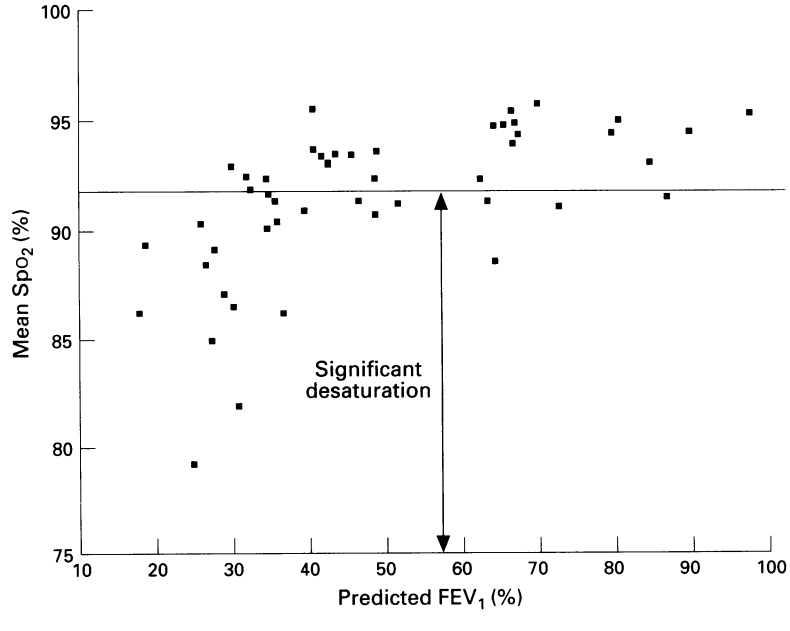

Figure 2 Mean Spo_2 versus percentage predicted FEV_1. Each point represents mean of admission values in individual patients (n=47). Significant desaturation=mean Spo_2 <92%.

On the day of admission and the day of discharge FEV_1 and FVC were recorded using one Vitalograph Compact spirometer. Patients were asked to repeat forced manoeuvres until the highest two readings differed by no more than 5%. FEV_1 and FVC obtained from the expiratory effort with the greatest FEV_1 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.

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

Patient no.	*n*	*Mean % predicted FEV_1*	*Mean % predicted FVC*	*Mean (mean Spo_2)*	*Correlation coefficient*
1	14	70·2	106·4	92·52	0·61
2	10	33·4	73·8	90·43	0·65
3	10	40·0	56·8	92·93	0·64
4	10	42·4	63·7	92·85	0·63
5	12	54·1	73·2	92·35	0·77
6	10	95·6	14·5	95·36	0·73
7	10	86·7	116·9	95·77	0·68
8	12	40·9	94·9	90·58	0·77
9	12	36·2	82·4	93·20	0·57
10	18	44·9	85·9	92·30	0·72
11	10	65·7	93·1	94·25	0·69

are shown in table 1. As expected, significant improvements were seen in all the measured parameters.

The percentage of recording time with Spo_2 <90% is plotted against the mean Spo_2 in fig 1 for admission and discharge values from all exacerbations. Between the limits of 0% and 100% the percentage of recording <90% decreases linearly with increasing mean Spo_2. There was a much weaker relation between the percentage of recording <90% and lowest recorded Spo_2. Significant hypoxaemia is usually considered to occur when Spo_2 is <90% for more than 10% of the recording. Mean Spo_2 of 92% is 98% sensitive and 74% specific in predicting this value, with positive and negative predictive values of 74% and 99·5%, respectively. The percentage of recording time with Spo_2 <90% can therefore be substituted by the much simpler mean Spo_2, with values of mean Spo_2 <92% representing significant hypoxaemia.

Mean Spo_2 is plotted against % FEV_1 on admission in fig 2. The discharge scatterplot was similar, with the points shifted to the right (after improvement with treatment). There was a better correlation between mean Spo_2 and % FEV_1 ($r=0·59$ on admission, 0·52 on discharge) than between mean Spo_2 and % FVC ($r=0·38$ on admission, 0·35 on discharge).

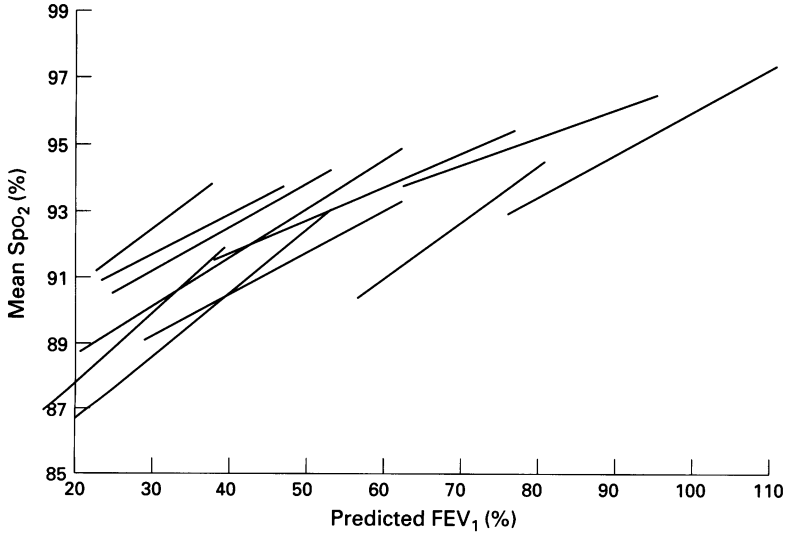

Figure 3 Regression of mean Spo_2 on percentage predicted FEV_1. Each regression line represents one of 11 individual patients with five or more exacerbations. Admission and discharge values are included, yielding a minimum of 10 observations per patient. General linear model for difference between slopes = NS, for difference between intercepts p<0·005. Pooled slope of mean Spo_2 on percentage predicted FEV_1 = 0·116.

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):

mean Spo_2 (admission) = 90·3 + 0·0471 % FEV_1 (admission) (p<0·0001)

mean Spo_2 (discharge) = 91·6 + 0·0377 % FEV_1 (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.[8] 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.[4-6 10] This corresponds to a mean Spo_2 of 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[4] 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 Spo_2, but for both the admission and discharge cases exclusion of patients with admission mean Spo_2 <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 Spo_2 and FEV_1 might be different on admission and discharge as the various therapeutic interventions employed in treating pulmonary exacerbations might have differential effects on FEV_1 and nocturnal Spo_2, 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 Spo_2 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 Spo_2 and FEV_1 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 FEV_1 >65%.[5] In our study significant desaturation occurred in three patients (12% of the total who desaturated) with predicted FEV_1 >65%. It is probably not possible to identify a value of FEV_1 above which desaturation will not occur in a cystic fibrosis population. Correlation between mean Spo_2 and % FEV_1 for the group as a whole was modest, as found by previous authors,[5 7 10 11] 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 % FEV_1 (fig 3) with a pooled slope of 0·116 – that is, for each 10% decrease in % FEV_1 mean Spo_2 decreased 1·16%. However, the value of % FEV_1 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 FEV_1, the FEV_1 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 FEV_1 can then guide whether pulmonary exacerbations are treated at home or in hospital where nocturnal desaturation would be more easily corrected, and FEV_1 can also guide the timing of assessment of suitability for continuous home overnight oxygen.

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