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Time course and recovery of arterial blood gases during exacerbations in adults with Cystic Fibrosis

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Abstract

Introduction: Hypoxia and hypercapnia are closely linked to morbidity and mortality in patients with Cystic Fibrosis (CF). The aims of this study were to describe the changes in blood gases during and following an acute pulmonary exacerbation in adults with CF.
Methods: We performed a prospective observational study of patients with CF admitted for management of an acute exacerbation. Blood gas and spirometric analysis was performed on admission, throughout the treatment period, and 31 days after discharge (day 45).
Results: At presentation, eight of nineteen patients had evidence of either hypoxia ($PaO_2 < 8$ kPa) and/or hypercapnia ($PaCO_2 > 6.6$ kPa). Blood gas parameters stabilized following two weeks of intravenous antibiotic therapy, with little difference evident in between treatment completion and subsequent review following discharge. Hypercapnia reversed in three patients, with persistent hypercapnia evident in two patients.
Conclusion: In our study group, hypoxemia and hypercapnia were frequently observed at presentation of the acute exacerbation. Blood gases stabilized following two weeks of intravenous antibiotic therapy, with arterial PCO_2 one month following hospital discharge generally similar to that at time of discharge.

Keywords: Arterial blood gas; Cystic Fibrosis; Hypercapnia; Hypoxia; Pulmonary exacerbation

1. Introduction

Survival of patients with Cystic Fibrosis (CF) has greatly improved over the past three decades [1] due to the aggressive treatment of pulmonary disease [2], the close monitoring of nutritional status[3,4] and the development of specialized CF centers [5]. However, despite these advances, the majority of morbidity and mortality in patients with CF remains related to pulmonary disease, with pulmonary failure accounting for 85% of deaths amongst the CF population [6,7]. Death in patients with CF is preceded by progressive deterioration in pulmonary function and gas exchange, with acute pulmonary exacerbations closely linked to morbidity and mortality.

Predictors of death in patients with CF include pulmonary hypertension related to chronic hypoxemia, hypoxemia on admission for pulmonary exacerbations, and chronic hypercarbia [8–10]. However, despite the central importance of both hypoxia and hypercapnia in patient outcome, there is very little detailed information available concerning hypoxia and hypercapnia during acute pulmonary exacerbations. We performed a prospective observational study to detail the pattern of ABG changes during acute exacerbations, to investigate the ABG changes following two weeks of intravenous antibiotic therapy, and finally, to assess ABG characteristics following resolution of the exacerbation, during a period of clinical stability.

2. Methods

We performed a prospective observational study of consecutive patients admitted to hospital for management of an acute pulmonary exacerbation of CF. Upon admission (day 1), each patient underwent clinical assessment, spirometry and

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blood gas analysis. Measurements were repeated 7, 14, and 45 days after admission. Following management of the acute pulmonary exacerbation, all patients reported major improvement in symptoms and, in all cases, the treating physician concluded that the acute exacerbation had resolved at the end of the 14 day treatment period. Notably, the data collected in this study did not influence treatment, or duration of treatment, of the acute exacerbation.

Patients were recruited from the inpatient department of the National Referral Centre for Adult Cystic Fibrosis at St. Vincent's University Hospital, Dublin. A diagnosis of CF was confirmed based on appropriate clinical features, abnormal sweat test (sweat $Cl^- > 70$ mmol/L) and/or genotyping [11]. Consecutive patients, with a confirmed diagnosis of CF, hospitalized for management of an acute pulmonary exacerbation, were recruited.

An acute exacerbation was diagnosed according to the criteria published by the 1994 Cystic Fibrosis Foundation Microbiology and Infectious Disease Consensus Conference [12] as the presence of three or more of the following new findings compared to the most recent visit: increased cough; increased sputum volume, thickness or increased darkness of sputum; increased dypsnoea, decreased exercise tolerance or both; weight loss ≥ 1 kg or 5% of bodyweight associated with anorexia; fatigue; temperature greater than 38 °C for at least 4 h in a 24 h period; 10% decrease in spirometry from best value achieved over the previous three months; new infiltrate on chest radiograph; school or work absenteeism due to illness in the past week. Patients had been unwell for no longer than 3–5 days prior to enrollment in the study.

Informed written consent was obtained from each participant prior to enrollment and the study was approved by the Ethics Committee of St. Vincent's University Hospital.

Upon diagnosis of an acute pulmonary exacerbation, and prior to commencement of intravenous antibiotic therapy, each patient had an ABG sample taken from their radial artery while in a supine position using a 25 gauge needle after a minimum of 30 min rest breathing room air. Topical anesthetic was offered to each patient prior to the ABG being performed to minimize discomfort. Upon drawing 2 ml of arterial blood, the sample was immediately analyzed for determination of PaO_2, $PaCO_2$ and pH. Standard electrode techniques (ABL 520 Radiometer, Copenhagen, Denmark) were used.

Subsequently, each patient received the standard of care for management of an acute pulmonary exacerbation, consisting of two weeks of a minimum of two intravenous antibiotics chosen according to the sensitivity of the bacteria isolated from previous sputum sample [13], nebulised antibiotics, bronchodilators as well as daily physiotherapy and nutritional support [14].

Further ABGs were taken throughout the treatment period on day 7, day 14 and one month after completion of the inpatient course during a period of clinical stability (day 45). Clinical stability was defined as no change in medication dosage or frequency and no exacerbations of disease or hospital admission in the preceding four weeks. ABGs were obtained at the same time of day on each occasion to control for circadian variations.

For interpretation of the ABG results, hypercapnia was defined as $PaCO_2$ greater than 6.6 kPa (50 mmHg) [15,16]. Hypoxemia was defined as PaO_2 less than 8 kPa (60 mmHg) [17].

Forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were assessed according to the American Thoracic Guidelines [18] using a spirometer (Vitalograph Compact II, Fannin, Ireland). Spirometry was performed with the patient in a seated position. Calibration of the spirometer was performed prior to each examination to ensure accuracy of reading.

Finally, C-reactive protein (CRP) was measured on days 1, 7, 14 and 45 using standard techniques.

3. Statistical analysis

All data was recorded on Microsoft Excel spreadsheets while statistical analysis was performed using a computerized statistical package (SPSS version 11, SPSS Inc 1989–2001, Chicago, Illinois, USA). The data is presented as median and range unless otherwise stated. The Mann Whitney *U* test was used to compare variables for evidence of statistically significant differences between the groups. A relationship was considered statistically significant if $p < 0.05$.

4. Results

Of the 42 patients initially approached to take part, 23 did not complete the study. The reasons for noncompletion of the study were declining further ABGs ($n = 21$) and self discharge from hospital prior to completion of study protocol ($n = 2$). This left a cohort of 19 patients which forms our study group (12 males (63%) and 7 females (37%)).

Median age for the study cohort was 24 years (range 19–45 years). The median baseline FEV_1, defined as the best FEV_1

Table 1
Median values for the study population throughout the study period

Variable	All patients initially enrolled ($n = 42$)	Study group ($n = 19$)			
	Day 1	Day 1	Day 7	Day 14	Day 45
FEV_1 (L)	0.91(0.5–3.3)	0.84(0.5–3.25)	0.88(0.53–3.66)	0.96(0.65–3.45)	1.08(0.71–3.76)
FEV_1 % predicted	25(16–78)	23(16–73)	26(16–83)	30(17–78)	32(20–81)
Blood pH	7.42(7.31–7.52)	7.43(7.32–7.52)	7.42(7.33–7.45)	7.42(7.30–7.47)	7.42(7.37–7.46)
PaO_2 (kPa)	8.9(6.7–12.2)	8.6(6.7–12.2)	9.2(5.9–12.7)	9.4(6.5–12.4)	10.6(7.2–12.2)
$PaCO_2$ (kPa)	5.5(4.5–8.4)	5.8(4.5–8.4)	5.9(4.75–9.21)	5.6(4.26–7.23)	5.3(4.80–7.12)
CRP	46(4–277)	44(4–277)	22(4–335)	11(4–49)	6(4–26)

Values presented as median (range).