

Reversible hypercapnia in acute exacerbations of chronic obstructive pulmonary disease (COPD)

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Reversible hypercapnia in acute exacerbations of chronic obstructive pulmonary disease (COPD). E. McNally, M. Fitzpatrick, S. Bourke, R. Costello, W.T. McNicholas. ©ERS Journals Ltd 1993.

ABSTRACT: We prospectively studied emergency hospitalizations due to acute exacerbations of chronic obstructive pulmonary disease (COPD) among 74 hypercapnic patients, in order to determine factors which predict reversal to normocapnia as a result of therapy.

Clinical, arterial blood gas and pulmonary function data on presentation were compared to predischarge values among those 58 patients who survived the admission. Patients were divided into those who reverted to normocapnia (reversible, 40% of surviving patients), and those who remained hypercapnic (chronic, 60% of surviving patients).

Reversible patients had higher admission arterial oxygen tension (P_{aO_2}) levels than those with chronic hypercapnia (6.4 ± 1.3 kPa (mean \pm SD), as compared to 5.7 ± 1.1 kPa) better pulmonary function (forced expiratory volume in one second (FEV₁) $35 \pm 16\%$ predicted, as compared to 26 ± 7.9), and a lower prevalence of cor pulmonale (30% as compared to 63% of patients).

No admission variable(s) distinguished individual patients as reversible or chronic hypercapnic, and, in particular, admission arterial carbon dioxide tension (P_{aCO_2}) and pH levels were similar in both groups. Furthermore, there were no differences between survivors and those 16 patients who died during the admission, apart from a higher urea level among those who died.

These findings suggest that reversible patients have milder underlying disease than those with chronic hypercapnia. Our data establish the high prevalence of reversible hypercapnia among patients hospitalized with exacerbations of COPD, and, furthermore, indicate that patients who are normocapnic in the stable state can develop similar levels of hypercapnia during exacerbations as those with chronic hypercapnia.

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The prognosis of chronic obstructive pulmonary disease (COPD) patients with hypercapnic respiratory failure is reported to be worse than those with normocapnia [1, 2], and some clinicians adopt a pessimistic attitude to management of hypercapnic patients, particularly when conservative therapy of an acute exacerbation has failed [3, 4]. Clinical experience and several previous reports [3-7], however, have indicated that patients with an exacerbation of COPD are prone to develop increased levels of arterial carbon dioxide tension (P_{aCO_2}), particularly if already hypercapnic. Therefore, the level of P_{aCO_2} during the acute illness is unlikely to be an accurate reflection of the P_{aCO_2} in the stable state, and indicates that some patients who are hypercapnic during an acute exacerbation may revert to normocapnia on recovery. No previous report, however, has examined the incidence of reversible hypercapnia during acute exacerbations of COPD.

We prospectively studied a group of patients admitted to our unit from the emergency department with an acute exacerbation of COPD, all of whom were in hypercapnic respiratory failure at the time of admission. The principal study aims were to assess the prevalence of reversible hypercapnia, and to seek admission variables which might

predict reversibility of hypercapnia in this patient population. We compared admission clinical, blood gas and pulmonary function data with the same variables measured after recovery, immediately prior to discharge from hospital. A secondary study aim was to compare the above variables on presentation between survivors and nonsurvivors of the admission, but the study was not designed with the specific aim of assessing factors which might predict survival during an acute exacerbation.

Methods

Consecutive patients admitted to our respiratory unit from the Accident and Emergency Department over a one year period, with an acute exacerbation of COPD, who were hypoxaemic (arterial oxygen tension (P_{aO_2}) < 8 kPa) and hypercapnic ($P_{aCO_2} > 6$ kPa), were considered for inclusion in the study. Patients on sedative or hypnotic therapy were excluded, and COPD was defined by standard criteria [8]. All patients were either current or ex-smokers. None had evidence of significant reversibility ($> 15\%$) of airflow obstruction after four puffs (400 μ g) of a salbutamol inhaler, and none had any features of asthma, such as

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sputum or blood eosinophilia, or elevation in serum immunoglobulin E (IgE) levels. An acute exacerbation was defined as a recent increase in dyspnoea, cough and sputum production of sufficient severity to warrant hospital admission. Cor pulmonale was diagnosed in patients who had clinical signs of right heart failure and electrocardiographic (ECG) criteria of right atrial or ventricular hypertrophy.

Arterial blood gases taken while breathing room air and prior to the institution of oxygen therapy, peak expiratory flow rate (PEFR), a chest radiograph and ECG were obtained in each patient on arrival in the Emergency Department, in addition to basic haematological profile, urea and electrolyte levels. In-hospital treatment consisted of parenteral corticosteroids and aminophylline, in addition to nebulized beta-agonists and ipratropium bromide and broad spectrum antibiotic therapy. All patients were given controlled low-flow oxygen therapy, using either a 24 or 28% Ventimask, or nasal prongs at a flow rate of 2 l·min⁻¹. The dose of oxygen was adjusted to maintain the Pao₂ above 6.7 kPa where necessary, but the flow rate was adjusted to minimize the degree of carbon dioxide retention. Three patients who completed the study required assisted ventilation. Thus, all patients admitted to our unit during the 12 month period of study, and who were not on sedative or hypnotic medications, are included in the analysis.

Arterial blood gases were repeated after 2 h of supplemental oxygen therapy, and at regular intervals on oxygen during the hospital admission. Blood gases taken while breathing room air (at least 2 h after cessation of supplemental oxygen in patients on chronic oxygen therapy), and spirometry, were also obtained in each patient within 24 h of discharge. Spirometry was recorded in the seated position using a Vitalograph spirometer and Wright peak flow meter, and the best of three efforts is reported. Reversibility was assessed after inhalation of 400 µg salbutamol.

Statistical analysis was by paired t-testing for within group comparisons between admission and discharge. Tukey's multiple range testing for multiple comparisons was performed on comparisons between reversible and chronic groups. Chi-squared analysis was used to compare the prevalence of cor pulmonale between groups. A p value <0.05 was taken as significant.

Results

Fifty eight patients survived the admission, of whom 23 (40%) reverted to normocapnia by the time of discharge (reversible), whereas 35 (60%) remained hypercapnic (chronic). Details of the survivors are given in table 1. No differences were identified in the clinical presentation and precipitating cause of the acute exacerbation between reversible and chronic hypercapnic groups. Symptoms of cough, sputum production and dyspnoea were similar in the two groups, and 28% of the reversible patients had consolidation on chest radiograph (defined as a focal infiltrate which cleared after therapy) as compared to 31% of chronic patients. Treatment regimens employed and duration of hospital stay (mean 15 days) were similar in both groups. There were no differences in other variables, such as haemoglobin and electrolyte levels, between the reversible and chronic groups (table 1), and bicarbonate

levels were also similar (table 2). Reversible patients had a lower body mass index (p<0.02) than chronic patients. One patient, who had chronic hypercapnia, was on home oxygen therapy.

Reversible patients had significantly higher Pao₂ levels on admission than chronic, but Paco₂ and pH levels were not different (table 2). By discharge, Pao₂ levels in reversible patients remained higher than in chronic patients, and pH levels remained similar in the two groups. As would be expected from the study design, Paco₂ levels fell significantly in reversible patients between admission and discharge, but also fell significantly in chronic patients (p<0.05). Pao₂ levels rose significantly in both groups between admission and discharge (p<0.05 for both comparisons). Reversible patients showed a trend towards a greater rise in CO₂ with supplemental oxygen therapy than chronic hypercapnic patients (fig. 1).

Table 1. — Anthropometric, clinical and haematological details on admission among 58 survivors

	Reversible hypercapnia	Chronic hypercapnia	p
Age yrs	68 (8.6)	66 (5.2)	NS
Sex M/F	11/12	22/13	
BMI	21 (1.0)	24 (0.8)	<0.02
Smoking history:			
Current nonsmokers	9	13	
Pack years	49 (10.3)	62 (16.0)	NS
Pulse b·min ⁻¹	104 (16)	106 (13.3)	NS
Haemoglobin g·dl ⁻¹	14.7 (1.6)	14.2 (2.0)	NS
PCV l·l ⁻²	0.45 (0.05)	0.45 (0.05)	NS
WBC count 10 ⁹ ·l ⁻¹	11.3 (3.9)	11.7 (5.2)	NS
Serum K mmol·l ⁻¹	4.1 (0.9)	4.2 (0.8)	NS
Serum Na mmol·l ⁻¹	136 (6.4)	138 (4.3)	NS
Urea mmol·l ⁻¹	7.8 (4.3)	6.8 (2.3)	NS

Data are presented as mean and (sd) in parenthesis. BMI: body mass index; PCV: packed cell volume; WBC: white blood cell; NS: not significant.

Table 2. — Blood gases and pulmonary function data among survivors

	Reversible hypercapnia	Chronic hypercapnia	p
Admission			
pH	7.34 (0.06)	7.36 (0.06)	NS
Pao ₂ kPa	6.4 (1.3)	5.7 (1.1)	<0.05
Paco ₂ kPa	7.7 (1.3)	8 (1.2)	NS
Bicarbonate mmol·l ⁻¹	33 (3.6)	35 (3.6)	NS
PEFR % pred	36 (16.6)	35 (11.7)	NS
Discharge			
pH	7.43 (0.10)	7.40 (0.5)	NS
Pao ₂ kPa	8.4 (1.1)	7.2 (1.3)	<0.05
Paco ₂ kPa	5.5 (0.4)	6.9 (0.6)	<0.05
Bicarbonate mmol·l ⁻¹	31 (3.8)	34 (3.6)	NS
FEV ₁ % pred	35 (16)	26 (7.9)	<0.05
FVC % pred	54 (15.7)	48 (14.3)	NS
PEFR % pred	36 (17.5)	34 (13.8)	NS

Data are presented as mean and (sd) in parenthesis. Pao₂: arterial oxygen tension; Paco₂: arterial carbon dioxide tension; FEV₁: forced expiratory volume in one second; % pred: percentage of predicted normal value; FVC: forced vital capacity; PEFR: peak expiratory flow rate; NS: not significant.

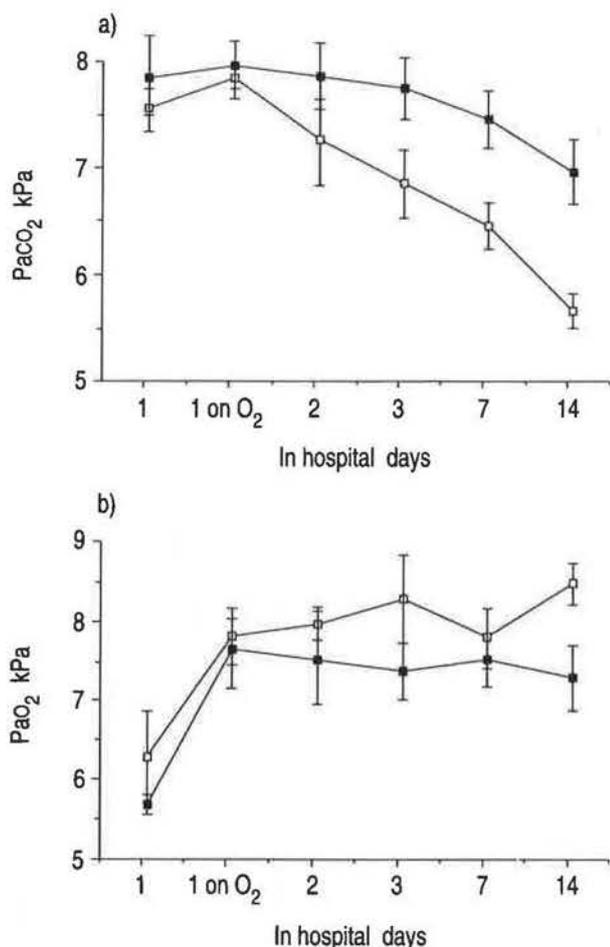


Fig. 1. — Course of arterial blood gases during hospitalization. a) PaCO₂; b) PaO₂. Values are presented as mean ± SD. Initial values represent room air blood gases taken in the Emergency Department, and are followed by those taken after 2 h of supplemental oxygen. Final values are those taken prior to discharge on room air. Reversible patients show a trend ($p < 0.1$) towards increased CO₂ retention following supplemental oxygen. —□—: reversible hypercapnic respiratory failure; —■—: chronic hypercapnic respiratory failure. PaCO₂: arterial carbon dioxide tension; PaO₂: arterial oxygen tension.

The degree of chronic airflow obstruction, as assessed by the pre-discharge forced expiratory volume in one second (FEV₁), was less in reversible than in chronic patients (table 2), and there was no significant change in PEF_R between admission and discharge, which underlines the largely irreversible nature of the chronic airflow obstruction in these patients. Furthermore, no patient showed significant (>15%) improvement in either FEV₁ or forced vital capacity (FVC) after 400 µg inhaled salbutamol. Cor pulmonale was much more prevalent in chronic (22 of 35 patients) than in reversible patients (7 of 23 patients) ($p = 0.02$). Combined analysis of admission pH and PaCO₂ did not help to distinguish reversible from chronic patients (fig. 2).

Comparison of admission characteristics among patients who died during the course of the hospital admission with those among survivors are given in table 3. There were no significant differences among these two groups, apart from a higher urea level among those patients who died ($p < 0.05$).

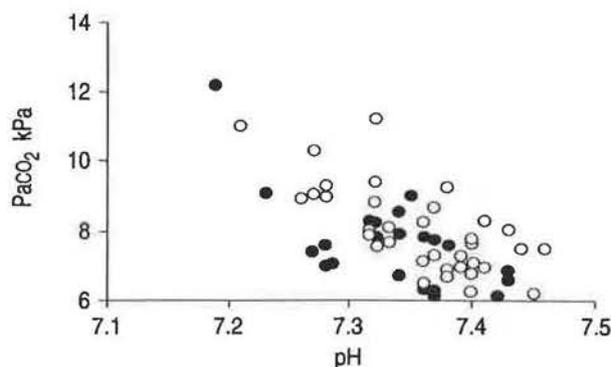


Fig. 2. — Graphic plot of admission pH against PaO₂ levels in reversible patients (closed circles) and chronic patients (open circles). See text for details. PaCO₂: arterial carbon dioxide tension.

Table 3. — Anthropometric, clinical and laboratory details on admission among total survivors and nonsurvivors

	Survivors	Nonsurvivors	Significance
Patients n	58	16	
Age yrs	67 (6.9)	66 (6.2)	NS
Smoking history pack years	54 (16)	51 (12)	
Pulse beats·min ⁻¹	106 (16)	104 (24)	NS
Haemoglobin g·dl ⁻²	14.4 (1.9)	14.1 (1.1)	NS
WBC count 10 ⁹ ·l ⁻¹	11.3 (4.0)	12.3 (5.4)	NS
Serum urea mmol·l ⁻¹	7.2 (3.5)	8.9 (3.8)	<0.05
Serum K mmol·l ⁻¹	4.2 (0.9)	4.0 (0.9)	NS
Serum Na mmol·l ⁻¹	137 (5.1)	135 (6)	NS
pH	7.34 (0.06)	7.36 (0.06)	NS
PaO ₂ kPa	6.0 (1.5)	5.4 (2.0)	NS
PaCO ₂ kPa	7.7 (1.4)	7.8 (1.3)	NS
Bicarbonate mmol·l ⁻¹	34 (4.2)	34 (5.2)	NS

Data are presented as mean and (SD) in parenthesis. For abbreviations see legends to tables 1 and 2.

Discussion

The principal finding of this study is that a substantial proportion of patients admitted with an exacerbation of COPD who are in hypercapnic respiratory failure will revert to normocapnia on recovery. Whilst this finding is not new, no previous study has examined the incidence of this phenomenon, or sought factors which might predict a reversibility of hypercapnia among such patients. Furthermore, reversible patients had similar PaCO₂ levels on admission to chronic patients. Thus, the finding of hypercapnia on admission should not be regarded as an indication of chronic hypercapnia in such patients, and the degree of hypercapnia on admission does not appear to help in the prediction of chronic hypercapnia.

This observation has particular clinical relevance in view of previous reports citing chronic hypercapnia as one of a number of poor prognostic indices in patients with COPD [2, 9]. We were unable to detect a single clinical or laboratory variable, nor indeed any group of variables, which would predict reversible from chronic hypercapnia at the time of admission. However, the finding that chronic patients also demonstrated a significant fall in PaCO₂ with recovery from the acute episode indicates that there are no fundamental differences between reversible and chronic hypercapnic patients.

Based on the better predischarge pulmonary function and lower incidence of cor pulmonale in reversible as opposed to chronic patients, we postulate that the reversible group represents a less severe end of the spectrum of COPD than the chronic group, and also that the long-term prognosis of reversible patients may be better than that of chronic hypercapnic patients. The latter possibility is supported by previous studies, which have indicated that poor pulmonary function and the presence of cor pulmonale correlate with a poor long-term survival [1, 2, 10]. A poor correlation of admission blood gases with survival has also been reported by JEFFREY *et al.* [11]. Long-term follow-up will be required to determine whether the survival of reversible patients in the present study is indeed better than chronically hypercapnic patients, and also to determine whether reversible patients become chronically hypercapnic at a later stage of their disease.

Hypercapnia with coexisting acidosis, variables which have traditionally been used to distinguish patients with an acute respiratory acidosis [6], were unreliable predictors of which patients would revert to normocapnia in the present study (fig. 2), in that many patients with reversible hypercapnia had a normal pH on admission. These criteria will, therefore, exclude many patients with reversible hypercapnia, whose acute respiratory acidosis may be masked by a concomitant metabolic alkalosis, as might occur in patients on regular diuretic therapy.

The absence of cor pulmonale proved a reasonable predictor of reversible hypercapnia, however, as only 30% of reversible patients had cor pulmonale compared to 63% of chronic hypercapnic patients. This finding is not surprising, given the better pulmonary function and higher predischarge P_{aO_2} levels in the reversible group. The higher prevalence of cor pulmonale in chronic hypercapnic patients is also the probable explanation for that group's higher body mass index (table 1), because of the tendency to fluid retention associated with cor pulmonale.

Acidosis has previously been reported as an indicator of poor short-term survival in exacerbations of COPD [4, 6, 7, 11]. MUIR and LEVI-VALENSI [4] noted that pH correlates better with prognosis than P_{aO_2} , with mortality increasing greatly when the pH falls below 7.32. Many of these studies however refer to worsening acidosis during the course of in-hospital therapy, and there is disagreement in the literature on the value of admission pH as a predictor of survival. The recent report of JEFFREY *et al.* [11] found that survivors of an acute exacerbation of COPD were significantly less acidotic on admission than nonsurvivors, whereas WARREN *et al.* [7] found no such difference. Our data show no significant differences between survivors and nonsurvivors in admission characteristics, apart from a higher urea level among those who died. However, the number of patients who died was small in the present study, and the study was not specifically designed to assess factors which predict survival in an acute exacerbation of COPD.

One problem in comparing previously reported literature in this field is that no two groups have used the same inclusion criteria, even when these have been based on arterial blood gas tensions. SLUITER *et al.* [3] defined respiratory insufficiency as a $P_{aO_2} < 55$ mmHg (7.3 kPa) and $P_{aCO_2} > 55$ mmHg (7.3 kPa), whereas WARREN *et al.* [7]

used $P_{aO_2} < 50$ mmHg (6.7 kPa) and $P_{aCO_2} > 50$ mmHg (6.7 kPa). Our criteria for respiratory failure were less stringent ($P_{aO_2} < 8$ kPa and $P_{aCO_2} > 6$ kPa), but were purposely so, in an effort to include patients at the "pink and puffing" end of the COPD spectrum. We feel that these inclusion criteria have allowed the observation that patients from both the "pink and puffing" and "blue and bloated" ends of the spectrum of COPD can develop similar degrees of hypercapnia and acidosis during an acute exacerbation.

An intriguing finding of the present study was that reversible patients appeared likely to retain more CO_2 with supplemental oxygen than chronic patients, although the differences did not quite reach statistical significance. This finding, if confirmed in a larger number of patients, may have important clinical implications for oxygen therapy to patients in hypercapnic respiratory failure during acute exacerbations of COPD, and would make a knowledge of the patients' previous stable P_{aCO_2} levels of practical clinical benefit.

We conclude from our findings that acute hypercapnia is common during severe exacerbations of COPD, and that reversible hypercapnia cannot be distinguished from chronic hypercapnia in such patients. Indeed, the data suggest that patients who are normocapnic in the stable state can develop similar degrees of hypercapnia during acute exacerbations to patients with chronic hypercapnia. These findings indicate that all COPD patients who are hypercapnic during an acute exacerbation should be regarded as having potentially reversible hypercapnia, unless chronic hypercapnia has previously been documented.

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