Spirometry and arterial blood gases in acute severe asthma

Peer review status:
No

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Article ID: WMC004600
Article Type: Research articles
Submitted on: 07-Apr-2014, 08:52:48 AM GMT Published on: 07-Apr-2014, 09:00:11 AM GMT
Article URL: http://www.webmedcentral.com/article_view/4600
Subject Categories: PULMONARY MEDICINE
Keywords: Acid base balance, Airway obstruction, Asthma, Lactic acidosis, Metabolic acidosis, spirometry

How to cite the article: Raimondi GA, Gonzalez S, Zaltsman J, Menga G. Spirometry and arterial blood gases in acute severe asthma. WebmedCentral PULMONARY MEDICINE 2014;5(4):WMC004600

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Source(s) of Funding:
None.

Competing Interests:
The authors declare no conflicts of interest.
Spirometry and arterial blood gases in acute severe asthma

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Abstract

Background: We studied in a group of patients admitted for acute severe asthma (ASA) arterial blood gases at admission and it relationship with airway obstruction. We also compared arterial gases of a subgroup of patients unable to perform spirometry because their poor clinical status with those able to complete the test. Methods. Data from arterial gases and spirometry were obtained from two previously published series of patients admitted for ASA to a State Hospital (Hospital María Ferrer, Buenos Aires, Argentina). Blood was drawn for arterial gases on arrival to the Emergency Department (ED) in 314 asthma patients. PaO₂, PaCO₂ and pH were measured using standard electrodes. Measurements of serum electrolytes were made in 250 of the patients. Anion gap was calculated as Na⁺ - (Cl⁻ + HCO₃⁻). Acid-base disturbances at presentation were classified according to commonly accepted criteria. Forced expiratory volume (FEV₁) was measured on ED arrival and expressed as % of theoretical values (FEV₁%). Forty eight patients presented poor clinical condition based on physician evaluation and were unable to carry out spirometry. Correlation was analyzed between FEV₁% and arterial gases and different acid base variables on arrival. PaO₂, PaCO₂, pH and other acid base data were compared between patients completing spirometry vs. and those unable to do so (n = 266 vs. 48). Results. Significant correlation (p < 0.05) was observed between FEV₁% vs PaO₂ (r=0.21), FEV₁% vs PaCO₂ (r=-0.33), pH vs PaCO₂ (r=-0.86), PaCO₂ vs PaO₂ (r=-0.36), lactic acid vs anion gap (r=0.58), lactic acid vs base excess (r=-0.50) and anion gap vs Bic (r=0.38). Significant differences were found between PaCO₂, pH and base excess, when comparing patients who could perform spirometry vs. those who could not. No significant differences were found between bicarbonate, anion gap and lactic acid. Comparison of patients able or unable to perform spirometry indicated: respiratory alkalosis (either alone or as a part of a mixed disturbance) in 56.6 vs. 37.8% of cases (p<0.03), respiratory acidosis (either alone or as a part of a mixed disturbance) in 22.8 vs 67.5% (p<0.001) and metabolic acidosis (either alone or as a part of a mixed disturbance) in 41.6 vs 51.3% (NS).

Conclusions. Our findings confirm the existence of a weak correlation between gas exchange, acid base status and magnitude of airway obstruction. We also observed that patients in poor clinical conditions who were unable to perform spirometry tests also had more severe acid base imbalance.

Introduction

In acute asthma during moderate or severe bronchospasm, arterial blood gas levels generally show slight decrease in partial carbon dioxide pressure without significant abnormality of arterial oxygen saturation. During more severe attacks, normal or increasing PaCO₂ with mild hypoxemia has been described (1,2), with sicker patients sometimes presenting metabolic acidosis (3,4). Findings on the relationship between airway obstruction PaCO₂, PaO₂ and acid base disturbances in asthma have also been published (1,5-10).

The objective of this study was to analyze, in a group of patients hospitalized for acute asthma, arterial blood gas levels at admission together with degree of airway obstruction, and establish whether there was any relation between them. Also, in a subgroup of patients too weak to perform spirometry, arterial gases were compared to levels observed in patients able to complete the test. Some of the results of this study have been previously reported elsewhere (11).

Methods

Data collected from 314 patients (90 men and 224 women, 18 to 83 years-old) admitted for acute severe asthma was analyzed, based on raw data previously published elsewhere relating to outpatient management of acute asthma in Argentina (12,13). Time elapsed between symptom onset and hospital admission was over 72 hours in 63% of patients, between 24 and 72 hours in 23%, between 3 and 24 hours in 13% and less than 3 hours in 2% of study patients. All patients met diagnostic criteria for bronchial asthma (14). Prior to admission 98.4 % of patients had been prescribed inhaled beta agonist bronchodilators, 60.7%, inhaled corticosteroids, 11.8% aminophylline. and 7.0% systemic corticosteroids.
Informed consent was obtained from all patients after approval of the study protocol by the Institutional Review Board. Blood was drawn for arterial gases on arrival to the Emergency Department (ED) in a heparinized syringe from the radial or brachial artery. pH, PaCO₂, and PaO₂ were measured using standard electrodes (Radiometer ABL 520). Measurements of serum electrolytes were made in 250 of the patients. Plasma electrolytes and lactate were assayed with Radiometer EML 105 electrodes and anion gap calculated as Na⁺ - (Cl⁻ + HCO₃⁻). Acid-base disturbances at presentation were classified according to commonly accepted criteria (15-18). Forced expiratory volume (FEV₁) (Vitalograph Pneumotrac) was measured on ED arrival. At least three maneuvers were performed and the higher result considered. Predicted values were calculated from normal values previously published by Knudson et al (19). Forty eight patients presented poor clinical condition based on physician evaluation and were unable to carry out spirometry.

Correlation was analyzed between FEV₁ values and arterial gases and different acid base variables on arrival. FEV₁ was expressed as % of theoretical values (FEV₁%). PaO₂, PaCO₂, pH and other acid base data were compared between patients completing spirometry vs. and those unable to do so (n = 266 vs. 48).

All results are presented as mean values ± standard deviation. Continuous variable comparisons were carried out using a two-tailed Student test. For dichotomous variables, contingency tables were used and Fischer’s exact test or chi square statistic employed. Correlations were analyzed using Pearson’s correlation coefficient of linear regression analysis. Statistical significance was taken as p < 0.05.

Results

Mean values of FEV₁%, PaO₂, PaCO₂, bicarbonate, base excess, anion gap and lactic acid on arrival are shown in Table 1. Significant correlation was observed between FEV₁% vs PaO₂ (r=0.21), FEV₁% vs PaCO₂ (r=0.33), pH vs PaCO₂ (r=0.86), PaCO₂ vs PaO₂ (r=0.36), lactic acid vs anion gap (r=0.58), lactic acid vs base excess (r=0.50) and anion gap vs Bic (r=0.38). (see Figures 1 to 7)

Significant differences were found between PaCO₂, pH and base excess, when comparing patients who could perform spirometry vs. those who could not. No significant differences were found between bicarbonate, anion gap and lactic acid (Table 2).

Acid base disturbances for the entire study group are shown in Table 3 as well as comparison between patients who could vs. could not perform spirometry in Table 4.

Comparison of patients able or unable to perform spirometry indicated: respiratory alkalosis (either alone or as a part of a mixed disturbance) in 56.6 vs. 37.8% of cases (p<0.03), respiratory acidosis (either alone or as a part of a mixed disturbance) in 22.8 vs 67.5% (p<0.001) and metabolic acidosis (either alone or as a part of a mixed disturbance) in 41.6 vs 51.3% (NS).

Discussion

Gas exchange results in patients with acute asthma here described are in agreement with earlier publications by other authors. PaO₂ and PaCO₂ ranged from nearly normal values to slightly abnormal, or extremely altered values, resulting in hypoxemia with or without hypercapnia (1-10). Most of these studies were conducted in patients in whom degree of airway obstruction varied greatly (20). As a whole, we found similar PaO₂ values to those obtained by McFadden et al. for a similar degree of airway obstruction (1).

We have found a weak correlation between PaO₂ and airway obstruction, nor are correlation coefficients in the literature strong with one exception (1), generally ranging from 0.36 to 0.41 (5-10). Loose correlation between PaO₂ and FEV₁ in acute asthma is in keeping with lack of correlation for VA/Q mismatch found during acute attack, measured as dispersion of blood flow distribution and air flow rates (21). When measured at different stages of recovery, this relationship may vary. Statistically significant negative correlation between air flow rate and gas exchange develops 3 to 4 weeks after discharge (21). Good correlation between PaO₂ and V/Q mismatch has been described in chronic stable asthma (22). An extreme example of the dissociation between spirometry and gas exchange is the effect of β-agonists, which simultaneously reduce airways obstruction and worsen gas exchange (23,24). These discrepancies suggest spirometry alone is insufficient to fully characterize lung function in acute asthma and indicates the need to also consider gas exchange measurements (21).

It has been described that patients with acute severe asthma requiring admission to hospital (compared to patients discharged after ER treatment), have lower air flow rates, PaO₂ and greater V/Q mismatch measured as blood flow distribution dispersion. (25). It is clearly known that V/Q mismatch is the principal mechanism
leading to abnormal arterial blood gas values, and the primary factor modulating variations in arterial hypoxemia levels (21,25-27). The hypothesis is that during acute severe asthma, air flow rates are determined mostly by properties of large airways, whereas gas exchange, specifically V/Q mismatch abnormalities, depends on airway narrowing and/or inflammation predominantly secondary to structural changes in small distal airways. (21,25-27)

In most of our patients, arterial blood gases were drawn on ED arrival breathing room air. Many of the patients unable to perform spirometry because of worse clinical condition were breathing different inspired oxygen concentrations or receiving nebulised medication driven by oxygen. For this reason it was impossible to compare PaO₂ values between patients able or unable to perform spirometry.

As observed by other authors, we also found a relationship between PaCO₂ and airway obstruction (1,5,10), suggesting mechanical properties of the airway could explain, at least in part, carbon dioxide retention. This could also be associated with V/Q inequality, although it is likely that alveolar hypoventilation related to respiratory muscle fatigue and/or weakness also plays a key role (27). On the other hand, the correlation we observed between arterial PaO₂ and PaCO₂ (also found in an earlier study by Simpson) (28), could suggest that alveolar hypoventilation may play a role as a mechanism for hypoxemia in acute severe asthma.

Respiratory alkalosis was the most common acid base disturbance found in this series, occurring either alone or as part of a mixed disturbance, in 13.3 and 42% of the patients, respectively. In a study by Mountain, respiratory alkalosis was found in 47.6% of episodes (3) and in the McFadden series in 72.3% of patients (1). Respiratory acidosis in our series was found, either alone or as a part of a mixed disturbance, in 30.4% of the episodes compared to 26.2% in the Mountain series and 6.9% in McFadden’s (1,3). These differences in incidence of respiratory alkalosis and respiratory acidosis could be ascribed to the magnitude of airway obstruction, as hypocapnia is described in patients with mild airway obstruction and hypercapnia in patients with severe airway obstruction. When comparing patients who could perform spirometry to those who could not, the former had more cases of respiratory alkalosis and the latter more cases of respiratory acidosis. We have to emphasize, that aside from the established relationship between degree of airway obstruction and acid base status, patients unable to perform spirometry show worse acid base status.

We found metabolic acidosis, either simple or combined, in 36.8% of cases. In other series this value ranged between 28% and 37.9% (3,4). Although lactic acid was not measured, some authors have considered it as the reason for metabolic acidosis, assuming anion gap increase during acute asthma was the result of lactic acid production (3). We have found a positive and significant relationship between anion gap and lactic acid, confirming anion gap increases were caused by lactic acid. Roncoroni et al at our hospital has provided direct evidence that the metabolic acidosis observed in acute asthma is a lactic acidosis (4).

Patients with metabolic acidosis have been described as more hypoxemic and with evidence of greater airflow obstruction compared to those without metabolic acidosis (3). In our series metabolic acidosis, measured either as bicarbonate, anion gap or lactic acid, was not related to degree of airway obstruction or hypoxemia severity. We found both groups of patients, i.e. those with less severe clinical condition that could perform spirometry as well as those who could not, had similar prevalence of metabolic acidosis and no differences in anion gap or lactic acid levels. It has been hypothesized that the mechanism of lactic acidosis in acute asthma is related to acid production by respiratory muscles and/or tissue hypoxia (3). However, lactic acidemia associated with severe exacerbations of asthma may occur in the absence of respiratory muscle activity, as is the case of patients requiring assisted ventilation and pharmacologic muscle relaxation (29). Other possible mechanisms described in acute asthma that may increase lactic acid are related to stimulation of β-adrenergic receptors as a result of a previous hyperadrenergic state or use of β-agonist treatment. Previous studies have suggested administration of β-agonists can lead to lactic acidemia in the absence of hypoxia or shock. Epinephrine infusion has been associated with increase in plasma lactate concentrations both in animals and in humans (30,31), as has salbutamol infusion in rabbits (32). Several studies have also linked lactic acidosis to inhaled β-agonists in patients with acute asthma (29,33-35). Rodrigo and Rodrigo (36) found, in a prospective study in patients with acute asthma treated in the ED with high doses of inhaled salbutamol, that increased lactate was associated with respiratory function improvement. The authors concluded that high lactate concentrations can develop during the first hours of inhaled beta agonist treatment and that the presence of a prior hyperadrenergic state may predispose to the development of this condition (36). These studies would suggest that increase in lactate level is mainly...
due to large doses of inhaled β-agonists administered during ED treatment.

Current practice guidelines for the treatment of an acute asthma exacerbation, such as in the ED setting, recommend objective measures of pulmonary function using peak expiratory flow (PEF) or FEV₁. At our hospital, all patients treated in the ED for acute asthma first perform spirometry tests. One study confirms, with strong emphasis on several quality measures, that spirometry for the purpose of obtaining an FEV₁ can be performed in acutely ill ED asthmatics (33). In that study, mean FEV₁ on ED arrival was 38% of the predicted value (37). We studied a subgroup of patients with a mean FEV₁ of 26% of the predicted value requiring admission after treatment in the ED, some of whom had arrived presenting near fatal asthma. Eighteen patients required intubation and mechanical ventilation within hours of arrival to the ED. Today, most adult patients seen for severe asthma exacerbations in an ED, even when obstruction is very severe (< 25% predicted), can successfully be coached to obtain criteria-specific acceptable and reproducible spirometry maneuvers (37).

In summary, our findings confirm the existence of limited correlation between gas exchange, acid base status and magnitude of airway obstruction measured by spirometry in acute severe asthma. We also observed that patients in poor clinical conditions who were unable to perform spirometry tests also had more severe acid base imbalance.

Conflict of interests

The authors declare that they have no competing interests.

Authors Contributions

All authors read and approved the final paper. G.A. Raimondi contributed to the study conception and design and analysis and interpretation of the results and drafting the manuscript for important intellectual content and revision. S. Gonzalez contributed to the study conception and design and analysis and interpretation of the results and revision. J. Zaltsman contributed to the study analysis and interpretation of the Results and revision. G. Menga contributed to the study analysis and interpretation of the Results and revision.

References

37. Silverman, RA, Flaster, E, Enright, PL, Simonson SG. FEV1 performance among patients with acute asthma. Results from a multicenter clinical trial. Chest 2007;131,164-171
Illustrations

Illustration 1

Table 1: Study population characteristics

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEV₁ (%predicted)</strong></td>
<td>25.6 ± 10.0</td>
</tr>
<tr>
<td><strong>PaO₂ (mmHg) †</strong></td>
<td>66.1 ± 11.9</td>
</tr>
<tr>
<td><strong>PaCO₂ (mmHg)</strong></td>
<td>37.5 ± 12.5</td>
</tr>
<tr>
<td><strong>AaDO₂ (mmHg) †</strong></td>
<td>39.3 ± 12.3</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>7.42 ± 0.09</td>
</tr>
<tr>
<td><strong>Bic (mEq/L)</strong></td>
<td>23.4 ± 3.6</td>
</tr>
<tr>
<td><strong>BE (mEq/L)</strong></td>
<td>-0.4 ± 3.9</td>
</tr>
<tr>
<td><strong>AG (mEq/L)</strong></td>
<td>14.1 ± 3.2</td>
</tr>
<tr>
<td><strong>Lactic acid (mEq/L)</strong></td>
<td>3.0 ± 1.5</td>
</tr>
</tbody>
</table>

† PaO₂ values of patients breathing room air only are shown.

BE, base excess; Bic, bicarbonate; AG, anion gap (Na – Cl – bicarbonate)
Illustration 2

Table 2: Comparison between patients able vs. unable to perform spirometry

<table>
<thead>
<tr>
<th>Could perform spirometry</th>
<th>Could not perform spirometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 266</td>
<td>48</td>
</tr>
<tr>
<td>PaCO\textsubscript{2} (mmHg)</td>
<td>35.1±6.5 vs. 50.9 ± 24.3 p&lt;0.0001</td>
</tr>
<tr>
<td>pH</td>
<td>7.44 ± 0.04 vs. 7.31 ± 0.18 p&lt;0.0001</td>
</tr>
<tr>
<td>BE (mEq/L)</td>
<td>0.1 ± 3.1 vs. −3.2 ± 5.6 p&lt;0.0001</td>
</tr>
<tr>
<td>Bic (mEq/L)</td>
<td>23.4 ± 3.5 vs. 23.4 ± 4.2 NS</td>
</tr>
<tr>
<td>AG (mEq/L)</td>
<td>14.1 ± 3.2 vs. 13.9 ± 3.4 NS</td>
</tr>
<tr>
<td>LA (mEq/L)</td>
<td>2.9 ± 1.4 vs. 3.1 ± 2.0 NS</td>
</tr>
</tbody>
</table>

BE, base excess; Bic, bicarbonate; AG, anion gap (Na – Cl – bicarbonate); LA, lactic acid
Illustration 3

Table 3: Acid base status at presentation in all cases

<table>
<thead>
<tr>
<th>Condition</th>
<th>% of episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory alkalosis+metabolic acidosis with increased AG</td>
<td>18.4</td>
</tr>
<tr>
<td>Normal</td>
<td>17.1</td>
</tr>
<tr>
<td>Respiratory acidosis+respiratory alkalosis</td>
<td>12.9</td>
</tr>
<tr>
<td>Respiratory acidosis+metabolic acidosis with increased AG</td>
<td>12.0</td>
</tr>
<tr>
<td>Acute respiratory alkalosis</td>
<td>9.2</td>
</tr>
<tr>
<td>Metabolic alkalosis+metabolic acidosis with increased AG</td>
<td>6.5</td>
</tr>
<tr>
<td>Respiratory alkalosis+metabolic alkalosis+metabolic acidosis with increased AG</td>
<td>4.6</td>
</tr>
<tr>
<td>Mixed respiratory alkalosis</td>
<td>4.1</td>
</tr>
<tr>
<td>Chronic respiratory alkalosis</td>
<td>4.1</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>3.7</td>
</tr>
<tr>
<td>Acute respiratory acidosis</td>
<td>3.7</td>
</tr>
<tr>
<td>Chronic respiratory acidosis</td>
<td>1.8</td>
</tr>
<tr>
<td>Metabolic acidosis with normal AG</td>
<td>0.9</td>
</tr>
<tr>
<td>Metabolic acidosis with increased AG</td>
<td>0.9</td>
</tr>
</tbody>
</table>
Illustration 4

Table 4: Acid base status at presentation in patients who could vs couldn’t perform spirometry

<table>
<thead>
<tr>
<th>Acid Base Status</th>
<th>Could perform Spirometry</th>
<th>Could not perform spirometry</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory alkalosis + metabolic acidosis with increased AG</td>
<td>18.4</td>
<td>13.5</td>
<td>0.47</td>
</tr>
<tr>
<td>Normal</td>
<td>17.1</td>
<td>5.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Respiratory acidosis + respiratory alkalosis</td>
<td>12.9</td>
<td>16.2</td>
<td>0.58</td>
</tr>
<tr>
<td>Respiratory acidosis + metabolic acidosis with increased AG</td>
<td>12.0</td>
<td>27.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Acute respiratory alkalosis</td>
<td>9.2</td>
<td>2.7</td>
<td>0.17</td>
</tr>
<tr>
<td>Metabolic alkalosis + metabolic acidosis with increased AG</td>
<td>6.5</td>
<td>2.7</td>
<td>0.36</td>
</tr>
<tr>
<td>Respiratory alkalosis + metabolic alkalosis + metabolic acidosis with increased AG</td>
<td>4.6</td>
<td>5.5</td>
<td>0.83</td>
</tr>
<tr>
<td>Mixed respiratory alkalosis</td>
<td>4.1</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Chronic respiratory alkalosis</td>
<td>4.1</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>3.7</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Condition</td>
<td>p-value</td>
<td>r</td>
<td>AG</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------</td>
<td>---</td>
<td>-----</td>
</tr>
<tr>
<td>Chronic respiratory acidosis</td>
<td>1.8</td>
<td>2.7</td>
<td>0.71</td>
</tr>
<tr>
<td>Metabolic acidosis with normal AG</td>
<td>0.9</td>
<td>2.7</td>
<td>0.19</td>
</tr>
<tr>
<td>Metabolic acidosis with increased AG</td>
<td>0.9</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>
Illustration 5

Figure 1

Relationship between $P_{A}O_2$ values breathing room air in mmHg and FEV1 % of theoretical values ($r=0.21, p<0.002$)

Illustration 6

Figure 2

Fig. 2: Relationship between $P_{A}CO_2$ values in mmHg and FEV1 % of theoretical (values $r=-0.33$, $p<0.001$)
Illustration 7

Figure 3

Fig. 4: Relationship between pH and PaCO2 values in mmHg (r = -0.86, p < 0.001)

Illustration 8

Figure 4

Fig. 4: Relationship between pH and PaCO2 values in mmHg (r = -0.86, p < 0.001)
Illustration 9

Figure 5

![Relationship between anion gap and lactic acid values in mEq/L](image)

*Fig. 5: Relationship between anion gap and lactic acid values in mEq/L (r=0.58, p<0.001)*

Illustration 10

Figure 6

![Relationship between base excess and lactic acid values in mEq/L](image)

*Fig. 6: Relationship between base excess and lactic acid values in mEq/L (r=-0.50, p<0.001)*
Illustration 11

Figure 7

Fig. 7: Relationship between anion gap and bicarbonate acid values in mmol/L ($r=-0.38, p<0.001$)