Hemodynamic Effects of Oxygen Therapy in Patients With Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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The effects of oxygen therapy in patients with stable COPD have been previously reported; however, the hemodynamic changes induced by oxygen therapy in patients during acute exacerbations of COPD are less well known. To investigate the hemodynamic effects of controlled oxygen therapy in patients with acute exacerbations of COPD shortly after arriving at the hospital, we studied 15 consecutive patients who came to the emergency room with acutely decompensated COPD that did not require mechanical ventilation. Patients were monitored with a pulmonary artery catheter and a radial artery catheter. Oxygen uptake was calculated by the modified Fick equation. Arterial and venous blood gas levels and hemodynamic parameters were measured while breathing room air (baseline) and after 30 min on oxygen therapy via face mask. Measurements were repeated after 24 and 48 h. The fractional concentration of oxygen in the inspired gas (FiO2) administered was adjusted to keep the PaO2 above 55 mm Hg. All patients had a PaO2 below 45 mm Hg at the beginning of the study. After 30 min of oxygen therapy, there was a significant (p<0.05) increase in arterial oxygen saturation (from 62 ± 16 to 87 ± 9 percent), mixed-venous oxygen pressure (from 25 ± 5 to 43 ± 11 mm Hg), and oxygen delivery (from 11.1 ± 3.7 to 19.3 ± 5.9 ml/kg/min). Oxygen uptake did not change significantly (from 4.1 ± 1.2 to 4.3 ± 1.6 ml/kg/min). The oxygen extraction ratio decreased from 37.5 ± 10.1 to 25.3 ± 9.6 percent. These changes were maintained during the following 48 h. There were no significant changes in cardiac output and systemic vascular resistance. A trend toward lower values of pulmonary vascular resistance did not reach statistical significance. We conclude that oxygen therapy in patients with acute exacerbations of COPD that do not require mechanical ventilation increases oxygen delivery without changes in cardiac output or oxygen uptake.

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CaO2 = arterial oxygen content; Do2 = oxygen delivery; FIO2 = fractional concentration of oxygen in inspired gas; FO2 = mixed-venous oxygen pressure; SaO2 = arterial oxygen saturation; SVO2 = mixed-venous oxygen saturation; Vo2 = oxygen consumption

The effects of long-term oxygen therapy in patients with COPD are well known. A decrease in pulmonary hypertension accompanied by an improvement in the quality of life and survival rate of these patients has been reported previously; however, the changes in hemodynamic and oxygen transport variables induced by oxygen therapy in patients during acute exacerbations are less well understood.

The reported hemodynamic effects of oxygen therapy during acute exacerbations differ among investigators. Abraham et al found no change in cardiac output. Degau et al8 studied 35 patients with acute exacerbations of COPD during the first day of admission after withdrawal of oxygen therapy. These investigators found that reintroduction of oxygen therapy caused a drop in the cardiac output and an increase in oxygen delivery (Do2) due to an improvement in arterial oxygen saturation (SaO2). Pulmonary artery pressure did not change. Lejeune et al, in a series of 17 patients with acute exacerbations of COPD studied during the first 3 days of hospitalization, observed a decrease in cardiac output induced by oxygen therapy, whereas pulmonary vascular resistance did not change.

All of those studies were done in patients during the first few days of hospitalization, and hemodynamic changes were investigated after withdrawal of oxygen therapy. We designed our study to investigate the effects of controlled oxygen therapy on hemodynamic parameters in patients with acute exacerbations of COPD shortly after arriving at the emergency department, before receiving oxygen therapy.

MATERIALS AND METHODS

We studied 15 consecutive patients (10 male patients; mean age, 62 ± 7 years) admitted to the emergency department with acutely decompensated COPD, due to acute bronchitis. The diagnosis of COPD was based on the patient's history, physical examination, chest x-ray film, arterial blood gas levels, and ECG. A history of daily expectoration during at least 3 months of the year during at least 2 consecutive years was required for the diagnosis of COPD. Eleven patients provided the results of previous pulmonary function tests showing airway obstruction (ratio of forced expiratory volume in 1 s over forced vital capacity <60 percent of the predicted value). The chest x-ray film obtained on admission showed no infiltrates, cardiomegaly, or significant pleural effusions. Four patients were febrile (peripheral temperature above 38.0°C) and became afebrile within the first 36 h in the ICU. The initial white blood cell count was 12,245/mm³ ± 782/mm³. The general condition of all patients improved while in the ICU, allowing discharge after a mean stay of 5.8 ± 0.5 days.

Hemodynamic parameters, SaO2, and mixed-venous oxygen sat-

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uration (SFiO2) were measured in all patients once they were monitored as described previously (breathing fractional concentration of oxygen in the inspired gas [Fl FiO2] = 0.21). Those values were taken as the baseline. Then oxygen therapy at an FiO2 sufficient to keep PaO2 above 55 mm Hg was started, and measurements were repeated at 30 min and at 24 and 48 h thereafter. When subsequent measurements were made, a steady state was ensured by a change in respiratory and heart rates less than 20 percent, systolic blood pressure less than 15 percent, and SaO2 less than 3 percent during the previous hour. All patients survived the ICU admission and were transferred to other medical wards when their condition improved.

Measurements and Calculations

Mean arterial pressure, right atrial pressure, pulmonary artery pressure, and pulmonary artery wedge pressure were measured using a stain-gauge transducer and recorded on a multichannel recorder (Siemens-Elema Mingograf 34). The zero reference was set at 4 cm below the sternal angle, with the patient in a semirecumbent position. The values for pressures were averaged for three successive respiratory cycles. Cardiac output was determined by the thermodilution technique, using a cardiac output computer. The mean value of 3 measurements within a range of 5 percent was used for calculation of derived variables. Cardiac index was calculated by dividing cardiac output by body surface area. Arterial and venous oxygen contents were calculated using the standard equation (oxygen content = 1.38 × hemoglobin concentration × O2 saturation + 0.0031 × PO2). Arterial and venous oxygen saturations were estimated from the corresponding PaO2 and mixed-venous oxygen pressure (PVO2) values, according to the Severinghaus nomogram, and corrected for pH, temperature, and hematocrit.13 Oxygen delivery was calculated as the product of cardiac output and arterial oxygen content (CaO2) by the following formula: DO2 = 10 × CaO2 × cardiac output. Oxygen uptake was calculated using the Fick equation (VO2 = 10 × cardiac output × [arterial O2 content - mixed-venous O2 content]). The oxygen extraction ratio was calculated as the ratio between VO2 and DO2. Hemoglobin concentration was measured by an automated analyzer (Coulter 5 Plus Analyzer). Blood gas levels were measured for arterial and mixed-venous blood samples (Instrumentation Laboratories Analyzer).

Data were analyzed by a one-way analysis of variance (ANOVA). A p value less than 0.05 was considered statistically significant.

RESULTS

Changes in hemodynamic and gas exchange parameters are summarized in Table 1 and Figure 1. The SaO2, PaO2, and PVO2 increased significantly after oxygen therapy. There was no significant change in cardiac output, mean blood pressure, and pulmonary artery pressure. Systemic and pulmonary vascular resistances tended to decrease, but the change did not reach statistical significance. Individual changes in pulmonary artery pressure and pulmonary vascular resistance were highly variable, and no particular relationship was found between disease severity and changes in the pulmonary vasculature after oxygen therapy. Following a significant increase in DO2 due to the increase in SaO2, calculated VO2 did not change, and the oxygen extraction ratio decreased.

DISCUSSION

Breathing oxygen-enriched air is an initial and standard treatment for patients with acute respiratory failure due to COPD. Restoration of PaO2 values above 50 to 55 mm Hg to relieve pulmonary vasoconstriction and tissue hypoxia are the accepted goals of oxygen therapy in these patients; however, there are few clinical studies on the effects of oxygen therapy on systemic and pulmonary hemodynamics during acute exacerbations of COPD. The baseline of most previous studies was obtained after withdrawing oxygen administration for variable periods of time once the patients were admitted.7,8,11,12 In trying to study patients during the acute hypoxic state, our baseline was the hemodynamic and gas-exchange status shortly after arrival at the hospital, before administering oxygen.

| Table 1—Hemodynamic and Oxygen Transport Variables After Administering Oxygen by Face Mask to Patients with Acutely Decompensated COPD* |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Baseline        | 30 min          | 24 h            | 48 h            |
| PaO2, mm Hg     | 36 ± 8          | 69 ± 26§        | 79 ± 46§        | 68 ± 21§        |
| SaO2, percent   | 87 ± 9          | 87 ± 11†        | 79 ± 14         | 88 ± 14         |
| PVO2, mm Hg     | 58 ± 9          | 58 ± 18         | 59 ± 14         | 55 ± 16         |
| pH              | 7.35 ± 0.05     | 7.36 ± 0.05     | 7.39 ± 0.07     | 7.39 ± 0.07     |
| Heart rate, beats per min | 95 ± 14 | 84 ± 13† | 82 ± 12§ | 83 ± 12         |
| CI, L/m²·min⁻¹  | 3.69 ± 1.30     | 3.89 ± 1.09     | 3.72 ± 0.95     | 3.72 ± 0.95     |
| Pra, mm Hg      | 13 ± 7          | 10 ± 3          | 7 ± 2           | 7 ± 2           |
| Pwpr, mm Hg     | 15 ± 5          | 16 ± 5          | 14 ± 5          | 14 ± 5          |
| Ppa, mm Hg      | 39 ± 9          | 39 ± 9          | 39 ± 9          | 39 ± 9          |
| SVR, dyn·cm⁻²·m⁻³ | 1.02 ± 2.42     | 1.14 ± 3.22     | 1.26 ± 2.62     | 1.26 ± 2.62     |
| PVR, dyn·cm⁻²·m⁻³ | 50 ± 2.12       | 46 ± 1.21       | 48 ± 1.21       | 48 ± 1.21       |
| DO2, ml/kg/min  | 19.8 ± 3.98     | 19.87 ± 3.98    | 19.87 ± 3.98    | 19.87 ± 3.98    |
| VO2, ml/kg/min  | 3.4 ± 1.6       | 3.3 ± 2.0       | 3.4 ± 1.6       | 3.4 ± 1.6       |
| OER, percent    | 25.3 ± 9.66     | 20.4 ± 6.98     | 25.2 ± 7.28§    | 25.2 ± 7.28§    |

*Data are means ± SEM.
†CI, cardiac index; Pra, right atrial pressure; Pwpr, pulmonary artery wedge pressure; Ppa, pulmonary artery pressure; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance; and OER, oxygen extraction ratio.
‡p < 0.01 vs baseline.
§p < 0.05 vs baseline.
Like other investigators, \(^{5,9}\) we did not find a decrease in pulmonary vascular resistance, although there was a trend toward lower values after oxygen therapy. There are contradictory results as to the changes in cardiac output after oxygen therapy in these patients. The systemic adaptation to hypoxia that includes an augmented cardiac output\(^{12}\) allowing maintenance of \(\text{DO}_2\)\(^{13}\) is likely to be attenuated when \(\text{PaO}_2\) increases after oxygen administration. In fact, a decrease in cardiac output during oxygen therapy has been reported in patients with decompensated COPD.\(^{5,9}\) In those studies, patients were studied once their condition was stable, after withdrawal of oxygen therapy; however, our patients' baseline was during the acute exacerbation before oxygen therapy. This fact may explain the different hemodynamic changes observed in our study. We found that cardiac output showed a nonsignificant trend toward higher values, probably due to a better \(\text{DO}_2\) allowing a better myocardial performance.

Standard treatment of these patients includes the administration of oxygen to increase the oxygen-carrying capacity of the blood. Therefore, defining whether increasing \(\text{SaO}_2\) in these patients leads to a rise in \(\text{VO}_2\) is of great clinical importance in order to determine if the excess oxygen supplied is actually used by the tissues. Degaute et al\(^{8}\) observed that increasing \(\text{FiO}_2\) from 0.21 to 0.28 leads to an increase in \(\text{PaO}_2\), \(\text{PrO}_2\), and the coefficient of oxygen delivery (the inverse of the oxygen extraction ratio) and to a decrease in cardiac output. A subgroup of patients with higher \(\text{PaO}_2\) showed no changes in \(\text{DO}_2\) and a decrease in cardiac output, whereas those with more severe pulmonary impairment presented an increase in \(\text{DO}_2\), with no change in cardiac output and greater decreases in the oxygen extraction ratio. Although no \(\text{VO}_2\) values are reported, it can be inferred from their data that \(\text{VO}_2\) decreased in the group in which \(\text{DO}_2\) did not change (due to the decrease in the oxygen extraction ratio), and \(\text{VO}_2\) possibly remained constant in the group in which \(\text{DO}_2\) increased, due to the coincident and more marked decrease in the oxygen extraction ratio.

Lejeune et al\(^{9}\) found in 22 patients with decompensated
sated COPD that increasing FIO₂ from 0.21 to 0.24 to 0.28 caused an increase in SaO₂ and SvO₂, accompanied by a drop in cardiac output. The DO₂ tended to increase, and VO₂ did not change. With higher FIO₂ (0.35 to 0.40), there was a significant increase in DO₂, whereas VO₂ did not change. These authors concluded that tissue oxygenation improves after oxygen therapy, as shown by increases in PVO₂. This finding could also reflect a lack of utilization of the oxygen supplied by increasing SaO₂ and therefore does not necessarily imply a better tissue oxygenation.

Kawakami et al. found in patients with stable COPD that breathing pure oxygen resulted in an increase in PVO₂ and an increase in cardiac output and the coefficient of oxygen delivery (decreased oxygen extraction ratio). Nonsurvivors presented lower baseline SVo₂ values compared to survivors. After the breathing of 100 percent oxygen, the SVo₂ in nonsurvivors rose to a level equivalent to that of survivors. Although not reported, the rise in SVo₂ should be accompanied by an increase in DO₂, since the coefficient of oxygen delivery (and therefore the oxygen extraction ratio) did not change significantly. Those findings suggest that VO₂ did not change after increasing DO₂.

An abnormal relationship between DO₂ and VO₂ has been reported in states of tissue hypoxia. When normally functioning mechanisms, such as an increase in the oxygen extraction ratio and blood flow, compensate for changes in DO₂, VO₂ is independent of supply. Only when DO₂ decreases below the so-called critical value, do those mechanisms become exhausted, and VO₂ becomes dependent on DO₂. Although criticized by some authors who did not find this abnormal relationship when VO₂ is measured by expired gas analysis, rather than calculated by the modified Fick equation, others accept that in certain clinical conditions (such as sepsis, the adult respiratory distress syndrome, pulmonary hypertension, and chronic congestive heart failure), there is an abnormal dependency of VO₂ on DO₂ for a wide range of supranormal values of DO₂. Since those patients have normal DO₂ values, it has been proposed that this dependency phenomenon reveals a covert tissue oxygen debt. It can be postulated that patients with uncompensated COPD suffer such an occult oxygen debt that could be demonstrated by increases in VO₂ when DO₂ increases.

The mean baseline value of DO₂ in our patients was 11.1 ± 3.7 ml/kg/min, and some values fell below what is considered the critical value of DO₂ in humans. Despite a significant rise in DO₂, VO₂ did not change. This lack of supply-dependence has several explanations. First, patients with COPD may have a normal DO₂/VO₂ relationship, and compensatory mechanisms keep VO₂ constant despite changes in DO₂; however, there have been reports of a pathologic supply-dependent VO₂ manifested by a vasodilatory intervention in patients with pulmonary hypertension, including patients with COPD. Secondly, patients with acutely decompensated COPD may have an occult oxygen debt, that is, one not manifest by increasing SaO₂. In fact, there are data to support that oxygen uptake is more limited by convective than diffusive transport. Increasing DO₂ by interventions that do not increase blood flow, such as increasing the hematocrit, does not uniformly lead to increases in oxygen uptake. Therefore, it could be that acutely decompensated patients with COPD present an occult oxygen debt that is not manifest after increasing DO₂ by increasing SaO₂. Since we could not include a control group (i.e., patients not given oxygen therapy), it is not possible to establish how much of the observed changes in DO₂ and VO₂ were attributable to oxygen therapy and how much to the natural history of this acute illness. It could be that a better control of infection and a decrease in the work of breathing as the effect of treatment takes place would contribute to a decrease in oxygen demand and therefore in VO₂. Nevertheless, our data support the concept that conventional treatment of these conditions and increasing DO₂ by means of oxygen therapy do not result in a higher VO₂. This can be due to the absence of a pathologic DO₂/VO₂ relationship in these patients, to a decrease in metabolic demands as the acute illness is controlled, or to the presence of a VO₂ more dependent on blood flow than on global DO₂.

REFERENCES


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