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Successful management of acute respiratory failure in an Idiopathic Pulmonary Fibrosis patient using an extracorporeal carbon dioxide removal system

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Abstract. Patients with Idiopathic Pulmonary Fibrosis (IPF) requiring Invasive Mechanical Ventilation (IMV) following unsuccessful treatment with Non-Invasive Ventilation (NIV) have a high mortality rate. IMV is, moreover, an independent predictor of poor outcome during the post-transplantation period in patients on waiting lists for Lung Transplantation (LT). Here we describe the successful management of an IPF patient with acute respiratory failure (ARF) using a pump-assisted veno-venous system for extracorporeal CO_2 removal (EC-CO_2R) (ProLUNG® system) as an alternative to endotracheal intubation (ETI) following NIV failure. Given this positive experience, further studies are warranted focusing on the ECCO_2R system's tolerability, safety, and efficacy in patients with IPF and severe ARF in whom NIV alone is ineffective. *(Sarcoidosis Vasc Diffuse Lung Dis 2016; 33: 186-190)*

Key words: Idiopathic Pulmonary Fibrosis, extracorporeal CO_2 removal, acute respiratory failure

Introduction

Accounting for nearly 30% of Lung Transplantation (LT) procedures performed worldwide, Idiopathic Pulmonary Fibrosis (IPF) is a chronic, progressive and generally fatal interstitial lung disease of unknown aetiology that causes death in nearly all patients within 6 years of diagnosis (1). Although most IPF patients die from slowly progressive respiratory failure, a small minority (approximately 5-10%) develop transient acute respiratory worsening and/or failure that may require ventilatory support and admission to an Intensive Care Unit (ICU) (2). Causes of acute deterioration include conditions such as pneumonia, pulmonary embolism, congestive heart failure, and pneumothorax; the term "acute exacerbation of IPF" was formulated to describe an acute respiratory deterioration without an identifiable cause (3,4).

Some observational studies have reported that Non-Invasive Ventilation (NIV) can efficaciously treat IPF patients who develop acute respiratory failure (ARF) requiring ventilatory assistance and prevent intubation (5,6); NIV application is, nevertheless, associated with a marked failure risk, and high mortality rates have been reported in IPF patients who require Invasive Mechanical Ventilation (IMV) following NIV failure (7).

A recently introduced procedure, Extracorporeal CO_2 removal (ECCO_2R) has been proposed as an intervention to eliminate CO_2 from the blood of patients undergoing NIV who are unable to achieve adequate gas exchange at maximal tolerable ventila-

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tion pressures in the attempt to avoid IMV and its complications. Sporadic case reports and case series have reported that $ECCO_2R$ systems have been used efficaciously in some cases of acute exacerbation of COPD (8-10), bronchiolitis obliterans (11) severe bronchial asthma (12), as well as non-Cystic Fibrosis (CF) bronchiectasis (13).

Despite increasing interest in the use of $ECCO_2R$ systems in patients who develop refractory hypercapnic ARF, its utility in IPF patients in the event of ARF has never been assessed. This report describes the successful management of an IPF patient with ARF who was treated efficaciously with $ECCO_2R$ following NIV failure.

Case Report

A 73-year-old male was admitted to the Respiratory Intensive Care Unit (RICU) of the University-City Hospital of Padova (Italy) for acute respiratory failure (ARF). In accordance with the American Thoracic Society/European Respiratory Society consensus statement criteria, the patient was disagnosed with IPF (at the age of 70) on the basis of High-Resolution CT (HRCT) findings (4). The patient presented at the Emergency Department complaining of increasing difficulty breathing and productive cough during the preceding week and reported suffering from recurrent episodes of ARF over the preceding 2 years. He was receiving treatment with pirfenidone therapy and long-term oxygen therapy (LTOT) with nocturnal NIV. He was also receiving steroid therapy during the four days preceding admittance. He was admitted to the Emergency Department of our hospital due to worsening of the clinical condition and was transferred to the RICU.

At admission to our unit the patient was polypneic, fatigued and moderately sleepy. Physical examination revealed tachypnea [Respiratory Rate (RR): 26b/min], weak productive cough, and diffuse subcrepitant bilateral rales. He was severely hypercapnic during supplemental oxygen therapy and his arterial blood gas (ABG) values were: pH, 7.32; $PaCO_2$, 69.4 mmHg; PaO_2, 95 mmHg; HCO_3-, 35.1 mmol/L; PaO_2/FiO_2 ratio: 190. A complete hematological work-up revealed mild anemia (Hb 12.5 g/L) and leukocytosis (WBC: 18,830 x 10^6/L); serum electrolytes were normal. NT-proBNP was slightly increased (1716 pg/mL). A chest X-ray revealed bilateral, reticular, coarse linear shadows. Blood cultures for pathogenic bacteria or fungi and serologic tests against major pneumotropic agents were all negative; but in view of the fact that a bronchoscopy was not feasible and acute bacterial infection could not be confidently excluded, the patient was prescribed intravenous antibiotic therapy (piperacillin and levofloxacin); he was also prescribed prednisone (1 mg·kg–1 per day) and diuretics.

Since ventilatory assistance was necessary, NIV was initiated using a portable ventilator (Elisée 150, ResMed Poway, CA, USA) set on the Pressure Support Ventilation (PSV) mode. The PSV was initially titrated to a moderate tidal volume (6-8 mL/kg); the ventilator setting was then readjusted according to arterial blood gas (ABG) values; we aimed to maintain arterial oxygen saturation (SaO_2) over 90% and partial pressure of carbon dioxide in arterial blood ($PaCO_2$) at approximately 50 mmHg and to reduce the RR. The initial PS level did not exceed 20 cm H_2O and was progressively elevated by 1-2 cmH_2O without exceeding 30 cm H_2O due to the high risk of pneumothorax. Positive End Expiratory Pressure (PEEP) was set at 6 cmH_2O to obtain the best oxygenation with minimal haemodynamic side effects, and the levels were raised by 1-2 cmH_2O without exceeding 6-8 cm H_2O. Supplemental oxygen was added to the ventilator circuit. The patient was connected to the ventilator by means of a full face mask; colloid dressings were placed on the major pressure points to minimize skin injury. NIV was delivered continuously except for brief "rest" (30-60 min) periods to allow the patient to receive dietary liquid supplements and to speak. A standard ICU monitoring system displaying electrocardiographic data, pulse oximetry, invasive blood pressure, and RR measurements was utilized.

A HRCT, performed 3 days after admission, showed honeycombing pattern and traction bronchiectases predominantly of the lower lobes; new or progressive infiltrates were not evident (Figure 1).

Despite continuous use of NIV, pulmonary gas exchange progressively deteriorated: on day 4 after admission ABG levels showed increasingly severe hypercapnia (pH, 7.39; PCO_2, 80 mmHg; PaO_2, 79 mmHg, during assisted ventilation). The patient also showed signs of exhaustion (RR was 30 to 35), increasing intolerance to uninterrupted NIV and an

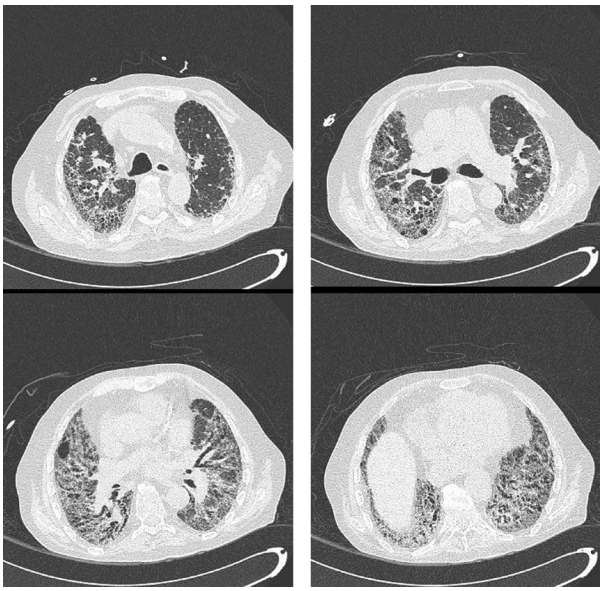

Fig. 1. Chest high-resolution computed tomography (HRCT) images taken at the patient's third day of hospitalization in the Respiratory Intensive Care Unit (RICU)

imminent need for IMV. Concerned about the high risk of complications linked to IMV, we informed the patient about an alternative veno-venous extracorporeal carbon dioxide removal ($ECCO_2R$) method, which had already been approved for an investigational feasibility study by our local ethics committee, that was available in our hospital. He was also provided detailed information about the benefits and risks of that system.

The $ECCO_2R$ device used in our center is the ProLUNG® system, a pump-driven veno-venous system which utilizes a small single veno-venous dual lumen catheter (size=13 Fr) that can be inserted into a femoral or jugular vein. It is characterized by a low blood flow rate (up to a maximum of 450mL/min) and a single-use-only gas exchange cartridge consisting of a hollow fiber polypropylene diffusion membrane network with an effective surface area of 1.35m^2. As the device uses a total volume circuit of only 120 mL, the hemodynamic impact on the patient is minimized. Oxygen flows as a carrier gas within the hollow fibers, and CO_2 moves by selective diffusion across the concentration gradient from the blood.

The patient freely gave consent to receiving treatment with the device. With the patient in a supine position, a 13 Fr catheter was inserted percutaneously through the right femoral vein without complication and connected to the extracorporeal circuit. The blood flow was initiated through the circuit by a centrifugal pump at 300 ml/min. The oxygen flow through the gas exchanger was initiated at 12 L/min to maximize CO_2 removal. In accordance with study protocol guidelines for anticoagulation, the patient was started on an intravenous heparin infusion to maintain an activated clotting time between 150 and 180 seconds.

The amount of CO_2 removed by the device was adjusted depending on the ABG and RR levels, which were measured every 4 hours. During use, the ProLUNG® circuit blood flow varied from 300 to 450 mL/min; the remainder of gas exchange occurred through the lungs using NIV adjusted to releasing low V_T (6-8 mL/kg) with a low/moderate PEEP level.

$PaCO_2$ decreased after $ECCO_2R$ therapy was initiated from 71 before cannulation to 50mmHg within 24 hours; the patient's RR also decreased from 30 to 20-22 b/min. $PaCO_2$ subsequently remained within a 52 to 48 mm Hg range for the duration of therapy (Figure 2). The patient's clinical status pro-

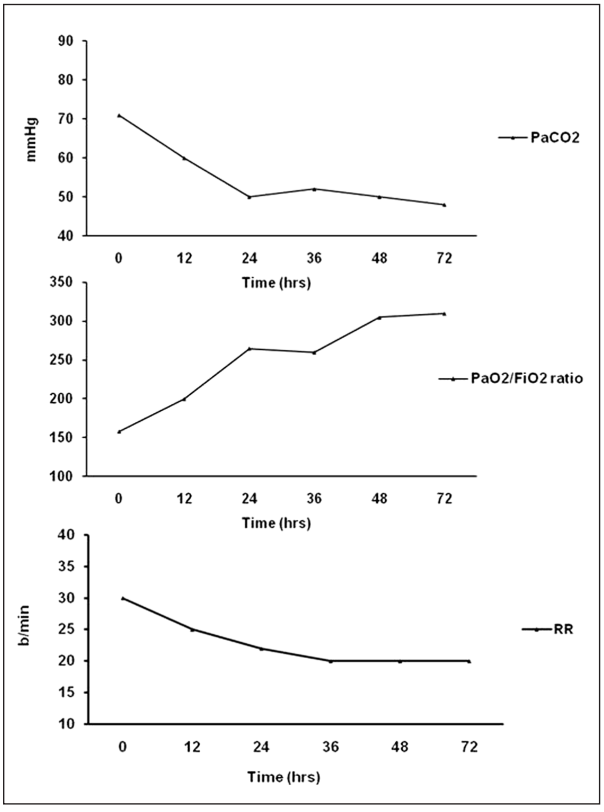

Fig. 2. Variations in the patient's $PaCO_2$, PaO_2/FiO_2 ratio and Respiratory Rate values after $ECCO_2R$ was initiated

gressively improved over the next 3 days, making it possible to reduce NIV application from continuous use, except for brief "rest" periods, to 3-4 hours off the ventilator by day 3. By day 4, the patient was able to breathe without ventilatory support for 10 consecutive hours; on the same day, the patient was increasingly active, clinically stable, and extracorporeal support was suspended. The catheter was removed, coagulation values were normal, and there was no additional bleeding. Subsequently, the patient continued to receive NIV at night. There were no complications during or after $ECCO_2R$. On day 7, the patient was transferred to the Pulmonary Division in good clinical condition; he was mildly hypercapnic during supplemental oxygen therapy and his ABG values were: pH, 7.48; $PaCO_2$, 46.9 mmHg; PaO_2, 82 mmHg; HCO_3-, 34.5 mmol/L; PaO_2/FiO_2 ratio: 314.3. When he was discharged from hospital he was prescribed night-time ventilation via a nasal mask.

Discussion

A major cause of morbidity and mortality, transient ARF, which leads to a high percentage of hospital admissions and up to 40% of all deaths, is a well known occurrence in IPF patients (14,15). When it presents, most patients develop hypercapnia and require ventilatory assistance: unfortunately, due to gross abnormalities in pulmonary mechanics such as alterations of the elastance of the lungs (16), mechanical ventilation continues to be a difficult task. Although potentially efficacious in selected IPF patients, NIV is associated with a relevant failure risk. Subsequent transitioning to IMV does not, moreover, substantially improve patients' outcome, as the mortality rate in these patients is approximately 90% (7).

The case described here is, to our knowledge, the first report concerning the utilization of an $ECCO_2R$ device as an alternative to IMV in a patient with acute worsening of IPF refractory to NIV support: findings from preliminary experiences had convinced us that this approach could prevent or reduce the need for endotracheal intubation thus avoiding problems linked to IMV.

Since a retrospective cohort study on adult patients awaiting Lung Transplant (LT) found that undergoing IMV before transplantation was an independent predictor of a longer time on IMV and in the ICU during the post-transplantation period, managing IPF patients on waiting lists for LT using an $ECCO_2R$ system to avoid IMV could prove to be particularly important (17).

Although extracorporeal support devices themselves are linked to some complications, such as vessel perforation, bleeding, and infections (18), those risks were minimized in our case by using a minimally invasive, well tolerated CO_2 removal system that is based on veno-venous cannulation as opposed to the traditional veno-arterial cannulation with insertion of a a small single veno-venous dual lumen catheter. Since the device, which does not require any specialized staff/training, proves easy to use, it is presumable that it could be safely utilized in any medical or surgical ICU.

In conclusion, given this and other positive experiences outlined in the literature in patients affected with a variety of conditions, further studies are warranted to verify the $ECCO_2R$ system's tolerability, safety, and efficacy in IFP patients with refractory hypercapnic ARF, with special regard to candidates awaiting LT.

This work was performed at the Padova University-City Hospital, Padova, Italy

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