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Extracorporeal CO_2 removal in combination with continuous renal replacement therapy[☆]

Sistema combinado de depuración de CO

To the Editor,

Extracorporeal carbon dioxide removal ($ECCO_2R$) systems are devices that provide partial respiratory support. They work with a blood flow of 250–1500 ml/min, less than that required for extracorporeal membrane oxygenation (ECMO), and use a smaller membrane surface (0.33–0.67 m^2). This system was first described in the 1980s by Gattinoni et al.,[1] while in 1990, Terragni et al.[2] published the first combined $ECCO_2R$ system. Using a neonatal membrane lung with a total membrane surface of 0.33 m^2 coupled with a continuous hemofiltration system in 32 patients with acute respiratory distress syndrome, they succeeded in reducing tidal volume (Vt) to less than 6 ml/kg ideal weight, achieving normalization of hypercapnia and a reduction of cytokines in bronchoalveolar lavage at 72 h, reflecting a reduction in mechanical ventilator-induced lung injury.

In patients with acute respiratory distress syndrome, these systems remove CO_2, allowing Vt to be reduced, so that protective or ultraprotective mechanical ventilation (MV) ($Vt \leq 6$ ml/kg or Vt 3–4 ml/kg, respectively) can be efficiently applied. These findings have been demonstrated in a recent international multicenter prospective study.[3] A greater reduction in Vt and plateau pressure would prevent alveolar overdistension, reduce mechanical ventilator-induced lung injury, and may reduce mortality in patients with acute respiratory distress syndrome.[4,5] These systems have several potential indications in hypercapnic patients.[4,5] In COPD, they could help avoid the use of MV, act as an alternative if non-invasive MV fails, or facilitate extubation.[6] In the bridge to lung transplant, they can improve physical conditions, obviating the complications derived from MV.[7,8]

Several $ECCO_2R$ systems are available, most of which are of the veno-venous type.[9] The use of this system combined with continuous renal replacement techniques (CRRT) has been shown to decrease vasopressor requirements,[10] in addition to sparing vascular access.

We report a case in which we used a combined $ECCO_2R$-CRRT system, describe the effects, and discuss the most important technical aspects.

Our patient was a 61-year-old woman admitted for an asthma exacerbation with progressive hypercapnia, who was intubated and connected to MV. On admission to the ICU, she had a pressure plateau of 35 cmH_2O and a peak pressure of 52 cmH_2O. Arterial blood gases with inspired oxygen fraction of 0.4 showed pH 7.3, $PaCO_2$ 120 mmHg, PaO_2 96 mmHg, bicarbonate 28.1 mmol/l, base deficit −7 mmol/l, and oxygen saturation 98%. She developed acute renal failure with urea 107 mg/dl and creatinine 1.36 mg/dl.

Antibiotic therapy, both empirical and targeted at pulmonary aspergillosis, was started, and she received corticosteroids, salbutamol, ipratropium, ketamine, and magnesium. MV was optimized by starting ECMO with ultraprotective MV, which was withdrawn on day 11. After 1 week, the patient's status deteriorated, with pH 7.32; $PaCO_2$, 83 mmHg; PaO_2, 181 mmHg; and bicarbonate, 37 mmol/l. A 13.5 Fr femoral Shaldon catheter was inserted for a combined $ECCO_2R$-CRRT system, with an 0.9 m^2 AN69 hemofilter, and CO_2 membrane lung with surface area of 0.32 m^2, blood flow of 350 ml/min, air 10 l/min, and anticoagulation with sodium heparin for an activated partial thromboplastin time (aPTT) of 2.1. After starting therapy, respiratory acidosis was corrected, with development of respiratory alkalosis after effective reduction of $PaCO_2$ to 30 mmHg in the first 3 h, allowing us to start protective MV with a Vt of 5 ml/kg and PEEP 8 cmH_2O. In the following hours, blood flow was reduced to 300 ml/min due to the development of alkalosis, and the fraction of inspired oxygen was reduced. Despite aPTT remaining within a good range, the hemofilter clotted at 24 h, so the system had to be removed. The patient died in the following 24 h due to severe global respiratory failure caused by pulmonary aspergillosis and septic shock, after ruling out the reintroduction of extracorporeal respiratory support systems, although no complications derived from the use of the system were observed.

In the case described, CO_2 removal was effective in the first hour, with maximum effect at 3 h, but effectiveness was later lost due to hemofilter clotting. It is important to emphasize that $ECCO_2R$ systems contribute only marginally to the improvement of oxygenation by several mechanisms.[11] The diffusing capacity of CO_2 is 20 times higher than that of oxygen, and these systems are theoretically able to eliminate 200–250 ml/min of CO_2 in an adult with a flow of 500 ml/min.[11,12] Hypercapnia should

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be corrected slowly[4] to avoid secondary alkalosis, as occurred in our case.

The main determining factor in CO_2 removal is airflow: up to a maximum of 10 l/min is recommended for most devices.[11,12] However, blood flow has also been studied as a related factor, and some authors determine that it should be increased in cases of severe respiratory acidosis (pH < 7.2).[13,14] The membrane surface area seems to play a less critical role in CO_2 clearance, although a membrane of 0.8 m^2 proved more effective than one of 0.4 m^2 in a bovine animal model.[13] The surface area of our polymethylpentene membrane was 0.32 m^2, similar to that used by Terragni et al.[2]

These $ECCO_2R$-CRRT systems can provide respiratory support alone, or both respiratory and renal support. This is important, because 60% of patients who suffer multiple organ failure and require MV also develop acute renal failure. In these patients, volume overload and increased alveolar permeability derived from acute renal failure negatively affect the lungs and, similarly, MV and biotrauma diminish renal function.[15]

Systemic anticoagulation is needed to maintain the whole system (hemofilter and $ECCO_2R$), maintaining an aPTT ratio of 1.5–2 to balance the risk of bleeding and/or clotting. In our case, clotting of the hemofilter (but not of the membrane lung) occurred after 24 h despite maintaining aPTT within the range, and this limited treatment. This complication has been previously described and may be related to the hemofilter surface.[15] Clotting of the membrane lung occurs in 14%–16.7% of cases.[3,10,11] These thrombotic complications in veno-venous $ECCO_2R$ systems are the most feared, since they require the system to be changed, or treatment to be discontinued, as in our case.

In summary, this combined $ECCO_2R$-TRRC system at a flow of less than 400 ml/min was very effective for CO_2 removal, but limited by rapid clotting of the hemofilter.

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