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UNDERSTANDING THE DISEASE

Understanding hypoxemia on $ECCO_2R$: back to the alveolar gas equation

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Extracorporeal CO_2 removal ($ECCO_2R$) is a promising technique for ARDS and for severe acute exacerbations of COPD [1]. However, $ECCO_2R$ carries its own risk of complications and side effects. Beyond hemorrhagic and thrombotic complications and hemolysis, the occurrence of progressive hypoxemia has been reported in COPD patients treated by $ECCO_2R$, leading to a tracheal intubation rate of 28% in the prospective series from Braune et al. [2]. Obviously, progressive hypoxemia can be explained by pulmonary complications such as evolving infiltrates, even if other factors such as modification of the respiratory quotient have been proposed [2, 3]. Accordingly, we illustrate such a mechanism, intrinsically linked to the $ECCO_2R$ technique and not involving any worsening of lung function by itself.

A 76-year-old man was admitted because of a very severe hypercapnic acute exacerbation of a chronic respiratory failure due to non-cystic fibrosis bronchiectasis. Invasive mechanical ventilation (Carescape R860 GE Healthcare) was initiated because of non-invasive ventilation failure. $ECCO_2R$ was started 24 h later with the goals of limiting hypercapnia and dynamic hyperinflation and promoting a rapid weaning process [4]. The iLA-Activve system (Xenios-Novalung, Heilbronn) was used with a 22-Fr right jugular veno-venous catheter. Since weaning was a very difficult process, the sweep gas flow was progressively increased during the next 7 days from 1 to 9 L/min, while the extracorporeal blood flow varied between 0.8 and 1.2 L/min. During the same period, the PaO_2/FiO_2 ratio progressively decreased from 251 to 145, with no obvious pulmonary complication. Table 1 indicates the corresponding ABG and PaO_2/FiO_2 values as well as the D_A-aO_2 values calculated either using the classical simplified alveolar air equation, i.e., $P_AO_2 = P_IO_2 - P_ACO_2/0.8$, or the exact simplified alveolar air equation using the 0.3 value of the respiratory quotient displayed by the ventilator. Despite the apparent changes in PaO_2/FiO_2 ratio, the correct D_A-aO_2 and P_AO_2 were compatible with clinically negligible changes in intrapulmonary shunt, oscillating around 15%, even if we cannot totally exclude confounding factors inferring with the shunt calculation such as a higher mixed venous PO_2 (even if it is generally believed that $ECCO_2R$ exerts only minimal oxygenation effects), a release of hypoxic pulmonary vasoconstriction due to a higher FiO_2, or a shunt decrease in relation to higher FiO_2 as described in moderate ARDS. The observed changes in PaO_2/FiO_2 were therefore mainly justified by changes in P_AO_2 due to changes in the VCO_2/VO_2 ratio of the patient's own lung, rather than to changes in its oxygenation function. Accordingly, no specific pulmonary complication was diagnosed during the following days.

$ECCO_2R$ exerts predominantly an effective extracorporeal CO_2 removal, without significant effect on oxygenation which accordingly occurs very predominantly in the native lungs, resulting in a decreased native lung respiratory quotient. It is therefore very important to use during $ECCO_2R$ the exact calculations of P_AO_2 and D_A-aO_2 when a suitable monitoring system is available, or at least to interpret with great caution any PaO_2/FiO_2 worsening, which could, at least in part, reflect an $ECCO_2R$-induced modification of the alveolar gas content [5].

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Table 1 Oxygenation values, ABG values, and invasive mechanical ventilation parameters recorded immediately before initiation of $ECCO_2R$ and under $ECCO_2R$ after raising the sweep gas flow to 9 L/min

	Immediately before $ECCO_2R$	$ECCO_2R$ day 7
PaO_2/FiO_2	251	145
P_AO_2 (mmHg) simplified	186	360
P_AO_2 (mmHg) exact	–	248
D_A-aO_2 (mmHg) simplified	98	273
D_A-aO_2 (mmHg) exact	–	161
R (native lungs) measured by the ventilator	–	0.3
pH	7.31	7.38
PaO_2 (mmHg)	88	87
$PaCO_2$(mmHg)	51	54
Ventilatory mode	ACV	ACV
VT (mL/kg IBW)	6	6
RR (/min)	12	10
PEEP (cmH_2O)	0	5
FiO_2	0.35	0.6

A alveolar, D_A-aO_2 difference between alveolar and arterial O_2 partial pressures, *R* respiratory quotient displayed by the ventilator, *simplified* assuming that *R* is equal to 0.8, *exact* using the measured value of *R*, *ACV* assist-controlled ventilation, *VT* tidal volume, *RR* respiratory rate

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Ethical statement
Treatment with $ECCO_2R$ was performed as part of a specific registry (Registry on the EXperience of Extracorporeal CO_2 Removal in Intensive Care Units, NCT02965079), benefiting from an approval (07 March 2016) from the Ethics Committee of the French Intensive Care Society.

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