



Extracorporeal Membrane Oxygenation for Management of Carbon Monoxide Intoxication

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Emergency use of extracorporeal membrane oxygenation (ECMO) for cardiopulmonary failure is well documented. However, the use of ECMO for carbon monoxide (CO) poisoning is rare. We report a case of a patient with severe CO poisoning that initially manifested as stunned myocardium-induced acute pulmonary edema. The patient was severely hypoxemic and refractory to mechanical ventilation at 7 hours after hospitalization. We applied veno-arterial ECMO for rescue life support for 3 days. The patient had a dramatic full recovery without immediate neurologic sequelae for the 3-day period. Under ECMO support, PaO₂ increased from 34.8 to 299.9 mmHg, and ventilator FiO₂ decreased to 0.4 within 3 days. The patient's consciousness also improved, with the Glasgow Coma Scale (GCS) score increasing from 8 to 15. Although the standard treatment for CO poisoning remains controversial, an aggressive rescue strategy is warranted for concurrent cardiovascular collapse and acute respiratory failure after severe CO poisoning in order to reduce the mortality of a reversible etiology.

Key words: extracorporeal life support, pulmonary edema, respiratory failure, carbon monoxide poisoning.

INTRODUCTION

Carbon monoxide (CO) poisoning is common and may be caused by faulty furnaces, inadequate ventilation of heating sources and exposure to engine exhaust.¹ Because the symptoms of CO poisoning are non-specific, a patient with subclinical exposure may only be recognized after an acute event or the coincidental discovery of a carbon monoxide leak.¹ CO exposure impairs cellular respiration and causes inflammation through multiple pathways,^{2,3,4,5} which result in neurological, pulmonary and cardiac injuries. Acute respiratory distress syndrome, myocardial injury and cognitive problems have been documented in many studies on CO poisoning.^{6,7,8,9}

For short-term management, administering normobaric oxygen at a high flow rate and 100% oxygen have been widely adopted.^{10,11} However, the use of hyperbaric oxygen (HBO) therapy remains controversial. A Cochrane review article does not support the use of hyperbaric oxygen therapy for CO poisoning,¹² although some randomized trials have reported potential benefits.^{13,14} The inflammatory consequences of CO exposure can induce tissue injury, although it remains unknown whether an anti-inflammatory strategy or the use of other neuroprotective techniques, such as induced hypothermia, can improve the prognosis of CO poisoning.¹

In general, extracorporeal membrane oxygenation (ECMO) may be indicated for patients with respiratory failure of a reversible etiology, but who do not respond to conventional medical treatment. To our knowledge, ECMO support for CO poisoning-related sequelae is a unique application. Here, we report a case of a patient with CO intoxication complicated by concurrent acute respiratory failure and cardiovascular collapse who received ECMO support for 3 days during the resuscitation period.

CASE REPORT

A 23-year-old, 110-kg male was found unconscious in

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Table 1. Hematologic and Biochemical Laboratory Data.

Variables	On Admission	7 Hours after Admission	72 Hours after ECMO	Reference Range, Adults
Hematocrit (%)	42.8	45.0	30.5	41.0-53.0 (men)
Hemoglobin (g/dl)	14.4	14.9	10.4	13.5-17.5 (men)
White cells (per mm ³)	21,300	19,900	16,500	4500-11,000
Differential count (%)				
Neutrophils	88.1	89.1	83.2	40-70
Lymphocytes	5.6	4.4	9.2	2.2-4.4
Monocytes	6.0	5.9	7.1	1-4
Eosinophils	0.1	0.0	0.4	0-8
Platelets (per mm ³)	290,000	208,000	55,000	150,000-350,000
Glucose (mg/dl)	101			70-110
Sodium (mmol/liter)	139	139	134	135-145
Potassium (mmol/liter)	4.2	3.5	3.4	3.4-4.8
Chloride (mmol/liter)	103	109		100-108
Urea nitrogen (mg/dl)	13	11	11	8-25
Creatinine (mg/dl)	0.7	0.8	0.4	0.6-1.5
Creatine kinase (U/liter)	307	919	150	38-174
Creatine kinase MB (U/liter)	35	41	11	7-25
Troponin I (ng/ml)	1.41	2.67	0.52	0.0-0.5
Arterial blood gas				
pH	7.413	7.32	7.433	7.35-7.45
PCO ₂ (mmHg)	27.4	30.0	36.0	35-45
HCO ₃ ⁻¹ (mmol/liter)	17.1	18.0	23.6	
PO ₂ (mmHg)	107.8	34.8	299.9	75-100
SaO ₂ (%)	99.2	78.8	97.9	92-98.5
FCOHb (%)	21.1	15.0	0.1	0.0-1.5
FiO ₂ (%)	60	100	40	
Lactate (mmol/liter)	5.9			0.7-2.1

the bathroom. On the previous evening, he had attended an overnight banquet, with heavy smoking in a closed environment, and had taken a shower for over an hour. Inadequate ventilation of a water heater with products of incomplete combustion was evident at the scene. He had no prior systemic disease or surgery and he was not taking any medications on a regular basis.

Upon his arrival at the emergency department, his clinical appearance showed a semi-comatose status with a body temperature of 36.8 °C, blood pressure of 105/64mmHg, pulse rate of 88/min and respiratory rate of 19/min. A drug screen, including amphetamine, benzodiazepam and morphine, was unremarkable. Emergency brain computed tomography showed no abnormal findings, and a lumbar puncture provided no evidence of meningitis. The laboratory test details are shown in Table 1.

Hypoxemia (SaO₂ = 88%) and drowsy consciousness were observed, and endotracheal intubation was performed. During and after the procedure, pinkish phlegm was noted from the endotracheal tube, leading to an impression of acute pulmonary edema (Fig 1). With the ventilator set in the pressure-controlled mode, positive end-expiratory pressure (PEEP) was 10.0 cmH₂O, respiratory rate was 24/min, pressure level was 25 cmH₂O and FiO₂ was 1.0. Ventilation initially resulted in improved blood oxygenation, but this subsequently deteriorated despite increasing the ventilation pressure and partial oxygen pressure. Blood gas analysis showed profound hypoxemia, with FiO₂ = 100%, SaO₂ = 80%, pH = 7.345, PaCO₂ = 30.0 mmHg, PaO₂ = 45.1 mmHg, HCO₃⁻¹ = 16.1 mmol/liter and COHb = 18%. Myocardial injury with myocardial suppression was diagnosed, which was compatible with emergency echocardiography that showed

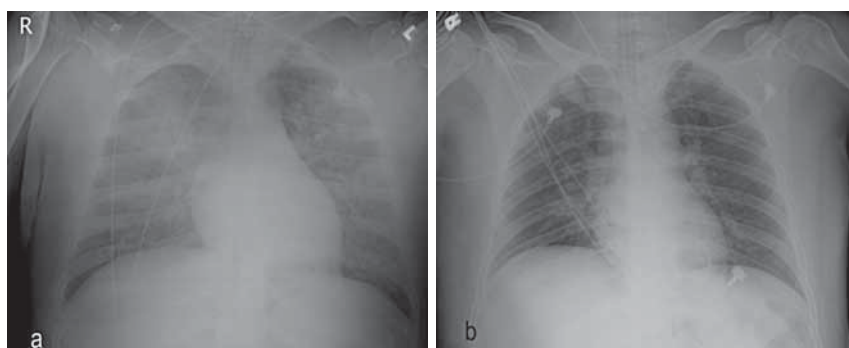


Fig. 1 Serial chest plain films. (a) Admission X-ray demonstrating patchy consolidations and ground-glass opacities of both lungs. (b) X-ray on Day 3 after ECMO with resolution of the consolidation.

an ejection fraction of 30% and generalized dyskinesia of the left ventricle.

The patient was admitted to the intensive care unit (ICU) for further treatment. In view of his poor ventilation (oxygenation index = 65; $AaDO_2$ = 637.9) complicated by deteriorating cardiac function and unstable hemodynamics, HBO therapy was postponed. Results of additional laboratory tests at 7 hours after admission are shown in Table 1. The difficulty with maintaining a satisfactory arterial oxygen level and effective cardiovascular flow was strong evidence for a grave prognosis, and he was referred for ECMO.

The ECMO system was comprised of a centrifugal pump and a microporous membrane oxygenator with an integrated heater (CB2505; Medtronic Inc., Minneapolis, MN, USA). The entire ECMO system had a heparin-binding surface in order to maintain an activated clotting time of 160-200 s. Because circulatory support was required, a veno-arterial ECMO was indicated, in which venous blood was drained from the right femoral vein, passed through the centrifugal pump, and returned to the patient via the right internal femoral artery after gas exchange in the oxygenator.

Under ECMO support, PaO_2 increased from 34.8 to 299.9 mmHg and ventilator FiO_2 decreased to 0.4 within 3 days. The patient's consciousness also improved, with the Glasgow Coma Scale (GCS) score increasing from 8 to 15. After 3 days, he was successfully weaned from ECMO and underwent 2 sessions of intensive HBO therapy. Laboratory test results at 3 days after using ECMO are shown in Table 1. The patient was weaned off the ventilator 2 days later and then transferred to a general care ward.

DISCUSSION

The affinity of CO for hemoglobin is approximately 200-fold greater than that of oxygen.² As a result, exposure to relatively low levels of CO can induce the formation of carboxyhemoglobin (COHb). COHb formation causes hypoxemia and impedes peripheral oxygen utilization by shifting the oxyhemoglobin dissociation curve to the left.¹⁰ CO also interrupts cellular respiration.³ This leads to an oxidative stress response⁴ and the production of reactive oxygen species⁵, which induces inflammation through multiple

pathways.¹ Consequently, CO poisoning results in various clinical manifestations, including neuropsychiatric impairment, myocardial dysfunction, respiratory failure and death. The signs and symptoms of CO poisoning are highly variable, depending on the acuity and duration of exposure. Although there is uncertainty regarding the level of CO exposure above which sequelae occur, it is well established that CO poisoning is confirmed by a COHb level greater than 2% in non-smokers and 9% in smokers.¹⁵

Worsening hypoxia from CO poisoning may cause severe respiratory failure. Acute respiratory distress syndrome, acute pulmonary edema and other acute lung injuries have been documented in many studies. Myocardial abnormalities due to CO toxicity have also been widely described. Although the cause of cardiovascular manifestations remains unclear, myocardial injury caused by impaired oxygen utilization, rather than by the absence of an oxygen supply, may be responsible for cardiac dysfunction.¹⁶ Satran et al.⁶ reported a 37% incidence of myocardial injury, assessed by biomarkers or electrocardiogram changes, among 230 patients with moderate to severe CO poisoning. Recently, Kao et al.¹⁷ reported a 59% incidence of cardiomyopathy and 2 cases of cardiogenic death (one due to cardiac arrest, and the other due to arrhythmia) among 81 patients with severe CO poisoning who were treated with mechanical ventilation-HBO therapy. Additionally, Kao et al.¹⁷ and Henry et al.¹⁸ identified the negative prognostic value of myocardial injury for long-term mortality for severe CO poisoning. Statistically, the standardized mortality ratio was 3.0, indicating that this group was 3 times more likely to die during the follow-up period.¹⁸

Traditionally, short-term management with high-flow

or 100% oxygen has been considered as the standard initial rescue strategy, as it is safe, readily available and economical.¹ However, if normobaric oxygen cannot maintain satisfactory arterial oxygen levels in patients who are too unstable to undergo HBO therapy, prolonged respiratory support with ECMO could be considered for patients with severe, but potentially reversible, respiratory and cardiac failure. This was particularly effective in our case, where life-threatening cardiogenic pulmonary edema caused by stunned myocardium and ischemic changes of cardiac enzymes were evident. In the studies by Kao et al.¹⁷ and Henry et al.,¹⁸ conventional mechanical ventilation and HBO therapy were used as the major therapeutic strategies. Most hospitals do not have a 24-hour HBO chamber, and mechanically ventilated CO-poisoned patients must be transferred to a specialty HBO center.

To the best of our knowledge, only one study has reported on extracorporeal support of a patient with severe CO poisoning, that by Maureen et al. in 2000.¹⁹ They concluded that it was possible to use extracorporeal lung assistance to treat a patient with severe CO poisoning and shock. Their patient had suffered from concurrent acute respiratory distress syndrome, which has been well-documented as an ECMO application,²⁰ and cardiovascular collapse. Compared to their patient, our patient manifested a more disastrous clinical presentation, with myocardial stunning (LVEF = 30%) and acute respiratory failure ($\text{PaO}_2/\text{FiO}_2 < 60$) that was precipitated by CO poisoning-induced pulmonary edema. Interestingly, both cases had impressive responses to ECMO, with improved arterial oxygenation and weaning from the ECMO circuit after approximately 3 days. Our patient received HBO therapy twice, which led to progressive improvements in cardiac markers and myocardial function. His consciousness recovered dramatically after ECMO, leading to a decreased total number of HBO therapy sessions.

While this intriguing case presented here was successfully treated, it does raise some interesting questions. First, the availability of ECMO compared to HBO might be an important issue. Although strong evidence is lacking to evaluate the advantage of ECMO availability, there is growing evidence in the literature emphasizing the feasibility of portable extracorporeal assistance for patients with cardiopulmonary failure in primary medical care centers. Arlt et al.²¹ and Haneya et al.²² have reported that the portable sizes and smaller weights of ECMO devices enable their use for critically ill patients, who then have a chance to reach a center of maximum medical care, including an HBO center. A British study shows

that this strategy is also likely to be cost-effective.²³ Thus, ECMO for patients while being transferred for specialized treatment, regardless of the patient's current location, can be carried out safely and cost-effectively.

Second, the association between ECMO and improved neurologic function is uncertain. The use of HBO has been classically looked at primarily in the setting of preventing delayed neurologic sequelae (DNS) in CO poisoning. Although the effect of ECMO on cerebral blood flow or oxygenation metabolism is controversial,^{24,25} the prevention of or rescue from neurologic dysfunction has never been previously reported as an indication for ECMO. While the use of ECMO for patients with severe, but potentially reversible, respiratory failure could be a rescue strategy, nonetheless, we need more well-designed studies of ECMO compared to HBO in the context of DNS.

Emergency application of ECMO for CO poisoning-related severe hypoxemia and cardiovascular collapse in adults has rarely been reported. We believe that ECMO was instrumental in saving our patient's life; nonetheless, we should be careful regarding any inferences made from single case reports. We hope that our clinical success promotes the application of ECMO and reminds clinicians of the rescue role for ECMO in the absence of alternative treatment strategies.²⁶

REFERENCES

1. Lindell K. Carbon monoxide poisoning. *N Engl J Med*. 2009;360:1217-1225.
2. Thom SR. Carbon monoxide pathophysiology and treatment. In: Neuman TS, Thom SR, eds. *Physiology and medicine of hyperbaric oxygen therapy*. Philadelphia: Saunders Elsevier, 2008;321-347.
3. Alonso JR, Cardellach F, Lopez S, Casademont J, Mir O. Carbon monoxide specifically inhibits cytochrome c oxidase of human mitochondrial respiratory chain. *Pharmacol Toxicol*. 2003;93:142-146.
4. Cronje FJ, Carraway MS, Freiburger JJ, Suliman HB, Piantadosi CA. Carbon monoxide actuates O(2)-limited heme degradation in the rat brain. *Free Radic Biol Med*. 2004;37:1802-1812.
5. Thom SR, Bhopale VM, Han ST, Clark JM, Hardy KR. Intravascular neutrophil activation due to carbon monoxide poisoning. *Am J Respir Crit Care Med*. 2006;174:1239-1248.
6. Satran D, Henry CR, Adkinson C, Nicholson CI, Bracha Y, Henry TD. Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. *J Am*

- Coll Cardiol. 2005;45:1513-1516.
7. Hopkins RO, Weaver LK. Cognitive outcomes 6 years after acute carbon monoxide poisoning. *Undersea Hyperb Med.* 2008;35:258.
8. Grieb G, Groger A, Bozkurt A, Stoffels I, Piatkowski A, Pallua N. The diversity of carbon monoxide intoxication: medical courses can differ extremely-a case report. *Inhal Toxicol.* 2008;20:911-915.
9. Barges L, Vaylet F, Le Bever H, L'Her P, Carsin H. Respiratory dysfunction in burned patients. *Rev Mal Respir.* 2005;22:449-460.
10. Ernst A, Zibrak JD. Carbon monoxide poisoning. *N Engl J Med.* 1998;339:1603-1608.
11. Weaver LK, Howe S, Hopkins R, Chan KJ. Carboxy-hemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. *Chest.* 2000;117:801-808.
12. Juurlink DN, Buckley NA, Stanbrook MB, Isbister GK, Bennett M, McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev.* 2005;1:CD002041.
13. Weaver LK, Hopkins RO, Chan KJ, Churchill S, Elliott CG, Clemmer TP, Orme JF Jr, Thomas FO, Morris AH. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med.* 2002;347:1057-1067.
14. Thom SR, Taber RL, Mendiguren II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae following carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. *Ann Emerg Med.* 1995;25:474-480.
15. Carbon monoxide - poisoning prevention clinical education: Centers for Disease Control and Prevention, 2009. (Accessed June 7, 2009, at <http://www2a.cdc.gov/phtn/webcast/copoisonprev>.)
16. Tritapepe L, Macchiarelli G, Rocco M, Scopinaro F, Schillaci O, Martuscelli E, Motta PM. Functional and ultrastructural evidence of myocardial stunning after acute carbon monoxide poisoning. *Crit Care Med.* 1998;26:797-801.
17. Kao HK, Lien TC, Kou YR, Wang JH. Assessment of myocardial injury in the emergency department independently predicts the short-term poor outcome in patients with severe carbon monoxide poisoning receiving mechanical ventilation and hyperbaric oxygen therapy. *Pulm Pharmacol Ther.* 2009;Apr 22 [Epub ahead of print].
18. Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI, Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. *JAMA* 2006;295:398-402.
19. McCunn, M, Reynolds HN, Cottingham CA, Scalea TM, Habashi NM. Extracorporeal support in an adult with severe carbon monoxide poisoning and shock following smoke inhalation: a case report. *Perfusion.* 2000;15:169-173.
20. International Summary of ECLS Registry, January 2005. Ann Arbor, MI: Extracorporeal Life Support Organization.
21. Arlt M, Philipp A, Zimmermann M, Voelkel S, Amann M, Bein T, Müller T, Foltan M, Schmid C, Graf B, Hilker M. Emergency use of extracorporeal membrane oxygenation in cardiopulmonary failure. *Artif Organs* 2009;33:696-703.
22. Haneya A, Philipp A, Foltan M, Mueller T, Camboni D, Rupperecht L, Puehler T, Hirt S, Hilker M, Kobuch R, Schmid C, Arlt M. Extracorporeal circulatory systems in the interhospital transfer of critically ill patients: experience of a single institution. *Ann Saudi Med* 2009;29:110-114.
23. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, Hibbert CL, Truesdale A, Clemens F, Cooper N, Firmin RK, Elbourne D; CESAR trial collaboration. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomized controlled trial. *Lancet* 2009;374:1351-1363.
24. Iijima T, Back T, Hossmann KA. Effect of extracorporeal life support on cerebral blood flow, metabolism and electrophysiology in normothermic cats. *Intensive Care Med.* 1995 Jan;21:38-44.
25. Ejike JC, Schenkman KA, Seidel K, Ramamoorthy C, Roberts JS. Cerebral oxygenation in neonatal and pediatric patients during veno-arterial extracorporeal life support. *Pediatr Crit Care Med.* 2006;7:154-158.
26. Egan TM, Duffin J, Glynn MF, Todd TR, DeMajo W, Murphy E, Fox L, Cooper JD. Ten year experience with extracorporeal membrane oxygenation for severe respiratory failure. *Chest.* 1988;94:681-687.