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Extracorporeal Membrane Oxygenation for Respiratory Failure

TOSHIHARU YAMAGISHI,[1] SUSUMU ISHIKAWA,[1] AKIO OTAKI,[1] YOSHIMI OTANI,[1] TORU TAKAHASHI,[1] YASUSHI SATO,[1] ICHIRO YOSHIDA,[1] FUMIO KUNIMOTO,[2] KENICHI ARAI,[2] AND YASUO MORISHITA[1]

[1] Second Department of Surgery, Gunma University School of Medicine and
[2] Intensive Care Unit, Gunma University Hospital, 3-39-15 Showa-machi, Maebashi, Gunma, 371 Japan

Abstract: We report herein our experience with extracorporeal membrane oxygenation (ECMO) for respiratory failure over a 3-year period. ECMO was employed in seven patients: in five for respiratory failure caused by adult respiratory distress syndrome (ARDS), Goodpasture's syndrome, hypoxia after ventricular septal defect closure, interstitial pneumonia, or lung metastasis from choriocarcinoma; and in two for tracheal obstruction. Nafamostat mesilate was used as the main anticoagulant with a small amount of heparin. The period of ECMO support for the five patients with respiratory failure ranged from 54 to 251 h, with an average time of 125 h. Five of the seven patients were able to be weaned from ECMO, and the two who had tracheal obstruction survived. The other three patients who were weaned from ECMO died of underlying diseases or complications 1–25 days after weaning. The complications which occurred during ECMO support were an abnormal electroencephalogram, multiple organ failure, and mediastinitis. Thus, we conclude that ECMO needs to be induced early to obtain a better outcome in patients with respiratory failure, and that it is particularly effective for transient airway obstruction.

Key Words: extracorporeal membrane oxygenation (ECMO), respiratory failure, ECMO criteria, nafamostat mesilate

Introduction

Extracorporeal membrane oxygenation (ECMO) has been used for the treatment of respiratory failure. However, although it has been successfully employed in cases of pediatric respiratory distress, the results have not always been satisfactory for adults, and therefore criteria for ECMO are not yet established. We report herein our 3-year experience with ECMO, highlighting the problems we encountered in its use.

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Patients and Methods

Since the beginning of November, 1990, ECMO has been employed in the treatment of seven patients ranging in age from 5 to 69 years, with an average age of 37 years (Table 1). There were four males and three females. Five patients had respiratory failure and two had tracheal obstruction. The respiratory failure was caused by adult respiratory distress syndrome (ARDS), Goodpasture's syndrome, hypoxia after ventricular septal defect closure, interstitial pneumonia, or lung metastasis from choriocarcinoma. The criteria for ECMO induction were: an arterial oxygen saturation (Sao_2) of less than 95% for at least 2 h at an inspired oxygen fraction (FIo_2) of 1.0 at a positive end-expiratory pressure (PEEP) of 5 cmH_2O or greater, a peak airway pressure of more than 40 cmH_2O, and no signs of recovery despite maximal medical therapy. The mean arterial oxygen pressure (Pao_2) at the time of ECMO induction was 60 mmHg, with a range of 53–76 mmHg, and the mean PEEP was 8.6 cmH_2O in the five patients with respiratory failure (Table 2). The tidal volume of these patients was 10%–15% of the estimated total lung capacity. The period of ECMO support for the five patients with respiratory failure ranged from 54 to 251 h, with an average time of 125 h. In the patients with tracheal obstruction, an intratracheal stent tube was inserted under ECMO support.

The ECMO circuit consisted of drainage and return cannulas, a blood reservoir, a membrane oxygenator (Menox AL-4000, Kuraray, Tokyo, Japan), and a roller pump (Stockert, Cobe, Lakewood, CO, USA). Venoarterial bypass circuits were used in four patients and venovenous bypass circuits in three. Nafamostat

Table 1. The type of circuit and duration of extracorporeal membrane oxygenation (ECMO) in the seven patients

Case	Age	Sex	Diagnosis	Circuit	Duration
1	52	M	ARDS	V-A	112 h
2	8	F	Goodpasture's syndrome	V-A	251 h
3	5	M	Hypoxia after VSD closure	V-V	110 h
4	55	M	Interstitial pneumonia, renal failure	V-A	98 h
5	32	F	Lung metastasis from choriocarcinoma	V-A	54 h
6	40	M	Tracheal obstruction from adenocarcinoma	V-V	105 min
7	69	F	Tracheal stenosis from old tuberculosis	V-V	176 min

ARDS, adult respiratory distress syndrome; VSD, ventricular septal defect; V-A, venoarterial bypass; V-V, venovenous bypass

Table 2. Blood gas values under mechanical ventilation at the time of ECMO induction

Case	FIo_2	PEEP (cmH_2O)	pH	$Paco_2$ (mmHg)	Pao_2 (mmHg)	Sao_2 (%)
1	1.0	10	7.41	58	55	88
2	1.0	10	7.48	35	61	92
3	1.0	5	7.46	25	53	89
4	1.0	10	7.22	45	54	79
5	1.0	8	7.35	31	76	95
mean	—	8.6	7.38	39	60	89

FIo_2, inspired oxygen fraction; PEEP, positive end-expiratory pressure; $Paco_2$, arterial carbon dioxide pressure; Pao_2, arterial oxygen pressure; Sao_2, arterial oxygen saturation

mesilate was infused at a rate of 10–50 mg/h with heparin 200–300 units/h to maintain a systemic activated coagulation time of about 200 s.

Results

Of the seven patients, five were able to be weaned from ECMO, including the two who had experienced tracheal obstruction, both of whom survived (Table 3). Thus, three of the five patients with respiratory failure were able to be weaned from ECMO; the period of ECMO support ranged from 98 to 251 h, with an average time of 153 h. However, all of these three patients died of underlying diseases or complications 1–25 days after weaning from ECMO, after a mean period of 10 days. The complications which developed during ECMO support were: an abnormal electroencephalogram (EEG), multiple organ failure, and mediastinitis. No bleeding originating from the anticoagulant therapy occurred. In the patient with an abnormal EEG (patient 2), slow waves appeared on the 3rd day after the induction of ECMO, and burst and suppression waves on the 10th day.

Figure 1 shows the clinical course of patient 4. A blood gas analysis prior to ECMO induction showed a Pao_2 of 54 mmHg, an SaO_2 of 79%, and a mean arterial CO_2 pressure ($Paco_2$) of 45 mmHg at an FIo_2 of 1.0 and a PEEP of 10 cmH_2O. On the 3rd day, the $Paco_2$ increased to 74 mmHg, following which a high-frequency jet ventilator was utilized for 6 days. Oxygenation was improved on the 5th day, after which

Table 3. Patient outcome

Case	ECMO weaning	Complications during ECMO	Result	Cause of death	Survival after ECMO
1	No	MOF	Died	MOF	—
2	Yes	Abnormal EEG	Died	Lung re-bleeding	21 h
3	Yes	Mediastinitis	Died	Sepsis	5 days
4	Yes	—	Died	Respiratory failure	25 days
5	No	—	Died	Rupture of liver metastasis	
6	Yes	—	Alive	—	—
7	Yes	—	Alive	—	—

MOF, multiple organ failure; EEG, electroencephalogram

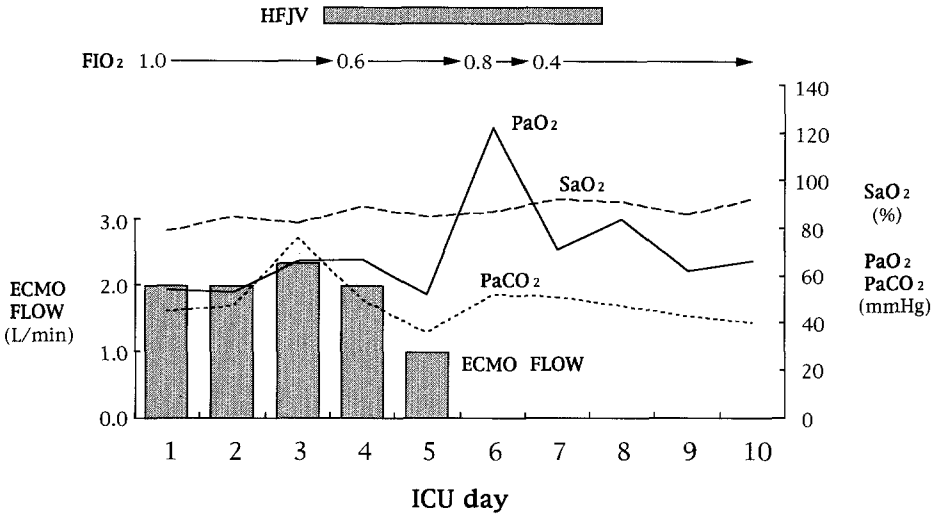

Fig. 1. Clinical course of patient 4. *ECMO*, extracorporeal membrane oxygenation; *FIo_2*, inspired oxygen fraction; *Pao_2*, arterial oxygen pressure; *$Paco_2$*, arterial carbon dioxide pressure; *Sao_2*, arterial oxygen saturation; *HFJV*, high-frequency jet ventilation

ECMO could be discontinued. The maximum flow and the period of ECMO were 2.4 l/min, with an index of 1.3 l/min per m^2, being 27% of the cardiac output, and 98 h, respectively. On the 10th day, the Pao_2 was 66 mmHg, $Paco_2$ 40 mmHg, and Sao_2 92% at an FIo_2 of 0.4. Renal failure, which was present prior to ECMO support, necessitated hemodialysis with a large amount of heparin (500–1,500 units/h) and a small amount of nafamostat mesilate (10 mg/h). No complications occurred during the ECMO perfusion.

Discussion

ECMO is principally indicated for patients with potentially reversible lung dysfunction,[1,2] the criteria for which according to Gattinoni et al.[3] are as follows:

1. For fast entry: a Pao_2 of less than 50 mmHg for more than 2 h when measured at an FIo_2 of 1.0 at a PEEP of 5 cmH_2O or greater.
2. For slow entry: after 48 h of maximal medical therapy, a Pao_2 of less than 50 mmHg for more than 12 h when measured at an FIo_2 of 0.6 or greater, at a PEEP of 5 cmH_2O or greater, with a right-to-left shunt greater than 30% of the cardiac output.

However, we believe that these criteria are too restrictive because they do not take into account the fact that high peak airway pressure,[4,5] high FIo_2,[6] and repeated hyperinflation[7] contribute to pulmonary injury. It has been shown that high inspiratory positive pressure breathing of 30 cmH_2O or greater induces pulmonary edema within 1 h in rats.[4,5] When 100% oxygen is given at normobaric pressures, damage to the lung occurs which may be reversible if exposure to hyperoxia is discontinued after 24–48 h.[6] Moreover, repeated hyperinflation reduces lung compliance.[7] The best respiratory treatment is to support gas exchange without incurring further damage to the lung.[3] To avoid these noxious factors, ECMO should be induced earlier, especially considering that 100% oxygen, which means an FIo_2 of 1.0, with a high peak airway pressure is very likely to inflict irreversible damage to the lung within several hours. Egan et al.[2] described that their objective after instituting ECMO was to reduce the FIo_2 to 0.5 or less, the PEEP to 5 cmH_2O, and the peak airway pressure to less than 40 cmH_2O. Gattinoni et al.[3] also reported that low-frequency positive pressure ventilation caused less damage to the lungs than continuous positive pressure ventilation. The early induction of ECMO and "resting" the lung are important to limit damage. With this in mind, we tried inducing ECMO early, before the above-mentioned criteria were met. The mean Pao_2 of our patients with respiratory failure was 60 mmHg at an FIo_2 of 1.0 with 5–10 cmH_2O PEEP at the time of ECMO induction. In fact, in patients 2, 4, and 5, ECMO was initiated before the final diagnosis of respiratory failure was made.

In our patients, the FIo_2, peak airway pressure, and respiration rates decreased relatively easily after ECMO induction, but it was difficult to maintain a PEEP of less than 10 cmH_2O, probably due to the low perfusion of ECMO. Soeter et al. reported that brachial artery perfusion on ECMO requires 45% of the cardiac output.[8] In our patient 4, because the ECMO perfusion was 27% of the cardiac output, respiration by his own lungs was needed. Pulmonary edema might have occurred, but a low PEEP helped protect against this eventuality.[4] In fact, a PEEP of less than 10 cmH_2O is likely to be beneficial.

Complications which may occur during ECMO, apart from technical or mechanical problems, generally

include bleeding, embolism and thrombosis, infecion, and renal failure.[2] Bleeding is the most common complication due to the anticoagulants and/or the decrease in the platelet count.[1] Intracranial hemorrhage and lung hemorrhage are often critical. We used nafamostat mesilate as the main anticoagulant with a low dose of heparin, which prevented massive bleeding during ECMO. Seizure is a major complication in infants, with an associated survival rate of only 69%.[1] In our patients, the major cause of death was the underlying disease. In fact, a positive correlation between mortality and the number of failing organs has been reported.[3] Thus, treatment for underlying diseases and additional organ failure, and the timely induction of ECMO are important to obtain better results.

According to some reports, venoarterial bypass significantly reduced pulmonary perfusion, which led to pulmonary infarction and decreased the possibility of lung repair;[9,10] however, no pulmonary infarction occurred in our patients. On the other hand, the venovenous bypass circuit is safe and sufficient for oxygenation and CO_2 removal in patients who need only respiratory assist. Therefore, patients who require insertion of an intratracheal stent tube under ventilatory standstill are good candidates for the transient use of ECMO.

The findings of this analysis led us to conclude that:

1. Peak airway pressure, the duration of exposure to high FIo_2, and blood gas analysis data should be taken into account when determining the induction criteria for ECMO therapy in patients with respiratory failure.
2. The use of nafamostat mesilate allows the amount of heparin needed to be reduced.
3. ECMO was found to be an effective means of treatment for transient airway obstruction.

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