Clinical application of extracorporeal membrane oxygenation in children with refractory cardiopulmonary failure

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Brief report

Background: **This study aimed to discribe the experience in supporting children with refractory cardiopulmonary failure with extracorporeal membrane oxygenation (ECMO).**

Methods: **We retrospectively reviewed 12 children with refractory cardiopulmonary failure supported with ECMO from February 2009 to August 2015 in the Pediatric Intensive Care Unit (PICU), Children's Hospital, Zhejiang University School of Medicine.**

Results: **Seven of the 12 patients were weaned successfully from ECMO and dischaged from the hospital, with a survival rate of 58.3% (7/12). Among them, five patients had acute fulminant myocarditis (AFM). Complications during ECMO included hemorrhage, hemolysis, thrombosis, acute kidney injury, and secondary hematogenous infection. During 1-24 month follow-up, the seven surviving patients recovered with normal cardiopulmonary function.**

Conclusion: **ECMO is useful for supporting children with refractory cardiopulmonary failure, especially for treatment of AFM.**

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Key words: **acute fulminant myocarditis; acute respiratory distress syndrome; extracorporeal membrane oxygenation**

Introduction

Extracorporeal membrane oxygenation (ECMO) is an extracorporeal method for improving functions of both the heart and lungs. During ECMO, a tube carries blood from the right side of the heart then pumps it through an artificial lung where it picks up oxygen. The oxygen-rich blood is then passed back into the person's blood system. Therefore, the circulatory blood volume and adequate oxygen supply can be maintained to meet the requirements of important organs in patients with cardiopulmonary arrest; this provides rest for the patient's cardiopulmonary system.[1,2] This study aimed to discribe our experience of using ECMO support in children with refractory cardiopulmonary failure.

Methods

This study was approved by the Ethics Committee of Children's Hospital of Zhejiang University School of Medicine. Written informed consent was obtained from the patients' parents.

We retrospective reviewed the clinical records of 12 children with acute cardiopulmonary failure in the Pediatric Intensive Care Unit (PICU), Children's Hospital, Zhejiang University School of Medicine, from February 2009 to August 2015. They included nine boys and three girls aged from 1 to 13 years (median, 7 years) with a weight range of 12-62 kg (mean, 23.5 kg). The ECMO support duration ranged from 70 to 569 hours, averaging 164.1 hours. Seven of the 12 patients had acute fulminant myocarditis (AFM), one had anaphylactic shock after antibiotic treatment,[3] and four had acute respiratory distress syndrome (ARDS) caused by severe pneumonia. Pediatric Critical Illness Scores for the patients were 66-74, with a mean value of 69.8. Two children (cases 3 and 5) suffered a cardiac arrest and received ECMO and cardiopulmonary resuscitation (CPR) simultaneously (Table 1). The twelve patients were refractory to other supportive therapies including mechanical ventilation and vasoactive medications. AFM patients were given large doses of vasoactive drugs, including adrenaline (0.3-1 μg/kg/min), dopamine (10-15 μg/kg/min), and/or dobutamine (10-20 μg/kg/min) prior to ECMO support. All patients were supported with synchronized intermittent mandatory ventilation (SIMV) with fraction of inspiration oxygen (FiO_2) of 40%-100%, breath rate of 40-50/min, tidal volume of 5-8 mL/kg, and positive end-expiratory pressure (PEEP) of 3-17 cmH_2O

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prior to ECMO support. During treatment, the four patients with ARDS were administered a small dose of methylprednisolone (2 mg/kg/day), while the seven children with AFM received large doses of intravenous immunoglobulin (2 g/kg) and methylprednisolone (20-30 mg/kg/day).

All patients were cannulated for veno-arterial (V-A) ECMO support except case 1, who underwent veno-venous (V-V) ECMO support initially before switching to the V-A mode after 24 hours because of poor oxygenation. Heparin at a dose of 1 mg/kg was administered intravenously 3 min before ECMO cannulation and remained at a dose which maintained the activated clotting time (ACT) between 180 and 220 s. Adjusted according to hemodynamic parameters, the adjunct flow volume was kept at 50-150 mL/min/kg to ensure venous oxygen saturation >65%. FiO_2 of the air/oxygen mixture was adjusted between 40% and 60% to keep arterial oxygen saturation ≥95%. Cardiac and pulmonary function during ECMO were assessed by echocardiography, chest X-ray, blood gas analysis. When the cardiac function recovered with better ejection fraction(EF), the adjunct flow volume was gradually decreased, vasoactive medicines were adjusted, and the ACT was adequately prolonged. When the adjunct flow volume decreased to 10%-20% of the total flow volume, ECMO was tentatively stopped for 30 min. The cervical vessel was ligated, and the femoral artery and vein were repaired. One patient with AFM was treated with combined ECMO and continuous renal replacement therapy (CRRT) because of secondary acute kidney injury for 53 h.

Results

The mean duration of ECMO support in the 12 patients was 164.1 h (70-569 h). During ECMO support, the amounts of vasoactive drugs given were reduced gradually, and the heart rate, blood pressure, and oxygen saturation were improved (Table 1).

Seven patients were weaned off ECMO support successfully, who were released from the hospital. The survival rate of all the patients was 58.3% (7/12). The survival rate in AFM patients was 71.4% (5/7). Three ARDS patients died of irreversible pulmonary failure secondary to pulmonary fibrosis; two AFM patients died of continued cardiac dysfunction. The main complications observed during ECMO support included hemorrhage (7 patients, 58.3%, including six cases of suture bleeding and one of retroperitoneal hemorrhage), hemolysis (3, 25%), thrombosis (1, 8.3%), acute kidney injury (1, 8.3%) and secondary hematogenous infection with proven staphylococcus aureus (1, 8.3%). The complications of ECMO support are summarized in Table 2. During the 4-24 month follow-up, the seven surviving patients recovered with normal cardiopulmonary function.

Discussion

Severe acute refractory cardiopulmonary failure without definitive treatment is considered a life-threatening situation in the PICU, with a high mortality rate.[4,5] ECMO support was considered as an effective therapy when conventional treatments such as medication and ventilation are not efficient in these patients.[6] ECMO is a modified form of cardiopulmonary bypass that can support the heart, circulation, and lungs for days to months. ECMO can be applicated in patients with respiratory failure, sepsis, cardiac arrest, and environmental hypothermia.[7] The two approaches of ECMO, V-A and V-V, are used to alleviate cardiopulmonary and pulmonary dysfunction, respectively.[8,9] The basic indications for V-A ECMO are refractory cardiac or cardiopulmonary failure.

Table 1. Comparison of indices before and after establishing extracorporeal membrane oxygenation

Patients	Heart rate (bmp)		Systolic pressure (mmHg)		CVP (cmH_2O)		SPO_2 (%)		FiO_2 (%)		PEEP (cmH_2O)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	138	120	92	90	8	9	66	85	100	60	12	6
2	165	145	94	118	4	8	75	100	98	80	17	12
3	20	85	30	80	3	8	55	95	100	45	6	4
4	118	104	98	100	7	10	90	92	70	30	9	6
5	0	40	0	30	3	5	40	90	100	70	7	4
6	180	148	78	112	12	9	90	96	70	50	6	4
7	170	108	65	82	10	8	98	98	40	40	5	3
8	98	105	80	85	11	7	80	89	100	40	12	6
9	180	172	68	83	18	12	98	100	50	40	6	3
10	120	118	66	75	11	9	95	98	50	40	5	3
11	140	125	60	85	10	8	85	95	60	40	3	3
12	122	114	108	98	8	9	85	94	90	55	7	5

CVP: central venous pressure; SPO_2: transcutaneous oxygen saturation; bmp: beat per minute; FiO_2: fraction of inspiration oxygen; PEEP: positive end-expiratory pressure.

Table 2. Clinical data for twelve children treated with extracorporeal membrane oxygenation (ECMO)

Patients	Sex	Age	Weight (kg)	Diagnosis	PCIS	Model	Duration (h)	Complications	Outcomes
1	Male	5 y	16	ARDS	70	V-V (right femoral vein- right cephalic vein) to V-A (right femoral vein-right femoral artery)	569	Suture bleeding, hemolysis	Death
2*	Male	9 y	30	Anaphylactic shock	68	V-A (right jugular vein-right femoral artery)	64	Suture bleeding	Survival
3	Female	8 y	21	AFM cardiac arrest	74	V-A (right jugular vein-right cephalic artery), E-CPR	70	Right jugularl vein thrombosis	Death
4	Male	11 mon	12	ARDS	72	V-A (right jugular vein-right femoral artery)	289	Suture bleeding, hemolysis	Death
5	Male	15 mon	11	AFM, cardiac arrest	68	V-A (right femoral vein-right femoral artery), E-CPR	98	Suture bleeding	Death
6	Male	6 y	20	AFM	74	V-A (right jugular vein-right cephalic artery)	116	Incision bleeding	Survival
7	Male	7 y	40	AFM	70	V-A (right jugular vein-right cephalic artery), CRRT	83	Retroperitoneal hemorrhage, AKI	Survival
8	Male	2 y	14	ARDS	68	V-A (right jugular vein-right femoral artery)	258	Suture bleeding, Hemolysis	Death
9	Female	6 y	21.5	AFM	68	V-A (right jugular vein-right cephalic artery)	95	No	Survival
10	Male	13 y	62	AFM	74	V-A (right jugular vein-right cephalic artery)	72	No	Survival
11	Male	3 y	16	AFM	66	V-A (right jugular vein-right cephalic artery)	287	Secondary hematogenous infection	Surviva
12	Female	6 y	19.5	ARDS	70	V-A (right jugular vein-right cephalic artery)	90	No	Survival

AFM: acute fulminant myocarditis; V-V: veno-venous; V-A: veno-arterial; E-CPR: simultaneous ECMO and cardiopulmonary resuscitation; PCIS: Pediatric Critical Illness Score; AKI: acute kidney injury; ARDS: acute respiratory distress syndrome; CRRT: continuous renal replacement therapy. *: This case has been reported by our team previously.[3]

V-V ECMO is considered as an excellent life-saving approach for patients with acute and life-threatening respiratory failure resulting from various causes, especially ARDS.

Some patients with arrhythmia or end-organ failure do not require ECMO; however, their cardiopulmonary system may stop at any given time. Therefore, it is essential to assess the clinical condition of each patient before making any decision regarding treatment. Rescue therapies for acute respiratory failure comprise airway pressure release ventilation, continuous neuromuscular blockade, inhaled nitric oxide, and ECMO.[10] ECMO can replace the lungs in providing oxygenation and depleting CO_2. In the present study, only one patient with ARDS (25%) was successfully weaned from ECMO, the survival rate in ARDS patients was lower than those reported previously.[11,12] The discrepancy may be mainly due to the small sample size. In addition, high mortality rate in ARDS might be explained by delayed ECMO, and the optimal time for ECMO application in ARDS needs further study.

The AFM patients in our study had a higher survival rate than those reported previously.[13,14] The small sample size might explain the differences. Mortality rate due to ECMO in adults with cardiac arrest (E-CPR) reached 40%.[15] As shown above, two individuals were subjected to E-CPR and both died; this might be due to the delayed time of ECMO application and poor CPR efficiency. And an Extracorporeal Life Support Organization (ELSO) study revealed that increases mortality in individuals with heart diseases.[16] Mean ECMO duration in the AFM patients was less than 5 days (105.7 h), suggesting that short-term ECMO for AFM might have a better outcome than prolonged ECMO.

Patient complications during ECMO support were classified according to the ELSO system[17] in ECMO circuit, multi-organ, infectious, and metabolic complications. The most common ECMO complication was hemorrhage in the present study, including a case of retroperitoneal hemorrhage, which was similar with Almond et al and Zanqrillo et al's reports.[14,18] In order to prevent hemorrhage and thrombosis, heparin was administered and adjusted to maintain the activated clotting time between 180 and 220 seconds, and monitored per 4 hours; in addition, hemorrhage of the catheter site was monitored closely as well as other physical parameters such as bilateral pupils, decompression fluid and urine color, and body skin color. All patients with hemorrhage were effectively controlled after heparin dose adjustment, blood transfusion, and symptomatic treatments as needed.

ECMO is an expeditious, cost-effective tool for rapid resuscitation of patients with cardiopulmonary

failure, especially for support in the treatment of AFM. Keys to successful ECMO support include patient selection, timely intervention, thorough assessment and close monitoring, complication prevention, and valuable experience from these successful cases.

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Ethical approval: All the content was approved by the patients' parents and the Ethics Committee of Children's Hospital of Zhejiang University School of Medicine.
Competing interest: There is no conflict interest in this study.
Contributors: Yang ZH wrote the draft; Ning BT proposed and designed the study; Zhang CM, Lin R, Ye S and Liu T collected the clinic data.

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