

Extracorporeal membranous oxygenation (ECMO) in neonates and children – experiences of a multidisciplinary paediatric intensive care unit

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ABSTRACT

Extracorporeal membranous oxygenation ECMO was applied in 18 patients. All children had deep hypoxia and 80% probability of dying. Average duration of ECMO in newborns was 131 hours, and in older patients 253 hours. Seven patients were discharged from the intensive care unit (late survivors), 5 of them are in perfect somatic and mental condition.

Key words: extracorporeal membranous oxygenation, neonate, child

Introduction

Extracorporeal membranous oxygenation (ECMO) is an established treatment of neonates and children with severe yet amenable lung or heart failure. From the technical point of view it follows the same principle as the extracorporeal circulation during the by-pass surgery, but it is adapted to the long-term use. In the year 1976, Bartlett (1) presented the first group of neonates treated by the ECMO. To initiate ECMO, cannulae are placed in large blood vessels to provide access to the patient's blood. Anticoagulant drugs (heparin) are given to prevent blood clotting. The ECMO machine continuously pumps blood from the patient through a membrane oxygenator that imitates the gas exchange process of the lungs, i.e. it removes carbon dioxide and adds oxygen. Oxygenated blood is then returned to the patient. There are several forms of ECMO, the two most common of which are veno-arterial (VA) and veno-venous (VV). In both modalities, blood drained from the

venous system is oxygenated outside of the body. In VA ECMO, this blood is returned to the arterial system and in VV ECMO the blood is returned to the venous system. In VV ECMO, no cardiac support is provided.

VV ECMO can provide sufficient oxygenation for several weeks, allowing diseased lungs to heal while the potential additional injury of aggressive mechanical ventilation is avoided. It may therefore be life-saving for some patients. However, due to the high technical demands, cost, and risk of complications (such as bleeding under anticoagulant medication), ECMO is usually only considered as a last resort therapy.

ECMO in neonatology

At the beginning ECMO was most commonly used in neonatal intensive care units, for newborns in pulmonary distress.

Indications:

Patients with the following two major neonatal diagnoses require the use of extracorporeal membrane oxygenation (ECMO):

- Primary diagnoses associated with primary pulmonary hypertension of the newborn (PPHN), including idiopathic PPHN, meconium aspiration syndrome, respiratory distress syndrome, group B streptococcal sepsis, and asphyxia
- Congenital diaphragmatic hernia (CDH)

Selection criteria

- Gestational age greater than or equal to 34 weeks (relative criteria)
- Birth weight greater than or equal to 2000 g (relative criteria)
- No significant coagulopathy or uncontrolled bleeding
- No major intracranial hemorrhage (grade 1 intracranial hemorrhage is not a contra-indication)
- Mechanical ventilation for 10-14 days or less (relative criteria)
- Reversible lung injury
- No lethal malformations
- No major untreatable cardiac malformation
- Failure of maximal medical therapy

Qualifying patient criteria for extracorporeal membrane oxygenation

Qualifying criteria are applied only when

the infant has reached maximal ventilatory support of fraction of inspired oxygen $[FiO_2]$ equals 1, with peak inspiratory pressures (PIP) often as high as 35 cm H_2O .

- Alveolar-arterial (A-a) gradient of 600-624 mm Hg for 4-12 hours at sea level, which may be computed as follows (where 47 = partial pressure of water vapor):

$(A-a)(\text{Diffusing capacity } [D] \text{ of } O_2 \text{ equals atmospheric pressure} - 47 - (\text{PaCO}_2 + \text{PaO}_2))/FiO_2$

- Oxygenation index (OI) greater than 40 in 3 of 5 postductal gas determinations obtained 30-60 minutes apart, which may be computed as follows (where MAP is mean airway pressure):

$OI = (\text{MAP} \times FiO_2 \times 100) / PaO_2$

- $PaO_2 = 35-50$ mm Hg for 2-12 hours
- Acute deterioration
 - PaO_2 less than or equal to 30-40 mm Hg for 2 hours
 - pH less than or equal to 7.25 for 2 hours
 - Intractable hypotension

ECMO in paediatric patients

Indications

- Low cardiac output resulting from right, left, and biventricular failure following repair of congenital heart defect (this indication is frequent in neonates as well)
- Pulmonary vasoreactive crisis following repair of congenital heart defect leading to severe hypoxemia, low cardiac output, or both
- As a bridge to cardiac surgery in patients with serious end-organ damage resulting from profound low cardiac output related to congenital heart disease
- As a bridge to cardiac transplant
- As a bridge to recovery in temporary cardiomyopathy secondary to renal failure, myocarditis, and burns

Unlike the situation in neonates, when ECMO is considered in a paediatric patient, no clear set of inclusion or exclusion criteria exists. Evaluation of a pediatric patient for ECMO support is largely based on an assessment of the patient's condition and the institutional experience with pediatric ECMO.

Management

Pulmonary system

ECMO is used temporarily while awaiting pulmonary recovery. In the classic use of neonatal ECMO, the typical ventilator settings are FiO_2 of 0.30, PIP of 15-25 cm H_2O , a positive end-expiratory pressure (PEEP) of 3-5 cm H_2O , and intermittent mechanical ventilation (IMV) of 10-20 breaths per minute. Sometimes, a high PEEP of 12-14 cm H_2O has been used to avoid atelectasis; this has been found to shorten the bypass time in infants. Pulmonary hygiene is strict and requires frequent endotracheal suctioning, usually every 4 hours depending on secretions, and a daily chest radiograph.

Cardiovascular system

Systemic perfusion and intravascular volume should be maintained. Volume status can be assessed clinically by urine output and physical signs of perfusion and by measuring the central venous pressure and the mean arterial blood pressure. Native cardiac output can be enhanced with inotropic agents. An echocardiogram should be performed to exclude any major congenital heart anomaly that may require immediate intervention other than ECMO (i.e., obstructed total anomalous pulmonary venous connection).

Central nervous system

Central nervous system complications are the most serious and are primarily related to the degree of hypoxia and acidosis. Avoiding paralytic agents and performing regular neurologic examinations are recommended. If feasible, a head ultrasound should be obtained before beginning ECMO in a neonate. Reevaluation with serial head ultrasounds may be needed on a daily basis, especially after any major event. In patients with seizures or suspected seizures, aggressive treatment is recommended (i.e., phenobarbital).

Renal system

During the first 24-48 hours on ECMO, oliguria and acute tubular necrosis associated with capillary leak and intra-

vascular volume depletion are common because ECMO triggers an acute inflammatorylike reaction. The diuretic phase, which usually begins within 48 hours, often is one of the earliest signs of recovery. If oliguria persists for 48-72 hours, diuretics are often required to reduce edema. When renal failure does not improve, hemofiltration or hemodialysis filters may be added to the circuit.

Haematologic considerations

To optimize oxygen delivery, the patient's hemoglobin should be maintained at 120-150 using packed red blood cells (pRBCs). As a result of platelet consumption during ECMO, platelet transfusions are required to maintain platelet counts above 100. ACT should be maintained at 180-240 seconds to avoid bleeding complications.

Infection control

Strict aseptic precautions are required. The presence of infection is monitored by obtaining cultures from the circuit at least once per day. Based on institutional experience, the protocol frequency may vary. Other appropriate cultures (eg, fungal and viral) should be sent as needed.

Fluids, electrolytes, and nutrition

Patients on ECMO require close monitoring of fluids and electrolytes. The high-energy requirements should be met using hyperalimentation techniques. The patient's weight increases in the first 1-3 days on ECMO because of fluid retention.

Medications

- Doses of most inotropic medications, such as dopamine, dobutamine, and epinephrine, usually can be decreased once the patient is on ECMO.
- Diuretics, such as furosemide, may be required for mobilization of tissue fluids.
- H_2 antagonists are usually administered for a prevention of a gastrointestinal tract bleeding.
- Only minimal sedation with fentanyl, midazolam, or morphine is required after stabilization.
- Phenobarbital can be used if the patient has seizures.

- Antibiotics are given, based on institutional experience.

Complications

Mechanical complications

- Clots in the circuit are the most common mechanical complication. Major clots can cause oxygenator failure, consumption coagulopathy, and pulmonary or systemic emboli.
- Cannula placement can cause damage to the internal jugular vein, which causes massive mediastinal bleeding. Dissection of the carotid arterial intima can lead to lethal aortic dissection. It never happened in our patients.
- Air in the circuit can range from a few bubbles to a complete venous air lock. This air can originate in the dislodgement of the venous cannula, a small tear in the membrane, or high partial pressure of oxygen in the blood. A large bolus of air can be fatal.
- Oxygenator failure is defined either as decreased oxygen or carbon dioxide transfer or as presence of consumptive coagulopathy. A failing membrane should be replaced immediately.
- Cracks in the connectors and tube rupture have become less serious problems.
- Pump malfunction may be a manifestation of inadequate venous return to the pump.
- Heat exchanger malfunction can cause severe hypothermia.
- Failure of the entire circuit, including the oxygen source and oxygen blenders, may occur.
- Failure of circuit-monitoring equipment may occur.

Management of circuit failure

Immediately clamp the venous line, open the bridge, and clamp the arterial line to remove the patient from the ECMO. Since the patient is ventilator dependent, immediately bag the patient with $FiO_2=1$ or shift the patient back to pre-ECMO ventilator settings.

Complications in patients

Neurologic complications

- Seizures may occur.
- Intracranial bleeds and infarction may

be due to ligation of the carotid artery and internal jugular vein, systemic heparinization, thrombocytopenia, coagulopathies, or systolic hypertension.

Haemorrhagic complications

- Hemolysis and consumption coagulopathy may occur.
- Haemorrhage at the surgical site, cannula site, or into the site of a previous invasive procedure is a frequent complication because of systemic heparinization.
- Intrathoracic, abdominal, or retroperitoneal hemorrhage may occur.
- Decreases in platelet count occur because of decreased production, increased consumption, sequestration, or dilution.

Cardiac complications

- Myocardial stun is defined as a decrease in the left ventricular shortening fraction by more than 25% with initiation of ECMO that returns to normal after 48 hours of ECMO.
- Hypertension is a dangerous complication because of the risk of haemorrhage and stroke. Arrhythmia may occur as a result of hypoxia and electrolyte imbalance.
- Symptomatic patent ductus arteriosus may occur.
- Pericardial tamponade may occur.

Pulmonary complications

- Pneumothorax is a potential complication.
- Pulmonary haemorrhage may occur.

Renal complications

- Oliguria is commonly observed during the early part of ECMO.
- Acute tubular necrosis is observed in some patients and may require haemofiltration and/or dialysis.

Gastrointestinal tract complications

- Haemorrhage may occur as a result of stress, ischaemia, or bleeding tendencies.
- Direct hyperbilirubinemia and biliary calculi occur secondary to prolonged fasting and total parenteral nutrition (TPN), haemolysis, and diuretics.

Complications resulting from infection and sepsis

The ECMO circuit represents a large intravascular foreign body; frequent manipulation increases the risk of sepsis.

Metabolic complications

- Acidosis or alkalosis
- Hyperkalaemia or hypokalaemia
- Hyponatraemia or hyponatraemia
- Hypercalcaemia or hypocalcaemia
- Hyperglycaemia or hypoglycaemia

Drug serum concentrations

- ECMO may alter serum concentration of drugs due to increased volume of distribution.
- Caution is warranted when narrow therapeutic drugs are administered. Dose alterations may be necessary.

Weaning or trial period without extracorporeal membrane oxygenation

In patients with a principal pre-ECMO diagnosis of respiratory failure, a trial period without ECMO is scheduled if (1) the patient demonstrates adequate gas exchange and is on reasonable ventilatory settings, and (2) the patient tolerates a pump flow of 10-20 ml/kg/min with the minimum of 200 ml/min.

Morbidity

Medical morbidity

- Difficulty in establishing full oral feeding is common after ECMO decannulation. Feeding difficulty is reported in as many as one third of babies, even in the presence of normal suck and swallow reflexes.
- Somatic growth is normal in infants who survive following ECMO. Poor growth should be evaluated for another underlying cause.
- Approximately 15% of infants still require oxygen at 28 days after ECMO. These children have a higher rate of rehospitalization for pulmonary indications, particularly in the first 6 months after ECMO. These children have a slightly higher prevalence of bronchial asthma.
- Infants who survive following ECMO have a higher rate of rehospitalization for nonpulmonary and surgical conditions.

Table 1. Neonates according to principle diagnosis, immediate survival and later survival after ECMO.

Number	Principle Diagnosis	Immediate Survival (IS)	% of IS	Later Death	Later Survival (LS)	% of LS
4	CDH ¹	3	75	2	1	25
4	MAS ²	2	50	-	2	50
2	PPH ³	2	100	1	1	50
1	HMD ⁴	1	100	-	1	100
1	Septic shock	0	0	-	0	0

Summary

12		8	66.6	3	5	41.6
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¹CDH, Congenital Diaphragmatic Hernia; ²MAS, Meconium Aspiration Syndrome; ³PPH, Primary Pulmonary Hypertension; ⁴HMD, Hyaline Membrane Disease.

Table 2. Older children according to the principle diagnosis, immediate survival and later survival after ECMO.

Number	Principle diagnosis	Immediate survival (IS)	% of IS	Later death	Later survival (LS)	% of LS
1	Abscedental Pneumonia	0	0	-	0	0
2	Dilatatory Cardiomyopathie	1	50	1	1	50
1	Viral (RSV ¹) Pneumonia	0	0	-	0	0
1	Stun Heart ²	1	100	-	1	100
1	Burns	1	100	-	1	100

Summary

6		3	50	1	2	33
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¹RSV, Respiratory Sinitial Virus; ²Following the Open Heart Surgery.

- The rate of sensorineural disabilities in infants who survive following ECMO averages 6% (range, 2-18%); developmental delay occurs in 9% (range, 0-21%).

- Abnormal brainstem auditory-evoked response (BAER) with mild-to-moderate threshold elevation is seen in 25% of

children following ECMO at discharge. This condition usually resolves. Sensorineural hearing loss is documented after age 1 year in 9% (range, 4-21%) of children following ECMO.

- Routine ophthalmic examinations during ECMO are not recommended because studies in term babies

have not shown any occurrence of retinopathy. In the rare neonate with birth weight less than 2 kg in whom ECMO is used, ophthalmic examination is required prior to discharge. Some degree of cortical visual impairment has been seen after posterior brain injury. However, in the long term,

visual function has been shown to improve.

- Both clinical and electroencephalographic seizure activity is reported in 20-70% of neonates while on ECMO. Epilepsy is reported in 2% of patients at age 5 years.
- Rare neuromotor deficits range from mild hypotonia to gross motor delay and spastic quadriparesis.
- Psychosocial morbidity

Increased frequency of social problems, academic difficulties at school age, and higher rates of attention deficit disorder are reported in children who received ECMO. The ECMO procedure is dramatic and highly invasive. Families can feel isolated if no other patients are on ECMO in the same institution. At age 1 year, the stress level of the mother of an infant previously on ECMO is the same as the stress level in the family of a preterm infant. By age 5 years, the family stress level is the same as that of the family of a healthy child in whom ECMO was not used.

Table 3. Mechanical Complications Related to ECMO Support in 18 Patients.

Type of the Mechanical Adverse Event	Number
Regular Replacement of the Oxygenator	2
Rupture of the Oxygenator Membrane	3
Tubing Rupture in the Raceway of the Pump	4
Weakening of the ECMO Circuit Tube Clamp	1
Rupture of the Balloon in the Servoregulator	1
Air Entry in the ECMO Circuit	3

Ljubljana's results 1994-2005

The first patient was treated by ECMO in our multidisciplinary paediatric intensive care unit in the year 1994. In the period of 1994-2005, i.e. in 12 years, there were 18 patients who underwent this procedure; 12 (66%) newborns, 6 (35%) children ranging in age from 2 months to 2 years, and 6 children older than 2 years (table 1,2). The immediate survival means that the death occurred in the first 24 hours after the decannulation and the late survival means that it occurred after 24 hours.

The most important mechanical com-

plications are summarized in table 3, and complications in patients are presented in table 4. The immediate survival of 18 patients was higher in the group of neonates (66%) compared to 33% in the group of older patients. In summary, there were 11 patients who survived the decannulation; of these eleven patients, four patients died within 24 hours after the decannulation. Five of seven late survivors have normal mental and somatic status. One child has mild motor and cognitive disturbances, but he is attending elementary school without any problems. One child is severely handicapped.

Table 4. The most Important Clinical Complications in 18 Patients During ECMO.

Type of Clinical Complication	No. of Survivors	No. of Non- survivors
Cerebral Paroxysms	2	-
Long Lasting Cerebral Convulsions	1	1
Jitterness (Tremor)	1	-
Brain Death	-	1
Nosocomial Sepsis (Positive Blood Culture)	1	2
Acute Renal Syndrome	3	3
Intracranial Bleeding	1	1
Bleeding at the Site of Cannulas	2	2
Cardiac Arrest and Resuscitation	1	4
Arrhythmias	-	2
Pneumothorax with Drainage	2	1
Pneumomediastinum	1	2
Pneumopericardium	-	1

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