Review Article

Neonatal ECMO

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Abstract

ECMO is a technique of providing cardiac & respiratory support to sustain life. Nowadays it is being increasingly used in newborns. Respiratory ECMO is used for severe respiratory distress syndrome, pneumonia & meconium aspiration syndrome. Cardiac ECMO is used after open heart surgery, myocarditis or myopathy. There are two types of ECMO, Veno-Venous (V-V) bypass & Arterio-Venous (A-V) bypass. ECMOcan be used to bridge patients with heart failure as they await heart transplantation & as an adjunct to cardiopulmonary resuscitation. ECMO should be used in reversible diseases only after analysing various factors. Qualifying criteria for ECMO are applied only when the infant has reached maximal ventilatory support. Only babies with gestational Age > 34 weeks, Birth Weight > 2,000 grams, without major coagulopathy, with mechanical ventilation < 14 days & reversible lung disease are eligible for ECMO. Absolute contraindications include Grade 3 or 4 IVH, irreversible brain injury, lethal malformations, non-treatable congenital heart disease & significant coagulopathy. The ECMO circuit consists of a cannula to drain deoxygenated blood from the patient, a pump, an artificial lung to provide oxygenation & ventilation, heat exchanger, a second cannula to return oxygenated blood back to the patient Management during ECMO includes Oxygenation, Inotropic support, Rest Ventilation & Sedation. Complications include Bleeding, Infection, myocardial stun, neurodevelopmental problems, Pneumothorax, pulmonary haemorrhage, bronchial asthma, Sensorineural disabilities,acute tubular necrosis, Feeding difficulty, metabolic derangements, Psychosocial morbidity & Neuromotor deficits .Early initiation of ECMO, monitoring & prompt management of expected complications will improve survivalwithout severe disability.

Key words: Neonatal ECMO, Respiratory ECMO, Cardio Respiratory Support.

Introduction

Extracorporeal membrane oxygenation (ECMO) is an extracorporeal technique of providing both cardiac & respiratory supporttopersons whose heart & lungs are unable to provide an adequate amount of gas exchange to sustain life. It works by removing blood from the person's body & artificially removing carbon dioxide & oxygenating red blood cells. It was first used successfully in 1976 [1] & is nowa proven treatment for life-threatening respiratory &/or cardiac failure in adults. Nowadays ECMO is being increasingly used in newbornsfor various conditions. Overall survival rates with the use of ECMO are approximately 80% in infants with a predicted survival of 20% [2]. The survival rate for neonates is much higher than for either pediatric or adult patients due to reversibility of the disease process & absence of chronic lung & heart disease [1]. ECMO use in newborns with respiratory failure started in 1982 [3,4]. Although invasive, ECMO results in a 94% survival rate for infants who have meconium aspiration syndrome who have failed to improve despite optimal ventilatory support [5]. It is merely a support modality & does not treat the cause or primary illness [6]. Early initiation of ECMO in acute disease process would reduce hospital days & cost [7]. A recent meta-analysis conducted by the Cochrane Collaborative concluded: A policy of ECMO in mature infants with severe but potentially reversible respiratory failure results in significantly improved survival without risk of severe disability [8]. The best survival-to-hospital discharge rate is among newborns supported with ECMO for neonatal respiratory failure around 75% [9].

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Types of ECMO: 1) Respiratory ECMO in children with very severe lung disease not responding to the

usual treatment of mechanical ventilation like severe respiratory distress syndrome, pneumonia, meconium aspiration syndrome. **2) Cardiac ECMO** in children with very poor cardiac function. It is used after open heart surgery, myocarditis or myopathy. There are two types of ECMO, Veno-Venous (V-V) bypass & Arterio-Venous (A-V) bypass. In A-V ECMO the tip of the arterial catheter should be within the aortic arch & the tip of the venous catheter should be within the right atrium. In V-V ECMO the tip of the sole venous catheter should be within the right atrium pointing towards the tricuspid valve.V-V ECMO consists of a double lumen cannula which can be inserted percutaneously.Adequate oxygenation in V-V ECMO causes pulmonary vasodilation & oxygenated coronary perfusion. However it is difficult to maintain adequate cardiac support thereby requiring high dose of inotropics. A-V ECMO involves two cannulas; one infemoral or carotid artery & other in internal jugular vein.As it involves carotid artery ligation there is a possibility of brain ischemia.Because of recirculation, VV ECMO cannot support >50% of cardiac output, which limitsadequate oxygenation [10]; so A-V ECMO is preferred in cardiac failure.

Indications: ECMO is being used in newborns with primary pulmonary hypertension of the newborn (PPHN), including idiopathic PPHN, meconium aspiration syndrome, respiratory distress syndrome, group B streptococcal sepsis, asphyxia,Congenital diaphragmatic hernia (CDH).It is used to bridge patients with heart failure as they await heart transplantation or placement of a long-term circulatory support device, such as a ventricular assist device. It is also used as an adjunct to cardiopulmonary resuscitation (ECPR) [11,12].

Eligibility criteria: ECMO was originally reserved for patients who were predicted to have only 20 % chance of survival. Since it involves lot of manpower, infrastructure along with huge cost, the decision to start on ECMO should be made only in reversible diseases only after analysing various factors. Factors like oxygenation index (OI) & blood gas help in predicting the reversibility & need of ECMO. Some factors where ECMO should be considered include 1) OI ≥ 30 - 60 for 0.5- 6 hours (OI ≥ 40 on conventional ventilation, OI ≥ 50-60 on High Frequency Oscillation); 2) PaO2 <40 mmHg for > 2 hours or PaO2 < 60 mmHg for 2-12 hours despite maximal ventilatory support; 3) Acidosis & Shock, pH <7.25 due to metabolic acidosis, Raised lactate, Intractable hypotension. 4) Barotrauma: Ventilator settings exceeding: PIP>35, MAP>20, Jet PIP or HFO AMP>45; Hypercarbia with pH <7.10 for 4 hours on: PIP>35, Jet PIP or HFO AMP >45; Severe air leak unresponsive to other therapies. 5) Acute Deterioration: PaO2 <30 at a single time point or preductal SaO2 <70%. 6) Cardiovascular/Oxygen Delivery Criteria: Plasma lactate: >45 mg/dl & not improving, despite volume expansion & inotropic support, Inotropic equivalent (IE):>50 for 1 hour or >45 for 8 hours, mixed venous saturation of <55% for 60 min. (<60% for CDH patients), Rapidly deteriorating or severe ventricular dysfunction, Intractable arrhythmia with poor perfusion. Qualifying criteria for ECMO are applied only when the infant has reached maximal ventilatory support of 100% oxygen with peak inspiratory pressures (PIP) often as high as 35 cm water with alveolar-arterial (A-a) gradient of 600-624 mm Hg for 4-12 hours at sea level. **1)** Only babies with gestational Age > 34 weeks are eligible for ECMO as premature infants have high risk for intracranial haemorrhage [13,14]. However a retrospective review of early ECMO patients by [15] concluded that with improvements in diagnosis, patient care& refinement of the ECMO technique, treatment of the premature infant may become possible. **2)** Only babies with Birth Weight > 2,000 grams are eligible for ECMO [16]. The reason for this limitation is non- availability of smaller cannulas lesser than 8 French (Fr). 3) Only babies withoutmajor coagulopathy or active bleeding are eligible for ECMO, becauseongoing systemic heparinization while on ECMO increases the risk for bleeding [17]. 4) Only babies with no major intracranial hemorrhageare eligible for ECMO as Heparin use during ECMO & altered cerebral blood flow increases the risk of extending a pre-existing intracranial bleed [18,19]. 5) Only babies with mechanical ventilation less than 14 days & reversible lung disease are eligible for ECMO as prolonged exposure to high concentrations of oxygen & positive pressure ventilation leads to bronchopulmonary dysplasia (BPD) [20]. In a retrospective study the risk for developing BPD was increased 11.4 fold when ECMO was initiated after prolonged assisted ventilation [21].

Contraindications: The absolute contraindiacations includeGrade 3 or 4 IVH, severe & irreversible brain injury, lethal malformations or congenital anomalies, significant non-treatable congenital heart disease, severe & irreversible lung, liver or kidney disease, significant coagulopathy or uncontrolled bleeding. The relative contraindications includegestational age < 34 weeks [22], birth weight < 2 kg, more than 14 days of

mechanical ventilation, IVH Grade 1-2, disease states with a high probability of a poor prognosis, CDH if pre-ductal PaO2 never > 70 mmHg or PaCO2 never < 80mmHg, Disseminated herpes.

Pre ECMO investigations: The usual work up done prior to initiation of ECMO include Chest X-Ray (CXR), Complete blood count, Differential count, INR, APTT, Fibrinogen, Electrolytes, Urea,Creatinine, Liver function test , Neurosonogram, Cardiac Echo, Crossmatch.

ECMO Circuit, Cannulation and Conduct: The ECMO circuit consists of a cannula to drain deoxygenated blood from the patient, a pump, an artificial lung to provide oxygenation & ventilation, heat exchanger, a second cannula to return oxygenated blood back to the patient [16]. Blood is drained into the ECMO by gravity, pumped into the membrane for gas exchange & returned to the patient after re-warming it to body temperature. Cannulation sites depend on age, size & indication. Venous cannulation sites include the internal jugular veins & femoral veins whereas arterial cannulation sites include the carotid arteries & femoral arteries .Intrathoraciccannulation of the right atrium and aorta is commonly used in children who have undergone recent cardiac surgery via a sternotomy. Various pumps (roller or centrifugal) & oxygenators (polymethylpentene hollow-fiber membrane or silicone membrane) are available. The roller pump causes less hemolysis and is used for neonatal ECMO. The venous reservoir is used with the roller pump for neonatal ECMO. Three types of commercial artificial lungs are available: bubble, membrane, and hollow-fiber devices. The heat exchanger warms the blood using a countercurrent mechanism. Blood is exposed to warm water that circulates within metal tubing.ECMO settings are adjusted to provide mechanical ventilation with low-tidal volumes & inspiratory pressure to avoid ventilation-induced lung injury & oxygen toxicity. The ECMO circuit is primed with the freshest blood available. The acid-base balance & blood gas of the primer are adjusted appropriately.

Management during ECMO: 1) Oxygenation: Very high PaO2 can occur with high flow VA bypass, flow and/or sweep gas are adjusted to keep the PaO2 under 100. If systemic oxygen delivery is not adequate (venous saturation less than 65% with elevated blood lactate levels) the pump flow is increased until perfusion is adequate. 2) Inotropes: Critically ill newborns placed on VA ECMO are often on high doses of inotropes & rapid increase in blood pressure with increased risk for intracranial haemorrhage can occur. Hence inotropy should be titrated down appropriately. Alternatively, as these drugs are titrated down, resistance falls & systemic pressure may fall proportionately. If the systemic perfusion pressure is inadequate pressure can be increased by adding blood or low doses of pressor drugs.3) Ventilation: Typical rest settings for a neonate on ECMO are, FiO2 0.21-0.3, PIP (15-22), PEEP (5-8), Rate (12-20), I-time (0.5sec). Using low PEEP may lead to alveolar collapse and increased edema. However, if the PEEP is set too high, venous return may be impaired. Rest settings are achieved in some centers with high frequency ventilation. 4) Air Leak: Air leak will usually resolve with decreasing ventilation settings like low CPAP settings or even capping-off the Endo tracheal tube for some time. Re-expanding the collapsed lung should be done gently over some period of time depending on the severity of the air leak (usually 24-48 hrs). 5) Sedation: Light sedation like narcotic & benzodiazepines may be used. 6) Bleeding: Neurosonogram should be performed every 24hrs for at least the first 5 days in stable neonates on ECMO.

Safety devices and monitors: Air bubble detectors identify microscopic air bubbles in the arterialized blood & automatically turn off the blood pump. Arterial line filters between the heat exchanger & the arterial cannula traps air, thrombi & other emboli. Pressure monitors placed before & after the oxygenator monitors for a dangerous rise in circuit pressure which can occur with thrombosis of the oxygenator or occlusion of the tubing or cannulae. A continuous venous oxygen saturation monitor & temperature monitor are other important safety features.

Complications: Since babies requiring ECMO are very sick many complications have been reported after initiation of ECMO, most of them are due to underlying disease process prior to ECMO.

Bleeding: Ongoing systemic Heparinisationtoprevent clots from forming within the ECMO increases the risk of bleeding.Hemolysis and consumption coagulopathy may occur. Hemorrhage at the surgical site, at the cannula site, Intrathoracic, abdominal, or retroperitoneal hemorrhage may occur. Thrombocytopenia occurs because of decreased production, increased consumption, sequestration, or dilution. Factor XIIa inhibitory antibody is now shown to provide thromboprotection in extracorporeal circulation without

increasing bleeding risk [23].

Infection: Sincetubes are inserted into blood vessels there is a high risk of infection on ECMO for which appropriate antibiotics are to be used.Moreover as frequent blood transfusions arerequired there is a risk of disease from donor blood.

Neurological: Intracranial bleeding, ischaemia or seizure activityoccur in up to 30 % of patients. Intracranial bleeds and infarction may be due to ligation of the carotid artery& internal jugular vein, systemic heparinization, thrombocytopenia, coagulopathies, or systolic hypertension. 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.Stenosis was considered as an adverse effect secondary to tying (ligation) of the carotid artery. However recent studies suggest there is no increased evidence of left-sided neurological damage in those with right carotid artery ligation.

Cardiac: Cardiac complications include myocardial stun, which is 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. Other complications include hypertension with a risk of haemorrhage& stroke, arrhythmia due to hypoxia &electrolyte imbalance, symptomatic patent ductusarteriosus & pericardial tamponade.

Neurodevelopmental: Upto 25 % of ECMO survivors have neurodevelopmental problems ranging from mild learning difficulties to severe neurological impairment which is comparable to those babies treated conventionally without ECMO.

Respiratory: The UK ECMO trial suggested increased respiratory problems & requirement for supplemental oxygen or respiratory medications, particularly bronchodilators in some children who had required respiratory ECMO.Pneumothorax is a potential pulmonary complication, along with pulmonary hemorrhage. Approximately 15% of infants still require oxygen at 28 days after ECMO & have a slightly higher prevalence of bronchial asthma.

Sensorineural Disabilities: About 6% of ECMO survivors havesensorineuraldisabilities ;developmental delay occurs in 9% ; Abnormal brainstem auditory-evoked response (BAER) with mild-to-moderate threshold elevation is seen in 25% of children following ECMO at discharge. Sensorineural hearing loss is documented after age 1 year in 9%.

Renal: Oliguria &acute tubular necrosis is observed in some patients and may require hemofiltration and dialysis.Neonates who suffer acute kidney injury in association with ECMO are at increased risk for developing chronic kidney disease (CKD) and/or hypertension.

Gastro Intestinal Tract: GI tract complications include hemorrhage, due to stress, ischemia, or bleeding tendencies. Direct hyperbilirubinemia&biliary calculi may occur secondary to prolonged fasting, total parenteral nutrition (TPN), hemolysis, & diuretics. 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. Experiments on neonatal animals showed that ECMO treatment leads to apoptosis of enterocytes, damage of the intestinal mucosal barrier & bacterial translocation which explains greater severity of systemic inflammatory response syndrome in neonates [24].

Metabolic: Disturbances in pH, potassium, sodium, calcium & glucose occur throughout the ECMO course.

Psychosocial morbidity: Increased frequency of social problems, academic difficulties at school age& higher rates of attention deficit disorder have been observed in children who received ECMO.

Neuromotor deficits: Neuromotor deficits range from mild hypotonia to gross motor delay & spastic quadriparesis. However studies have proven that the neurodevelopmental outcome of the ECMO cohort is comparable to other high-risk neonatal groups& similar to neonates with the same condition managed conventionally.

Conclusion: With advances in critical care, ECMO proves to be a promising therapy for cardiac & respiratory support to sustain life in sick infants. Early initiation of ECMO, religious monitoring& prompt management of expected complications will improve survivalwithout severe disability.

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