Veno-Venous Extracorporeal Membrane Oxygenation for Continuous Renal Replacement in a Neonate with Propionic Acidemia

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Abstract: The usual indications for extra corporeal membrane oxygenation (ECMO) are for respiratory or cardiac failure. Although continuous renal replacement therapy (CRRT) is frequently used when patients are on ECMO, the need for CRRT as the primary indication for ECMO is rare. A case of a neonate placed onto veno-venous ECMO for the use of CRRT to treat hyperammonemia from propionic acidemia is presented. Keywords: veno-venous extracorporeal membrane oxygenation, continuous renal replacement, propionic academia, neonate, renal failure, hyperammonemia.

The Extracorporeal Life Support registry has over 44,000 cases with 67% being for pulmonary and 25% for cardiac support indications (1). During courses on extra corporeal membrane oxygenation (ECMO), patients are often placed onto continuous renal replacement therapy (CRRT) to aid in fluid and waste product removal. Occasionally, it will be performed to remove specific substances, such as ammonia. Hemodialysis driven by venoarterial ECMO has been reported to remove ammonia rapidly in a case report of two patients with urea cycle disorders (2).

Propionic acidemia is a disease that occurs due to a deficiency in propionyl-CoA carboxylase (3). This is an enzyme in mitochondria that converts propionyl-CoA, to methylmalonyl-CoA to eventually be used in the Krebs cycle. Propionic acid, a metabolite of isoleucine, valine, threonine, methionine, odd chain fatty acids, and cholesterol catabolism, builds up in tissues. Elevations of methylcitrate and propionylglycine, metabolites of propionic acid, in urine confirm the diagnosis. The increased amount of propionic acid leads to an anion gap acidosis and hyperammonemia. When levels of ammonia remain high, patients can suffer seizures, encephalopathy and coma that may result in death. Duration of hyperammonemia and peak levels greater than 300 umol/L represent risk factors for the development of neurotoxicity (4). Rapid removal of ammonia can be lifesaving in these patients and critical to prevent irreversible neurologic complications (3).

Renal replacement therapy is generally considered for ammonia levels greater than 400 umol/L (5). Peritoneal dialysis (PD) can remove ammonia but is considered a less efficacious modality when compared to intermittent hemodialysis and CRRT (6,7). Hemodialysis and CRRT have been demonstrated to rapidly remove ammonia, however vascular access for neonates may be technically challenging. Blood flow rate may be an additional issue, as standard catheters for hemodialysis procedures in a neonate may not be able to support a rate greater than 50 mL/min (4). This may make the ammonia removal too slow to prevent neurologic sequelae. In addition, CRRT often requires frequent stopping and re-priming of a circuit which can both delay ammonia dialysis and lead to blood volume loss. ECMO offers the advantages of more assured vascular access, while allowing a higher blood flow rates conducive for quick ammonia removal. We report the first use of veno-venous (VV) ECMO for...
CRRT to aid in rapid ammonia removal in a neonate with propionic acidemia.

DESCRIPTION

A 5-day-old, 2.2-kg infant girl born at term presented to an outside facility with lethargy and poor oral intake. The child had been exclusively breast fed, with poor feeding effort, hypotonia, tachypnea and poor urine output over a 2-day period. On presentation, the patient was hypotensive, noted to have a metabolic acidosis and an ammonia level of 1,730 umol/L. An echocardiogram revealed no significant congenital heart disease. She was started on vasopressors, dextrose containing fluids, broad spectrum antibiotics for possible sepsis, and transferred to our institution.

On arrival to the pediatric intensive care unit, the patient was orotracheally intubated. The pediatric genetics team was urgently consulted and concerned for an inborn error of organic acid metabolism. Given her small size, pediatric nephrology recommended ECMO with an in-line CRRT circuit as the most reliable and expeditious way to remove ammonia. A 13-French VV cannula was inserted through the right internal jugular vein. ECMO at a flow of 75 mL/kg/min and CRRT at a blood flow rate of 100 mL/min were initiated. The dialysis flow rate was 1,000 mL/h Primsate 4/0/1.2 (Baxter, Deerfield, IL) was used for dialysate. The CRRT in-line dialysis circuit was connected to the ECMO circuit post-oxygenator and returned pre-oxygenator. The child was heparinized as per our institution’s usual protocol. The acidosis improved and by 24 hours the ammonia levels were in a normal range. Elevated organic acids, methyl citrate and propionylglycine, were detected in the urine confirming the diagnosis of propionic acidemia. This was later confirmed by the newborn screen. A low-protein formula was started via nasogastric tube. Seizures were detected while on ECMO and controlled with phenobarbital.

After 72 hours of ECMO and CRRT, the circuit was clamped and the child was observed. Ammonia remained at normal levels and the ECMO cannulas were successfully removed. After decannulation, the child remained stable on the low-protein diet. She was discharged on hospital day 26 with mild left-sided weakness.

COMMENT

Dialysis in neonates presents a unique challenge due to the small size of their blood vessels and fluid shifts when initiated. This is why PD catheters are often used in this patient population for acute renal failure. When rapid removal of toxins is required, hemodialysis or CRRT are preferred. However, size limitations of the catheter and the smaller volume of the dialysis circuit can limit clearance (8). We were able to overcome these constraints with use of ECMO with in-line CRRT. In addition, this treatment strategy was able to confer a more hemodynamically stable approach. Typically, the extracorporeal blood volume of a CRRT/HD circuit represents a potential risk for cardiovascular compromise for the neonate. By utilization of an ECMO circuit in this case, we were able to significantly increase the patient’s circulating blood volume and avoid major hemodynamic changes.

The typical indications for ECMO in neonates are cardiac or respiratory failure. Although CRRT is often used while on ECMO, its use as a primary indication is rare. ECMO has been used for dialysis for hyperammonemia from urea cycle disorders as well as hemodynamic support for patients with other inborn errors of metabolism (9). Cardiac failure from propionic acidemia necessitating ECMO and liver transplant has been described (10). Our patient was diagnosed with propionic academia and did have mild hemodynamic lability from the acidosis from hyperammonemia. However, the primary indication for ECMO in our case was to effectively and rapidly remove ammonia with CRRT.

Arbeiter et al. described 21 patients whom dialysis was used for elevated ammonia from inborn errors of metabolism (8). CRRT was used in fifteen neonates. In this study, the maximal blood flow rate achieved was 50 mL/min. The mean time to a level under 200 was 22 hours with a standard deviation of 18 hours. In our case, the ammonia was under 200 by 17 hours. Although it is difficult to compare between patients, as each case started at a different value, it appears that using the larger cannula and ECMO circuit for CRRT allowed for rapid reduction in this patient’s ammonia values.

The previous studies that report the use of ECMO for hemodialysis (2) or for the use of support for a patient in metabolic disarray from propionic acidemia (9,10) all used veno-arterial ECMO. In using the carotid artery, there is a risk for immediate stroke as well as long-term neurologic problems. In our case, the use of VV ECMO though the internal jugular vein obviates this risk. A 13-french VV cannula was able to generate enough flow to drive CRRT.

While this case only required minimal oxygenation and hemodynamic support, and the argument could be made that this was not true extracorporeal life support, it is important to describe this method for successful dialysis of ammonia in a small (2.2 kg) neonate. In this case, the large cannula and volume in the circuit did allow for efficient and rapid removal of ammonia in a tenuous patient. The risks of using anticoagulation in a patient who otherwise would not have needed it for purely CRRT was considered; however, the ability to remove the ammonia was felt to be much more important.
Dialysis is rarely needed in the neonatal population. When dialysis is indicated, PD is more commonly instituted. Neonatal presentation of an organic acidemia is a metabolic emergency, requiring emergent dialysis, which can be technically challenging as the small catheter size and volume in the circuits can limit the dialysis flow rates. CRRT driven by VV ECMO can overcome both of these problems. When a neonate needs dialysis for rapid removal of a toxin, the use of VV ECMO should be strongly considered.

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REFERENCES