Original Research Article

When CRRT on ECMO Is Not Enough for Potassium Clearance: A Case Report

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Abstract

Background: Continuous renal replacement therapy (CRRT) is an excellent method used to remove fluid and solutes. It may also reduce the systemic inflammatory response for patients on extracorporeal membrane oxygenation (ECMO) support. The objective of this report is to describe a case where CRRT in combination with ECMO was insufficient to control hyperkalemia.

Methods: We report the case of an adolescent patient with refractory symptomatic hyperkalemia due to substantial rhabdomyolysis in which CRRT insufficiently cleared the patient’s excess potassium.

Results: Intermittent hemodialysis (IHD) was added and proved successful. The patient was weaned off ECMO, CRRT, and IHD, and his cardiac and renal function eventually normalized.

Conclusions: Two important lessons can be learned from this case report: (1) If CRRT is insufficient in achieving a desirable potassium balance, additional IHD should be considered and (2) separate IHD access should be considered to improve efficacy.

Keywords
ECMO, CRRT, IHD, hyperkalemia, pediatrics

What was known before

While continuous renal replacement therapy (CRRT) is the default renal replacement method in patients with acute kidney injury (AKI) and extracorporeal membrane oxygenation (ECMO), the clearance of potassium and other small solutes is superior on hemodialysis.

What this adds

Consultation with a nephrologist can assist the intensivist with the choice of the best method for renal replacement

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therapy, specific to the therapeutic goal. CRRT may not always compensate for multiple sources of endogenous potassium and thus may not adequately clear potassium.

**Introduction**

Acute kidney injury (AKI) is very common in patients placed on extracorporeal membrane oxygenation (ECMO) for cardiac failure. This result is multifactorial: hypoperfusion from a low cardiac output, nonpulsatile renal blood flow in venoarterial-ECMO (VA-ECMO), ischemia/reperfusion injury, systemic inflammatory response syndrome, and hemolysis. AKI can also have direct negative effects on the heart. The etiology of the resulting cardiac damage is also multifactorial and includes systemic inflammatory response syndrome with increased vascular permeability, electrolyte disturbances, acidosis, and uremia. These influences lead to a poor prognosis for patients on VA-ECMO for cardiac failure who develop AKI.

Accordingly, initiating continuous renal replacement therapy (CRRT) early in patients on ECMO may be beneficial as it ameliorates the impact of AKI as shown by Antonucci et al. CRRT is excellent for removing fluid and solutes and may reduce the systemic inflammatory response.

**Methods**

We present the case of an adolescent who underwent cardiogenic shock and required VA-ECMO. He developed refractory hyperkalemia and worsening azotemia from multiple causes despite early initiation and optimization of CRRT. Adding intermittent hemodialysis (IHD) successfully led to an improvement in the patient’s hyperkalemia and azotemia. There are little data describing the addition of IHD to continuous venovenous hemodiafiltration (CVVHDF) for a patient on VA-ECMO, especially in pediatrics. Informed consent for this report was obtained both from the patient and from his parents.

**Results**

A 17-year-old male (47 kg) with a history of Crohn disease presented to our hospital in cardiogenic shock. He was treated with broad-spectrum antibiotics for septic shock and was aggressively supported with fluid boluses, inotropes, vasoactives, and steroids. He also developed a pericardial effusion that required the percutaneous drainage of 150 mL of serous fluid. Within a few hours of admission and despite these interventions, he progressed to cardiac standstill and required extracorporeal cardiopulmonary resuscitation, that is, he was cannulated to a VA-ECMO circuit while cardiopulmonary resuscitation was performed.

Within 24 hours of ECMO cannulation, the patient developed hyperkalemia. The etiology of the hyperkalemia was thought to be multifactorial. The patient had significant hemolysis, rhabdomyolysis, and AKI. The hyperkalemia (8.2 mmol/L) was refractory despite the administration of low-dose dopamine, encouraging urine output with diuretics, optimizing ECMO circuit flows to minimize hemolysis, minimizing nephrotoxic medications, and giving medications for hyperkalemia (sodium bicarbonate, diuretics, insulin and dextrose, and salbutamol, all within a 6-hour window) (Figure 1).

The hyperkalemia produced a wide Q wave, R wave, and S wave (QRS) complex (despite the administration of calcium infusions and normal ionized calcium values on point-of-care testing), and the patient developed anuria. His laboratory results at the time were as follows: urea 12.9 mmol/L (normal ≤ 8.3), creatinine 234 µmol/L (normal = 62-120), phosphate 2.73 mmol/L (normal = 0.8-1.33), creatine kinase ≥ 25 300 U/L (normal ≤ 190), haptoglobin < 0.7 g/L (normal = 0.2-2.26), total bilirubin 21.3 µmol/L (normal = 3.4-17.1) and direct bilirubin 6.9 µmol/L (normal = 0-5), lactate dehydrogenase 1219 U/L (normal ≤ 225), and lactate 7.9 mmol/L (normal ≤ 2.4).

We introduced CVVHDF to the ECMO circuit proximal to the oxygenator using the Prismaflex system (Figure 2). The CRRT circuit was connected in parallel to avoid high access pressures, with the outflow line originating from the
patient’s venous line and the inflow line attached to the patient’s arterial cannula before the oxygenator. Nonetheless, high access pressures from the ECMO circuit limited the blood flow rate, so it was set at 150 mL/min. The pre-blood pump (PBP) was set to 1000 mL/h, which is the rate given on standard preprinted orders. The dialysate (PrismaSol 0) rate was set to 1000 mL/h, which is also the rate on standard pre-printed orders, and increased to 6000 mL/h, while the postfilter replacement (PrismaSol 0) rate was set to 1000 mL/h. The Prismaflex has broad flow rate capabilities for blood flows, dialysate, and replacement rates and can deliver up to 8000 mL/h of dialysate (replacement plus PBP). Potassium levels did not improve, so we elected to add IHD to improve the potassium balance (Figure 2). An additional central venous line was inserted for this purpose. His IHD treatment duration was 4 hours, with a dialysate flow rate of 800 mL/min (normal dialysate flow for maintenance dialysis 500 mL/min) and a maximal blood flow rate of 300 mL/min (normal pediatric blood flow rate 4-8 mL/kg/min for maintenance dialysis). The maximum blood flow rate that the dialysis machine that we used could produce was 300 mL/min. The dialyzer employed an F200NR filter to achieve maximum clearance. There was no potassium in the dialysate. We were successful in reducing potassium levels (Figure 3), and the ECG changes normalized with the additional hemodialysis.

After normalization of the hyperkalemia, the patient’s CVVHDF was discontinued after 4.5 days and switched to continuous venovenous hemodialysis (CVVHD). The patient was weaned off ECMO after 1 week, came off CVVHD after 13 days, and continued IHD 3 to 4 times per week for a total of 7 weeks until the AKI improved. His cystatin C estimated glomerular filtration rate (eGFR)\textsuperscript{15} was 23 (normal $\geq 91$) 3 weeks after presentation and is now (6 months later) only mildly impaired at 71 mL/min/1.73 m\textsuperscript{2}(chronic kidney disease [CKD] stage II, normal eGFR at this age 90-135 mL/min/1.73 m\textsuperscript{2}). His urea and creatinine normalized within 3 months of presentation and have remained normal.

**Discussion**

The concomitant use of CRRT and ECMO is common. In one case series, 71% of pediatric cardiac patients on ECMO suffered AKI.\textsuperscript{2} Of 155 pediatric patients cannulated onto VA-ECMO for heart failure secondary to myocarditis, 42 (27%) patients required dialysis.\textsuperscript{12} In a large series of pediatric patients who required ECMO for a variety of indications, 144 (41%) required CRRT.\textsuperscript{10} CRRT is typically sufficient for managing fluid overload, acidosis, and electrolyte disturbances. We present a case where CRRT (in this case CVVHDF) was not sufficient in managing severe refractory hyperkalemia despite maximal settings on CVVHDF and ongoing medical management of the hyperkalemia. While we cannot ascertain beyond a doubt that IHD really had to be introduced, the intensivist felt that medical treatment was exhausted and that a higher blood flow (the treatment was already at maximum with 8 L/h) was unacceptable because of the high access pressures. High access pressures on CVVHDF connected to an ECMO circuit are a documented complication.\textsuperscript{17} The refractory hyperkalemia was likely due to the patient’s continuing massive rhabdomyolysis in addition to hemolysis secondary to ECMO. The addition of IHD rapidly reduced potassium levels in a case of severe ongoing rhabdomyolysis.

It is important for a clinician to consider high-dose CRRT in patients like this when AKI develops, and if this fails, adding IHD to CRRT or replacing CRRT with IHD if a patient...
adolescent on VA-ECMO for cardiogenic shock who sufficiently clear potassium. We present the unique case of an
sources of endogenous potassium and thus may not adequately add IHD to correct the potassium imbalance. Indeed, the dialysis prescription of the CVVHDF was low, and perhaps the refractory hyperkalemia could have been avoided with a much higher prescription been introduced earlier.

In the latest Extracorporeal Life Support Organization (ELSO) report, between 35% and 52% of pediatric patients who required ECMO for cardiogenic shock survived to discharge or transfer. The survival rate was lower in those who underwent extracorporeal cardiopulmonary resuscitation (E-CPR) and further decreased in those who developed acute renal failure. Our patient would have had ongoing cardiac insult, undesirable potassium levels despite the use of CRRT, and a lower likelihood of recovery if we had not aggressively added IHD to correct the potassium imbalance. Of course, IHD could have been chosen instead of CRRT, but this has the disadvantage of discontinuous fluid removal. Still, adding IHD can pose some risks. Large fluid shifts in intermittent dialysis can create hemodynamic instability, and there is a risk of catastrophic bleed when inserting a central access line in an anticoagulated patient. We considered using peritoneal dialysis, our choice was IHD. Second, consider separate vascular access to maximize the efficacy of the additional renal replacement therapy.

Conclusion

To conclude, CRRT may not always compensate for multiple sources of endogenous potassium and thus may not adequately clear potassium. We present the unique case of an adolescent on VA-ECMO for cardiogenic shock who survived and regained full renal and cardiac function after IHD was added to CRRT to manage his persistent refractory hyperkalemia. There are 2 important teachable moments: First, in consultation with a nephrologist, consider adding an additional renal replacement modality if the balance of any uremic toxin remains unfavorable despite optimizing CRRT. Given that potassium is best cleared by conventional hemodialysis, our choice was IHD. Second, consider separate vascular access to maximize the efficacy of the additional renal replacement therapy.

Ethics Approval and Consent to Participate

Ethics approval is waived for a case report in our institution.

Consent for Publication

Written informed consent to publish was obtained from the patient and the caregivers.

Availability of Data and Materials

Not applicable.

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Declaration of Conflicting Interests

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References

1. Chen YC, Tsai FC, Fang JT, Yang CW. Acute kidney injury in adults receiving extracorporeal membrane oxygenation. J Formos Med Assoc. 2014;113(11):778-785.
2. Smith AH, Hardison DC, Worden CR, Fleming GM, Taylor MB. Acute renal failure during extracorporeal support in the pediatric cardiac patient. ASAIO J. 2009;55:412-416.
3. Virzi GM, Clementi A, Brocca A, et al. The hemodynamic and nonhemodynamic crosstalk in cardiorenal syndromes type 1. Cardiorenal Med. 2014;4:103-112.
4. Cruz DN. Cardiorenal syndrome in critical care: the acute cardiorenal and renocardiac syndromes. Adv Chronic Kidney Dis. 2013;20:56-66.
5. Betrus C, Remenapp R, Charpie J, et al. Enhanced hemolysis in pediatric patients requiring extracorporeal membrane oxygenation and continuous renal replacement therapy. Ann Thorac Cardiovasc Surg. 2007;13:378-383.
6. Bagshaw SM, Hoste EA, Braam B, et al. Cardiorenal syndrome type 3: pathophysiologic and epidemiologic considerations. Contrib Nephrol. 2013;182:137-157.
7. Balasubramanian SK, Tiruvoipati R, Amin M, et al. Factors influencing the outcome of paediatric cardiac surgical patients during extracorporeal circulatory support. J Cardiothorac Surg. 2007;2:4.
8. Kolovos NS, Bratton SL, Moler FW, et al. Outcome of pediatric patients treated with extracorporeal life support after cardiac surgery. *Ann Thorac Surg*. 2003;76:1435-41;discussion 41-42.

9. Tsai TY, Tsai FC, Chang CH, et al. Prognosis of patients on extracorporeal membrane oxygenation plus continuous arteriovenous hemofiltration. *Chang Gung Med J*. 2011;34:636-643.

10. Huang SC, Wu ET, Wang CC, et al. Eleven years of experience with extracorporeal cardiopulmonary resuscitation for pediatric patients with in-hospital cardiac arrest. *Resuscitation*. 2012;83:710-714.

11. Morris MC, Ittenbach RF, Godinez RI, et al. Risk factors for mortality in 137 pediatric cardiac intensive care unit patients managed with extracorporeal membrane oxygenation. *Crit Care Med*. 2004;32:1061-1069.

12. Rajagopal SK, Almond CS, Laussen PC, Rycus PT, Wypij D, Thiagarajan RR. Extracorporeal membrane oxygenation for the support of infants, children, and young adults with acute myocarditis: a review of the Extracorporeal Life Support Organization registry. *Crit Care Med*. 2010;38:382-387.

13. Antonucci E, Lamanna I, Fagnoul D, Vincent JL, De Backer D, Silvio Taccone F. The impact of renal failure and renal replacement therapy on outcome during extracorporeal membrane oxygenation therapy. *Artif Organs*. 2016;40:746-754.

14. Mu TS, Palmer EG, Batts SG, Lentz-Kapua SL, Uyehara-Lock JH, Uyehara CF. Continuous renal replacement therapy to reduce inflammation in a piglet hemorrhage-reperfusion extracorporeal membrane oxygenation model. *Pediatr Res*. 2012;72:249-255.

15. Filler G, Lepage N. Should the Schwartz formula for estimation of GFR be replaced by cystatin C formula? *Pediatr Nephrol*. 2003;18:981-985.

16. Paden ML, Warshaw BL, Heard ML, Fortenberry JD. Recovery of renal function and survival after continuous renal replacement therapy during extracorporeal membrane oxygenation. *Pediatr Crit Care Med*. 2011;12:153-158.

17. Askenazi DJ, Selewski DT, Paden ML, et al. Renal replacement therapy in critically ill patients receiving extracorporeal membrane oxygenation. *Clin J Am Soc Nephrol*. 2012;7:1328-1336.

18. Schetz M. Vascular access for HD and CRRT. *Contrib Nephrol*. 2007;156:275-286.

19. Paden ML, Conrad SA, Rycus PT, Thiagarajan RR; ELSO Registry. Extracorporeal Life Support Organization Registry Report 2012. *ASAIO J*. 2013;59:202-210.

20. Hei F, Lou S, Li J, et al. Five-year results of 121 consecutive patients treated with extracorporeal membrane oxygenation at Fu Wai Hospital. *Artif Organs*. 2011;35:572-578.