Research Article

Continuous Renal Replacement Therapy Applications on Extracorporeal Membrane Oxygenation Circuit

Ayse Filiz Yetimakman, Murat Tanyildiz, Selman Kesici[1], Esra Kockuzu, Benan Bayrakci[2]

Department of Pediatric Intensive Care Medicine, Hacettepe University, [1]Department of Pediatric Intensive Care Medicine, Dr. Sami Ulus Maternity and Children's Training and Research Hospital, [2]Center for Life Support Clinics and Research, Hacettepe University, Ankara, Turkey

Abstract

Background and Aims: Continuous venovenous hemofiltration or hemodiafiltration is used frequently in pediatric patients, but experience of continuous renal replacement therapy (CRRT) application on extracorporeal membrane oxygenation (ECMO) circuit is still limited. Among several methods used for applying CRRT on ECMO patients, we aim to share our experience on inclusion of a CRRT device in the ECMO circuit which we believe is easier and safer to apply. **Materials and Methods:** The data were collected on demographics, outcomes, and details of the treatment of ECMO patients who had CRRT. During the study period of 3 years, venous cannula of ECMO circuit before pump was used for CRRT access for both the filter inlet and outlet of CRRT machine to minimize the thromboembolic complications. The common indication for CRRT was fluid overload. **Results:** CRRT was used in 3.68% of a total number of patients admitted and 43% of patients on ECMO. The patients have undergone renal replacement therapy for periods of time ranging between 24 h and 25 days (260 h mean). The survival rate of this group of patients with multiorgan failure was 33%. Renal recovery occurred in all of the survivors. Complications such as electrolyte imbalance, hypothermia, and bradykinin syndrome were easily managed. **Conclusions:** Adding a CRRT device on ECMO circuit is a safe and effective technique. The major advantages of this technique are easy to access, applying CRRT without extra anticoagulation process, preventing potential hemodynamic disturbances, and increased clearance of solutes and fluid overload using larger hemofilter.

Keywords: Continuous venovenous hemodiafiltration, continuous venovenous hemofiltration, extracorporeal membrane oxygenation, renal replacement therapy

Introduction

Successful utilization of extracorporeal membrane oxygenation (ECMO) in children was defined as early as the 1970s.[1,2] Beginning of continuous renal replacement therapies (CRRTs) also dates back to 1970s, and expectations from the therapy as well as the technique has evolved since then.[3,4] In our day, continuous venovenous hemofiltration or hemodiafiltration is used frequently in Pediatric Intensive Care Units (PICUs) for renal replacement therapy, but experience of CRRT application on ECMO circuit is still limited.

Acute kidney injury is frequently observed in ECMO patients. The hypoxic insult and systemic inflammatory response associated with the ECMO process or the underlying condition are the two important factors causing acute kidney injury. Reduced perfusion of the kidneys before ECMO, reperfusion injury after ECMO, and disrupted hormonal mechanisms are predisposing factors.[5] Acute kidney injury and requirement of renal replacement are associated with increased mortality in these patients.[6]

Even when the kidneys are minimally injured and functioning as in a normal child, the massive fluid overload at the beginning of ECMO process cannot be easily overcome solely by the kidneys. It is well described that fluid overload affects survival in critically ill children and CRRT enhances fluid management in ECMO patients.[7,8] Slow but continuous nature of the renal replacement is superior to intermittent hemodialysis in this hemodynamically unstable patient group.[9]

Access this article online

Quick Response Code:

Website: www.ijccm.org

DOI: 10.4103/ijccm.IJCCM_128_17

Address for correspondence: Dr. Ayse Filiz Yetimakman, Department of Pediatric Intensive Care Medicine, Hacettepe University, Section 35, 06100 Ankara, Turkey.
E-mail: filizyetimakman@hotmail.com

How to cite this article: Yetimakman AF, Tanyildiz M, Kesici S, Kockuzu E, Bayrakci B. Continuous renal replacement therapy applications on extracorporeal membrane oxygenation circuit. Indian J Crit Care Med 2017;21:355-8.

There are several methods for performing CRRT during ECMO: (1) performing RRT through venous access independent of the ECMO circuit, (2) introduction of a hemofiltration filter into the ECMO circuit, and (3) inclusion of a CRRT device in the ECMO circuit.[10] Hereby, we aim to share our experience on the third technique which we believe is easier and safer to apply on an ECMO run.

Materials and Methods

On average, 600 patients are admitted annually to our PICU, for both surgical and medical PICU needs. During the study period, 1.6% of all patients underwent ECMO (All centrifugal pumps, nine patients with Rotafl ow® [Maquet Cardiopulmonary AG, Rastatt, Germany], and 26 patients with DeltaStream® DP3 [Medos Cardiopulmonary Solutions, Stolberg, Germany]). Data on patients admitted from April 2013 to September 2016 were collected on demographics, outcomes, and details of ECMO treatment and CRRT.

The decision for CRRT was given in all of the patients when the fluid overload exceeded 10% of the body weight or anticipated to reach 10% within 24 h. All of the CRRT procedures were carried out with a CRRT machine (Prismaflex® system, Baxter Healthcare, Illinois, USA). Venous cannula of ECMO circuit before pump was used for CRRT access for both the filter inlet and outlet of CRRT machine [Figure 1]. During CRRT, the blood flow rates were set 4–12 ml/kg/min and total effluent rates were 2–3 l/1.73 m^2/h. Hemofiltration was used with predilution in all of the patients, whereas hemodialysis was added as needed. Normal saline or packed red blood cells were used for priming. In our usual practice, we use polyarylethersulfone membranes (circuit volume 60 ml) for children under 15 kg and AN69 membranes (circuit volume 93 ml or 152 ml) for children over 15 kg. As CRRT machine was connected to an ECMO circuit, membranes with large circuit volumes (93 or 152 ml) were used in seven patients whose weights were under 15 kg. Heparin was used for anticoagulation of ECMO circuit and titrated up to 30 IU/kg/h for a target activated clotting time between 160 and 180 s. No additional anticoagulation was used for CRRT system. After the maintenance of the metabolic homeostasis and fluid balance, the CRRT was discontinued when urinary output was sufficient.

Results

During the study period, 35 ECMO patients were followed in PICU and 15 of these patients underwent CRRT, with a machine added on the ECMO circuit. The mean age of the group was 4.6 years and the mean body weight was 16.3 kg. Five patients were in the newborn period and a total of nine patients were under the age of two. Within the study period, the number of patients who had undergone renal replacement therapy was 3.68% of a total number of patients admitted to our PICU. This rate was 43% among ECMO patients treated in the unit. All of the patients were on venoarterial ECMO. The number and distribution of the underlying diseases as well as demographic information of patients are listed in Table 1. The majority of the patients had primary cardiac pathologies or severe pulmonary hypertension. The survival rate of the subgroup (ECMO + CRRT) was 33% with a mean ECMO runtime of 733 h, whereas the overall ECMO survival was 57% in our unit during the study period. The patients have undergone renal replacement therapy for periods of time ranging between 24 h and 25 days (260 h mean). Renal recovery occurred in all of the survivors. The most common complications of the process were clotting of the membrane, electrolyte imbalances (hypophosphatemia 80%, hypokalemia 93%), and bradykinin release syndrome (33%). All of the bradykinin syndromes were observed when an AN69 membrane was primed by packed red blood cells.

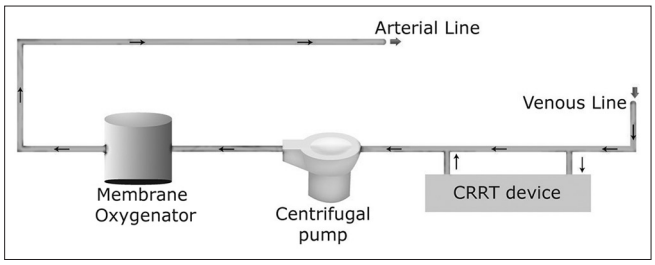

Figure 1: Configuration of the system

Discussion

The aim of this report is to share the pediatric experience on combination therapy. We want to emphasize some main advantages of the technique in the foreground as well as listing the common but easily manageable complications.

All CRRT support was given by a CRRT machine because in-line filter technique without a machine carries the disadvantages of lack of blood flow adjustment and inability to detect clots early as well as inaccurate ultrafiltration rates.[11]

Since most of the patients are young with low body weights, the venous access had a high probability of being difficult in our patient group where direct access from ECMO circuit becomes a significant advantage. Venous cannula of ECMO circuit was used for CRRT access to minimize the thromboembolic complications, with both the filter inlet and outlet of CRRT machine connected before ECMO pump. When the filter inlet is connected after the pump and outlet before the pump, shunting of blood occurs which was prevented by our method. We believe that preventing resistance which would occur when both the filter inlet and outlet were connected after the pump is another advantage.[12] Although air entrapment into the ECMO pump has previously been presented as a major concern when the CRRT machine is connected before ECMO pump,[6] we did not observe any complications concerning the pump.

Use of ECMO pump for cardiac function enables us to use membranes with larger surface areas in small children. Higher flow rates used with membranes with larger surface areas result in increased solute clearance and shortened time of fluid removal.[13,14] Since the relationship between mortality and fluid overload in CRRT patients is defined,[7,15] this advantage was

Table 1: Patient characteristics

Patient number	Age (month)	Weight (kg)	Underlying disease	Type of CVVH membrane	Blood prime/bradykinin release
1	112	40	Dilated cardiomyopathy	AN69 (M60®)	-/-
2	6	7	ASD, VSD	PAES (HF20®)	-/-
3	0	3.5	Congenital diaphragmatic hernia	AN69 (M60®) + PAES	+/+
4	0	3.5	Congenital diaphragmatic hernia	AN69 (M60®) + PAES	+/+
5	6	7	VSD	AN69 (M60®) + PAES	+/+
6	0	3.5	Congenital diaphragmatic hernia	AN69 (M60®) + PAES	+/+
7	0	3.5	Congenital diaphragmatic hernia	AN69 (M60®)	+/+
8	27	11	AV canal defect	PAES	-/-
9	223	38	Kidney transplantation, sepsis	AN69 (M100®)	-/-
10	0	3.5	Congenital diaphragmatic hernia	AN69 (M60®)	+/-
11	18	10	Dilated cardiomyopathy	AN69 (M60®)	+/-
12	6	7	Tetralogy of Fallot	PAES	-/-
13	198	57	Colchicine intoxication	AN69 (M100®)	-/-
14	144	25	Tetralogy of Fallot	AN69 (M60®)	-/-
15	98	25	Dilated cardiomyopathy	AN69 (M60®)	-/-

Blood prime: (-) stands for absent (+) stands for present; bradykinin release: (-) stands for 'not observed' (+) stands for 'observed'; Type of CVVH membrane: (+) stands for 'and'. ASD: Atrial septal defect; VSD: Ventricular septal defect; AV: Atrioventricular; PAES: Polyarylethersulfone; CVVH: Continuous venovenous hemofiltration

gratefully utilized. CRRT was started with the anticipation of fluid overload to reach more than 10% of body weight, to facilitate fluid balance and caloric intake.[8]

The rate of renal replacement therapy in ECMO patient group is almost 12 times the rate in the general patient population of the unit. This finding is consistent with the increased disease severity and rate of multiorgan failure. Furthermore, the survival rate of 33% reflects the disease severity of these patients and is similar to previously reported rates.[16] The overall survival rate of all CRRT patients in our unit is 38.5%. There are variable reports of survival rates in CRRT patients, but the patient populations are not homogeneous among different patient series as well as within any sample patient group.[16-18] The 33% survival rate is lower than the overall rate of survival in our ECMO patients. Again, this is not related to failure of CRRT treatment but caused by the increased disease burden.[19] Similar to previous reports, renal recovery occurred in all of the survivors.[19,20]

Because of the common denominator of severe cardiac failure and multiorgan failure in our patients, no comparison could be made between survivors and nonsurvivors depending on the inotrope scores, organ failure scores, or mortality scores. From this aspect, future randomized studies with larger number of patients are needed to correlate the outcomes with several clinical variables and to validate the effect of CRRT therapy on mortality in ECMO patients.

All of the patients experienced temporary electrolyte imbalances. The rate of bradykinin syndrome was higher (33%) than the overall rate in CRRT patients in our unit (11%) and all of the reactions occurred if an AN69 membrane is blood primed. Complications were easily managed by the experienced staff.

Bigger membranes were an advantage that we wanted to continue to use, but the small weight infants needed blood priming causing bradykinin syndrome. For that reason, we started using "bypass system" described by Brophy *et al*. for priming. This technique involves transfusing the packed red blood cells mixed 1:1 with normal saline at a rate of 10–15 ml/min, postfilter into the patient, while the saline-primed circuit drains into a bag.[21] By the help of this technique, we overcame bradykinin syndrome [Table 1; patients 10 and 11].

Conclusions

In our experience, adding a CRRT device on ECMO circuit is a safe and effective technique that improves fluid balance and metabolic disturbances. None of the complications resulted in mortality, and fluid balance is definitely a target of therapy in ECMO patients. The major advantages of this technique are easy access for a patient on continuous anticoagulation, applying CRRT without extra anticoagulation process, preventing potential hemodynamic disturbances, and increased clearance of solutes and fluid overload using larger hemofilter. Prospective randomized studies are needed to verify the effect of technique on weaning of ECMO, length of PICU stay, and survival.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Bartlett RH, Gazzaniga AB, Jefferies MR, Huxtable RF, Haiduc NJ, Fong SW. Extracorporeal membrane oxygenation (ECMO) cardiopulmonary support in infancy. Trans Am Soc Artif Intern Organs 1976;22:80-93.
2. Bartlett RH, Gazzaniga AB, Fong SW, Jefferies MR, Roohk HV, Haiduc N. Extracorporeal membrane oxygenator support for cardiopulmonary failure. Experience in 28 cases. J Thorac Cardiovasc Surg 1977;73:375-86.

3. Kramer P, Wigger W, Rieger J, Matthaei D, Scheler F. Arteriovenous haemofiltration: A new and simple method for treatment of over-hydrated patients resistant to diuretics. Klin Wochenschr 1977;55:1121-2.
4. Garzotto F, Zanella M, Ronco C. The evolution of pediatric continuous renal replacement therapy. Nephron Clin Pract 2014;127:172-5.
5. Villa G, Katz N, Ronco C. Extracorporeal membrane oxygenation and the kidney. Cardiorenal Med 2015;6:50-60.
6. Askenazi DJ, Selewski DT, Paden ML, Cooper DS, Bridges BC, Zappitelli M, *et al.* Renal replacement therapy in critically ill patients receiving extracorporeal membrane oxygenation. Clin J Am Soc Nephrol 2012;7:1328-36.
7. Foland JA, Fortenberry JD, Warshaw BL, Pettignano R, Merritt RK, Heard ML, *et al.* Fluid overload before continuous hemofiltration and survival in critically ill children: A retrospective analysis. Crit Care Med 2004;32:1771-6.
8. Hoover NG, Heard M, Reid C, Wagoner S, Rogers K, Foland J, *et al.* Enhanced fluid management with continuous venovenous hemofiltration in pediatric respiratory failure patients receiving extracorporeal membrane oxygenation support. Intensive Care Med 2008;34:2241-7.
9. Bellomo R, Ronco C. Continuous versus intermittent renal replacement therapy in the Intensive Care Unit. Kidney Int Suppl 1998;66:S125-8.
10. Chen H, Yu RG, Yin NN, Zhou JX. Combination of extracorporeal membrane oxygenation and continuous renal replacement therapy in critically ill patients: A systematic review. Crit Care 2014;18:675.
11. Santiago MJ, Sánchez A, López-Herce J, Pérez R, del Castillo J, Urbano J, *et al.* The use of continuous renal replacement therapy in series with extracorporeal membrane oxygenation. Kidney Int 2009;76:1289-92.
12. Ricci Z, Ronco C, Picardo S. CRRT in series with extracorporeal membrane oxygenation in pediatric patients. Kidney Int 2010;77:469-70.
13. Clark WR, Ronco C. Determinants of haemodialyser performance and the potential effect on clinical outcome. Nephrol Dial Transplant 2001;16 Suppl 5:56-60.
14. Henderson L. Biophysics of ultrafiltration and hemofiltration. In: Jacobs C, Kjellstrand C, Koch K, Winchester J, editors. Replacement of Renal Function by Dialysis. 4th ed. Dordrecht: Kluwer Academic Publishers; 1996. p. 114-45.
15. Goldstein SL, Currier H, Graf CD, Cosio CC, Brewer ED, Sachdeva R. Outcome in children receiving continuous venovenous hemofiltration. Pediatrics 2001;107:1309-12.
16. Shaheen IS, Harvey B, Watson AR, Pandya HC, Mayer A, Thomas D. Continuous venovenous hemofiltration with or without extracorporeal membrane oxygenation in children. Pediatr Crit Care Med 2007;8:362-5.
17. Goldstein SL, Somers MJ, Baum MA, Symons JM, Brophy PD, Blowey D, *et al.* Pediatric patients with multi-organ dysfunction syndrome receiving continuous renal replacement therapy. Kidney Int 2005;67:653-8.
18. Bunchman TE, McBryde KD, Mottes TE, Gardner JJ, Maxvold NJ, Brophy PD. Pediatric acute renal failure: Outcome by modality and disease. Pediatr Nephrol 2001;16:1067-71.
19. 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;12:153-8.
20. Meyer RJ, Brophy PD, Bunchman TE, Annich GM, Maxvold NJ, Mottes TA, *et al*. Survival and renal function in pediatric patients following extracorporeal life support with hemofiltration. Pediatr Crit Care Med 2001;2:238-42.
21. Brophy PD, Mottes TA, Kudelka TL, McBryde KD, Gardner JJ, Maxvold NJ, *et al*. AN-69 membrane reactions are pH-dependent and preventable. Am J Kidney Dis 2001;38:173-8.