Clinical Case Report

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Co-initiation of continuous renal replacement therapy, peritoneal dialysis, and extracorporeal membrane oxygenation in neonatal life-threatening hyaline membrane disease

A case report

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Abstract

Rationale: Extracorporeal membrane oxygenation (ECMO) is a well-known technique to provide cardio-pulmonary support. Although continuous renal replacement therapy (CRRT) is frequently indicated, the need for faster fluid removal as the primary indication for ECMO is uncommon. Experiences on concomitant applications of ECMO, peritoneal dialysis (PD) and CRRT in neonates are relatively limited.

Patient concerns: We report a 2-day-old male neonate with life-threatening hyaline membrane disease (HMD), accompained by severe systemic fluid retention, sepsis and abdominal compartment syndrome.

Diagnosis: Hyaline membrane disease (HMD), neonatal respiratory distress syndrome, sepsis, capillary leakage syndrome, and abdominal compartment syndrome.

Intervention: Veno-arterial ECMO, CRRT, and PD were synchronously initiated for the sake of faster fluid removal possible.

Outcomes: The infant was successfully weaned from ECMO circuit and fluid overload was greatly improved four days after extracorporeal life support (ECLS), without major complications.

Lessons: Initiation of CRRT and PD during ECMO therapy is effective and safe to release fluid overload in neonates, and severe complications are absent. When a neonate requires dialysis of urgency, ECMO offers assured vascular access to hemodialysis, allowing faster fluid removal.

Abbreviations: AKI = acute kidney injury, CRRT = continuous renal replacement therapy, ECLS = extracorporeal life support, ECMO = extracorporeal membrane oxygenation, HMD = hyaline membrane disease, PD = peritoneal dialysis.

Keywords: continuous renal replacement therapy, extracorporeal membrane oxygenation, hyaline membrane disease, neonate, peritoneal dialysis

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All authors declare no conflict of interest.

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1. Introduction

Extracorporeal membrane oxygenation (ECMO) provides cardio-pulmonary support to critically life-threatening patients with clinically reversible disorders when traditional approaches are ineffective. Neonates, mostly for acute respiratory failure, constitute the largest population of patients requiring ECMO support. However, in-hospital mortality of neonates receiving extracorporeal life support (ECLS) is significantly higher compared to children and adult candidates, and one important reason is that subsequent fluid overload and acute kidney injury (AKI) frequently occur in critically ill newborns.[1]

Many critically ill infants have inflammatory response with severe capillary leakage before ECLS owing to hypoxemia, low cardiac output, sepsis and shock, and ECMO itself may also induce systemic inflammatory response syndrome and capillary leakage syndrome, resulting in severe fluid overload.[2] Blood pressure will decrease because of fluid and protein loss, and deficient organ perfusion causes multiple organ failure, of which AKI is prominent. During ECMO support, maintenance of effective fluid volume for sufficient venous return is vital for optimizing ECLS.[3] Apparently, rapid management of fluid overload can be lifesaving in these patients and pivotal to prevent irreversible complications.

Peritoneal dialysis (PD) is widely used in infants to remove excessive fluid, but is less efficacious and slower when compared

to CRRT. Vascular access maybe a technically challenging issue that impedes the speed of hemodialysis, as standard catheters in neonates for CRRT is unable to reach a rate over 50 mL/min.[4] These approaches may be too slow to remove overloaded fluid to prevent successive sequela. Conjugation of CRRT device to neonate ECMO patients is advantageous because ECMO offers assured vascular access, permitting higher flow rates conducive for prompt fluid removal.[4]

Studies on neonatal ECLS have shown that continuous renal replacement therapy (CRRT) improves clinical outcome when post-procedural renal complications and refractory fluid disturbances develop.[5,6] Previous report showed that utilization of CRRT during neonatal ECMO support not only reduced duration of ECLS and mechanical ventilation, but also enabled faster cardiac function recovery.[2,7] Here, our group describes the co-initiation of CRRT and PD during ECLS in a critically ill neonate with lethal hyaline membrane disease (HMD) manifesting as serious systemic fluid overload.

2. Case presentation

A 2-day-old male neonate was transferred from a private clinic with a diagnosis of HMD. He was a preterm infant, born via normal vaginal delivery in 36 weeks of gestational age, with a birth weight of 2.4 kg and a normal Apgar score. Five hours after birth, aggressive symptoms of respiratory distress developed apparently, including dyspnea, mild cyanosis, and abdominal distension. He was, therefore, intubated, mechanically ventilated and referred to the neonatal intensive care unit, Guangdong General Hospital for further treatment. Initial finding of physical examination included dusky appearance, tachypnea with respiratory rate 56 per minute, intercostal retractions and reduced breath sounds bilaterally. A cardiac echocardiogram indicated a 3 mm of patent ductus arteriosus with normal cardiac contractivity. Both metabolic and respiratory acidosis were confirmed by arterial blood gas, showing that PH value of 7.18, BE value of −10.2 mmol/L, PaO_2 54 mmHg, $PaCO_2$ 48 mmHg, and lactic acid level of 10.3 mmol/L. Laboratory workups revealed that serum creatinine was 157 umol/L (normal range: 44–107 umol/L), and blood urea nitrogen was 8.20 mg/dL (normal range: 7–21 mg/dL). In routine blood test, platelet count was 27×10^9/L (normal range: $100–300 \times 10^9$/L), and streptococcus agalactiae was detected via blood culture. Main changes of chest X-ray were reduction of lung transparency and frosted glass-like changes of the lung fields, which were in accordance with the diagnosis of HMD (Fig. 1A).

Situation was deteriorating after admission, and manifestations of systemic fluid overload developed abruptly. As a result of capillary leakage syndrome, generalized anasarca, ascitic fluid retention, and increasing abdominal distension were presented. Hepatomegaly and systemic edema aggravated, which was partially because of little urinary volume, and also a result of AKI secondary to renal mal-perfusion. He was noted to have sepsis, for which broad spectrum antibiotics were used. The baby was then hypotensive, though high dose inotropes (dopamine 10 ug/kg/min and adrenaline 0.1 ug/kg/min) had been administered. The diagnosis of severe pulmonary hypertension (92 mmHg) and a right-to-left shunting patent ductus arteriosus (4.5 mm) were confirmed by repeated echocardiography, with dilated right ventricle and moderate tricuspid insufficiency. Oxygen saturation was, therefore, dropping, with a pre-ductal oxygen saturation of 70% and a post-ductal SpO_2 of 30%. Hemodynamics was unstable, presenting as refractory electrolyte disturbance and progressive acidosis. Abdominal distension was increasing markedly, with elevated bladder pressure by a urinary bladder catheter of 23 mmHg, which was noted to have abdominal compartment syndrome according to the criteria of diagnosis.[8,9] In spite of all attempts including nitric oxide inhalation and high-frequency oscillatory ventilation, therapeutic effect was poor.

Given his small age and the life-threatening conditions, the pediatric multi-disciplinary team recommended ECMO, PD, and CRRT to overcome this vicious cycle. Twenty hours after admission, a veno-arterial ECMO (Pump head: Maquet Getinge Group, Rastatt, Germany; Oxygenator: Medos Medizintechnik AG, Stolberg, Germany) was commenced (Fig. 2A), allowing the heart and lung to rest. An 8-Fr arterial cannula was inserted into the right common carotid artery, while the right internal jugular vein was cannulated by a 12-Fr venous cannula. Repeated chest X-ray confirmed the appropriate position of cannulas of ECMO circuit, also revealed diffuse exudation of both lung fields which was the so-called "white-out", and exacerbation of fluid overload was obvious (Fig. 1B). The ECMO blood flow was maintained

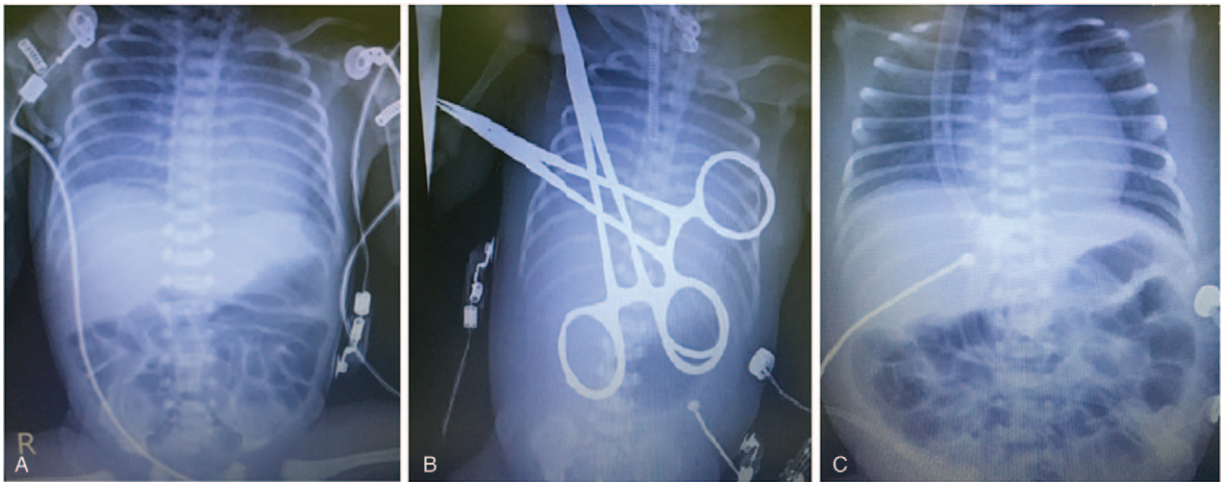

Figure 1. Chest X-rays in a critically ill neonate with PHMD receiving ECMO and CRRT therapy. Notes: (A) Before ECMO therapy; (B) Seven hours after initiation of ECMO; (C) Decannulation of ECMO. CRRT = continuous renal replacement therapy, ECMO = extracorporeal membrane oxygenation, PHMD = pulmonary hyaline membrane disease.

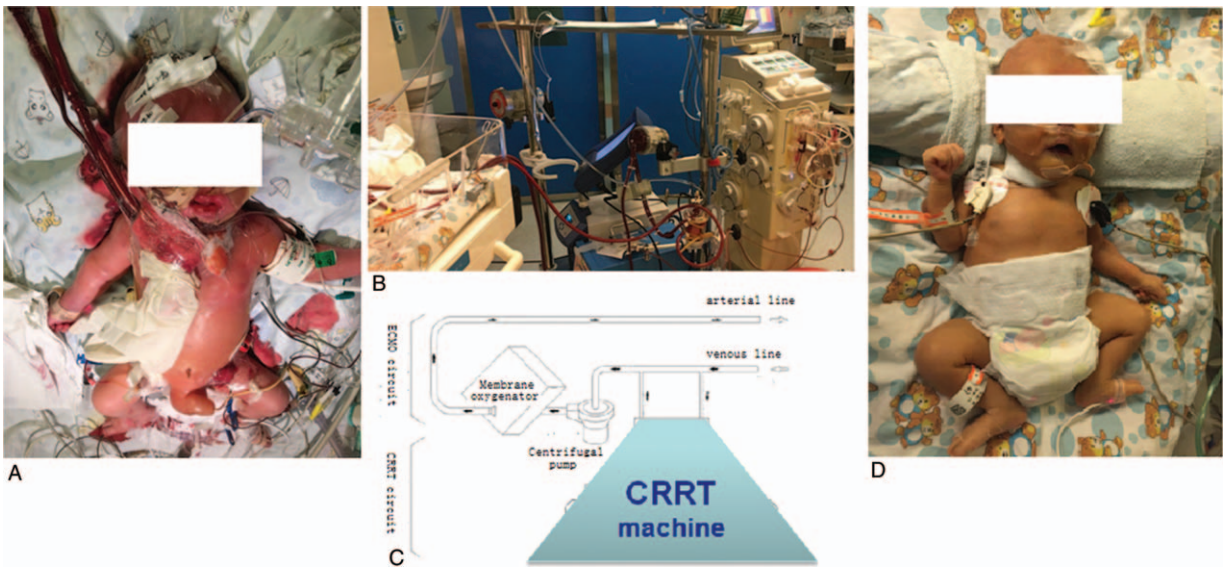

Figure 2. Description of incorporating a CRRT device to ECMO circuit. Notes: (A) Initiation of ECMO; (B) Inclusion of a CRRT device to ECMO circuit; (C) Schematic diagram of incorporating a CRRT device to the ECMO circuit; (D) Discontinuation of mechanical support (29 days post-ECMO). CRRT = continuous renal replacement therapy, ECMO = extracorporeal membrane oxygenation.

from 75 to 100 mL/kg/min, and the child was heparinized to keep an activated clotting time ranging from 180 to 220 s. Immediate after the initiation of ECLS, CRRT circuit was connected the post-oxygenator and returned pre-oxygenator of ECMO (Fig. 2B and C). The targeted blood flow rate of CRRT was 100 mL/min, with a dialysis flow rate of 1L/h Primasate 4/0/1.2 (Baxter, Deerfield, IL). Based on the presence of abdominal compartment syndrome, PD was also carried out, with PD catheter (Tenckhoff, Quinton Instrument Cor., Bothell, WA) inserted, then approximately 350 mL peritoneal fluid was drained immediately. Hemodynamics improved soon after the establishment of ECMO, PD, and CRRT, and mean arterial pressure and oxygen saturation reached normal level. Repeated transfusion of blood components and surfactant were administered.

Four days after ECLS, PD, and CRRT, improvements of pulmonary exudation and pulmonary vascular resistance were evident. Systemic edema also improved greatly, and serum creatinine was in a normal range. Result of repeated arterial blood gas was satisfactory, and repeated echocardiogram demonstrated spontaneous closure of patent ductus arteriosus, decrease of pulmonary artery pressure (45 mmHg), as well as the absence of right ventricle enlargement.

With the improvement of overall conditions, the pediatric multi-disciplinary team weaned the ECMO circuit on the fifth day of admission, and vascular cannulas were removed smoothly. Repeated chest film revealed significant improvement regarding to fluid overload (Fig. 1C). Hemodynamic was stable after decannulation, without the support of high dose inotropes.

The bladder pressures decreased to 8 mmHg, with a soft abdomen on palpation, PD was therefore discontinued on ninth day of admission. After sepsis and respiratory disorder were properly managed, the neonate was extubated and weaned from mechanical support 29 days after ECLS (Fig. 2D). The child was discharged 38 days after his admission, without any complications relevant to ECMO, PD, and CRRT. On follow-up, the patient was uneventful, with stable electrolyte parameters, renal function and fluid balance.

Approval of ethical committee of Guangdong General Hospital was obtained. Written informed consent for the use of patient information, clinical data, images and permission of publication have been obtained from the neonate's parents.

3. Discussion

We describe a neonatal ECMO case diagnosed with fatal HMD and acute respiratory failure, accompanying with severe systemic fluid retention, sepsis and abdominal compartment syndrome, which required fast fluid removal. When fast removal of overloaded fluid is imminent, renal replacement therapy is usually the most reliable way. However, dialyzing a neonate presents a clinically challenging issue due to the limitation of peripheral vascular access at this age. But in this case, obstacle of vascular access was easily overcome by the incorporation of a CRRT machine to ECMO. Faster fluid removal was done by CRRT, PD, and ECMO.

Abdominal compartment syndrome, usually clinically underreported, is typically defined as sustained intra-abdominal pressure of 20 mmHg and above.[10] Abdominal compartment syndrome was usually secondary to peritoneal fluid accumulation in the setting of capillary leakage during sepsis. The reported mortality of abdominal compartment syndrome in critically ill patients might be as high as 50%.[10] In patients receiving ECMO, abdominal compartment syndrome and increasing intra-abdominal pressure give rise to negative effects on ECMO venous return and flow. Placement of PD catheter is a technically simple method to release abdominal pressure and remove overloaded fluid in peritoneal cavity.

No special CRRT device was designed for ECLS. With respect to the initiation of hemodialysis, one approach is to utilize the CRRT machine or a hemofilter into the ECMO.[11] Hemofilter is a fast, convenient, and cost-effective method, but drawbacks exist in many aspects, in relation to the absence of pressure monitoring, regulation of blood flow and ultra-filtration volume. While the CRRT machine is considered to be the best way to

precisely manage intake and output volume for dialysis, as well as the supervision of circuit pressure, especially in critically life-threatening patients, although it requires more priming volume which might adversely cause harmful consequences to hemodynamics in neonates.[11] Further, the possibilities of clotting and rupture of membrane, are proved to be significantly lower in CRRT machine compared to hemofilter.

Experiences available in the literature on concomitant applications of CRRT, PD and ECMO in neonates are relatively limited. Despite of the feasibility of CRRT to ECMO, CRRT is deemed to be an extra-burden and risk factor for ECLS. Some studies report that CRRT increases mortality for ECMO patients, and may negatively influence clinical outcome.[12] The pathological process of AKI, frequently occurred in neonates after ECLS, is poorly acknowledged. Following the development of AKI or other severe complications, neither the improvement of mortality, nor recovery of renal function, could be easily achieved by efforts at simple fluid removal. Clearly, conjugating a CRRT device into ECMO prolongs ECMO treatment duration, and might in turn contribute to negative impacts and other critical complications.

Optimal timing for CRRT initiation during ECLS in neonates is controversial, and some published results are conflicting since CRRT was used in many studies only when complications such as AKI or unmanageable fluid overload had developed.[13] Experiences from our institution, constituting the largest pediatric ECMO series in southern China, confirm the beneficial effects of early initiation of CRRT to ECMO. It is our common practice to introduce CRRT device to ECMO for the prevention of complications induced by fluid overload, rather than for a palliative salvage when multiple organ dysfunction has developed. It is probably not the application of CRRT per se but the presence of uncontrollable condition that raises the risk for in-hospital death. In such uncontrollable conditions, survival rate of ECMO is significantly lower, and CRRT adds complexity to the ECMO circuit and might even worsen the situation.

We conclude that co-initiation of CRRT and PD to ECMO is an effective and safe approach to improve fluid overload in neonates, and severe complications are absent. Based on these advantages, when a neonate requires dialysis of urgency, for the purpose of prompt fluid removal, the concomitant use of CRRT and ECMO is recommended.

4. Conclusion

Co-initiation of CRRT and PD during ECMO therapy is effective and safe to release fluid overload in neonates, and severe complications are absent. In critically ill neonates receiving ECMO, the influence of abdominal compartment syndrome should not be ignored. When a neonate requires dialysis of urgency, ECMO offers assured vascular access to hemodialysis, allowing faster fluid removal.

Author contributions

Chengbin Zhou, Guanhua Li designed the report; Chengbin Zhou, Li Zhang and Yunxia Sun collected the patient‘s clinical data; Guanhua Li and Jimei Chen analyzed the patient‘s data; Guanhua Li wrote the paper. Author Guanhua Li and Li Zhang contributed equally to this work. Author Li Zhang should be considered as the first co-author.
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Writing – original draft: Guanhua Li.
Writing – review & editing: Guanhua Li.

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