ORIGINAL RESEARCH

Early Continuous Renal Replacement Therapy Improves Nutrition Delivery in Neonates During Extracorporeal Life Support

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Objective: Optimizing nutrition in neonatal patients as soon as possible after extracorporeal life support (ECLS) initiation is imperative as malnutrition can worsen both short- and long-term outcomes. Fluid restriction, used to manage the fluid overload that commonly complicates neonatal ECLS, severely impairs nutrition delivery. Continuous renal replacement therapy (CRRT) can be used to help manage fluid overload. We hypothesize that early CRRT utilization ameliorates the need for fluid restriction and allows providers to prescribe higher parenteral nutrition (PN) volumes leading to better nutrition delivery.

Design: The design of the study was a retrospective chart review, and the setting was a single, level III neonatal intensive care unit.

Subjects: Neonatal patients ($n = 42$) treated with ECLS between January 1, 2008, and December 31, 2013.

Interventions: Comparisons were made between 2 groups: neonates who received ECLS without early CRRT initiation (group 1; $n = 23$) and with early CRRT initiation (group 2; $n = 19$).

Main Outcome Measures: The main outcome measures were goal total fluid intake, prescribed PN volume, protein, glucose infusion rate, intralipid, and kilocalories.

Results: Infants who received early CRRT were prescribed higher mean total fluid intake goals (group 1: 99 mL/kg/day vs. group 2: 119 mL/kg/day, $P < .001$) and higher mean volumes of PN (group 1: 61 mL/kg/day vs. group 2: 81 mL/kg/day, $P < .001$) over the first 72 hours of ECLS compared with infants who did not receive early CRRT. Early CRRT receivers also were prescribed greater mean amounts of protein during the first 72 hours of ECLS (group 1: 2.7 g/kg/day vs. group 2: 3 g/kg/day, $P = 0.03$). There were no significant changes noted in prescribed glucose infusion rates, intralipid, or total kilocalories.

Conclusions: Institution of early CRRT in neonates on ECLS allows for administration of greater volumes of PN with improved protein delivery. This study characterizes one benefit of early CRRT initiation in neonates on ECLS and suggests these patients could experience improved nutritional outcomes.

Introduction

EXTRACORPOREAL LIFE SUPPORT (ECLS) is a supportive therapy that provides temporary cardiopulmonary support to critically ill patients with certain reversible diseases. Neonatal patients requiring ECLS are at high risk for malnutrition, which can worsen both short- and long-term outcomes.[1-5] Protein catabolism specifically is markedly increased during ECLS.[2] Optimizing nutrition in neonatal patients as soon as possible after ECLS cannulation is imperative; and in fact, expeditious nutritional support is the first of 4 clinical guidelines prescribed by the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) for nutrition support in neonates requiring ECLS.[1,4] Refractory fluid overload regularly complicates neonatal ECLS, further compounding the risk of malnutrition and increasing both morbidity and mortality.[6-8] Nutrition delivery can be severely impaired, particularly in neonatal patients, by fluid restriction, a commonly used strategy for the management of refractory fluid overload.[9,10]

Continuous renal replacement therapy (CRRT) is an adjunct therapy used to manage fluid overload during ECLS. CRRT is most commonly used after initial attempts to manage fluid overload with fluid restrictions and/or diuretics during ECLS.[10-14] Emerging data suggest early CRRT initiation (CRRT initiation before the development of fluid overload or acute kidney injury) may improve morbidity and mortality during ECLS by preventing significant fluid overload and associated

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sequelae.[6,8] Because severe fluid restriction is unnecessary when a patient receives CRRT, CRRT utilization should allow for delivery of more adequate nutrition to neonates, particularly via parenteral nutrition (PN), and early CRRT use may improve fluid balance enabling more expeditious delivery of adequate nutrition during neonatal ECLS. A study of pediatric patients with respiratory failure receiving ECLS alone case-matched to patients receiving ECLS with CRRT demonstrated associations between concurrent ECLS and CRRT with not only improved fluid balance but also improved caloric intake and less diuretic use; however, this study did not include neonates.[10] We hypothesize that early initiation of CRRT during neonatal ECLS will allow clinicians to prescribe larger volumes of PN with improved concentrations of key components, earlier.

Methods

Data Collection and Statistical Analysis

We conducted a retrospective chart review, collecting data from the medical records of neonates who received ECLS in a single center, level III neonatal intensive care unit (NICU) between January 1, 2008, and December 31, 2013. Patients were excluded if (1) their care was transitioned from NICU to another intensive care unit at our institution within the first 72 hours of cannulation, (2) medical records data were unavailable, or (3) slow continuous ultrafiltration therapy was initiated within first 72 hours of cannulation. Data including patient demographics, PN orders, date and time of initiation of ECLS, date and time of initiation of CRRT, and length of ECLS were collected. Morbidity data including neurodevelopmental testing results, specifically Cognitive Adaptive Test (CAT) and Clinical Linguistic and Auditory Milestone Scale (CLAMS) results, were also collected. Comparisons were made between 2 groups: (1) neonates who received ECLS without early CRRT initiation (group 1) and (2) neonates who received ECLS with early CRRT initiation (group 2). Early CRRT initiation was defined as CRRT initiation within 48 hours of ECLS cannulation.

ECLS With CRRT Configuration

CRRT during this time was done in our institution as described by Weber et al and Hoover et al with an inline HF1000 polyarylethersulfone filter with tubing (Gambro, Hechingen, Germany) added to the ECLS circuit.[10,15] Ultrafiltration from the hemofilter was achieved with the use of IV tubing and IV pumps (Alaris by Becton, Dickinson, and Company; Franklin Lakes, NJ), and ultrafiltrate was collected and measured with a urine drainage bag system (C.R. Bard, Incorporated, Convington, GA). Patient fluid removal rate was determined each day by the neonatology team in consultation with pediatric nephrology. All patients who received early CRRT were treated with continuous veno-venous (VV) hemofiltration, continuous VV hemodialysis, or a combination of both at the discretion of the treating pediatric nephrologist.

Parenteral Nutrition

PN initial orders and escalation orders for neonates in our NICU are standardized by protocols stratified by gestational age. PN orders were retrieved, and data from the first 3 days after ECLS cannulation were recorded. No patients in our cohort received enteral feeds during the first 72 hours of ECLS due to underlying pathology.

Statistical Analysis

Quantitative data are reported as median (interquartile range) or mean (±standard deviation) for continuous data and proportions (percentile) for categorical variables. Univariate comparisons between groups were conducted using Student t-tests, chi-square tests, Fisher's exact tests, or Wilcoxon rank-sum tests, as appropriate. All analyses were performed using SPSS Statistics, version 23 (IBM, Armonk, NY), and statistical significance was determined at a P value $\leq .05$. The university's Institutional Review Board approved the study (Pro00048737).

Results

A total of 46 neonatal patient charts were reviewed and 42 patient charts were included in comparison (Figure 1). Baseline characteristics of patients in both groups were similar including birth weight, gestational age at birth, age at ECLS initiation, duration of ECLS, duration of hospitalization, mode of ECLS (venoarterial versus VV), or survival (survival of ECLS as well as survival to hospital discharge); however, the groups were statistically different with regard to gender (group 1: 65% male vs. group 2: 32% male; $P = .03$; Table 1). The indication for ECLS in each group is also indicated in Table 1; several infants were classified as "other" including 1 patient in group 1 with hydrops, 1 patient in group 2 with tracheal stenosis, 1 patient in group 2 with alveolar capillary dysplasia, and 1 patient in group 2 with late-onset pulmonary hypertension.

Infants who received early CRRT were prescribed higher mean total fluid intake (TFI) goals (group 1: 99 mL/kg/day vs. group 2: 119 mL/kg/day, $P < .001$) and higher mean volumes of PN (group 1: 61 mL/kg/day vs. group 2: 81 mL/kg/day, $P < .001$) over the first 72 hours of ECLS compared with infants who did not receive early CRRT (Table 2). Specifically, on the second and third days of ECLS, statistically significant differences were noted between groups in prescribed TFI goals and PN volumes. Early CRRT receivers also were prescribed greater mean amounts of protein during the first 72 hours of ECLS (group 1: 2.7 g/kg/day vs. group 2: 3 g/kg/day, $P = .03$), with statistically significant differences between groups noted on the first and second days of ECLS (Table 2; Figure 2). On each of the first 3 days of ECLS, more infants in group 2 met goal protein delivery (3 g/kg/day) than infants in group 1 with a statistically