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Fluid overload and outcomes in critically ill children: A single center prospective cohort study

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ABSTRACT

Objective: To prospectively evaluate the association between fluid overload (FO) and clinical outcomes, mortality, mechanical ventilation (MV), and duration and length of stay in a pediatric intensive care unit (PICU).
Methods: Over a 12-month period, patients who were on MV for >24 h or vasoactive support were prospectively included. Demographic and clinical data were recorded. Daily FO was calculated as [(fluid in − fluid out) / admission weight] × 100%. Multivariate stepwise logistic regression analysis was used to determine predictors of survival.
Results: 224 patients were included; median age was 3.3 (IQR 0.7, 9.9) years, mortality was 15.6%. The median peak FO (PFO) was 12.5% (IQR 5, 25), PFO > 10% was present in 55.8% of patients, and PFO > 20% was present in 33%. The PFO in non-survivors was 17.8% (IQR 8, 30) and 11% (IQR 4, 23) in survivors ($p = 0.028$). A survival analysis showed no association between PFO and mortality. A multivariate analysis identified vasoactive support, >3 organ failures and acute kidney injury (AKI) but not FO as independent risk factors for mortality. FO was associated with MV duration and PICU length of stay.
Conclusion: FO is frequent in a general PICU population, but PFO is not an independent risk factor for mortality. Future studies of FO should focus on patients with AKI and multiorgan failure for better classification of severity and potential interventions.

1. Introduction

Intravenous fluid is a common treatment for critically ill patients and is thought to be the cornerstone of initial treatment for many conditions. The development of fluid overload (FO) because of therapeutic interventions is common, particularly in critically ill children, who are at higher risk because of systemic inflammation, reduced plasma oncotic pressure and capillary leak, among other factors. Detrimental effects of FO have been recently described, and most experts now recommend caution when generalizing the beneficial effects of the so-called early goal-directed therapy to situations outside the initial resuscitation phase [1-6]. Our group and others have reported an association between the degree of FO and mortality in children requiring renal replacement therapy [7-15]. Recent data support the association between FO and unfavorable outcomes in other subgroups of critically ill children, such as those with pediatric acute lung injury and respiratory failure [16-19], those who have cardiac surgery and are receiving extracorporeal life support after congenital heart disease surgery [20-22] and newborns [23], but there is still debate regarding whether FO is an epiphenomenon in critically ill patients or is independently related to mortality [24,25].

The purpose of this study was to prospectively evaluate the association between fluid overload and mortality in a general pediatric intensive care unit (PICU) population. The secondary outcomes were evaluations of the associations between FO and mechanical ventilation (MV) duration, hospital and PICU length of stay (LOS). Although positive fluid balance has been related to mortality in many critically illnesses, we hypothesize that FO is an indirect marker of severity in the general population of critically ill children and it is not directly related to mortality.

2. Patients and methods

The Institutional Review Board for Human Use at The University of Alabama at Birmingham approved this study, waiving the requirement for informed consent from individual patients.

Abbreviations: FO, fluid overload; PICU, pediatric intensive care unit; AKI, acute kidney injury; MV, mechanical ventilation; LOS, length of stay; MODS, multiple organ dysfunction syndrome; P-MODS, Pediatric Multiple Organ Dysfunction Score; SCr, serum creatinine.

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2.1. Patients

During a 12-month period (January to December 2007), all children admitted to the PICU at Children's of Alabama were screened each day during their admission. Our unit is a general medical and surgical PICU, but children are admitted to another specialized unit after congenital heart surgery.

All patients who received MV for >24 h or required vasoactive support (>5 mcg/kg/min dopamine) were prospectively identified and included in a relational database. Each admission to the PICU was recorded separately for children with multiple admissions. Patients were excluded if their age at admission was younger than 30 days or older than 21 years; if they had preexisting chronic renal insufficiency or end-stage renal disease; or if admission to the PICU was for a renal transplantation.

2.2. Data collection

Data were recorded at time of inclusion and daily until discharge from the PICU or death. All data recorded, including demographic, laboratory and clinical information, were obtained through medical record review. The treating physician determined the primary diagnosis and cause of death. Pediatric Risk of Mortality 2 (PRISM2) scores at the time of admission to the PICU were recorded as calculated by a single data analyst. Admissions were classified as either having or not having sepsis and as either having or not having multiple organ dysfunction syndrome (MODS). Sepsis was defined using the International Pediatric Sepsis Consensus Conference definitions [26]. MODS was defined as the presence of at least 2 failed organs at any time during PICU admission. Organ system failures were defined using the International Pediatric Sepsis Consensus Conference definitions [26]. Acute kidney injury (AKI) was classified according to pRIFLE criteria. The Pediatric Multiple Organ Dysfunction Score (P-MODS) was calculated [27].

The primary outcome was survival to hospital discharge. The secondary outcomes were hospital and PICU LOS. A retrospective analysis of the prospective collected data was done looking for association between peak FO and duration of MV.

2.3. Fluid overload

The daily and total fluid intake and output were recorded during PICU stay. The percent of FO was calculated using the following formula: [(total fluid intake (L) − total fluid output in liters (L)) / (admission weight in kilograms) * 100] [8,9].

Peak FO was defined as the maximum percentage of FO relative to PICU admission on any day during the PICU stay. Twenty percent FO was chosen as a breaking point based on prior studies [7-10]. Peak FO in patients with continuous renal replacement therapy (CRRT) was considered the FO prior to the initiation of CRRT.

2.4. Statistical considerations

Descriptive statistics were used to summarize all continuous and categorical variables. Comparisons between patient groups were performed using Fisher's exact test for categorical variables and the Mann-Whitney *U* test for continuous variables because of concerns about the normality of the distributions of these variables. Multivariate stepwise logistic regression analysis (with entry criteria of $\alpha = 0.20$ and

Table 1
Demographic and clinical information of all population and survivors. Data as median and interquartile range unless listed. PRISM-2, pediatric risk of mortality score; PICU, pediatric intensive care unit; LOS, length of stay; MV, mechanical ventilation; MODS, multiple organ dysfunction syndrome; PMODS, pediatric multiple organ dysfunction score; AKI, acute kidney injury.

	All $n = 224$	Survivors $n = 189$	Nonsurvivors $n = 35$	*p*-Value
Age (years)	3.3 (0.7,9.9)	2.6 (0.5,9.3)	5.5 (0.9,13.9)	0.035
Weight (kg)	14.3 (6.6–35)	13.1 (6.1–33.3)	19.3 (10.0,47.5)	0.059
Height (cm)	90 (62,136)	89 (60,134)	113 (72,155)	0.044
Gender (%)				0.713
Male	59.8	60.3	57.1	
Female	40.2	39.7	42.9	
Race (%)				0.58
White	48.7	47.6	45.3	
Black	42.4	43.4	37.1	
Hispanic	7.1	7.4	5.7	
Other	1.8	1.6	2.9	
PRISM2 (mean ± SD)	13.2 ± 8.7	11.5 ± 7.2	22.4 ± 10.4	<0.01
PICU LOS (days)	6 (4,9)	6 (4,10)	5 (3,10)	0.84
Hospital LOS (days)	12 (7,22)	14 (5,23)	6 (2,12)	<0.01
MV support (%)	90.6	89.9	94.3	0.542
MV duration (days)	4 (2–7)	4 (2,7)	4 (3,7)	0.324
MODS (%)	92	90.5	100	0.084
PMOD Score	1 (0,3)	1 (0,2)	3 (1,7)	<0.01
≥3 organ failures (%)	70	20.63	100	<0.01
pRIFLE				<0.01
no AKI	17.9	21.2	0	
R or I	64.7	66.2	47.1	
F	17.4	12.7	42.9	
Vasoactive support (%)				
≥1 drug	40.2	30.7	91.4	<0.01
≥2 drugs	25	15.9	77.1	<0.01
Diagnosis (%)				0.067
Respiratory	30.8	34.4	11.4	
Trauma	17.9	16.9	22.9	
Neurological	15.2	15.3	14.3	
Cardiac	11.6	12.2	8.6	
Sepsis	7.6	6.3	14.3	
Oncology	7.6	6.3	14.3	
Liver	2.2	1.6	5.7	
Renal	2.2	2.1	2.9	
other	4.9	4.9	5.6	

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