Prophylactic Peritoneal Dialysis Following Cardiopulmonary Bypass in Children Is Associated with Decreased Inflammation and Improved Clinical Outcomes

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ABSTRACT

Objective. To investigate impact of prophylactic peritoneal dialysis (PD) on clinical outcomes and inflammatory cytokines in children following cardiac surgery with cardiopulmonary bypass.
Design. Prospective before-and-after nonrandomized cohort study.
Setting. Pediatric cardiovascular intensive care unit in tertiary hospital.
Patients. Fifty-two consecutive neonates and infants at high risk for postoperative fluid overload following cardiopulmonary bypass. All had PD catheters placed during primary cardiac surgery.
Intervention. Initial 27 patients were managed with passive peritoneal drainage and diuretics (controls). Following 25 patients were started on prophylactic PD in immediate postoperative period and managed per PD protocol (+PD).
Outcome Measures. Cumulative fluid balance, indices of disease severity, and clinical outcomes were prospectively collected. Plasma interleukin-6 and interleukin-8 were measured immediately before-and-after cardiopulmonary bypass and at 24 and 48 hours post–cardiopulmonary bypass.
Results. Demographics, diagnoses, and intraoperative variables were similar. Median net fluid balance was more negative in +PD at 24 hours, –24 mL/kg (interquartile range: –62, 11) vs. +18 mL/kg (interquartile range: –26, 11), $P = .003$, and 48 hours, –88 mL/kg (interquartile range: –132, –54) vs. –46 mL/kg (interquartile range: –84, –12), $P = .004$. +PD had median 55 mL/kg less fluid intake at 24 hours, $P = .058$. Peritoneal drain, urine, and chest tube output were comparable over first 24 hours. Mean inotrope score was lower in +PD at 24 hours. +PD had earlier sternal closure—24 hours (interquartile range: 20, 40) vs. 63 hours (interquartile range: 44, 72), $P < .001$—and a trend toward shorter duration of mechanical ventilation—71 hours (interquartile range: 49, 135) vs. 125 hours (interquartile range: 70, 195), $P = .10$. +PD experienced lower serum concentrations of interleukin-6 and interleukin-8 at 24 hours.
Conclusions. Prophylactic PD is associated with greater net negative fluid balance, decreased inotrope requirements, and lower serum concentrations of inflammatory cytokines in the early postoperative period.

Key Words. Congenital Heart Disease; Postoperative Care; Peritoneal Dialysis; Fluid Overload; Cardiopulmonary Bypass; Neonate

Introduction

Fluid overload (FO) is common in neonates after cardiac surgery with cardiopulmonary bypass (CPB)[1,2] and may be associated with increased morbidity and mortality. Fluid overload may result from hemodilution from CPB, capillary leak, fluid/blood product administration, low cardiac output, low oncotic pressure, and/or impaired renal function. Systemic inflammation induced by CPB may worsen FO via deleterious effects on endothelial cell integrity[3] and myocardial function.[4] Excess fluid accumulation impairs pulmonary gas exchange and can contribute to renal, myocardial, and neurological dysfunction.[5]

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Collectively, the harmful effects of FO may increase duration of mechanical ventilation, delay sternal closure, increase inotrope requirements, and prevent optimal nutrition.

Common strategies to limit FO include intraoperative and postoperative ultrafiltration,[6,7] restriction of fluid intake, diuretic administration,[8] and passive peritoneal drainage.[9] Several uncontrolled studies have suggested that peritoneal dialysis (PD) is a safe and effective method of fluid removal in neonates and infants after CPB.[10–19] Others have suggested that postoperative PD ameliorates post-CPB inflammation via cytokine removal.[20,21] Unfortunately, these descriptive studies are limited by small sample sizes, retrospective data collection, and the lack of substantive control groups.

We conducted a prospective before-and-after nonrandomized cohort study in neonates and infants undergoing high-risk cardiac surgery to evaluate the effectiveness of a goal-directed PD fluid removal protocol. Cumulative fluid balance, indices of disease severity, and clinical outcomes in patients managed with the PD protocol (+PD) were compared with a group of similar patients managed with passive peritoneal drainage and diuretics (controls). We hypothesized that +PD would be associated with shorter mechanical ventilation duration and superior fluid removal. We also hypothesized that +PD would have lower postoperative inflammatory cytokine serum concentrations.

Methods

Study Design

Neonates and infants undergoing complex congenital heart surgery with CPB at our institution receive peritoneal drains during their primary cardiac procedures. We prospectively collected data on 52 consecutive patients who received intraoperative PD catheters during two management eras: a control period from July 1, 2010 to December 31, 2010 and a +PD study period from January 1, 2011 until December 31, 2011. Inclusion and exclusion criteria were the same for both groups. During the control period, patients were managed with passive peritoneal drainage and diuretics. Patients in the +PD era were managed with our PD protocol, in which PD was initiated within 6 hours of cardiac intensive care unit (CICU) admission.

The only definitive inclusion criterion was PD catheter placement during primary cardiac procedure. Placement of peritoneal catheters was routinely performed in neonates and infants at the discretion of the cardiothoracic surgeons (R.D. and J.K.) in the following circumstances: complex neonatal cardiac surgery, patients at high risk for postoperative right ventricular dysfunction, and patients requiring high inotropic support upon weaning from CPB. Exclusion criteria included preoperative renal replacement therapy, extracorporeal membrane oxygenation (ECMO) initiation within 6 hours of CICU admission, or lack of informed consent. Institutional Review Board of the University of Alabama at Birmingham approved this study.

Control Study Period

Participants enrolled before January 1, 2011 had peritoneal catheters placed to gravity drainage. Furosemide infusions were started on postoperative day (POD) #1 (titrated between 0.05 and 0.5 mg/kg/h), targeting net negative fluid balance. Dialysis was initiated only for traditional indications per judgment of the attending physician (e.g., renal insufficiency and severe FO refractory to diuretics). Twenty-five percent albumin was administered to maintain serum albumin $\geq$3 g/dL; there was no prophylactic replacement of peritoneal drainage with plasma or albumin.

Prophylactic PD Protocol Study Period

Participants enrolled between January 1, 2011 and December 31, 2011 received PD once hemodynamics stabilized, goal initiation time within 6 hours of CICU admission. We utilized neonatal "Dialy-Nate" disposable PD delivery system (Utah Medical Products, Midvale, UT, USA); dialysate solutions of 1.5%, 2.5%, and 4.25% dextrose were connected to an enclosed system and warmed prior to infusion. Dialysis was initiated with 10 mL/kg fill volume of 1.5% dextrose dialysate. Hourly cycles consisted of 10-minute fill, 40-minute dwell, and 10-minute drain. Dextrose concentration was titrated to target the following goals: zero fluid balance by first postoperative morning and negative 50–100 mL/kg for each subsequent 24-hour period. Fill volumes and time of dwell were kept constant. Diuretics were not used during active PD. Peritoneal dialysis was continued for a minimum of 48 hours; after 48 hours, discontinuation of PD occurred for the following (if urinary output $\geq$2 mL/kg/h): (1) net negative fluid balance from admission; (2) resolution of anasarca; or (3) per discretion of attending physician. Peritoneal dialysis catheters were left to straight drain for an additional 24 hours before

removal. Dextrose concentration was lowered if serum glucose persistently >200 mg/dL.

Postoperative Management

Management of both control and +PD groups was protocolized to target age and defect-specific hemodynamic and respiratory goals via inotrope titration, colloid boluses, and ventilator adjustments as described elsewhere.[22] All patients were managed via fluid restrictive protocol including 25% maintenance intravenous fluids during the first 24 hours and maximally concentrated infusions. Adjunctive therapy included high protein total parenteral nutrition and repletion of albumin, electrolytes, and serum immunoglobulins. Serum albumin was checked daily and oncotic pressure was maintained with 25% albumin infusions to keep serum albumin ≥3 g/dL. Renal and cerebral near-infrared spectroscopies (NIRSs) monitors were used in all patients per unit protocol. NIRSs data was used in conjunction with other hemodynamic and laboratory data to assess cardiac output and oxygen consumption, though interventions to target specific NIRS values were not routinely conducted.

Intraoperative Management

After primary surgical procedure, a 39-cm single-cuffed silicone PD catheter (Pediatric Tenckhoff Curl Catheter; Tyco, Mansfield, MA, USA) was inserted into abdominal cavity via sternotomy incision and brought through left abdominal wall with cuff external to skin or through direct, tunneled periumbilical approach. During CPB, patients were cooled to either 22°C (Norwood patients) or 25–28°C (all others). A strategy of selective cerebral perfusion was used during all aortic arch reconstructions; deep hypothermic circulatory arrest was not employed in any patients. Sternum was left open in Norwood patients and others experiencing high inotrope requirements or excessive bleeding. All patients received zero-balance ultrafiltration during CPB and single-pass ultrafiltration after CPB. All patients received 10 mg/kg of methylprednisolone 8 and 1 hour before surgery. Intraoperative steroids were not given.

Sample Analysis for Interleukin-6 and Interleukin-8

Whole blood samples were obtained, processed, and stored at −80°C at four time points until analysis: immediately pre-CPB, post-CPB upon arrival to CICU, and at 24 and 48 hours post-CPB. Serum interleukin (IL)-6 and IL-8 were measured via multiplex electrochemiluminescence detection method (MSD 2400 imager, Meso Scale Diagnostics, Gaithersburg, MD, USA). Minimum sensitivities were 0.018 pg/mL for IL-6 and 0.10 pg/mL for IL-8.

Definitions

For time-dependent variables, time of admission to CICU was considered time zero. Inotrope score was calculated as follows: 1 × dopamine dose (μg/kg/min), plus 100 × epinephrine or norepinephrine dose (μg/kg/min), plus 10 × phenylephrine dose (μg/kg/min), plus 10 000 × vasopressin dose (units/kg/min).[23,24] Percent FO was calculated as follows: ([total mL fluid intake − total mL fluid output]/preoperative kg weight) × 100.[25]

Statistical Analysis

This study was powered to determine a 1-day difference in duration of mechanical ventilation between groups. Data were summarized as means with SD or medians with interquartile range (IQR) where appropriate. All analyses were performed in intention to treat manner. Continuous variables were compared using Wilcoxon Mann–Whitney or Student's *t*-test where appropriate. Categorical data were compared using Fisher's exact test. Two-tailed *P* values of <.05 were considered statistically significant. Cytokine analysis was performed using analysis of variance after log transformation of data given lack of normal distribution. Bonferroni correction was used to control for multiple comparisons in cytokine analysis. SPSS 19 (SPSS Inc, Chicago, IL, USA) was used for all statistical tests.

Results

Fifty-eight patients were eligible for this study; six were excluded (five ECMO and one refusal parental consent). Controls (n = 27) and +PD (n = 25) were not different with respect to age, weight, CPB and aortic cross clamp times, surgical diagnosis, and risk-adjusted classification for congenital heart surgery category (Table 1). Dialysis was initiated in +PD at median 2.5 hours (IQR: 2, 4.4) and continued for median 86 hours (IQR: 41, 122). The majority of subjects (44/52, 85%) remained on their allocated strategies of fluid removal. Deviations included the following: one control subject who received bolus furosemide dosing (instead of continuous infusion), two +PD patients who received a single dose of furosemide during active PD, and five control patients who were

Table 1. Demographics and Surgical Procedures

	Control (n = 27)	+PD (n = 25)	*P*
Preoperative weight (kg)	3.26 ± 0.90	3.67 ± 1.15	.20
Age (d) at operation	7 (4, 13)	10 (6, 74)	.20
Gestational age (wk)	37.9 ± 2.0	37.2 ± 3.5	.89
Male gender, n (%)	19 (70)	19 (76)	.76
Race (n)			
White	13	13	1.00
Black	11	10	1.00
Other	3	2	1.00
Duration of cardiopulmonary bypass (min)	177.8 ± 56.1	176.4 ± 58.7	.93
Duration of aorta cross clamp (min)	81.1 ± 25.6	90.9 ± 27.0	.19
RACHS-1 category	4.4 ± 1.7	3.9 ± 1.5	.24
Delayed sternal closure, n (%)	20 (80)	21 (78)	1.0
Diagnosis			
Stage 1 Norwood	13	6	.09
Arterial switch operation with VSD repair	2	5	.24
Arterial switch operation	2	4	.41
TAPVR repair	3	0	1.00
Tetralogy of Fallot repair	3	2	.24
Aortic arch reconstruction	2	4	.70
Atrioventricular canal repair	0	4	.05
Truncus arteriosus repair	1	0	1.00
TAPVR/unifocalization/central shunt	1	0	1.00

Data presented as median (IQR) or mean (SD).
+PD, patients receiving prophylactic peritoneal dialysis; Control, patients not receiving prophylactic peritoneal dialysis; RACHS-1, risk-adjusted classification for congenital heart surgery-1; VSD, ventricular septal defect; TAPVR, total anomalous pulmonary venous return; IQR, interquartile range.

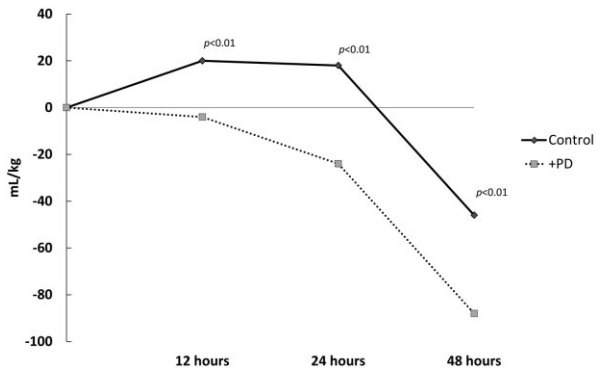

Figure 1. Median net fluid balance after admission to the cardiac intensive care unit for prophylactic peritoneal dialysis patients (+PD) and those that received passive peritoneal drainage and diuretic therapy alone (controls). +PD achieved more negative fluid balance by 12 hours and remained more negative at all three time points.

started on PD for FO and oliguria. In these five subjects, median time to PD initiation was 20.9 hours (IQR: 16.3, 23.5), with median duration of PD = 223 hours (IQR: 166.5, 263).

Fluid Balance

Relative to controls, +PD achieved negative fluid balance more rapidly and remained more negative than control through 48 hours (Figure 1). Through the first 24 hours, there was a trend toward less fluid intake in +PD relative to controls (median 176 mL/kg [IQR 142, 246] vs. median 231 mL/kg [IQR 189, 290], P = .058). Urine output, net PD output, and chest tube output were similar between groups. From 24 to 48 hours, +PD had greater PD output but lower urine output than controls (Table 2). Percent FO was significantly lower in +PD subjects relative to controls at 24 hours: median −6.5% (IQR: −12.5, 0.9) vs. +6.3% (IQR: −7.7, 22.8), P = .004. At 48 hours, 9/27 (33%) control patients had ≥15% FO compared with only 1/25 (4%) +PD subjects, P = .01. Serum albumin and hematocrit were similar between the groups at 24 and 48 hours (Table 2).

Clinical Outcomes

There was a trend toward shorter duration of mechanical ventilation in +PD: 71 hours (IQR: 49, 135) vs. 125 hours (IQR: 70, 195), P = .10. Sternal closure was delayed in 20/25 (80%) of +PD and 21/27 (79%) of control patients. Sternal closure occurred sooner in +PD (24 hours [IQR: 20, 40] vs. 63 hours [IQR: 44, 72], P < .001). Mean inotrope scores were lower in +PD over first 24 hours (7.6 ± 4.5 vs. 10.9 ± 5.6, P = .04) and from 24 to 48 hours (4.2 ± 3.4 vs. 7.8 ± 5.9, P = .04). Median central venous pressure was similar between groups over the first 24 hours but higher in +PD from 24 to 48 hours (mean 12 ± 3 vs. 10 ± 2 cm H_20, P = .004). There were no differences in any other respiratory or hemodynamic variables (Table 3). Median days to PD catheter removal

Table 2. Comparison of Fluid Balance, Hematologic, and Renal Variables

	Control (n = 27)	+PD (n = 25)	*P*
24-h intake (mL/kg)	231 (189, 290)	176 (142, 246)	.058
24-h output (mL/kg)	223 (178, 269)	201 (175, 221)	.34
Urinary output first 24 h (mL/kg)	42 (36, 60)	38 (25, 49)	.20
Net PD catheter output first 24 h (mL/kg)	99 (72, 130)	110 (64, 115)	.37
Chest tube output first 24 h (mL/kg)	62 (50, 75)	53 (41, 87)	.44
Net fluid balance at 24 h (mL/kg)	+18 (–26, 72)	–24 (–62, 11)	.003
24- to 48-h intake (mL/kg)	120 (100, 152)	130 (110, 153)	.43
24- to 48-h output (mL/kg)	193 (167, 237)	211 (173, 234)	.59
Net PD catheter output 24–48 h (mL/kg)	37 (22, 60)	120 (97, 155)	<.001
Urinary output 24–48 h (mL/kg)	135 (94, 165)	29 (14, 49)	<.001
Net fluid balance at 48 h (mL/kg)	–46 (–84, –12)	–88 (–132, –54)	.004
Baseline serum creatinine (mg/dL)	0.5 (0.2, 0.6)	0.4 (0.3, 0.5)	.61
Maximum serum creatinine (mg/dL)	0.7 (0.6, 1)	0.7 (0.5, 0.9)	.48
Incidence serum creatinine ≥150% baseline (n)	24 (89%)	18 (72%)	.17
Albumin, serum (g/dL) 24 h	3.3 ± 0.5	3.3 ± 0.5	.95
Albumin, serum (g/dL) 48 h	2.9 ± 0.5	3.0 ± 0.4	.46
Hematocrit (%) on admission	44 ± 8	42 ± 6	.2
Hematocrit (%) 24 h	45 ± 7	42 ± 6	.08

Data presented as median (IQR) or means (SD); net fluid balance since CICU admission.
PD, peritoneal dialysis, +PD, patients receiving prophylactic peritoneal dialysis; Control, patients not receiving prophylactic peritoneal dialysis; CICU, cardiac intensive care unit; IQR, interquartile range.

Table 3. Comparison of Hemodynamic Variables

	Control (n = 27)	+PD (n = 25)	*P*
Inotrope score, admission	9.1 ± 4.7	8.5 ± 5.1	.79
Inotrope score first 24 h	10.9 ± 5.6	7.6 ± 4.5	.04
Inotrope score 24–48 h	7.8 ± 5.9	4.2 ± 3.4	.04
HR first 24 h (per min)	159 ± 14	153 ± 17	.15
HR 25–48 h (per min)	156 ± 15	151 ± 21	.37
MAP first 24 h (mm Hg)	54 ± 9	52 ± 6	.43
MAP 25–48 h (mm Hg)	56 ± 9	57 ± 7	.57
CVP first 24 h (cm H_2O)	11 ± 2	12 ± 2	.49
CVP 25–48 h (cm H_2O)	10 ± 2	12 ± 3	.004
Maximum lactate (mmol/L)	8 ± 5	7 ± 4	.54
Renal near-infrared spectroscopy first 24 h (%)	70 ± 11	76 ± 11	.07

Data presented as median (IQR) or mean (SD) of hourly averages.
+PD, patients receiving prophylactic peritoneal dialysis; Control, patients not receiving prophylactic peritoneal dialysis; HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; IQR, interquartile range.

were similar: six (IQR: 3, 7) for controls and five (IQR: 4, 6) for +PD. Duration of CICU stay was not different between groups.

Inflammatory Cytokines

+PD and control groups had similar preoperative serum IL-6 and IL-8 levels and similar elevation after CPB (Figure 2). At 24 hours, +PD was associated with significantly lower serum concentrations of both cytokines (IL-6: 66.8 ± 26.7 pg/mL vs. 106.9 ± 75.4 pg/mL, $P = .01$; IL-8: 87.1 ± 61.8 pg/mL vs. 125.3 ± 31.3 pg/mL, $P = .02$). At 48 hours, serum IL-6 and IL-8 concentrations were similar between groups, approaching preoperative concentrations. The mean percent decrease in serum IL-6 from CICU admission to 24 hours post-CPB was greater in +PD (–24%) compared with controls (+7%), $P = .007$. Percent change in serum IL-8 was not different between +PD and controls: –22% and –32%, respectively, $P = .32$.

Norwood Patients

Consecutive patient enrollment resulted in an unequal distribution of Norwood patients in the study groups ($P = .09$). To determine if the larger number of Norwood patients in control era (13 vs. 6 in +PD) influenced clinically important outcomes, a subanalysis of the Norwood population was performed. Comparison of all Norwood patients (control and +PD) vs. all other surgical diagnoses demonstrated no difference in duration of mechanical ventilation, time to sternal closure, 24-hour fluid intake, 24- or 48-hour net fluid balance, or 24-hour average inotrope scores. Similar to overall study findings, +PD Norwood

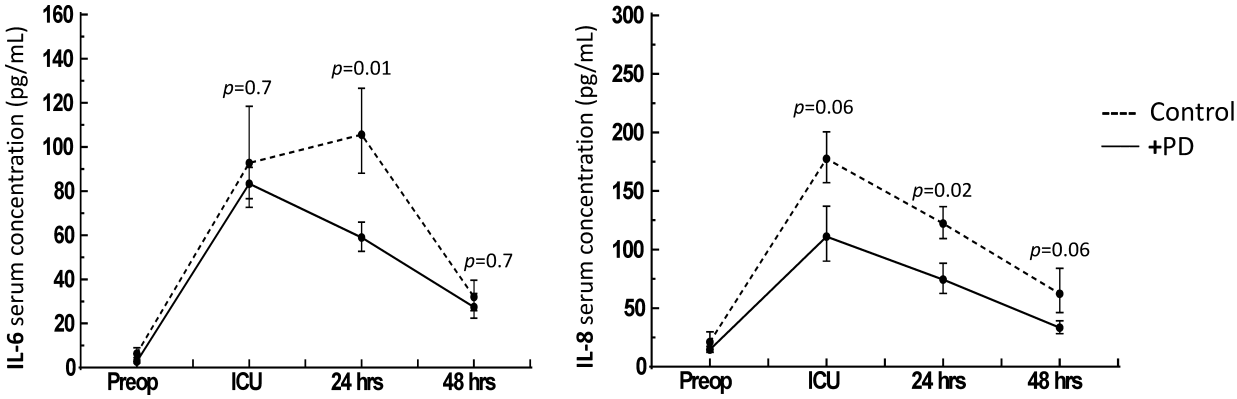

Figure 2. Serum interleukin (IL)-6 and IL-8 concentrations for control and patients receiving prophylactic peritoneal dialysis (+PD) patients over time (geometric mean values ± one standard error). Samples draw immediately precardiopulmonary bypass (CPB), shortly after arrival to intensive care unit (ICU) following CPB (labeled "ICU" on *y*-axis), 24 hours after CPB, and 48 hours after CPB. +PD had significantly lower IL-6 and IL-8 concentrations 24 hours after CPB.

Table 4. Complications of Peritoneal Dialysis

Complication, n (%)	Control (n = 27)	+PD (n = 25)	*P*
Peritonitis (suspected)	0	1	.48
PD fluid draining from chest tubes	2	3	.67
PD fluid from catheter exit site	1	2	.46
Peritoneal catheter difficulty draining	0	3	.10
Omentum herniation	1	0	1.00
Hemoperitoneum	2	3	.67
Chyloperitoneum	2	2	1.00
Serum glucose >180 (mg/dL)	12	12	1.00
Serum glucose <50 (mg/dL)	5	3	.71
Serum phosphorus <2.5 (mg/dL)	6	8	.54
Serum potassium <3.1 (mmol/L)	16	17	.57
Peak inspiratory pressure >35 (cm H_2O)	8	9	.77

PD, peritoneal dialysis; +PD, patients receiving prophylactic peritoneal dialysis; Control, patients not receiving prophylactic peritoneal dialysis.

patients had shorter time to sternal closure (22 hours [IQR: 21, 32] vs. 63 hours [IQR: 43, 106], $P < .001$) and less fluid intake at 24 hours (159 mL/kg [IQR: 137.8, 253.1] vs. 247.6 mL/kg [IQR: 210.7, 313.2], $P = .04$) than control period Norwood.

Complications

Table 4 displays complications related to PD or peritoneal catheters. Peritoneal dialysis was stopped early in two patients (38 and 44 hours) due to obstruction of catheter and excessive drainage from PD exit site. One +PD patient had suspected peritonitis (elevated peritoneal fluid white blood cell count but negative gram stain and culture). Hemoperitoneum self-resolved in all cases. Frequency of electrolyte disturbances was not different. One patient in each group required hemodialysis due to acute renal failure and ineffective clearance from PD. No +PD patients required termination of PD for hemodynamic instability.

There were four deaths (one control and three +PD, $P = 1$), thought unlikely to be directly influenced by the use of PD: Norwood from sepsis and multiorgan dysfunction on POD #11, atrioventricular canal/double outlet right ventricle repair from pulmonary hypertension after pulmonary hemorrhage on POD #7, interrupted aortic arch/ventricular septal defect repair from multiorgan dysfunction on POD #17, and interrupted aortic arch repair from multiorgan dysfunction on POD #37. Only one patient was receiving PD at time of death.

Discussion

Our study found that compared with management with passive peritoneal drainage and furosemide infusions, early initiation of PD was associated with less FO, shorter time to sternal closure, lower inotrope scores, and lower levels of serum proinflammatory cytokines in children high risk for post-CPB FO.

Severe FO has been associated with increased morbidity and mortality in several populations of critically ill children: those requiring renal replacement therapy,[25–28] with diagnosis of respiratory failure,[29] and receiving postcardiotomy ECMO support.[30] While data specifically assessing implications of FO in the post-CPB pediatric population are limited, failure to achieve net negative fluid balance has been associated with increased morbidity in this population.[31] Our study found that the use of prophylactic PD is associated with decreased incidence of severe FO in neonates and infants after CPB. By 24 hours of admission, +PD patients actually had a negative mean fluid balance, and at 48 hours, incidence of 15% FO was significantly lower in +PD. As FO may impair cardiac and pulmonary function,[5] we believe that many of +PD's favorable clinical outcomes were related to the group's decreased fluid accumulation.

Prophylactic PD was associated with shorter time to sternal closure, occurring almost 2 days sooner than control patients. Delayed sternal closure has acknowledged benefits after complex cardiac surgery but is also associated with increased risk of mediastinitis[32] and prolonged ICU stay.[33,34] It is likely that prevention and/or reduction of anasarca in +PD influenced earlier sternal closure.

There was a trend toward shorter duration of mechanical ventilation in +PD. It is notable that exclusion of one outlier in the +PD group (postoperative course complicated by pulmonary hemorrhage with 570 ventilation hours) would shorten the median duration of mechanical ventilation in this group to 69 hours, which would be 56 hours shorter than controls, $P = .04$. Length of CICU stay was not different between groups. Our unit policy predicates that neonates tolerate full enteral feeds prior to transfer. Variability in feeding tolerance in this population despite otherwise normal postsurgical convalescence may have contributed to lack of difference in duration of CICU stay.

Contrary to our hypothesis of superior fluid removal by PD, +PD's net negative fluid balance through first 24 hours was more heavily influenced by less fluid intake in +PD (Table 3). Lack of statistical significance ($P = .058$) between groups' fluid intake may be secondary to our relatively small sample size and large variability in data. As all study patients received protocolized maintenance fluid and medication infusions, any difference in intake predominantly represents colloid resuscitation. Prophylactic PD was also associated with lower inotrope score over first 48 hours and trend toward higher renal NIRS during the first 24 hours. Arguments against the use of PD in critically ill children often cite concern about potential negative hemodynamic effects, specifically impairment in preload during filling and dwelling cycles. We found that PD was well tolerated, even in the early postoperative period. Our data suggest that PD may actually help stabilize the tenuous hemodynamics during the early postoperative period, as evidenced by association with less fluid resuscitation, decreased inotrope escalation, and trend toward higher renal NIRS in +PD.

Aside from fluid removal benefits, evidence suggests that PD removes inflammatory cytokines,[20,21] potentially ameliorating their deleterious impact on organ function. The systemic inflammatory response induced by CPB has been implicated as a trigger of capillary leak and multiorgan dysfunction in children after cardiac surgery.[2,3,35] In particular, IL-6 and IL-8 levels have been correlated with surrogates for severity of illness, including 24-hour lactate in infants after CPB.[36] In +PD, IL-6 and IL-8 serum concentrations were significantly lower 24 hours post-CPB. In addition, it appears that clearance of IL-6 occurred faster in +PD. It is feasible that decreased colloid resuscitation and inotrope support in +PD was facilitated by enhanced inflammatory cytokine clearance via PD ultrafiltration. Removal of substantial concentrations of IL-6 and IL-8 by PD has been previously described.[20,21] We did not analyze PD fluid in our current study. Despite this major limitation, we are the first to show that PD is associated with lower serum cytokines after CPB when compared with a similar group of neonates and infants that did not receive PD. This promising potential link between improved clinical outcomes and inflammatory cytokine removal in +PD patients warrants further investigation.

Our study is the first to evaluate clinical outcomes in patients managed with prophylactic PD compared with controls of similar patient population. Several single-center studies have described PD after CPB in neonates and infants in the setting of FO or acute kidney injury, demonstrating that PD is safe and effective for fluid removal,[10–19] and may improve hemodynamic[10,12,13,19] and pulmonary outcomes.[12] A few studies describe benefits of early/prophylactic PD.[10,13,19,37] A recently published retrospective study by Bojan et al. demonstrated decreased mortality among neonates following CPB who

received "early" PD compared with "late" PD after adjusting for multiple clinical variables.[37] The absence of a control group in this and other studies makes it difficult to support benefits as much more than association with normal convalescence.

The safety and ease of PD make it an appealing modality of fluid removal following CPB. Many institutions regularly place peritoneal catheters in neonates and other children at risk for right ventricle dysfunction during their primary cardiac procedures. Like other studies of PD after CPB,[10,13,15–19,37] we found that side effects of PD were minimal and did not occur more frequently than control group. There were no cases of culture proven peritonitis. While it was common to see a transient rise in central venous pressure by 2–3 cm H_2O during filling cycles (majority of infants had femoral central venous lines per institution preference), impairment in preload was not a common observation.

The goal of our PD protocol was prevention, not treatment of FO. As data were analyzed in intention to treat fashion, it is important to note that five control patients received active PD secondary to oliguria and/or FO. All five received PD almost 1 day later in their CICU course compared with +PD. While fluid removal was effective in all cases, these patients tended to receive PD over twice as long as +PD. Given the association between degree of FO at onset of renal replacement therapy and mortality in critically ill children,[25–28] these patients may have had improved outcomes if PD had been started empirically prior to development of significant FO. It remains to be seen whether the association between degree of FO at onset of dialysis and mortality exists in patients managed with PD after CPB.

This study is limited by the inherent weaknesses of its relatively small sample size and single-center design. Several measured outcome variables, including our primary outcome and fluid intake, would have reached statistical significance with the exclusion of one extreme outlier. While our CICU has strict management protocols, we cannot discount interprovider variability. The higher percentage of Norwood patients in the control group could lead one to speculate that +PD achieved much of its benefit via decreased number of "sicker" patients. However, analysis of the Norwood population vs. all others reveals that fluid and time-dependent variables were not different. We cannot conclude that PD catheters offer benefit over patients without them, though a recent study of children undergoing complete atrioventricular canal repair demonstrated that patients managed with passive PD drainage had greater negative fluid balance compared with those without PD drains.[9]

In conclusion, we found that a protocol centered on early initiation of PD in neonates and infants following high-risk cardiac surgery is associated with greater negative fluid balance and decreased inotrope requirements in the early postoperative period. Patients receiving prophylactic PD had earlier sternal closure and trend toward shorter duration of mechanical ventilation. Prophylactic PD was also associated with decreased serum levels of proinflammatory cytokines in the first 24 hours after CPB. These potentially important findings should be confirmed in a larger multicenter randomized clinical trial.

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