Inotropic support and peritoneal dialysis adequacy in neonates after cardiac surgery

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Abstract

We describe the impact of cardiovascular pharmacologic support on peritoneal dialysis adequacy in 20 neonates who required postoperative renal replacement therapy following cardiopulmonary bypass exposure. Peritoneal dialysis was administered for 2.5 (2) days. Peritoneal dialysis creatinine clearance was 3.4 (2.1) ml/min/1.73 m² and ultrafiltration rate was 9.75 (10) ml/h. Residual creatinine clearance was 31 (26) ml/min/1.73 m². Peritoneal dialysis creatinine clearance appeared to be a function of dialysate flow up to 100 ml/h. No correlation was present between inotropes and vasopressors infusion and peritoneal dialysis creatinine clearance/ultrafiltration rate. LDH clearance was 0.59 (0.85) ml/min/1.73 m² and it did not appear to have a correlation with dialysate flow. Patients in-hospital mortality was 20%, significantly higher than overall neonatal population admitted to our ICU (4.8%, P=0.02). Peritoneal dialysis in neonates allows optimal ultrafiltration rate and adequate small solute clearance, irrespective of hemodynamic status or vasopressor support.

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1. Introduction

Renal replacement therapy (RRT) is delivered in up to 10% of children undergoing cardiac surgery for correction of congenital heart disease and is associated with an increased mortality rate [1–3]. Cardiopulmonary bypass (CPB) and low flow states likely contribute to the development of acute kidney injury (AKI) [4, 5]. Even in the absence of evident signs of renal dysfunction, a clinical condition of fluid retention and generalized edema is common in neonates after major cardiovascular interventions [3]. While various therapeutic options are available, early peritoneal dialysis (PD) administration is the treatment of choice for these patients in many centers [2]. Optimization of fluid balance is primarily targeted by PD initiation. Nonetheless, clearance of nitrogenous waste products and other solutes is also likely to be important in children who develop AKI. Efficiency of PD in the immediate postoperative period following CPB, however, may be affected by several factors: small dialysate exchange volumes are often prescribed and delivered in order to minimize hemodynamic derangements, excessive abdominal pressure rise and leakage of abdominal catheters [6]. Furthermore, blood flow to the peritoneum may be reduced secondary to diminished cardiac output, high vasopressors dose, changes in vascular resistance, or capillary leak [6].

PD is currently accepted as a feasible, safe and effective therapy but information on clearance and ultrafiltration patterns during PD in this specific subset of patients is missing. This study aimed to describe the impact of hemodynamic pharmacologic support on PD adequacy in neonates who require postoperative PD following CPB exposure.

2. Materials and methods

2.1. Study protocol

We conducted a prospective observational study on a cohort of 20 consecutive neonates who received postoperative PD after cardiac surgery requiring CPB. Indications to PD were the presence of oliguria (defined as urine output <0.5 ml/kg/h for more than 4 h) and/or generalized edema with need for supplementary ultrafiltration. At the time of enrollment, demographic and clinical data (age, sex, body surface area, primary diagnosis, surgery, duration of CPB) were collected (Table 1). Cycling peritoneal dialysis was performed in all subjects using a cuffed Tenckhoff catheter. A fixed exchange volume of 10 ml/kg was always infused. Dwell and drainage times varied depending on patients needs. Hence, final dialysate flow (hourly Qd: exchange volume×number of exchanges per hour) was exclusive function of dwell and drainage times and not of volume infused per cycle. Dialysis fluid glucose concentration (ATC B05DA, AIC Baxter SpA, Rome, Italy) was 1.35%.
After the institution of PD and every 24 h for a period of three days a simultaneous sample of blood and 6 h PD drainage were analyzed locally for creatinine, lactic dehydrogenase (LDH), sodium, potassium, glucose and lactates. These solutes were selected among those routinely available in our laboratory. Six-hour urine collection was also analyzed for creatinine clearance in patients with residual renal function. Mean arterial pressure, heart rate, vasoressors dose, diuretics, ultrafiltration rate, fluid balance and significant clinical events occurring during the study period were recorded. Duration of PD, length of intensive care unit stay and out of hospital mortality were also documented. The Institutional Review Board of Bambino Gesù Hospital approved the protocol and waived the need for consent from patient parents because of the observational nature of the study.

2.2. Measurements

Body surface area (BSA) was determined using duBois formula as follows:

\[
\text{BSA m}^2 = 0.007184 \times \text{wt}^{0.425} \times \text{ht}^{0.725}.
\]

PD solute clearance was calculated by multiplying a 6 h dialysate volume by the ratio between solute concentration in dialysate and plasma \((D/P_{\text{solute}})\). Residual creatinine clearance was calculated when present multiplying 6 h urine volume (simultaneous to dialysate collection) by the ratio between creatinine concentration in urine and plasma. The period of 6 h was selected in order to include periods with constant hemodynamic parameters and drug infusions that could occur over a broader time. Clearances were always indexed to 1.73 m².

Inotropic score (IS) was calculated as previously described [7]: dopamine \(\mu g/\text{kg/min} \times 1\) + dobutamine \(\mu g/\text{kg/min} \times 1\) + milrinone \(\mu g/\text{kg/min} \times 15\) + epinephrine \(\mu g/\text{kg/min} \times 100\). IS is represented by a wide range of values indicating different inotropic and vasopressor drug regimens. In the absence of other direct instrumental measures of cardiac performance, that are not currently available for neonates, different ISs correlate with different dosages of vasoactive drugs indirectly indicating different cardiac output states. In order to compare subgroups subjected to different ISs, we stratified patients into three pre determined categories: low IS (value < 20), intermediate IS (value between 21 and 30), high IS (value over 31). A further stratification was obtained dividing patients in low Qd (30–40 ml/h), intermediate Qd (60–75 ml/h) and high Qd (90–120 ml/h).

2.3. Statistical analysis

All data are expressed as mean (S.D.). One-way analysis of variance was utilized for analysis of hemodynamic parameters among the three IS categories. Two-way analysis of variance with Qd and IS as sources of variation was utilized to show the impact of these parameters on solute clearances and ultrafiltration. Wilcoxon signed rank test was utilized to compare groups where appropriate. Spearman test was used for correlations. A P-value < 0.05 was considered significant.

3. Results

Twenty consecutive neonates who underwent post CPB PD were considered eligible and no one was excluded from the protocol. Indication to RRT was oliguria in 13 cases and generalized edema with need for supplementary ultrafiltration in seven patients. In all cases AKI developed after
surgery. Age at operation was 21 (17) days and weight 2.8 (0.6) kg. Fifty-five dialysate collections were performed. Five patients out of 20 stopped PD before the third protocol day. PD was administered for 2.5 (2) days. Heart rate, systolic arterial pressure, central venous pressure and lactate levels did not show statistical differences between the three IS categories (P > 0.05) (Table 2). Serum creatinine concentration at PD start was 0.97 mg/dl (0.9); it was 0.8 (0.6) at PD stop (P < 0.05) (Fig. 1). Mean prescribed Qd was 60 (45) ml/h. PD creatinine clearance was 3.4 (2.1) ml/min/1.73 m² and ultrafiltration rate was 9.75 (10) ml/h. As expected, D/Pcreatine showed a direct correlation with dwell time duration (r = 0.37, P = 0.009) (Fig. 2a). PD creatinine clearance appeared to be correlated Qd up to a dialysate of 100 ml/h (P = 0.02) (Fig. 3). No correlation was present between IS and PD creatinine clearance (r = 0.178, P = 0.2). This tendency was maintained when patients were stratified into three IS classes and three Qd classes (Fig. 4): Qd but not IS was found to affect peritoneal creatinine clearance (P = 0.0135). Residual renal creatinine clearance was present in seven patients and was 31 (26) ml/min/1.73 m². Ultrafiltration rate was not correlated to Qd but IS showed a direct correlation with dwell times duration (r = 0.28, P = 0.048) (Fig. 2b) but linear regression did not show any correlation between LDH clearance and Qd. Albumin loss was present through peritoneal drainage. Mean D/Palbumin was 0.05 (0.06) without significant differences within the three IS classes (P > 0.05). Mean albumin concentration in peritoneal drainage was 0.27 g/dl (0.46) with a mean albumin loss in the 24 h of 2.2 g (1.3); in particular, daily albumin loss ranged from 0.01 to 4.3 g.

Table 2

<table>
<thead>
<tr>
<th>Parameters</th>
<th>IS 1</th>
<th>IS 2</th>
<th>IS 3</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactates (mg/dl)</td>
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<td>36 (51)</td>
<td>41 (41)</td>
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<tr>
<td>MAP (mmHg)</td>
<td>48 (7)</td>
<td>53 (9)</td>
<td>48 (10)</td>
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</tr>
<tr>
<td>CVP (mmHg)</td>
<td>8 (3)</td>
<td>9 (2)</td>
<td>7 (3)</td>
<td>0.43</td>
</tr>
<tr>
<td>HR (b/min)</td>
<td>152 (6)</td>
<td>152 (15)</td>
<td>163 (14)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

MAP; mean arterial pressure; CVP; central venous pressure; HR, heart rate.

Fig. 2. Both PD creatinine (a) and LDH (b) dialysate to plasma ratio (D/P) showed a direct correlation with dwell times duration. In the case of LDH, longer dwell times allowed a relatively higher increase in D/P ratio with respect to creatinine. This effect might elucidate the role of allowing longer dwell times in order to optimize clearance of higher molecular weight solutes.

In-hospital mortality among this cohort of patients was 20%, that was significantly higher than the overall neonatal population admitted to our ICU (4.8%, P = 0.02). There was full renal recovery in 19 patients (95%) at PD stop. No major complications were reported. Catheter site leakage from catheter insertion was observed in two patients but did not require any specific intervention. Hemodynamic derangements were never described in correlation with DP cycles.
4. Discussion

PD represents a simple and safe system for fluid removal, depending on osmolarity, volume and dwell-time of the dialysis fluid. Prevention and treatment of fluid overload, main goal of acute renal support, are more likely to be achieved by application of high dialysate volumes [8–10]. Unfavorably, modifications of atrial and mean pulmonary artery and systemic pressure have been observed in chronic PD and in children after cardiac surgery [11]. For this reason, a PD prescription of 10 ml/kg, previously defined ‘low volume PD’, is commonly prescribed during neonatal RRT [8]. The aim of our study was to show adequacy of low flow PD, evaluating if its efficiency at different dwell times was affected by vasopressor drug administration and patients hemodynamic conditions. Our cohort of 20 post-cardiosurgical neonates was very homogeneous about age, weight and BSA. Interestingly, our patients tended to maintain a similar mean arterial pressure and heart rate independently from IS, probably due to the fact that in our center inotropes and vasopressors dose is targeted on these parameters. In all patients, ultrafiltration needs were adequately fulfilled by PD with an ultrafiltration rate of about 10 ml/h and a negative fluid balance ranging from 50 to 500 ml/day. Net ultrafiltration depends mainly on glucose concentration of dialysis bags: in our cohort, ultrafiltration was not influenced by Qd nor by IS. Our PD prescription determined a relatively low creatinine clearance with a tendency to increase with Qd: since cycle volumes were predetermined at 10 ml/kg, Qd was augmented only by the increase of cycles per hour and by the consequent decrease of dwell times. Creatinine molecular weight is sufficiently small to cross efficiently the peritoneal membrane (high D/P creatinine) even when dwell times were very short (Fig. 2a): for this reason low flow PD is able to progressively increase creatinine clearance at high Qd with short dwell times.

IS seemed to have no impact on PD efficiency and creatinine clearance was never affected by hemodynamic status. Peritoneal blood flow is generally considered high enough to avoid any limitations in solute clearance. Nonetheless, the real impact of effective peritoneal blood flow is still controversial [12]. In our patients, the absence of correlation between IS and PD creatinine clearance might suggest that during low volume PD mesenteric blood flow never decreased to a level able to impact PD efficiency. It remains to be elucidated however, if vasopressor administration actually causes mesenteric blood flow reduction, when hemodynamic parameters are maintained close to normal levels [13]. The direct correlation between creatinine clearance and Qd tended to reach a plateau for flows above 100 ml/h, that were rarely achieved in our patients. This threshold might represent the point where mesenteric blood flow is considered to be a limiting factor to further clearance rise: it can be speculated that only after reaching this level of PD dose, IS and hemodynamic status might impact treatment efficiency. For larger solutes, the low diffusion coefficients of the molecule may represent the most important limitation to transport [14, 15]. In our treatments, analysis of LDH clearance, a 140 kD molecular weight solute, showed a different clearance pattern from creatinine: dwell times influenced D/P LDH (Fig. 2b) to the point that the increase of cycles per hour and the consequent decrease of dwell times did not determine any clearance rise. Differently from what is described above about creatinine, higher molecular solutes clearance might be improved by high exchange volumes with prolonged dwell times, in order to optimize peritoneal diffusion. We found a significant albumin loss through peritoneal drainage: such amount of proteins is routinely infused in excess by fresh frozen plasma and human albumin to our patients. Furthermore, the clinical meaning of such finding is unclear: particularly, the wide range of albumin loss does not allow to understand whether the albumin was lost due to ascites, secondary to heart failure, or to capillary leakage, secondary either to generalized inflammation and to chemical peritonitis.

A major limit of this study was its observational nature and no definitive conclusions can be drawn by these results. Measured solutes and PD prescriptions were not modified with respect to the routine of our department. Nonetheless, this is the first attempt to monitor PD prescription and delivery. Further prospective studies should analyze different PD exchange models and specific mediators clearances to verify our suggestions.

5. Conclusions

Low flow PD in neonates shows optimal ultrafiltration patterns and adequate small solute clearances, irrespective of hemodynamic status or vasopressor support.

References


![Fig. 4. Patients were stratified into three IS classes and three Qd classes: Qd but not IS was found to affect peritoneal creatinine clearance (P=0.0135).](image-url)