Using Zero-Balance Ultrafiltration With Dialysate as a Replacement Solution for Toxin and Eptifibatide Removal on a Dialysis-Dependent Patient During Cardiopulmonary Bypass

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CARDIAC DISEASE is very prevalent in patients with end-stage renal disease (ESRD) dependent on hemodialysis (HD).[1] While HD-dependent patients commonly are referred for cardiac surgery, their multiple comorbidities, including diabetes, peripheral vascular disease, anemia and cachexia, and others, make perioperative management challenging.[2,3] It has been shown that perioperative management of fluid balance, electrolytes, metabolic acidosis, and azotemia plays an important role in operative morbidity and mortality in these patients.[2–10] Previous research has shown that intraoperative fluid removal and toxin clearance using intraoperative hemodialysis (IHD),[3–7,9] continuous hemodiafiltration (CVVH),[8,10,11] IHD using a hemoconcentrator,[12–14] and zero-balance ultrafiltration (Z-BUF)[15] all have been shown to decrease the incidences of perioperative and postoperative complications in chronic dialysis patients undergoing cardiac surgery.

While commonly used, IHD and CVVH increase the cost and complexity of the procedure.[2] A hemoconcentrator is typically a standard component of the cardiopulmonary (CPB) circuit and can be utilized to perform ultrafiltration, Z-BUF or, less commonly, hemodialysis with the addition of a roller pump to control the dialysate. While the cost of a hemoconcentrator for hemodialysis is minimal, there is still added complexity for the perfusionist.[12–14] Z-BUF with dialysate as replacement fluid is the only intraoperative renal replacement therapy option that is low in both cost and complexity.

Journois et al originally introduced the concept of Z-BUF in the pediatric population in order to decrease the concentration of inflammatory mediators by removing plasma water with a hemoconcentrator while replacing it with an equal amount of crystalloid fluid, leading to a shorter time to extubation.[16] Fluid overload also can be addressed with this technique by simply removing more fluid than is replaced. In addition to removing inflammatory and uremic toxins that contribute to cardiogenic shock and lung dysfunction,[2,17] Z-BUF also allows for the removal of any unwanted circulating drugs such as eptifibatide (Integrilin®, Merck & Co. Inc. Whitehouse Station, NJ), a platelet glycoprotein IIb-IIIa inhibitor.[18–20] By using specific replacement fluids, Z-BUF also can be used to normalize pH or electrolyte concentrations, most commonly to treat hyperkalemia.[21] Because dialysis-dependent patients are unable to excrete a potassium load, the use of hyperkalemic cardioplegia solutions to induce electrical arrest of the heart often causes intraoperative and postoperative hyperkalemia.[4,15]

Since most electrolyte-balanced solutions such as Plasma-Lyte A® (Baxter®, Deerfield, IL) or Normosol™-R (Hospira, Lake Forest, IL) contain potassium, many centers avoid these and use normal saline (NS) as a replacement fluid when treating or anticipating hyperkalemia.[13,15,22] Although NS is used commonly as a replacement fluid for Z-BUF, it is not an ideal replacement fluid due to its high chloride content. It is well-documented that intravenous resuscitation with the high chloride content of NS will increase serum chloride concentration, exacerbating hyperkalemia by inducing a hyperchloremic acidosis.[21,23,24]

Mick et al reported using Z-BUF using a 0 K^+ [potassium] dialysate solution to correct acute acidosis after a period of deep hypothermic circulatory arrest.[25] The authors report use of a 2 K^+ dialysate solution as a replacement fluid with Z-BUF in the treatment of azotemia, acidosis, and unwanted circulating eptifibatide as well as the prevention of hyperkalemia in a dialysis-dependent patient.

CASE

A 59-year-old, 69-kg man with ESRD (on HD three times a week), type-II diabetes, hypertension, hyperlipidemia, peripheral arterial disease, history of a left femoral-arterial bypass, and prior stroke with residual right-sided weakness presented with 3 days of unstable angina after undergoing HD. Notably, the patient had been volume-resuscitated aggressively due to hypotensive episodes and required an extra HD session for additional fluid removal. A left heart catheterization was performed and demonstrated severe 3-vessel coronary artery disease, including 99% occlusive left main disease with a possible ruptured ostial LAD plaque. The patient experienced transient episodes of hypotension during the catheterization procedure; he was placed on heparin (1,050 units/hour) and eptifibitide (1 μg/kg/min) and transferred to the coronary care unit. During the patient's time in the coronary care unit he had transient episodes of hypotension that responded to fluid boluses and was scheduled for CABG. Due to the patient's persistent episodes of hypotension it was determined that he would not tolerate HD prior to surgery. The eptifibatide infusion was stopped 18 hours prior to surgery, and the heparin drip was stopped 4 hours prior to surgery; the patient's creatinine (Cr) was 11.5 mg/dL on the morning of surgery.

Intraoperatively, a left radial arterial catheter was placed before induction, and general anesthesia was induced with fentanyl and propofol. Cisatracurium was used for a neuromuscular blockade. Central venous access was obtained with a sheath introducer in the right internal jugular vein, and a pulmonary artery catheter was inserted for monitoring of filling

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pressures and cardiac output. Anesthesia was maintained with fentanyl, isoflurane, and a mixture of oxygen/air, titrated to maintain an MAP >65 mmHg and a BIS 40 to 60. Intermittent doses of phenylephrine were used to support the blood pressure in the prebypass period, while epinephrine at 0.04 μg/kg/min was used as an inotrope in the post-bypass period. Transesophageal echocardiography was used for monitoring throughout the case.

A median sternotomy was performed and the left internal mammary artery was harvested as a pedicle. The patient received 35,000 units of heparin with a resulting pre-CPB activated coagulation time of 841 seconds. The aorta and right atrium were cannulated, and CPB was initiated.

The bypass circuit consisted of a Capiox® FX25 oxygenator with an integrated arterial filter and reservoir (Terumo®, Ann Arbor, MI) and was primed with 1 L of Plasma-Lyte A®, 10,000 units of heparin, and 50 mEq of sodium bicarbonate. There was sufficient cardiotomy suction return to the CPB circuit to ultrafiltrate and remove the prime, leaving the circuit autologously primed before CPB was initiated. Plegisol™ solution (Hospira®, Lake Forest, IL) was used for cardioplegia with a concentration of 96 mEq/L, for the induction dose and 26 mEq/L, for subsequent maintenance doses at a 4:1 blood-to-cardioplegia ratio.

The pre-CPB arterial blood gas showed worsening acidosis (Table 1). The hypercarbia may have been due to the transient periods of hypoventilation during harvesting of the left internal mammary artery given the frequent interruptions in ventilation that are needed in order to allow surgical access to the harvesting site. Once CPB was initiated, Z-BUF was started with a CAPIOX® HC11 hemoconcentrator (Terumo®, Ann Arbor, MI) to remove plasma water, and Nx STAGE® PureFlow™ B RFP400 (2 K^+) Solution® (NxStage®, Lawrence, MA) was used as replacement fluid (Fig 1). After 15 minutes of CPB, 1,500 mL had been removed and replaced with 1,200 mL of dialysate. Then, the aorta was cross-clamped and 1,200 mL of cold blood cardioplegia were given. During the 68-minute cross-clamp period, his low hemoglobin concentration was treated with a unit of packed red blood cells and 12.5 g of albumin. The patient's acidosis further worsened with the transfusion of 2 units of fresh frozen plasma and 2 units of packed red blood cells despite continuing to Z-BUF. The authors were able, however, to remove additional plasma water after the extra volume of the blood products was added. The final blood sample on CPB showed a highly improved acid base with a pH of 7.42.

Although the K^+ level was 5.3 mEq/L prior to the administration of hyperkalemic cardioplegia solution, systemic hyperkalemia was successfully avoided with Z-BUF using $2K^+$ dialysate (Fig 2). Although the authors had planned to use $4K^+$ dialysate solution in case of hypokalemia, this was not necessary.

CPB time was 140 minutes, during which 13 L of fluid were removed. The fluid added, including dialysate, blood products, and cardioplegia, totaled 13 L, resulting in a fluid balance of zero.

The patient subsequently was transferred to the intensive care unit, and CVVH was initiated. He was on CVVH for 5 days and then successfully transitioned back to HD. He was discharged home on postoperative day 7.

DISCUSSION

In addition to the multiple coexisting noncardiac comorbidities, the intraoperative management of ESRD patients undergoing cardiac surgery often is complicated by hyperkalemia, fluid balance derangements, and uremic and inflammatory mediator toxicity as well as alterations in drug clearance. By replacing the absent renal function, Z-BUF allows for proper management of all of these problems. The potassium burden from cardioplegia and blood products is not well-tolerated by those with renal dysfunction, and, additionally, their inherent acidosis tends to worsen hyperkalemia. Potassium will shift out of cells and into the extracellular space in response to acidosis to maintain charge neutrality. Avoiding a hyperchloremic acidosis by using a normochloremic dialysate solution as Z-BUF replacement fluid enabled the author to adjust fluid balance. In this particular case, the authors used a $2K^+$ replacement solution in order to successfully avoid hyperkalemia. Also, with the transfusion of more than 1 L of blood products while on CPB, they we were able to remove 1 L of plasma water in order to correct the fluid balance.

While they did not measure specific inflammatory mediator and cardiopulmonary toxin levels, Z-BUF has been shown to lower these levels, specifically IL-1β, IL-6, IL-8, IL-10, tumor

Table 1. Laboratory Values and Events During Surgery

	Heparin	CPB On, Z-BUF Start	1 RBC	2 RBC, 2 FFP	CPB Off, Z-BUF Stop	
Time	Before 09:27	9:27–10:18	10:18–10:43	10:43–11:23	12:31–13:41	
pH	7.19	7.36	7.3	7.27	7.42	7.30
pCO_2 (mmHg)	57	39	42	41	33	37
pO_2 (mmHg)	59	503	265	221	282	423
Na^+ (mEq/L)	133	133	135	136	138	138
K^+ (mEq/L)	5.0	5.3	4.6	4.2	3.9	3.4
Cl^- (mEq/L)	94	95	97	97	101	102
Ca^{++} (mEq/L)	1.12	0.96	1.03	1.03	1.00	0.99
Glu (mg/dL)	154	129	155	125	115	127
Lac (mEq/L)	0.7	1.4	2.1	2.2	2.6	4.5
Hb (g/dL)	8.5	7.8	7.2	10.2	6.7	7.8
BE (mEq/L)	-6.3	-3.2	-5.3	-7.6	-2.8	-7.6
AG (mEq/L)	22	21	22	24	20	21
HCO_3 (mEq/L)	21.8	22.0	20.7	18.8	21.4	18.2

Abbreviations: CPB, cardiopulmonary bypass; FFP, fresh frozen plasma; Glu, glucose; Lac, Lactate; RBC, red blood count; Z-BUF, zero-balance ultrafiltration.