

Using Zero Balance Ultrafiltration with Dialysate as a Replacement Fluid for Hyperkalemia during Cardiopulmonary Bypass

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Abstract: Avoiding or managing hyperkalemia during cardiac surgery, especially in a patient with chronic renal insufficiency, can be challenging. Hyperkalemic cardioplegia solution is usually administered to achieve and maintain an electrical arrest of the heart. This solution eventually mixes in with the systemic circulation, contributing to elevated systemic potassium levels. Administration of packed red blood cells, hemolysis, tissue damage, and acidosis are also common causes of hyperkalemia. Current strategies to avoid or manage hyperkalemia include minimizing the volume of cardioplegia administered, shifting potassium from the extracellular into the intracellular space (by the administration of sodium bicar-

bonate when the pH is low and/or dextrose–insulin when effects relatively independent of serum pH are desired), using zero-balanced ultrafiltration (Z-BUF) with normal saline as the replacement fluid (to remove potassium from the body rather than simply shift the electrolyte across cellular membranes), and, occasionally, hemodialysis (1). We report the application of Z-BUF using an electrolyte-balanced, low potassium dialysate solution rather than isotonic saline to avoid a high chloride load and the potential for hyperchloremic acidosis to successfully treat hyperkalemia while on cardiopulmonary bypass. **Keywords:** cardioplegia, cardiopulmonary bypass (CPB), kidney *JECT. 2014;46:262–266*

Although there are many types of cardioplegia solutions used to arrest the heart during cardiac surgery, almost all contain high levels of potassium. This hyperkalemic solution eventually mixes into the systemic circulation, raising extracellular potassium levels (1). Although potassium is predominantly an intracellular cation, a high extracellular concentration affects cardiac rhythm and hence myocardial contraction (2). Etiologies of systemic hyperkalemia include infusion of potassium (K⁺) containing solutions (e.g., packed red blood cells [pRBCs]), a transcellular shift of K⁺ (typically from acidosis), and decreased K⁺ clearance (usually from renal insufficiency) (1). Using even minimal amounts of cardioplegia can cause hyperkalemia while on cardiopulmonary bypass (CPB) in a patient with renal insufficiency.

Hyperkalemia can be treated by decreasing the total amount of K⁺ in the body or by causing a shift of K⁺ from

the extracellular into the intracellular space. Shifting K⁺ intracellularly is only a temporary fix because the ion will eventually shift back into circulation. Ways to reduce the total K⁺ load include stimulating renal excretion of K⁺ with diuretics, ultrafiltration, or hemodialysis. Journois et al. (3) originally introduced the concept of zero-balanced ultrafiltration (Z-BUF) in the pediatric population during the rewarming phase to decrease the concentration of inflammatory mediators and subsequently lower time to extubation by removing plasma water with a hemoconcentrator while replacing with an equal amount of crystalloid fluid. By using specific replacement fluids, Z-BUF can also now be used to normalize pH or electrolyte concentrations. Because most electrolyte-balanced solutions such as Plasma-Lyte A[®] (Baxter[®], Deerfield, IL) or Normosol[™]-R (Hospira, Lake Forest, IL) contain K⁺, many centers avoid these and use normal saline (NS) as a replacement fluid to treat hyperkalemia (1,2,4).

Normal saline is also not an ideal replacement fluid as a result of its high chloride content as well as its capacity to exacerbate hyperkalemia as a result of hyperchloremic acidosis (5). It is well documented that intravenous resuscitation with NS will increase serum chloride concentration leading to acidosis (6). The Stewart approach to acid base evaluation succinctly explains this observation

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Table 1. Components of normal plasma, PureFlow™ B RFP 400 and RFP 402 dialysate, normal saline, and Plasma-Lyte A®*

	Normal Plasma	PureFlow™ B RFP 400 Dialysate Solution	PureFlow™ B RFP 402 Dialysate Solution	.9% Normal Saline	Plasma-Lyte A®
K ⁺ (mEq/L)	3.5–5.0	2	0	—	5
Na ⁺ (mEq/L)	140	140	140	154	140
Ca ⁺⁺ (mEq/L)	2.3–2.6	3	3	—	—
Mg ⁺⁺ (mEq/L)	1.4–2.0	1	1	—	3
Cl ⁻ (mEq/L)	100–108	111	109	154	98
HCO ₃ ⁻ (mEq/L)	22–26	35	35	—	—
Glucose mg/dL	80–120	100	100	—	23
Osmolarity mOsmol/L	280–296	296		310	294

*We used the PureFlow™ B RFP 400 with 2 K⁺.

using the concept of the strong ion difference (SID). Most ions in the body such as bicarbonate, phosphate, or albumin are weak acids or bases, acting to buffer physiologic pH changes. The remaining “strong ions” are those that are fully dissociated at physiologic pH such as Na⁺, K⁺, Mg²⁺, Ca²⁺, Cl⁻, sulfate, and lactate. The SID can be estimated as $SID = ([Na^+] + [K^+]) - ([Cl^-] + [lactate])$ with a normal value of 40 ± 2 ; positive deviations correspond to alkalosis, whereas negative deviations correspond to acidosis (6). At relevant physiologic concentrations, sodium and chloride dominate the equation by several orders of magnitude. Because NS has a SID of zero ($[154] - [154] = 0$), administration of NS will dilute normal plasma SID leading to acidosis. Potassium will shift out of cells in response to acidosis and into the extracellular space to buffer hydrogen ions, which must move reciprocally to maintain charge neutrality, thus exacerbating the hyperkalemia.

Mick et al. (7) reported using Z-BUF using a (a 0 K⁺) dialysate solution to correct acute acidosis after a period of deep hypothermic circulatory arrest. We report use of (a 2 K⁺) dialysate solution as a replacement fluid with Z-BUF in the treatment of hyperkalemia in a patient on CPB with chronic renal insufficiency. The components of .9% normal saline, Plasma-Lyte A®, and PureFlow™ Dialysate Solutions .9%→0.9% in Table 1 and compared to normal plasma.

DESCRIPTION

A 57-year-old man with a history of hypertension, hyperlipidemia, 40 pack-year smoking history, and prior coronary stents presented to the catheterization laboratory with hypertensive urgency and underwent left heart catheterization showing three-vessel coronary artery disease. The serum creatinine went from a baseline value of 1.8 mg/dL to 2.3 mg/dL postcatheterization (normal range of .7–1.3 mg/dL). His estimated glomerular filtration rate declined from 41.5 mL/min (100–140 mL/min is normal) to 31.3 mL/min 5 days after the catheterization.

Two weeks later the patient presented for coronary artery bypass grafting. A midline incision was made and a median sternotomy was performed. After the left internal mammary was dissected, the patient received 40,000 units of heparin followed by two subsequent 10,000-unit boluses for a final pre-CPB activated clotting time of 508 seconds. The aorta and right atrium were cannulated and CPB was initiated.

The bypass circuit consisted of a Capiiox® FX25 oxygenator with integrated arterial filter and reservoir (Terumo®, Ann Arbor, MI) and was primed with 1 L of Plasmalyte A®, 10,000 units of heparin, and 50 mEq of sodium bicarbonate. Plegisol™ solution (Hospira) was used for cardioplegia with a concentration of 96 mEq/L for the induction dose and 26 mEq/L for subsequent maintenance doses.

After 10 minutes of CPB, but before the cross-clamp was placed on the aorta, a blood sample (see Table 2) revealed a K⁺ of 6.0 mEq/L, increased from a baseline value of 5.0 mEq/L. The pH increased from 7.25 to 7.37, most likely as a result of our ability to treat the hypercarbia more effectively on CPB by simply adjusting the sweep rate. The aorta was then cross-clamped and 1200 mL of cold blood cardioplegia was given. After allowing the cardioplegia to wash out and recirculate systemically for 10 minutes, another blood sample was tested showing a K⁺ of 7.1 mEq/L. Although the pCO₂ stayed stable, the acidosis had worsened. With little urine output and such a high K⁺, the decision was made to begin Z-BUF. We used a CAPIOX® HC11 hemoconcentrator (Terumo®) to remove plasma water and Nx STAGE® PureFlow™ B RFP400 Solution® (NxStage®, Lawrence, MA) with the lowest K⁺ level (2 mEq/L) our hospital had available as the replacement fluid (the Z-BUF and CPB circuit can be seen in Figure 1).

Approximately 10 minutes after beginning Z-BUF, another sample was run with a K⁺ of 7.5 mEq/L. In response, Z-BUF was continued in addition to the administration of 50 mEq of sodium bicarbonate and an insulin drip at two units per hour was initiated. Twenty minutes later, the patient had a pH of 7.38, base excess -1.3 mEq/L, and K⁺ 6.6 mEq/L. A five-unit bolus of insulin was given

Table 2. Laboratory values and events during the operation.

	Heparin	CPB On	XCl On	Z-BUF Start	XCl Off	CPB Off		
Time	8:57	9:24	10:06	10:43	11:26	11:49	12:08	12:54
pH	7.23	7.25	7.37	7.27	7.31	7.38	7.28	7.3
pCO ₂ (mmHg)	56	51	42	46	41	40	49	43
pO ₂ (mmHg)	88	108	230	254	258	?	77	95
Na ⁺ (mEq/L)	140	138	137	137	137	139	140	142
K ⁺ (mEq/L)	5	5.2	6.0	7.1	7.5	6.6	4.9	4.5
Cl ⁻ (mEq/L)	107	106	107	106	107	110	110	111
Ca ⁺⁺ (mEq/L)	1.24	1.19	1.09	1.06	1.04	1.41	1.25	1.17
Glucose (mg/dL)	134	138	142	169	166	152	130	117
Lactate (mEq/L)	1.3	1.1	1.1	1.7	1.2	1.8	2.8	2.1
Hemoglobin (g/dL)	12.6	12.1	10.8	11.4	11.6	10.8	9.5	10.3
Base excess (mEq/L)	-4.7	-5.1	-1.0	-5.7	-5.3	-1.3	-3.8	-5
AG (mEq/L)	15	15	12	17	17	12	12	14
HCO ₃ (mEq/L)	23.5	22.4	24.3	21.1	20.6	23.7	23	21.2

CPB, cardiopulmonary bypass; Z-BUF, zero-balanced ultrafiltration, AG, anion gap.

and one additional liter of Z-BUF (4000 mL total) was performed before terminating CPB. A sample was obtained shortly after coming off CPB with a K⁺ concentration of 4.9 mEq/L. The potassium concentration remained in a normal range throughout the entire postoperative period.

COMMENT

This patient was known to have chronic renal insufficiency and produced only 100 mL of urine on CPB. As shown in Figure 2, the serum K⁺ concentration spiked

to 6.0 mEq/L from 5.0 mEq/L in an hour timespan, before cardioplegia administration. Possible causes for this include hemolysis, tissue damage, metabolic acidosis, or acute heparin-induced hyperkalemia (HIH). HIH is a recognized cause of hyperkalemia with hypoaldosteronism being the presumed cause, but typically onset is recognized 1–3 days after heparin therapy is started (8,9). It is tough to pinpoint the exact cause of the acute rise of K⁺ concentration, especially because no K⁺ or K⁺-containing solutions were administered and nothing was notably atypical from other cardiac surgery cases, but a K⁺ burden may not be handled by a patient with renal dysfunction. In addition, acidosis further exacerbates hyperkalemia.

Although this patient was not transfused, allogenic blood product use is another common cause of hyperkalemia during cardiac surgery. The K⁺ content of pRBCs increases linearly as they age because the cells lose the ability to maintain a physiologically normal Na⁺/K⁺ gradient (10).

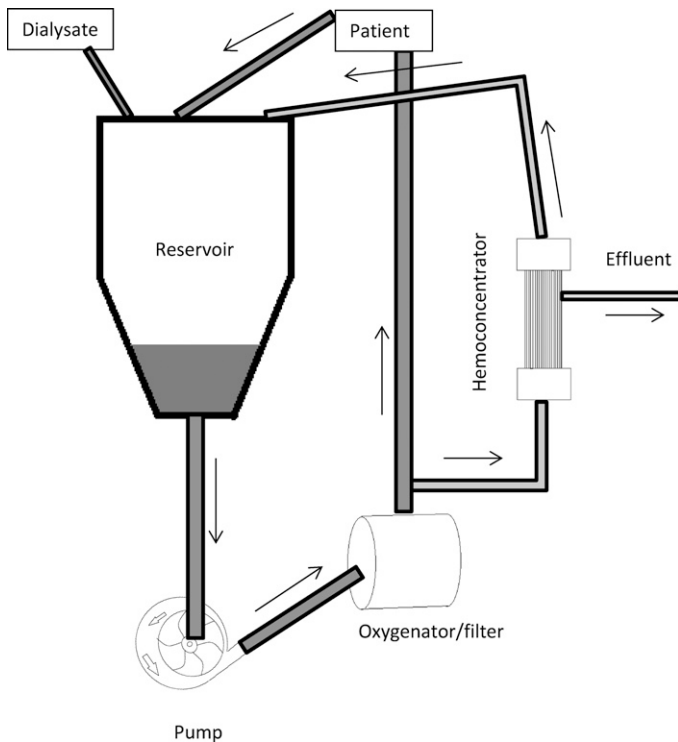


Figure 1. Schematic layout of CPB circuit.

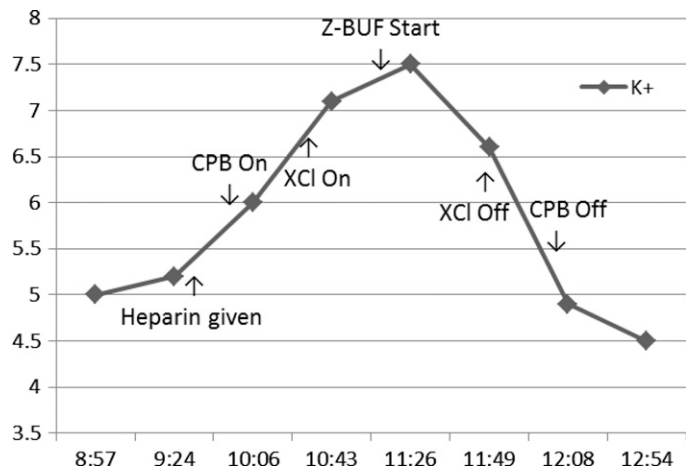


Figure 2. Potassium levels throughout the case, with significant events labels. Hyperkalemia had begun before cardioplegia was administered and zero-balanced ultrafiltration (Z-BUF) successfully lowered the potassium concentration.

Delaney et al. found fresher pRBCs (less than 1 week old) given at their institution to have a K^+ concentration approximately 10 mEq/L, whereas others have reported older pRBCs to have K^+ concentrations of greater than 20 mEq/L (1,10). Many have suggested washing pRBCs with a cell saver to reduce the high extracellular K^+ concentration (10). In the pediatric population, where pRBCs are often added to the prime, prebypass ultrafiltration can be used to lower the K^+ in the prime to a normal level (11).

Cost is always a concern when it comes to treatment options. A hemoconcentrator is used on every case at our institution and the dialysate comes as a 5-L bag with a cost of approximately \$30, or approximately \$6/L. The per-liter cost is not drastically different from a balanced electrolyte solution such as Normosol[®]. Because the extracellular K^+ is in equilibrium with the intracellular levels, the amount of K^+ removal to achieve the desired K^+ is unpredictable, so blood samples must be analyzed often (2). An inline blood gas analyzer such as the Terumo[®] CDI 500[™] (Terumo[®]) can assist in following the K^+ trend and potentially increase the time between samples sent outside the operating room for analysis.

The Nx STAGE[®] PureFlow[™] B RFP400 Solution[®] is indicated for use with renal replacement systems that use sterile premixed dialysate. This includes the application of continuous venovenous hemodialysis, although its use in continuous venovenous hemofiltration (CVVH), where replacement fluid is added pre- or postfilter to the venous blood, is technically considered off-label. It is however common to use this and other dialysate solutions off-label as a prefilter replacement fluid for CVVH in the intensive care unit (ICU) and to date there are no published reports of observed adverse effects (12). Our application for using the dialysate is essentially the same because we are removing the solutes by convection without dialysate and replacing the volume with dialysate prefilter.

Our solution fell within the following recommended concentrations for replacement fluids with CVVH: sodium 140 mEq/L; chloride 109–112 mEq/L; potassium 0–4 mEq/L; calcium 3.0–3.5 mEq/L; magnesium 1.0–1.5 mEq/L; glucose 0–15.00 g/L; and 25–45 mEq/L lactate or sodium bicarbonate buffer (11–14). It is commonly recommended that bicarbonate be used as a buffer in replacement fluids for CVVH for critically ill cardiac or ICU patients (13–15). Not only does a bicarbonate buffer preserve lactic acid as a marker, but several studies also show a better improvement in acid-base status and reduced incidence of cardiovascular events compared with lactate (13–15). Of note, it is important to realize that the recommended bicarbonate level in the replacement fluid is greater than the normal plasma concentration of 22–26 mEq/L because the sieving coefficient of bicarbonate is greater than 1 (14).

The Nx STAGE[®] PureFlow[™] B RFP400 Solution[®] is very similar in composition to the two most popular replace-

ment fluids, PrismoSol[®] (Gambro[®], Lakewood, CO) and PrismaSATE (Gambro[®], Lakewood, CO), except lactate is used as a buffer in these solutions, which would not be ideal for our patients. In July 2006, Normocarb HF[™] (Dialysis Solutions Inc., Ontario, Canada) received U.S. Food and Drug Administration approval as the first and only lactate- and dextrose-free hemofiltration solution (infusate) for use in a continuous renal replacement therapy circuit (16). Normocarb HF35[™] contains the same concentration of sodium bicarbonate as PureFlow[™] B RFP400 Solution[®], but only sodium, chloride, and magnesium are present in the solution with recommendations to add K^+ , calcium, and glucose at desired levels. Although this allows for some customization, it is recommended that this be done by the pharmacy and must be made as needed as a result of the low subsequent shelf life (12). Because we have a limited therapy window (CPB runs are typically 1–3 hours), the preparation time as well as the increased risk for human error with homemade solutions is not ideal (12). To our knowledge, there are no off-the-shelf ready, lactate-free fluids indicated specifically approved for use as a replacement fluid for CVVH (17).

In addition to the composition and osmolarity, we also found that the sterility of the solution was similar to those that are approved for intravenous use. According to NxStage, PureFlow dialysate solutions are terminally sterilized, pyrogen-free, and meet Association for the Advancement of Medical Instrumentation, U.S. Pharmacopeia, and European Pharmacopoeia specifications and standards (18).

When treating hyperkalemia, it may not be necessary to avoid K^+ containing solutions altogether. A transcellular shift in K^+ rather than its “removal” from the body may be the main mechanism for reduction in plasma concentration of K^+ . During Z-BUF, the routine use of isotonic saline may not be optimal. Paradoxically, hyperchloremic acidosis induced by saline could worsen hyperkalemia (5). A benefit of using balanced crystalloids may be physiologic chloride content resulting in maintenance of normal SID. The association of acidosis and hyperkalemia during and after CPB has not been thoroughly evaluated in the literature. Metabolic acidosis after CPB, however, has been shown to be associated with changes in the SID as a result of fluid administration while on CPB (19). Even changes in priming solutions have been shown to affect acidosis through the SID (20). Although the clinical effect of acidosis resulting from increased SID on morbidity and mortality is a topic of debate, it is reasonable to conclude that in a population with impaired renal function, a balanced solution with a minimal effect on SID may be a useful adjunct in preventing and treating hyperkalemia. Hence, although balanced solutions contain K^+ , they may be better for the treatment for hyperkalemia by avoiding hyperchloremic acidosis. Similarly, the effects of sodium

bicarbonate on hyperkalemia may be a result of high SID (=50) moving plasma pH toward neutral rather than the influence of bicarbonate on pH.

Because cardiac surgery often involves the administration of hyperkalemic cardioplegia, systemic hyperkalemia is often an issue, especially for patients with advanced renal insufficiency or dialysis dependence. Although there are many techniques to address hyperkalemia, Z-BUF using dialysate as a replacement fluid corrects and also preserves the fluid, electrolyte, and acid base balance toward a normal value.

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