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Hyperkalemic Death during Use of a High-capacity Fluid Warmer for Massive Transfusion

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Blood transfusions carry significant risks to the patient, such as hemolytic transfusion reaction, both immediate and delayed allergic reaction, and infection. Despite these risks, the morbidity and mortality associated with routine blood transfusion remain low. Massive transfusion (1.5 blood volumes in 24 h) has long been recognized to engender patient risks due to the composition of and effects of preservation and storage of packed red blood cells (PRBCs).[1–3] New technology, such as the high-capacity fluid (HCF) warmer and the large-caliber iv cannula, allows anesthesiologists to transfuse more than four blood volumes per hour. In humans, the most extensively studied transfusion-related complication has been hypocalcemia.[4–6] Hyperkalemia and cardiac arrest caused from rapid K^+ infusion rates and rapid blood transfusion have been studied extensively in animals.[7–9] Hyperkalemic arrest due to rapid blood transfusion has been documented to occur in humans.[10] It has been an infrequent transfusion complication, since the technology has not previously allowed very rapid blood infusion rates (up to 500 ml/min).

This paper describes one adult case of hyperkalemic arrest due to rapid transfusion with the use of a HCF warmer. The electrolyte composition of adenosine dextrose saline (ADSOL)-preserved PRBC was determined to document the source of the potassium. Suggestions for prevention of the transfusion-associated hyperkalemia are discussed.

CASE REPORT

A 33-yr-old, 65.3-kg man came to the operating room for left hemipelvectomy. He was known to have hereditary osteochondromatosis and presented with recurrence of a left pelvic chondrosarcoma with extension into the musculature, bowel, bladder, and spine. Physical exam was unremarkable except for the tumor. Preoperative laboratory values were normal and included a K^+ of 3.7 mEq/l. Anesthesia was induced with thiopental, and after paralysis with vecuronium, anesthesia was maintained with air/O_2, isoflurane, and fentanyl. The right axillary artery, pulmonary artery (*via* the right internal jugular vein), and three arm veins were cannulated with one 8.5 French and two 7.0 French ivs. The three peripheral iv cannula were connected to a HCF warmer (model D100, Level 1 Technologies, Marshfield, MA), which is capable of warming blood from 4 to 36° C at a fluid flow rate of 500 ml/min. Continuous intraoperative monitoring included ECG, central venous pressure (CVP), pulmonary artery pressures, core temperature, pulse oximetry, and all respiratory gases.

For 5 h the patient was hemodynamically stable. During this interval, 14 U PRBCs, 10 U fresh frozen plasma (FFP), and 10 U platelets were infused. All PRBC units were partially backfilled with 0.9% normal saline. The patient's esophageal temperature was 35.5° C. Removal of the pelvis produced a marked increase in blood loss. In the 25 min prior to the cardiac arrest, the blood pressure (BP) was maintained at 100–90/50–60 mmHg by the rapid infusion of 10 U PRBCs. Calcium $CaCl_2$ was empirically administered whenever 5 U PRBCs were given in less than 15 min. Just prior to the cardiac arrest, increased blood loss and increased BP lability were treated with transfusion of 7 U PRBCs over 5 min.

As an arterial blood gases (ABG) sample was being drawn, the ECG changed in the following sequence: 1) the QRS interval widened; 2) a sine wave appeared; 3) ventricular fibrillation occurred; and 4) the ECG became isoelectric. Despite effective cardiopulmonary resuscitation (CPR) and maintenance of the core body temperature at 35° C, defibrillation with direct current (DC) countershock was unsuccessful. The ABG drawn at the moment of arrest contained a K^+ of 10.7 mEq/l. The postarrest transfusion increased the K^+ to 12.6 mEq/l. After 45 min of therapy, which included $CaCl_2$, glucose and insulin, hyperventilation, $NaHCO_3$, epinephrine bolus and infusion, and hemodilution, the K^+ had decreased to 6.4 mEq/l. A junctional rhythm was obtained briefly but could not be maintained. The attempt at resuscitation ended approximately 1 h after the hyperkalemic arrest. All PRBCs were ADSOL-preserved. Laboratory work-up for intravascular hemolysis was negative. Table 1 chronicles the laboratory values during the operative procedure.

Laboratory Methods. The administration time for each PRBC unit was established from separate blood product administration records kept by anesthesia technicians. The empty PRBC units were collected and placed in a refrigerator. Potassium was determined (model KNAI; Radiometer, Medford, MA) in both the bag and the whole-blood crossmatch tags in all PRBC units given within the 25 min prior to, the 5 min prior to, and the 5 min after the cardiac arrest. Estimates of blood flow rates were made.

Laboratory Results. All of the units administered to this patient in the periarrest period had K^+ levels that were within the expected values for the storage age of the individual units (table 2). The transfusion rate was estimated to be 420 ml/min or 6.43 $ml \cdot kg^{-1} \cdot min^{-1}$ just prior to the cardiac arrest. This rate is under the established maximum transfusion rate of the HCF warmer.

DISCUSSION

Evidence strongly suggests that this patient underwent a hyperkalemic cardiac arrest due to rapid infusion of a hyperkalemic solution, the PRBC (table 1). There was no evidence of a hemolytic transfusion reaction or of any other endogenous source of K^+. Other possible causes for a cardiac arrest, such as hypovolemia, hypothermia, or

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TABLE 1. Perioperative Patient Laboratory Values

Periarrest Time	Units PRBC Transfused	Patient Temperature (° C)	Arterial Blood Gases $O_2/CO_2/pHa/BE$ (mmHg/mmHg/)	Hb (mg/dl)	Ca^{++} (mEq/l)	K^+ (mEq/l)	Glucose (mg/dl)
5 h prearrest	0	37	177/42/7.38/0.3	11.9	2.3	3.81	75
20 min prearrest	20	36.0	226/33/7.39/−3.7	9.8	2.8	4.35	119
Arrest	36	35.5	228/16/7.51/−6.8	12.4	3.7	10.7	383
5 min postarrest	41	35.5	535/11/7.42/−12.7	15.1	4.8	12.6	540
45 min postarrest	46	34.1	615/29/7.33/−9.3	8.5	2.6	6.4	458

acidosis, were not present. The ECG sequence seen was comparable to that described in ponies,[7] dogs,[8] and humans.[9,10] Increased extracellular K^+ increases the resting membrane potential. This decreases the speed of depolarization of the myocardial fiber and decreases the rate of the spontaneous depolarization in pacemaker cells. As in the current case, these effects produce the characteristic widening of the QRS interval and eventually produce asystole. During asystole, the myocardial cell cannot develop a negative intracellular potential to repolarize.[11]

The hyperkalemia continued (K^+ = 12.6 mEq/l) in large part due to continued transfusion. Continued transfusion, therefore, prevented normalization of serum potassium and the establishment of a cardiac rhythm. This patient's base deficit had begun to increase prior to the cardiac arrest. The *p*H of the transfused blood and the poor serum-buffering capacity due to probable hypoproteinemia both contributed to the developing deficit. Due to the administration of $NaHCO_3$, the patient was not acidotic (table 1). Cardiac arrest and hyperkalemia due to blood transfusion have been reported at much lower total blood unit transfusion rates than this patient underwent. Linko and Tigerstedt[9] described a series of 21 patients who received more than 10 U whole blood. Eleven of 21 developed significant increases in K^+, and 3 of the 11 experienced cardiac arrest. In this study cardiac arrest occurred at a K^+ level of approximately 7.0 mM (7.0 mEq/l).

In the current case, the transfusion rate was the major factor causing the patient's hyperkalemia, as there was insufficient time for K^+ distribution into the interstitial fluid and intracellular space. These very high flow rates are possible only with a HCF warmer. Separate standard blood warmers on four iv catheters do not allow a fluid flow rate in excess of 500 ml/min or 7 $ml \cdot kg^{-1} \cdot min^{-1}$ (in a 70-kg person). The fluid administered had an average K^+ of 29.6 mEq/l. Miller and Brzica state bank blood must be given at rates exceeding 120 ml/min to produce significant risk of hyperkalemia.[1] Linko and Saxelin[10] found significant transient hyperkalemia occurring at transfusion rates >90 ml/min or 0.3 $ml \cdot kg^{-1} \cdot min^{-1}$. Miller *et al.* found that swine could not survive "old blood" transfusion rates in excess of 1.5 $ml \cdot kg^{-1} \cdot min^{-1}$ once one blood volume had been infused.[11] Hiatt and Hiatt[13] found that when dogs received 2 $mM \cdot kg^{-1} \cdot h^{-1}$ ($mEq \cdot kg^{-1} \cdot h^{-1}$) K^+, they developed cardiac toxicity within 2 h and ventricular fibrillation at 0.1 mM/kg rapid infusion. Our patient received up to 420 ml/min of blood (6.43 $ml \cdot kg^{-1} \cdot min^{-1}$), equivalent to 9.9 mEq/min of K^+ (9.1 $mEq \cdot kg^{-1} hr^{-1}$), just prior to cardiac arrest, and had received more than 2.0 $mEq \cdot kg^{-1} \cdot h^{-1}$ during the previous 5 h. This patient received blood, or K^+, in rates that far exceeded rates shown to cause cardiac toxicity in humans and animals.

Neither the PRBC K^+ nor the H^+ concentration was excessive for the storage time. The hyperkalemic event was the cumulative effect of a continuous rapid infusion of a hyperkalemic acidotic solution. The $CaCl_2$, glucose–insulin infusion, $NaHCO_3$, and epinephrine (table 1) were used prior to and during the cardiac arrest to increase cellular uptake of K^+ and to protect the heart from the effects of increased K^+. Magnesium was not administered. Kraft *et al.* found that Mg antagonized K^+-induced depolarization in isolated canine atria and ventricle tissue. In addition, they reported that hypermagnesemia prevented ECG changes associated with hyperkalemia in four patients.[14] At the blood infusion rates administered in the reported case, these standard treatments proved ineffec-

TABLE 2. Measured Potassium in Blood Transfused Before and During Cardiac Arrest

Periarrest Time	PRBC Transfused During Time Interval (U)	Days PRBC Stored (mean ± SD)	PRBC Composition (mean ± SD)		Estimated Transfusion Rate*	
			K^+ (mEq/l)	*p*H	(ml/min)	($ml \cdot kg^{-1} \cdot min^{-1}$)†
25 to 5 min prearrest	10 in 20 min	34.2 ± 6.5	31.8 ± 7.2	6.43 ± 0.11	150	2.30
5 to 0 min prearrest	7 in 5 min	24.7 ± 4.9	23.6 ± 5.9	6.51 ± 0.12	420	6.43
5 min postarrest	4 in 5 min	27.5 ± 9.3	34.4 ± 4.1	6.54 ± 0.11	240	3.68

* Estimated unit volume was 300 ml.

† Patient weight 65.3 kg.

tive. Once arrest occurred, inadequate tissue perfusion and continued transfusion made the cellular uptake of excess K^+ inadequate.

In clinical situations in which massive transfusions remain inevitable, the blood product infused must more closely approximate normal intravascular fluid. Suggestions to accomplish this include: 1) decreasing PRBC serum K^+ by superpacking or by using glycerol-washed RBC[15,16]; 2) using "fresh" (<5 storage days) blood[17]; 3) washing PRBC with saline in a cell saver; and 4) performing standard saline dilution of each PRBC unit.

The most efficient alternative is the use of a cell saver to process banked blood as well as the recycled blood from the surgical field. Washing PRBC would decrease the H^+ and K^+ concentrations of the blood transfused. Cell savers can process four to six PRBC units in 15 min and are already currently in use by operating room personnel. Standard PRBC have significant clotting factors; thus, washing PRBC may increase the incidence of dilutional coagulopathy. In addition, the risk of patient heparinization exists. Serum K^+ concentrations would need to be monitored, since eventually hypokalemia develops as the transfused red cells become metabolically active. Dilution of PRBC with saline is imprecise and sometimes very difficult during very rapid transfusion situations. Care must be used to prevent dilutional anemia and fluid overload in patients who are already anemic due to blood loss.

Current surgical and anesthetic techniques allow blood loss and blood replacement at rates that far exceed the human body's ability to equilibrate Ca^+ and K^+. The rapid ECG change from peaked T waves to a sine wave and flat line may not be observed. A high level of suspicion for hyperkalemia is necessary when one or more HCF warmers are being used or when only PRBCs are being administered.

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