Received: 5 November 2021 | Accepted: 10 November 2021

DOI: 10.1111/jocs.16157

COMMENTARY

JOURNAL OF CARDIAC SURGERY WILEY

Preventing transfusion-associated hyperkalemia in pediatric cardiac surgery: Measure the levels of potassium in packed red blood cells before using – Invited commentary

Ali Baran Budak MD

Department of Cardiovascular Surgery, Faculty of Medicine, Alanya Practice and Research Center, Başkent University, Antalya, Turkey

Correspondance
Ali Baran Budak, MD, Cumhuriyet Mah. Sanatokulu Cad. Selçuklu Konakları A2 Blok D: 6 07400 Alanya, Antalya, Turkey.
Email: drbaranbudak@gmail.com

Abstract

The authors present a revolutionary study aiming to evaluate the effect of alterations in potassium concentrations in transfused packed red blood cells (PRBC) on the neonate and infant potassium levels after congenital cardiac surgery. By establishing a strict protocol that restricts the rate of transfusion, the age of the transfused PRBC, and not transfusing a PRBC with a potassium level above 15 mmol/L, they accomplished to suggest a safe and easy way for preventing transfusion-associated hyperkalemia.

KEYWORDS

blood transfusion, congenital cardiac surgery, hyperkalemia, infant, neonatal

In this issue of the Journal of Cardiac Surgery, Altun et al.[1] presented the results of a prospective, single-center, interesting study aiming to evaluate the effect of alterations in potassium concentrations in transfused packed red blood cells (PRBC) on the neonate and infant potassium levels after congenital cardiac surgery to prevent transfusion-associated hyperkalemia (TAH).

Seventy-four patients with a normal renal function who underwent pediatric cardiac surgery were enrolled in the study. The median age and weight were 20 days and 3.6 kg, respectively. Patients requiring ventricular assist device or extracorporeal membrane oxygenation support, massive transfusion, or reoperation due to ongoing bleeding, peritoneal dialysis, and potent diuretics that affect K + balance were excluded. PRBC units older than 7 days for infants and 5 days for neonates (mean 3.8 ± 1.4 days), which have $K^+ > 15$ mmoL/L (mean 9.9 ± 2.4 mmol/L) were not administered to the patients. None of the patients developed TAH (defined as $K^+ > 5.5$ mEq/L) and associated complications. They maintained a transfusion rate between 10 and 20 ml/kg within 1–2 h. The surgical team used moderate hypothermia and standard cardioplegia techniques in every patient. There were no differences between the groups in terms of acid–base state, duration of aortic cross-clamp or cardiopulmonary bypass (CPB), and surgical technique, which may influence extracellular potassium regulation. They found that when you followed a strict policy for transfusion, the actual rise in serum potassium level was significantly lower than expected (mean difference 0.95 ± 0.35 mmol/L).

Since CPB can result in serious physiological alterations, the conduct of CPB requires meticulous planning of the circuit design, degree of hemodilution, choice of cannulae, priming fluid, flow rates, and degree of hypothermia. Furthermore, we know that children's absolute blood volume is low although their circulating blood volume is relatively higher than adults.[2] Small blood volume, which is significantly affected by major fluid shifts during and after CPB, immune system maturity, hematologic values, and physiological responses to hypovolemia and hypoxia vary widely and contribute to the complexity of pediatric transfusion practice in patients undergoing complex operations. Additionally, small blood volume creates practical limitations on the use of certain blood conservation strategies in a pediatric population, such as autologous donation and cell saver. Swindell et al showed that[3] cell saver washing of PRBCs before adding to the prime or filtering the circuit against a potassium-free buffer has been shown to be superior to blood bank washing because the acid metabolites are truly "washed off" rather than hemodiluted. Fleming et al.[4] claimed that in patients < 10 kg, increased K^+ concentration in CPB circuits do not produce hyperkalemia. However, in that study, the authors removed supernatant additives from most (69.7%) of the PRBC units, which resulted in a significant reduction in extracellular potassium in the PRBC units.

In light of randomized controlled studies in the literature, an intraoperative target hematocrit (Htc) value of > 25% was recommended to not adversely affect neurocognitive development in

the pediatric age group, but a definite and "safe" Htc value could not be determined due to alterations in parameters (pH strategy, flow rate, age, diagnosis, etc.).[2,5] Reduction in the CPB circuit prime volume and subsequent elimination of blood transfusion are main goals in pediatric surgery; however, in infants and small children with complex congenital heart disease, a higher hematocrit has generally been required to maintain the optimal hemodynamics and neurological protection. Adjustment of target Htc level according to the planned procedure, the size of the patient, the lowest planned temperature requires an accurate calculation of blood prime volumes. In this gray area, the strict protocols of experienced clinics have gained importance. PRBCs are generally used in the prime solution of pediatric extracorporeal circuits for the induction of CPB to minimize excessive hemodilution. Another way to reduce hemodilution is a miniaturization of the CPB circuit to reduce the foreign surface area that comes in continuous contact with the patient circulating blood volume and reduces the amount of prime volume. In this way, a decrease in platelet activation and regression in the inflammatory process can be achieved, and surgery can be performed with bloodless priming in the majority of patients with a bodyweight of 4–5 kg and above.[6] Smaller, lower prime-volume circuits are now available with low line pressures and excellent reliability, and it is now possible to review the basic need for hemodilution and hypothermia.[2]

Potassium is a predominant intracellular cation, but an extracellular concentration greater than 5.5 mEq/L has significant effects on cardiac rhythm, which may lead to cardiac arrest.[7] Stored PRBCs are depleted of ATP, which alters the cell membrane, resulting in hemolysis and dysfunction of cation transporters, including impairment of Na^+/K^+ ATPase,[8] which leads to a progressive increase in extracellular K^+ in the PRBC unit supernatant.[9] Furthermore, gamma irradiation, which is used to prevent graft-versus-host disease, increases hemolysis, resulting in potentiated K^+ leakage. As a result, rapid or large-volume transfusions and transfusion of an aged unit can predispose patients to hyperkalemia. It is widely accepted that the longer the blood is stored, the more likely are the chances of electrolyte disturbances.[10] Therefore, K^+ concentration in the supernatant of PRBC is important for predicting the effect of transfused blood on the levels of K^+. In addition to the duration of PRBC storage, transfusion rate, the volume of the transfusion relative to the patient's circulating blood volume, the volume status of the patient also contributes to TAH in an infant with inadequate renal function, impaired Na^+/K^+ ATPase activity, and hormonal tolerance. However, the risks and reasons for such complications remain debatable.

Since it has been proven that extracellular potassium levels are elevated in "old" units as compared with "fresh" units and storage age is associated with cardiac complications, I think it is a very smart, cheap, and safety enhancing protocol to measure the potassium level in the PRBC. Restricting the rate of transfusion, the age of the transfused PRBC, and not transfusing a PRBC with a potassium level above 15 mmol/L weakened the statistical correlation between the patients' potassium change and the age of the transfused PRBC and the correlation between the potassium value of PRBC and the age of PRBC. Similar to Altun et al.,[1] Strauss[11] claimed that correct prescription and administration in a child prevents TAH; however, their study group included patients with normal cardiovascular functions. Ramon and Cortes[12] pointed out the striking differences in patterns of PRBC use among countries, hospitals, and Patel et al.[13] noted the lack of detailed neonatal PRBC transfusion data set in the United States.

One important limitation of the study is that the authors did not evaluate and compare the levels of preoperative, intraoperative, and postoperative values of glucose, calcium, and serum osmolality. The citrate in citrate-phosphate-dextrose, which is added to stored blood as an anticoagulant, binds to the Ca^{++} in serum and leads to low Ca^{++} levels. Because of the anaerobic metabolism of the red blood cells, an increment in the lactate and pyruvate levels with H^+ ion concentration results in a more acidotic stored blood unit. Acidosis and hyperglycemia contribute to increased serum potassium levels. Similarly, hypothermia slows the metabolism of citrate, which exacerbates hypocalcemic states. Further studies should evaluate alterations in potassium levels after PRBC transfusion through these factors.

Another limitation is that the authors failed to document which patients used ultrafiltration and which type of ultrafiltration was used. Prebypass ultrafiltration (PBUF) is commonly used in pediatric cardiac surgery to improve the electrolyte balance of stored PRBC and to create a more physiologic circuit priming solution before the initiation of CPB. A randomized controlled trial comparing conventional ultrafiltration techniques (continuous and zero-balance) and modified ultrafiltration techniques in pediatric patients weighing 15 kg or less concluded that when a standard fluid volume was restored, neither method was superior to the other.[14] There are different sentiments about both techniques in the literature, suggesting that both techniques can be applied safely.[15,16] Some centers do not recommend the routine use of modified ultrafiltration or ultrafiltration for patients with fluid overload, acidosis, or low Hct at the end of CPB.[17]

ACKNOWLEDGMENT

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

Dr. Ali Baran Budak has no conflicts of interest.

ORCID

Ali Baran Budak https://orcid.org/0000-0002-9772-1765

REFERENCES

1. Altun D, Arnaz A, Doğan A, et al. Measuring potassium level in packed red blood cells before using: word of caution for congenital cardiac surgery.
2. Budak AB, McCusker K, Gunaydin S. A structured blood conservation program in pediatric cardiac surgery. *Eur Rev Med Pharmacol Sci*. 2017;21(5):1074-1079.
3. Swindell CG, Barker TA, McGuirk SP, et al. Washing of irradiated red blood cells prevents hyperkalaemia during cardiopulmonary bypass

in neonates and infants undergoing surgery for complex congenital heart disease. *Eur J Cardiothorac Surg*. 2007;31(4):659-664.
4. Fleming GM, Remenapp RT, Bartlett RH, Annich RH. Hyperkalemia of the blood-primed ECLS circuit does not result in post-initiation hyperkalemia in infants < 10 kg. *Perfusion*. 2006;21:173-177.
5. Naguib AN, Winch PD, Tobias JD, et al. A single-center strategy to minimize blood transfusion in neonates and children undergoing cardiac surgery. *Paediatr Anaesth*. 2015;25:477-486.
6. Miyaji K, Kohira S, Miyamoto T. Pediatric cardiac surgery without homologous blood transfusion, using a miniaturized baypas system in infants with lower body weight. *J Thorac Cardiovasc Surg*. 2007;134:284-289.
7. Yamada C, Edelson M, Lee A, Saifee NH, Bahar B, Delaney M. Transfusion - associated hyperkalemia in pediatric population: prevalence, risk factors, survival, infusion rate, and RBC unit features. *Transfusion*. 2021;61(4):1093-1101.
8. Reilly M, Bruno CD, Prudencio TM, et al. Potential consequences of the red blood cell storage lesion on cardiac electrophysiology. *J Am Heart Assoc*. 2020;9(21):e017748.
9. Hess JR. Red cell changes during storage. *Transfus Apher Sci*. 2010;43:51-59.
10. Belpulsi D, Spitalnik S, Hod E. The controversy over the age of blood: What do the clinical trials really teach us? *Blood Transfus*. 2017;15:112-115.
11. Strauss RG. How I transfuse red blood cells and platelets to infants with the anemia and thrombocytopenia of prematurity. *Transfusion*. 2008;48(2):209-217.
12. Romon I, Cortes MA. Hyperkalemia: the Trojan horse of pediatric transfusion? *Transfusion*. 2021;61(4):996-999.
13. Patel RM, Meyer EK, Widness JA. Research opportunities to improve neonatal red blood cell transfusion. *Transfus Med Rev*. 2016;30(4):165-173.
14. Thompson LD, McElhinney DB, Findlay P, et al. A prospective randomized study comparing volume-standardized modified and conventional ultrafiltration in pediatric cardiac surgery. *J Thorac Cardiovasc Surg*. 2001;122:220-228.
15. Golab HD, Kissler J, de Jong PL, van de Woestijne PC, Takkenberg JJM, Bogers AJJC. Clinical outcome and blood transfusion after infant cardiac surgery with a routine use of conventional ultrafiltration. *Perfusion*. 2015;30(4):323-331.
16. Kuratani N, Bunsangjaroen P, Srimueang T, Masaki E, Suzuki T, Katogi T. Modified versus conventional ultrafiltration in pediatric cardiac surgery: a meta-analysis of randomized controlled trials comparing clinical outcome parameters. *J Thorac Cardiovasc Surg*. 2011;142(4):861-867.
17. Vohra HA, Adluri K, Willets R, Horsburgh A, Barron DJ, Brawn WJ. Changes in potassium concentration and haematocrit associated with cardiopulmonary bypass in paediatric cardiac surgery. *Perfusion*. 2007;22(2):87-92.

How to cite this article: Budak AB. Preventing transfusion-associated hyperkalemia in pediatric cardiac surgery: measure the levels of potassium in packed red blood cells before using – Invited commentary. *J Card Surg*. 2022;37:542-544. doi:10.1111/jocs.16157