Potassium Changes Associated With Blood Transfusion in Pediatric Patients

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Key Words: Pediatric transfusion; Potassium; AS-5; Storage; Segment potassium concentration

Abstract

Storing packed red blood cells (pRBCs) increases the potassium concentration. This effect is characterized in citrate phosphate dextrose/citrate phosphate dextrose adenine units but not published for Adsol (AS-5) units. The change in whole-blood potassium concentration in pediatric patients during routine transfusion is also poorly characterized. In this study, pediatric patients undergoing transfusion had pre- and posttransfusion whole-blood potassium measurements. The pRBC unit transfused and the unit’s segment were sampled, with potassium concentration measured. In addition, potassium concentration in AS-5 units was measured over 42 days of storage. Unit extracellular potassium increased in AS-5 units after day 7 at 0.83 mmol/L/d. The mean change in patient potassium concentration was 0.08 mmol/L (range, –0.5 to 0.5 mmol/L). No correlation with unit age or unit potassium concentration was identified with change in patient whole-blood potassium concentration. The lack of clinical effect on patient potassium does not support the use of “fresh” pRBC units with routine pediatric transfusion.

A known effect of storing and irradiating packed red blood cells (pRBCs) is an increase in potassium concentration in the supernatant suspending the pRBCs.1 When a transfusion is given, thought must be given to the amount of potassium being infused. Children with disturbances in their potassium levels are susceptible to muscle weakness, paralysis, cardiac arrhythmia, and death. The changes in serum potassium in children due to transfusion have been poorly characterized and may or may not be clinically significant. These changes have been studied in the past,2 although in the past 30 years, many changes in transfusion medicine practice have occurred. These include different anticoagulants, storage, and additive solutions. We set out to determine what effect transfusion has on a patient’s whole-blood potassium concentration with modern transfusion practice.

Since the 1970s, there have been 11 case reports of transfusion-associated hyperkalemia in children; 4 of those 11 cases resulted in death.3 To mitigate this risk, some providers have switched to using washed RBCs in pediatric patients. However the evidence supporting this use is weak,4 although the reasoning behind it is judged to be sound by some authors.5 We quantify the changes in whole-blood potassium concentrations in patients undergoing small-volume (up to 450 mL) transfusions in a routine manner.

When blood is stored, potassium passively leaks from the cells, building in the medium surrounding the cells and leaving the red cells deficient in intracellular potassium. When the stored unit of blood is transfused, this extracellular potassium is also infused. The RBCs restore intracellular potassium by active transport after the transfused RBCs...
recover metabolic activity and adenosine-5'-triphosphate production. Because of the delay in recovery of metabolic activity by the transfused RBCs, a transient increase in plasma potassium may occur in the recipient.

This unintended “transient hyperkalemia” is an undesirable adverse effect of transfusion. Much has been written about strategies to deal with this potassium influx. However, in the setting of routine, nonemergent, or high-volume transfusion, the changes in serum potassium caused by giving nonwashed, irradiated RBCs are not well characterized.

Published data exist for potassium concentrations in units preserved with citrate phosphate dextrose (CPD) and citrate phosphate dextrose adenine 1 (CPDA-1). However, to our knowledge, no published data have detailed potassium concentration as Adsol (AS-5)–preserved unit ages. In this study, we also determine potassium concentration in AS-5–preserved RBC units as they age.

Materials and Methods

This study was reviewed and approved by the Penn State Hershey Medical Center Institutional Review Board (protocol number 38407). The study was powered to detect a significant change in serum potassium of 0.1 mmol/L. With the laboratory methods being used, this results in the need for 17 transfusion events to be analyzed. Because of the (relatively) high number of pediatric hematology and oncology patients undergoing transfusion, this patient population was selected to be representative of the pediatric population receiving transfusions at academic medical centers and to shorten patient accrual time. When a patient with central venous access was to undergo transfusion for any reason, the clinicians identified the child, and the child and parent or guardian provided consent. Only patients with central access were accrued in the study to maximize patient comfort, minimize hemolysis with blood draws, and ensure more uniform infusion rates.

A pretransfusion blood draw of 3 mL was performed through a central venous catheter and sent for analysis by the GEM3500 (Instrumentation Laboratories, Bedford, MA) blood gas analyzer, which uses an ion-selective electrode to assess whole-blood potassium in the core clinical laboratory. Whole-blood potassium was measured for ease of sampling, speed of specimen handling, speed of analysis, and to avoid the small and variable increase in potassium that occurs during centrifugation of whole blood to prepare plasma.

Concurrently, a 3-mL sample was taken from the unit to be transfused. In addition, the segments from the unit were sampled. Both the unit sample and segment sample underwent measurement of potassium concentration on the VITROS 5,1 (Ortho Clinical Diagnostics, Rochester, NY) chemistry analyzer using ion-selective slide technology. The details of the unit, such as draw date, volume of transfusion, and date of transfusion, were recorded.

All analytic instruments used in this study, which undergo daily in-house calibration, were always within calibration limits during the study.

The transfusion was then given as clinically indicated. No patients in the study received a transfusion of more than 450 mL at one time, and transfusions were given at a rate of 50 to 150 mL/h based on the clinician’s orders, the patient’s weight, and the patient’s clinical situation. No transfusion-related complications were noted during or after transfusions. All units were leukoreduced by filtration at the time of initial unit processing and irradiated within the 24 hours prior to sampling and transfusion. No product was irradiated without a transfusion ordered and scheduled within the 24 hours after irradiation occurred. All units were anticoagulated and preserved with AS-5 solution (Terumo, Tokyo, Japan).

A second patient blood sample was drawn through the patient’s central venous access 1 hour after the transfusion and analyzed on the GEM3500 blood gas analyzer (Instrumentation Laboratories), measuring whole-blood potassium.

Patient information was obtained by medical record review. The most recent available result prior to transfusion was recorded for age, weight, sex, estimated glomerular filtration rate (eGFR), serum creatinine, and primary diagnosis. Total blood volume was calculated using the patient’s most current pretransfusion weight and pediatric blood volume normal values. eGFR was calculated by the electronic medical record with established formulas using serum creatinine, age, and height.

Data were entered into computer spreadsheet software (Microsoft Excel 2011; Microsoft, Redmond, WA) and analyzed with STATA version 12 software (StataCorp LP, College Station, TX). Correlation coefficients were calculated by STATA using the product-moment correlation coefficient. A paired sample t test was used to determine whether unit potassium and segment potassium concentrations were equal. Significance for all statistical tests was set at P ≤ .05.

AS-5–preserved units for the determination of potassium concentration changes over time were collected and processed at the Hershey Medical Center donor center, per normal protocol, on the day prior to unit selection. All units selected were collected without difficulty during phlebotomy in an Immuflex Terumo BCT bag (Terumo, Tokyo, Japan), leukoreduced by filtration, and processed for plasma and platelet collection as well as pRBCs. Units were then stored on their own shelf in the blood bank refrigerator and disturbed only for sampling. Potassium concentration was measured on the day of selection (day 0) and every 7 days afterward, until day 42. Blood samples were collected for testing with the use of a neonatal aliquot system (Charter Medical, Winston-Salem, NC) to avoid puncturing the unit,
and care was taken to avoid hemolysis when samples were obtained. A 3-mL sample was obtained from the aliquot bag into a heparin-Vacutainer tube. This was hand carried to the Hershey Medical Center clinical chemistry laboratory, spun for 7 minutes at 3200 rpm, and measured on the VITROS 5,1 (Ortho Diagnostics) chemistry platform via ion-selective slide technology.

Results

A total of 9 individual patients received 17 distinct transfusions. The children ranged in age from 1 to 14 years and weighed between 8.8 and 57 kg. Six of the 9 patients were female. Their calculated blood volumes ranged from 692 to 4,971 mL. Their eGFR at the time of transfusion ranged between 100 and 308 mL/min; thus, all patients had normal renal function. No patient had auto- or alloantibodies identified on their pretransfusion type and screen, nor was there any evidence of a transfusion reaction or hemolysis posttransfusion.

The change in whole-blood potassium from the pretransfusion sample to 1-hour posttransfusion sample ranged from –0.5 to 0.5 mmol/L. The mean change was +0.08 mmol/L. No patient developed hyperkalemia (as defined by a whole-blood potassium concentration >5.0 mmol/L), and no complication from transfusion was noted.

A total of 17 distinct units were transfused for the 17 transfusions included in this study. Unit age ranged between 3 and 38 days (mean, 26.5 days). Unit potassium concentration averaged 54.9 mmol/L (range, 19.1-79.9 mmol/L). The segment potassium concentration averaged 48.1 mmol/L (range, 8.2-69.7 mmol/L). Unit potassium concentration and segment potassium concentration were significantly different (P = .015). The mean absolute difference between segment potassium and unit potassium was 9.1 mmol/L. Six segments had higher and 11 segments had lower potassium concentrations than the units. The segments had potassium concentrations that ranged from 8.6 mmol/L higher than the units to 28.4 mmol/L lower than the units. The transfusion volumes ranged between 140 and 450 mL (6.1-16.4 mL/kg). By multiplying the unit potassium concentration by the volume transfused, the amount of potassium infused with each transfusion averaged 0.6 mmol/kg (range, 0.3-1.3 mmol/kg).

No correlation was identified between unit potassium concentration and change in patient whole-blood potassium (P = .72). Figure 1A, potassium dose transfused and change in patient whole-blood potassium (P = .18). Figure 1B, unit age and change in patient whole-blood potassium (P = .89). Figure 1C, calculated blood volume and change in patient whole-blood potassium (P = .24), and patient GFR and change in patient whole-blood potassium (P = .18).

There was a positive correlation between unit age and unit potassium concentration (P = .003). Figure 2, unit age and segment potassium concentration (P = .001), and unit potassium concentration and segment potassium concentration (P = .001). Figure 3.

The amount of potassium infused with the transfusion was calculated by multiplying the transfusion volume by the transfused unit potassium concentration. After calculating patient blood volume based on sex and weight, the amount of potassium infused was divided by the total blood volume to estimate the maximum expected rise in patient potassium concentration. This obviously does not take into account the tight metabolic control that humans have over potassium and the ability of potassium to quickly redistribute throughout the body. However, for purposes of comparison, a calculation of the “worst-case” scenario for transfusions causing hyperkalemia is made, which is that all the transfused potassium stays in the bloodstream. This calculation is not physiologic, but it is a starting point for discussion.

The mean maximum calculated expected rise was 7.4 mmol/L (range, 3.1-15.2 mmol/L). Figure 4. The mean difference in the observed change as compared with the mean calculated expected change was 7.4 mmol/L (range, 2.8-14.7 mmol/L).

The mean ± SD serum potassium concentration on day 0 was 1.4 ± 0.3 mmol/L. The mean ± SD serum potassium concentration was 22.7 ± 7.5 mmol/L on day 7 and 51.0 ± 6.7 mmol/L on day 42. A linear mixed-effects regression was fit to the data starting on day 7, as potassium increases were observed to be linear starting from the day 7 time point. The slope of this was 0.83 mmol/L/d, with a standard error of 0.037. Figure 5.

Discussion

There is currently much concern regarding hyperkalemia after blood transfusion in children. However, our study did not demonstrate a predictable or clinically significant change in patient whole-blood potassium concentration after transfusion. The changes in potassium observed in this study were also small, ranging from –0.5 to 0.5 mmol/L.

The most likely explanation for our findings is that the transfusions were given at a moderate rate, with the posttransfusion whole-blood potassium measurement performed 1 hour after the transfusion had finished. In our patient population, the mean total infused potassium dose was 54.9 mmol, and the mean calculated expected rise was 7.4 mmol/L. The mean observed rise was +0.08 mmol/L.

The observed value is much smaller than the measured whole-blood potassium increase at 1 hour due to the combined effects of potassium excretion in the kidneys and
Figure 1 A. Potassium concentration from the unit is plotted on the y-axis against the observed change in recipient whole-blood potassium concentration at 1 hour posttransfusion. There is no correlation ($P = .72$) between unit potassium concentration (mmol/L) and the change in patient whole-blood potassium (mmol/L). A best-fit linear trend line is provided for reference, $R^2 = 0.01$.

B. The calculated potassium dose delivered with each transfusion is plotted against the observed change in recipient whole-blood potassium concentration at 1 hour posttransfusion. There is no correlation ($P = .18$) between the amount of potassium (mmol/kg) and the change in patient whole-blood potassium (mmol/L). A best-fit linear trend line is provided for reference, $R^2 = 0.12$.

C. The age of the transfused unit (x-axis) is plotted against the observed change in recipient whole-blood potassium concentration at 1 hour posttransfusion. There is no correlation ($P = .89$) between the change in patient whole-blood potassium (mmol/L). Trend line, $R^2 = 0.001$.

Figure 2 A. The age of the transfused unit (x-axis) is plotted against the potassium concentration in that unit (y-axis). There is a positive correlation ($P = .003$) between unit age (days) and unit potassium concentration (mmol/L). Trend line, $R^2 = 0.45$.

B. The potassium concentration in the unit (x-axis) is plotted against the potassium concentration in the segment attached to the unit (y-axis). A best-fit linear trend line is provided ($y = 0.71x + 8.99$, $R^2 = 0.54$).
potassium “redistribution” in the transfused RBCs as they recover metabolic activity and actively transport potassium from plasma to the RBC cytosol. As our data clearly demonstrate, the combined effects of potassium excretion by the kidneys and uptake by the transfused RBCs mitigate the changes in plasma potassium after RBC infusion such that the observed 1-hour posttransfusion increase in whole-blood potassium was not clinically significant.

Of note, our study did not include patients with severely compromised renal function. In this patient population, potassium homeostasis is more tenuous, and the shifts observed in this study may not be reflective of the changes seen in this population. Our study also did not look at the potassium shifts with extremely rapid or large-volume transfusions.

A limitation of this study is the small sample size. Because of concerns by the institutional review board about pediatric patient blood drawing, efforts were made to reduce the number of participants to the minimum needed to power the study so a clinically significant change in potassium of 0.1 mmol/L could be identified. Because of this, only 17 transfusion events were included in the study. By including more participants, a wider demographic of patients could be observed, including patients with renal failure, patients receiving larger volume transfusions or high infusion rate transfusions, and those in an intensive care unit setting.

An interesting finding in this study was that the potassium concentration of the unit and of the segment was significantly different. The unit potassium concentration was on average higher (54.9 mmol/L) compared with the segment from the unit (48.1 mmol/L). This may be due to the differences in the storage microenvironment. The unit bag is more breathable, and differences in RBC metabolism during storage may account for the differences. However, more investigation is warranted into this poorly studied topic.

To our knowledge, this is the first description of the changes in unit serum potassium concentration in AS-5–preserved units. Although not significantly different from the potassium changes seen in CPD- and CPDA-1–stored blood, the 42-day shelf life of the AS-5–stored units allows for higher potassium concentrations to build in the unit serum. However, our study does not imply that this higher potassium concentration changes the patients’ serum potassium levels 1 hour after a routine transfusion.

This study used exclusively nonwashed, irradiated, leukoreduced RBC units preserved with AS-5. Our current blood bank protocol is to irradiate units just prior to the time of issue. However, this should not imply that irradiation within 24 hours of issue provides an RBC product that is significantly different from one that is irradiated beyond 24 hours prior to issue. Leukoreduction does not increase unit potassium, and although irradiation does raise potassium concentration in RBC units, it has been shown by this study and others that routine washing of these units is not warranted.

This study also used blood that was generally “older.” Two units were drawn less than 8 days after the transfusion, but the remaining 15 were older than 16 days, with 8 of these older than 30 days. The potassium concentrations in these units were higher than the “fresh” units. However, there was
no correlation to change in whole-blood potassium concentration with the transfusion of these “old” units.

This study provides good evidence that in the scope of “routine” blood transfusion (ie, not as part of large-volume resuscitation efforts) in children with normal renal function, serum potassium is not drastically shifted by transfusion. The need for washing or providing “fresh” or more recently collected blood for “routine” pediatric blood transfusion is not supported by this study.

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Source of support: Penn State Hershey Departmental Research Award.

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Acknowledgments: We thank Michael Creer, MD, Dani Zander, MD, Teresa Shapiro, MSN, AOCNP, Melanie Comito, MD, and the entire Penn State Hershey Medical Center Blood Bank staff.

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