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Evaluation of a Tiered Potassium Replacement Protocol in Post-Operative Patients Admitted to a Pediatric Cardiac Intensive Care Unit

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OBJECTIVE To evaluate the efficacy and safety of our institution's tiered intravenous potassium replacement protocol in pediatric patients admitted post-operatively to the pediatric cardiac intensive care unit. To our knowledge, this is the only study evaluating the specific parameters of a potassium replacement protocol similar to ours.

METHODS This retrospective, single-center, observational study evaluated children up to 18 years of age admitted post-operatively to the pediatric cardiac intensive care unit between September 1, 2022 and January 31, 2023 who received 1 or more doses of intravenous potassium per our institutional replacement protocol for a hypokalemic episode (serum potassium concentration less than or equal to 3.7 mEq/L). All patients, hypokalemia episodes, replacement doses, and subsequent serum potassium concentrations were evaluated until post-operative day 5.

RESULTS There were 23 patients included with a total of 95 episodes of hypokalemia. For both tiers of the replacement protocol, a median of 1 dose was required to resolve hypokalemia. Two incidences of hyperkalemia (serum potassium greater than or equal to 5.5 mEq/L), 2.1% of total, were proven or suspected to be true, both classified as moderate hyperkalemia. All episodes of hyperkalemia were not associated with ECG abnormalities and did not require treatment.

CONCLUSIONS Despite utilizing higher serum potassium concentration thresholds for replacement as well as higher maximum dosing than published literature, our protocol was effective at resolving hypokalemia, as defined by our protocol, without leading to significant hyperkalemia.

ABBREVIATIONS ACE, angiotensin converting enzyme; ARB, angiotensin 2 receptor blocker; ASD, atrial septal defect; BUN, blood urea nitrogen; CPB, cardiopulmonary bypass; ECG, electrocardiogram; IV, intravenous; NSAIDs, non-steroidal anti-inflammatory drugs; PDA, patent ductus arteriosus; SCr, serum creatinine; STAT, Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery; TOF, Tetralogy of Fallot; VSD, ventricular septal defect

KEYWORDS cardiovascular surgical procedure; electrolyte; pediatric; pediatric cardiac intensive care unit; pediatric intensive care unit; potassium

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Introduction

Potassium is an intracellular cation that plays a major role in many physiologic functions, including the regulation of cardiovascular electrical activity.[1,2] A disruption in the balance between intracellular and extracellular (3.5–5.5 mEq/L) concentrations can have significant and life threatening consequences.[1]

Hypokalemia is considered one of the most common electrolyte disturbances in critically ill patients and can cause disruptions in the electrical activity of cardiac, skeletal, and smooth muscles. These effects may lead to arrhythmias, cardiac arrest, respiratory failure, and muscular paralysis.[2,3] Pediatric patients undergoing cardiovascular surgery are highly susceptible to hypokalemia in the post-operative period. During this time, patients often require vasopressors, inotropes, and high-dose diuretics, which can contribute to hypokalemia by shifting potassium intracellularly or disturbing the renal mechanisms for regulation. In addition, the clinical picture is often further clouded by the dilutional effect seen during procedures requiring cardiopulmonary bypass (CPB) as well as the need for intravenous (IV) fluid management until enteral feeds begin.[1,3,4]

Pediatric patients undergoing cardiovascular surgery are also highly susceptible to hyperkalemia in the post-operative period due to the use of blood products,

potential for over-supplementation, and the risk of transient acute kidney injury after CPB.[3] Hyperkalemia can be further classified into mild (serum potassium 5.5–6.5 mEq/L), moderate (serum potassium 6.6–7.5 mEq/L) and severe (serum potassium greater than 7.5 mEq/L).[1] In most cases, the cause of hyperkalemia can be attributed to either an impaired elimination of potassium or a shift of potassium extracellularly.[1]

A retrospective cohort review published in 2020 by Amirnovin et al[3] compared the safety and efficacy of 3 separate potassium replacement protocols in pediatric patients who were admitted to the cardiac intensive care unit post-operatively. The authors assessed a low-dose protocol (using 0.5 mEq/kg of IV potassium chloride for potassium concentrations less than or equal to 3.2 mEq/L), a high-dose protocol (using 1 mEq/kg of IV potassium chloride for potassium concentrations less than or equal to 3.2 mEq/L), and a tiered-dose protocol (using 0.5 mEq/kg of IV potassium chloride for potassium concentrations 2.9 to 3.2 mEq/L and 1 mEq/kg of IV potassium chloride for potassium concentrations less than or equal to 2.8 mEq/L) with a maximum dose of 10 mEq in all 3 protocols. The authors concluded that the tiered-dose protocol improved the efficacy of the low-dose protocol while maintaining its safety profile.[3]

In 2019, our institution implemented a tiered-dose potassium replacement protocol, presented in Table 1, utilizing 0.5 mEq/kg (maximum of 20 mEq/dose) of IV potassium chloride for serum potassium concentrations of 3.3 to 3.7 mEq/L (Tier 1) and 1 mEq/kg (maximum of 40 mEq/dose) of IV potassium chloride for serum potassium concentrations of less than or equal to 3.2 mEq/L (Tier 2). The replacement dose is administered over 2 hours and a repeat serum potassium concentration is drawn 1 hour after the end of infusion. This protocol is ordered for all patients post-operatively, unless omitted by the physician due to patient characteristics warranting against use, such as patients with significant renal impairment or requiring renal replacement therapy. Routine potassium concentrations are obtained per provider order and if hypokalemia is present, the nurse requests the appropriate protocol replacement dose. This protocol was implemented due to an increased incidence of junctional ectopic tachycardia observed in this population in an effort to be more proactive and have a higher sensitivity of capturing hypokalemia. Our protocol is also entirely nurse-driven with no maximum number of doses. This design allows the nurse to continue giving replacement doses as needed to resolve the hypokalemia without additional provider orders, to help eliminate any potential delay in serum electrolyte correction. In contrast to the protocol evaluated by Amirnovin et al,[3] this protocol utilizes a more aggressive dosing strategy requiring supplementation for potassium concentrations less than 3.7 mEq/L and allowing up to 40 mEq per dose. The purpose of this study was to evaluate the efficacy and safety of our potassium replacement protocol in pediatric patients admitted post-operatively to the pediatric cardiac intensive care unit.

Table 1. Institutional Intravenous Potassium Replacement Protocol

Protocol Parameter	Tier 1	Tier 2
Serum potassium concentration threshold	3.3 to 3.7 mEq/L	≤ 3.2 mEq/L
Potassium chloride intravenous dose*	0.5 mEq/kg single dose	1 mEq/kg single dose
Maximum dose	20 mEq	40 mEq
Time to repeat serum potassium concentration	1 hr after end of infusion	

* Intravenous potassium dose administered over 2 hr.

Materials and Methods

Study Design. This was a retrospective, single-center, observational study of patients admitted post-operatively to the pediatric cardiac intensive care unit to assess the efficacy and safety of our institutional potassium replacement protocol.

Selection of Participants. Patients were included in the study if they were less than 18 years of age and admitted post-operatively to the pediatric cardiac intensive care unit at AdventHealth for Children between September 1, 2022, and January 31, 2023. Once identified, included patients were then screened to ensure they received one or more potassium replacement doses within the protocol parameters. Patients were followed through post-operative day 5 to identify the presence of hypokalemia, which we defined as a serum potassium less than or equal to 3.7 mEq/L as this is when the replacement protocol is initiated. An episode of hypokalemia was defined as the time from a serum potassium concentration less than or equal to 3.7 mEq/L to the resolution of hypokalemia. For patients with multiple episodes of hypokalemia during the study period, each episode was counted separately. Episodes of hypokalemia were excluded if the potassium replacement protocol was not followed, if the serum potassium concentration was not drawn within 6 hours of the start of the replacement dose, or if no serum potassium concentration was drawn prior to administering an additional dose.

Endpoints and Statistical Analysis. The primary endpoint evaluated was the amount of potassium required to resolve a hypokalemia episode, measured in number of doses and total dose (mEq/kg) given. Secondary endpoints included the percentage of protocol doses leading to hyperkalemia (serum potassium greater than or equal to 5.5 mEq/L), the percentage of hyperkalemia

episodes with documented electrocardiogram (ECG) abnormalities, and the percentage of hyperkalemia episodes that were treated with pharmacologic measures or renal replacement therapy. Hyperkalemia was further classified into mild, moderate, and severe. An additional analysis was performed to evaluate the timeliness in administering a replacement dose as well as repeating serum potassium per protocol. All endpoints and additional analyses were evaluated using descriptive statistics.

Data Collection. Baseline patient characteristics including age, sex, weight used for protocol, history of arrhythmias, presence of intraoperative arrhythmias, type of surgery performed including STAT category, use of CPB, pre-surgery labs (serum potassium, blood urea nitrogen, and serum creatinine), and immediate post-operative labs (serum potassium, blood urea nitrogen, and serum creatinine) were collected. For each episode of hypokalemia, data points were collected to include mechanism for potassium concentration analysis (i.e., point of care testing obtained for arterial blood gas analysis or lab-analyzed), concomitant medications that have been associated with alterations in serum potassium concentrations, the presence of potassium from continuous intravenous fluids or parenteral nutrition, time from hypokalemia concentration to administration of potassium replacement dose, and time from administration of potassium replacement dose to repeat serum potassium concentration. Evaluated medications associated with hypokalemia included insulin, fludrocortisone, bumetanide, furosemide, chlorothiazide, and metolazone. Daily doses of diuretics were collected, as these are heavily used in this population, to establish a baseline and identify outliers from usual dosing practices. At our institution, bumetanide continuous infusions or intermittent furosemide in combination with intravenous or oral chlorothiazide, as needed, is our standard practice. Medications associated with hyperkalemia, including spironolactone, cyclosporine, tacrolimus, trimethoprim, pentamidine, non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme (ACE) inhibitors, angiotensin 2 receptor blockers (ARBs), beta blockers, and therapeutic heparin were also evaluated.[1]

Results

Study Population. Demographic data and clinical characteristics for patients are presented in Table 2. Of the 40 patients screened for inclusion, 17 patients were excluded. The reasons for exclusion included: age greater than or equal to 18 years of age (6 patients) and protocol not followed (11 patients). Patients classified as not following the protocol included those with dose rounding greater than 10% (3 patients), those who did not receive a potassium replacement dose within the specified time frame (5 patients), and those in which no episodes of hypokalemia were treated following the protocol (3 patients).

Table 2. Baseline Patient Characteristics

Characteristic	n = 23 Patients
Age in mo, median (IQR)	3.5 (0.8–6.4)
Female, n (%)	15 (65.2)
Weight in kg, median (IQR)	5.1 (3.5–6.9)
Arrhythmias, patients, n (%)	
History	2 (8.7)
Intraoperative	4 (17.4)
Use of CPB, patients, n (%)	21 (91.3)
STAT category (procedures), n	
STAT 1 (ASD repair, TOF repair, VSD repair, PDA closure)	13
STAT 2 (Bidirectional Glenn, coarctation repair)	4
STAT 3 (aortic arch repair, arterial switch)	3
STAT 4 (arterial switch with VSD repair)	1
STAT 5 (Norwood)	1
Not categorized	1
Pre-operative laboratory values, average (SD)	
Serum potassium in mEq/L	3.7 (± 0.6)
BUN in mg/dL	12.2 (± 5.3)
SCr in mg/dL	0.37 (± 0.08)
Immediate post-operative laboratory values, average (SD)	
Serum potassium in mEq/L	3.9 (± 0.8)
BUN in mg/dL	11.5 (± 4.5)
SCr in mg/dL	0.31 (± 0.07)

ASD, atrial septal defect; BUN, blood urea nitrogen; CPB, cardiopulmonary bypass; PDA, patent ductus arteriosus; SCr, serum creatinine; STAT, Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery; TOF, Tetralogy of Fallot; VSD, ventricular septal defect

In the 23 patients who met inclusion, a total of 153 hypokalemia episodes were identified with 95 episodes meeting inclusion criteria. The primary reason for episode exclusion was due to not following the protocol (43 episodes), followed by repeat serum potassium concentration being drawn too early (11 episodes) and no serum potassium concentration being drawn within 6 hours of administering the replacement dose (4 episodes). Episodes grouped as not following the protocol were most commonly excluded due to no protocol dose being administered for a hypokalemia concentration or the administered replacement dose did not match the protocol (see Supplemental Figure). Concomitant medications that are known to cause hypokalemia or hyperkalemia for each episode are presented in Table 3. Doses of diuretics utilized during episodes of hypokalemia are presented in Table 4.

Efficacy. Of the 95 episodes of hypokalemia included, 76 (80%) episodes had an initial serum potassium concentration between 3.3 and 3.7 mEq/L (Tier 1) and 19 (20%) episodes had an initial serum potassium concentration that was less or equal to than 3.2 mEq/L (Tier 2) (Table 5).

For Tier 1 episodes, the average number of doses needed to resolve hypokalemia was 1.3 (SD 0.36) with a median of 1. The average dose, in mEq/kg, to resolve hypokalemia was 0.68 (SD 0.41) with a median of 0.5.

For Tier 2 episodes, the average number of doses needed to resolve hypokalemia was 2.05 (SD 2.44) with a median of 1. The average dose, in mEq/kg, to resolve hypokalemia was 1.92 (SD 2.28) with a median of 1. The average values for this group were largely influenced by 3 outlier episodes. One of these outlier episodes required a total of 4 doses (4 mEq/kg), 1 of these outlier episodes required a total of 5 doses (4 mEq/kg) and 1 of these outlier episodes required a total of 11 doses (10.5 mEq/kg) to correct the hypokalemia.

Safety. A total of 9 incidences of hyperkalemia were identified (Table 6). Five incidences of hyperkalemia were determined to be false with proven or suspected hemolysis as a repeat concentration was performed within 10 minutes of the elevated result and returned within normal limits. One incidence of hyperkalemia was noted to be drawn during the

Table 3. Important Concomitant Medications Associated With Hypokalemic Episodes

Medication	n = 95 Episodes
Potassium, n (%)	
Scheduled intravenous	1 (1)
Intravenous fluids/parenteral nutrition	44 (46.3)
Receiving medications associated with hypokalemia,* episodes, n (%)	
Bumetanide	46 (48.4)
Furosemide	40 (42.1)
Chlorothiazide	25 (26.3)
Total	80 (84.2)
Mean number of medications associated with hypokalemia per episode, n (SD)	1.04 (± 0.69)
Receiving medications associated with hyperkalemia,* episodes, n (%)	
NSAIDs	30 (31.6)
Therapeutic heparin	16 (16.8)
ACE inhibitors	3 (3.2)
Beta-blockers	2 (2.1)
Total	45 (47.4)
Median number of medications associated with hyperkalemia per episode, n (SD)	1.03 (± 0.61)

ACE, angiotensin converting enzyme; NSAIDs, non-steroidal anti-inflammatory drugs

* Other evaluated medications not listed were not present during any episodes during study period. A full list of medications is detailed in Methods.

Table 4. Diuretic Doses Utilized During Hypokalemic Episodes

Medication	Number of Episodes (%)	Mean Dose (SD)
Bumetanide intravenous, mcg/kg/day	46 (48.42)	146.4 (± 0.07)
Furosemide oral, mg/kg/day	3 (3.16)	4.24 (± 2.12)
Furosemide intravenous, mg/kg/day	37 (38.95)	2.74 (± 1.57)
Chlorothiazide oral, mg/kg/day	1 (1.05)	26
Chlorothiazide intravenous, mg/kg/day	24 (25.26)	14.14 (± 8.12)

Table 5. Primary Outcome

Tier 1 (Initial Potassium 3.3–3.7 mEq/L)	n = 76 episodes
Number of IV potassium doses to resolve hypokalemia, episodes, n (%)	
1 dose	60 (78.9)
2 doses	12 (15.9)
3 doses	1 (1.3)
4 doses	3 (3.9)
Mean potassium dose (SD) to resolve hypokalemia episode, in mEq/kg	0.68 (± 0.41)
Median potassium dose (IQR) to resolve hypokalemia episode, in mEq/kg	0.5 (0.5–0.5)
Tier 2 (Initial Potassium ≤ 3.2 mEq/L)	**n = 19 episodes**
Number of IV potassium doses to resolve hypokalemia, episodes, n (%)	
1 dose	13 (68.4)
2 doses	3 (15.7)
4 doses	1 (5.3)
5 doses	1 (5.3)
11 doses	1 (5.3)
Mean potassium dose (SD) to resolve hypokalemia episode, in mEq/kg	1.92 (± 2.28)
Median potassium dose (IQR) to resolve hypokalemia episode, in mEq/kg	1 (1–1)

IV, intravenous

Table 6. Secondary Outcomes

Outcome	n = 95 Episodes
Number of IV potassium doses leading to hyperkalemia episodes, episodes, n (%)	2 (2.1)
Mild (5.5–6.5 mEq/L), episodes, n (%)	0 (0)
Moderate (6.6–7.5 mEq/L), episodes, n (%)	2 (2.1)
Severe (>7.5 mEq/L), episodes, n (%)	0 (0)
Number of IV potassium doses leading to ECG abnormalities, episodes, n (%)	0 (0)
Number of hyperkalemia episodes requiring treatment, episodes, n (%)	0 (0)
Time from hypokalemic level to dose given in hr, median (IQR)	0.73 (0.22–1.48)
Time to repeat serum potassium concentration in hr after start of IV potassium infusion, median (IQR)	3.08 (2.36–3.82)

ECG, electrocardiogram; IV, intravenous

infusion of a potassium replacement dose and another was drawn during administration of massive transfusion protocol. Due to this, both incidences were excluded. The remaining 2 incidences (2.1% of the total episodes) were suspected or proven to be true hyperkalemia, but neither was associated with ECG abnormalities or required treatment. Of the 2 incidences of hyperkalemia, only 1 was associated with a high-dose (Tier 2) replacement.

Additional Analysis. The average time between the serum potassium concentration being drawn and the start of the replacement dose infusion was 1.06 hours (SD 1.07) with a median of 0.73 hours. The average time to repeat serum potassium concentration after the start of the replacement dose was 3.18 hours (SD 1.05) with a median of 3.08 hours, which aligns with our protocol.

Serum potassium concentrations were analyzed through both point of care and our institutional chemistry laboratory. Initial post-operative serum potassium concentrations were lab-analyzed and repeat potassium concentrations after a replacement infusion were typically point of care, although the method sometimes varied depending on the patient's lab and blood gas schedule. The initial hypokalemia level was identified more commonly from lab-analyzed values (83 episodes, 87.37%).

Discussion

We used a serum potassium greater than 3.7 mEq/L after replacement as a marker of efficacy. Sixty episodes (78.9%) with an initial serum potassium concentration of 3.3 to 3.7 mEq/L (Tier 1) were corrected after 1 dose. Thirteen episodes (68.4%) with an initial serum potassium concentration less than 3.2 mEq/L (Tier 2) were corrected after 1 dose. For both tiers of our potassium replacement protocol, the median number of IV doses to correct hypokalemia was 1, which indicates that our protocol is effective. The average dose to resolve hypokalemia in Tier 2 episodes was largely influenced by 3 outliers. For each of these episodes, patients were receiving diuretics at doses higher than the mean for the population, which may have impacted the need for additional potassium replacements. The types of diuretics and mean doses observed in this study are consistent with our unit practice.

The study conducted by Amirnovin et al[3] found a hyperkalemia rate, which they defined as a serum potassium concentration greater than or equal to 4.8 mEq/L, of 0.5% (associated with 3 doses) with the tiered-dose protocol. They utilized a high-normal potassium concentration as a marker for safety to increase sensitivity. We found a hyperkalemia rate of 2.1% (associated with 2 doses) with our tiered-dose protocol, which included no incidences of severe hyperkalemia. Our protocol, although more aggressive than that studied by Amirnovin et al,[3] does not appear to lead to clinically significant higher rates of hyperkalemia for our population.

There was significant variability in time to administration of an IV potassium replacement dose given inconsistencies in our unit practice. Our protocol is entirely nurse driven and requires the nurse to request a replacement dose to be made and sent from the pharmacy. Some nurses proactively request replacements to have available on the unit when needed, but this is not standard practice nor part of our protocol, making it entirely dependent on the nurse and the patient's presumed level of acuity. This also varies with time, as nurses are more likely to maintain replacement doses on the unit for the first 24 to 48 hours after surgery compared with post-operative day 5. There was less variability in time to repeat serum potassium concentration. Our protocol defaults to a 2-hour infusion time for each dose with a minimum infusion time of 1 hour. Nurses are prompted to repeat a serum potassium concentration 1 hour after the replacement dose completes. Given this, an average time to repeat concentration of 3.18 hours from the start of infusion aligns with our protocol.

This study adds to the limited existing literature for potassium replacement in this population. However, given that this is a retrospective and observational study, the ability to capture safety parameters, such as ECG abnormalities, is restricted, and our study lacked a comparison group. This study was also performed after a recent change in our institution's electronic health record which limited the time frame for data collection. This study followed patients through post-operative day 5 and did not evaluate efficacy or safety in non-surgical pediatric patients admitted to the pediatric cardiac intensive care unit. The median age of 3.5 months in this study may limit the

generalizability to other pediatric cardiac intensive care units. Limitations also exist in the ability to accurately measure serum potassium and the level of hemolysis present, as our unit commonly uses point of care testing via samples obtained for blood gas analysis for repeat serum potassium concentrations. Additionally, we were unable to quantify the impact of potassium administration outside of the protocol, such as through intravenous fluids or parenteral nutrition, as these varied throughout the study period and were impacted by many other factors. Our unit largely relies on nurses and pharmacists to monitor and dispense potassium replacement doses, which could be an area of opportunity to improve timely potassium replacement. At the time this study was conducted, to our knowledge, there was no published literature evaluating the higher parameters used for our potassium replacement protocol or a completely nurse-driven protocol. Future prospective studies with a larger sample size may be warranted.

Conclusion

The presence of hypokalemia is common in pediatric patients following cardiac surgery. This study aimed to evaluate the efficacy and safety of our tiered IV potassium infusion replacement protocol in pediatric patients admitted post-operatively to the pediatric cardiac intensive care unit. This protocol utilizes higher serum potassium concentrations for replacement and higher maximum dosing than published protocols. We found our protocol to be effective at resolving hypokalemia, as defined by our protocol, with minimal hyperkalemia that was comparable to prior studies.

Article Information

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