JPPT | Single-Center Retrospective Study

Evaluation of Parenteral Potassium Supplementation in Pediatric Patients

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OBJECTIVE The primary objective was to evaluate the effect of parenteral potassium chloride (KCl) supplementation on potassium (K^+) concentrations in a non-cardiac pediatric population. Secondary outcomes were to identify variables that may influence response to KCl supplementation (i.e., change in K^+ concentration after KCl administration) and assess the incidence of hyperkalemia.

METHODS This single-center, retrospective study evaluated infants and children who received parenteral KCl supplementation of 0.5 or 1 mEq/kg between January 2017 and December 2019.

RESULTS The study included 102 patients with a median age of 1 year (IQR, 0.4–3.9) and weight of 9.1 kg (IQR, 4.9–14.2) who received 288 parenteral KCl administrations. One hundred seventy-three administrations were in the 1 mEq/kg group, and 115 administrations were in the 0.5 mEq/kg group. The median changes in K^+ were 0.8 and 0.5 mEq/L in the 1 mEq/kg and 0.5 mEq/kg groups, respectively. Patients who had a repeat K^+ concentration within 4 hours of the end of a 1 to 2–hour infusion had a higher median change in K^+ compared with those who had a concentration drawn after this time frame (0.8 vs 0.6 mEq/L; $p < 0.01$).

CONCLUSIONS There is a paucity of data on the correlation between parenteral KCl supplementation and change in K^+ concentrations in pediatric patients. Our study demonstrated an association between KCl supplementation doses of 1 and 0.5 mEq/kg and changes in K^+ of 0.8 and 0.5 mEq/L, respectively, in non-cardiac pediatric patients, with low observed incidence of hyperkalemia.

ABBREVIATIONS BMP, basic metabolic panel; CICU, cardiac intensive care unit; ICU, intensive care unit; IV, intravenous; K^+, potassium; KCl, potassium chloride

KEYWORDS hypokalemia; pediatrics; pharmacokinetics; potassium

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Introduction

Hypokalemia is a common electrolyte imbalance in pediatric patients. In pediatric intensive care units, common causes of hypokalemia include renal disease, shock, and gastrointestinal losses, while in pediatric cardiac units, hypokalemia is most often associated with diuretic usage.[1–3] In adult patients, studies[4,5] have shown that for every 10 mEq of intravenous (IV) potassium chloride (KCl) administered, there is a respective increase of approximately 0.1 mEq/L in serum concentration. Furthermore, several studies[5–7] have suggested that response to KCl supplementation can be influenced by degree of hypokalemia. In pediatrics, there is a paucity of data regarding patients' response to parenteral KCl, with publications limited to the pediatric cardiac intensive care unit (CICU) population.[8–10] Potassium homeostasis may be different in this population because of altered clearance of medications and differences in physiology.[11,12] Comparable data have not been published in the broader pediatric population. Given the potential population differences, the objective of this study was to describe the response to IV KCl administration in pediatric patients admitted to non-cardiac units.

Materials and Methods

This was a single-center, retrospective cohort study of patients admitted to Hassenfeld Children's Hospital at NYU Langone Health (New York, NY) from January 2017 through December 2019. Patients were included if they were at least 7 days old and less than 21 years of age, had received IV KCl doses of 0.5 or 1 mEq/kg for the treatment of hypokalemia, and had a baseline and follow-up potassium (K^+) concentration surrounding IV KCl administration. Hypokalemia was defined as a K^+ of less than 3.5 mEq/L. An institutional protocol did not exist at the time of this study; therefore, dosing and monitoring was at the discretion of the prescriber. Likewise, while infusion times were not standardized, most KCl doses were administered over the course of 2 hours. Patients could be included more than once in the study if more than one parenteral KCl supplementation

Table 1. Baseline Patient Demographics, N = 102 Patients

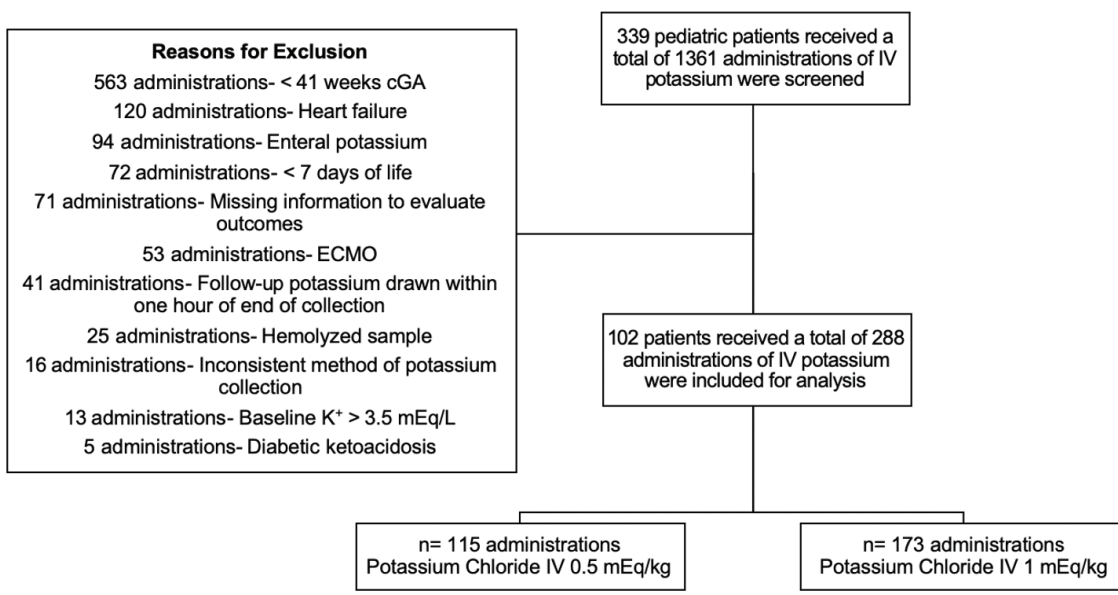
Variable	Value
Male sex, n (%)	51 (50)
Age, median (IQR), yr	1.0 (0.4–3.9)
Weight, median (IQR), kg	9.1 (4.9–14.2)
Comorbidities*, n (%)	55 (53.9)
Acute kidney injury	24 (23.5)
Acyanotic heart defects	24 (23.5)
Hypertension	19 (18.6)
Pulmonary hypertension	16 (15.7)
Chronic kidney disease	2 (2)
Admission unit, n (%)	
PICU	77 (75.5)
NICU	15 (14.7)
Acute care	10 (9.8)
Total IV KCl doses administered	288
Administrations by age, n (%)	
Neonates ≤ 28 days	19 (6.6)
Infants 29 days to ≤1 yr	158 (54.9)
Children >1 yr	111 (38.5)

IV, intravenous; KCl, potassium chloride; NICU, neonatal intensive care unit; PICU, pediatric intensive care unit

occurred during the hospital admission. If IV KCl administration occurred 4 hours or greater from the last dose, any subsequent IV KCl supplementation was counted as a second administration for that patient. Patients were excluded if they were less than 41 weeks corrected gestational age, owing to the concern for delayed renal maturation in premature infants. Patients were also excluded if they had been admitted to the CICU, were on extracorporeal membrane oxygenation, had a history of heart failure, had diabetic ketoacidosis or a blood glucose of greater than 500 mg/dL at the time of repletion, had received concomitant enteral KCl supplementation, had follow-up K^+ concentrations drawn within 1 hour of the end of the infusion or more than 24 hours after the beginning of the infusion, or had hemolyzed blood samples. Patients were also excluded if their K^+ concentrations were collected via different methods before and after KCl administration. As an example, if a patient had a baseline serum K^+ determination from a basic metabolic panel (BMP), they were excluded if the follow-up K^+ concentration was from a whole blood gas sample, and vice versa.

The purpose of this study was to describe IV KCl administration in this pediatric population and the resulting change in K^+ concentrations. The response to IV KCl was expressed as delta K^+ and calculated with the following equation: Follow-up $[K^+]$ − baseline $[K^+]$. Serum K^+ from BMP results was used when available. When BMP results were not available for both baseline and follow-up K^+ concentrations, results from whole blood samples for venous or arterial blood gases were used. The secondary objectives of this study were to identify the factors that might affect a patient's response to IV KCl administration and to assess the incidence of hyperkalemia within

Figure. Study enrollment.



cGA, corrected gestational age; ECMO, extracorporeal membrane oxygenation; IV, intravenous; K^+, potassium.

Table 2. Intravenous Potassium Administration Characteristics, N = 288 Doses Administered

Characteristic	Value
Doses per patient, median (IQR)	2 (1–3)
Dose of potassium administered, n (%)	
0.5 mEq/kg	115 (40)
1 mEq/kg	173 (60)
Method of potassium collection, n (%)	
Basic metabolic panel	194 (67.4)
Blood gas	94 (32.6)
Baseline potassium concentration, median (IQR), mEq/L	2.7 (2.5–2.9)
Severity of hypokalemia, n (%)	
Mild (K^+ 3.0–3.5 mEq/L)	62 (21.5)
Moderate (K^+ 2.6–2.9 mEq/L)	139 (48.3)
Severe (K^+ <2.6 mEq/L)	87 (30.2)
Administrations with baseline pH also collected, n (%)	226 (78.5)
pH, median (IQR)	7.40 (7.36–7.45)
Urine output, median (IQR), mL/kg/hr	3.2 (1.7–5.0)
Serum creatinine, median (IQR), mg/dL	0.41 (0.32–0.51)
Serum magnesium, median (IQR), mg/dL	1.8 (1.5–2)

K^+, potassium

24 hours after KCl administration. Hyperkalemia was defined as a K^+ concentration of greater than 5.5 mEq/L. Degree of hypokalemia was defined as mild (K^+ = 3.0–3.5 mEq/L), moderate (K^+ = 2.6–2.9 mEq/L), or severe (K^+ < 2.6 mEq/L). Electronic health records were retrospectively reviewed for baseline demographics, medical history, serum creatinine, baseline pH, baseline serum magnesium, and medications known to effect K^+ concentrations. Potassium chloride dose, rate of administration, and time between the end of infusion and repeat K^+ concentrations were also collected.

Descriptive statistics were used to analyze the data. Independent-samples *t*-tests were run to determine if there were differences in the change of K^+ based on a patient's baseline K^+ concentration (degree of hypokalemia) and KCl dose (0.5 vs 1 mEq/kg) received. Binary logistic regression was used to estimate the association between achieving a K^+ concentration of 3.5 to 5.0 mEq/L and patient-specific risk factors and KCl dosing strategy. Covariates for the multivariate model were selected based on significance on univariate analysis at a p value of 0.05 or less. All data were secure, and statistics were obtained by the investigators using SPSS Statistics Software (IBM Corp, Armonk, NY; version 25.0).

Results

There were 339 patients and 1361 administrations of IV KCl screened (Figure). A total of 102 patients who received 288 administrations were included (Table 1). The median patient age was 1 year (IQR, 0.4–3.9), and median weight was 9.1 kg (IQR, 4.9–14.2). Infants 29 days to 1 year of life represented the largest group that received IV KCl (158 administrations, 54.9%). Most IV KCl administrations were to patients admitted to an intensive care unit (ICU; n = 92 patients, 271 administrations) compared with patients admitted to an acute care pediatric unit (n = 10 patients, 17 administrations). In total, patients received a median of 2 doses (IQR, 1–3) of IV KCl. The median baseline K^+ concentration was 2.7 mEq/L (IQR, 2.5–2.9), and most KCl administrations were given for moderate hypokalemia (138 administrations, 47.9%). The overall median delta change in K^+ concentration was 0.7 mEq/L (IQR, 0.3–1.1). This did not differ significantly between doses administered in the ICU vs those administered on the acute care floor: 0.7 mEq/L (IQR, 0.2–1.3) vs 0.7 mEq/L (IQR, 0.3–1.1) (p = 0.93). Further details regarding K^+ administration characteristics are summarized in Table 2.

The most common dose of IV KCl received in this study was 1 mEq/kg (173 administrations, 60%), followed by 0.5 mEq/kg (115 administrations, 40%), and most IV KCl administrations were infused over the course of 2 hours (258 administrations, 90%). The observed changes in K^+ concentration after receiving IV KCl were 0.8 mEq/L (IQR, 0.5–1.2) and 0.5 mEq/L (IQR, 0.2–0.8) for doses of 1 and 0.5 mEq/kg, respectively. Baseline hypokalemia was stratified into 3 distinct categories: mild, moderate, and severe hypokalemia. Most IV KCl administrations given for mild hypokalemia were 0.5 mEq/kg (57.1% vs 42.9%). In the setting of moderate and

Table 3. Assessment of Potassium Supplementation

Characteristic	0.5 mEq/kg N = 115 Doses Administered	1 mEq/kg N = 173 Doses Administered	p value
Patient degree of hypokalemia, n (%)			
Mild hypokalemia (K^+ 3.0–3.5 mEq/L)	35 (30.4)	27 (15.6)	0.003
Moderate hypokalemia (K^+ 2.6–2.9 mEq/L)	56 (48.7)	83 (48)	0.91
Severe hypokalemia (K^+ <2.6 mEq/L)	24 (20.9)	63 (36.4)	0.005
Change in potassium concentration (overall), median (IQR)	0.5 (0.2–0.8)	0.8 (0.5–1.2)	0.001
Change in potassium concentration by age, median (IQR)			
Neonates ≤28 days	0.6 (0.4–1.0)	0.9 (0.6–1.2)	0.272
Infants 29 days to ≤1 yr	0.4 (0.1–0.7)	0.9 (0.6–1.3)	0.001
Children >1 yr	0.5 (0.2–0.9)	0.8 (0.3–1.1)	0.112
Change in potassium concentration by method of collection, median (IQR)	0.4 (0.2–0.8)	0.8 (0.4–1.2)	0.001
Basic metabolic panel	0.6 (0.4–0.9)	0.9 (0.6–1.3)	0.001
Blood gas			
Change in potassium concentration by degree of hypokalemia, mean ± SD	0.4 ± 0.53	0.9 ± 0.66	0.018
Mild hypokalemia (K^+ 3.0–3.5 mEq/L)	0.5 ± 0.5	0.9 ± 0.52	0.001
Moderate hypokalemia (K^+ 2.6–2.9 mEq/L)	0.6 ± 0.38	0.9 ± 0.57	0.004
Severe hypokalemia (K^+ <2.6 mEq/L)			
Time from end of infusion to repeat serum potassium concentration, median (IQR), hr	4.7 (2.8–8.8)	4.1 (2.3–8.5)	0.235
Concomitant potassium lowering therapies, n (%)	73 (63.5)	152 (87.9)	0.236
Loop diuretic	52 (45.2)	93 (53.8)	0.156
Albuterol	41 (35.7)	65 (37.6)	0.741
Thiazide diuretic	22 (19.1)	47 (27.2)	0.118
Other*	4 (3.5)	6 (3.4)	0.295
Concomitant potassium increasing therapies, n (%)	100 (87.0)	146 (84.4)	0.546
IV fluids/TPN containing potassium	99 (86.1)	142 (82.1)	0.368
Aldosterone antagonists	3 (2.6)	9 (5.2)	0.374
ACE inhibitors/ARBs	1 (0.9)	0 (0)	N/A
Amount of potassium received from other sources within 24 hr, median (IQR), mEq/kg, N = 241	1.1 (0.5–1.7)	1.2 (0.7–2.2)	0.018

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; IV, intravenous; TPN, total parenteral nutrition

* Other is defined as amphotericin B and insulin regular.

severe hypokalemia, the 1 mEq/kg dose was prescribed more frequently, as compared with the 0.5 mEq/kg dose (60.1% vs 39.9% and 72.4% vs 27.6%, respectively). The IV KCl doses of 1 mEq/kg resulted in a mean change in K^+ concentration of 0.9 ± 0.66, 0.9 ± 0.52, and 0.9 ± 0.57 mEq/L for mild, moderate, and severe hypokalemia, respectively. Doses of 0.5 mEq/kg IV KCl resulted in a mean change in K^+ concentration of 0.4, 0.5, and 0.6 mEq/L for mild, moderate, and severe hypokalemia, respectively. For each category of hypokalemia, doses of 1 mEq/kg resulted in a significantly higher change in potassium than did doses of 0.5 mEq/kg, as shown in Table 3.

The median time to a repeat K^+ concentration was 4.5 hours (IQR, 2.4–8.6) from the end of IV KCl infusion. This did not differ significantly between the 0.5 mEq/kg and 1 mEq/kg groups (p = 0.235) or between patients admitted to the ICU vs those admitted to the acute care floor (p = 0.691). Of note, when a repeat K^+ concentration occurred within 4 hours of the end of the KCl infusion, a significantly higher median change in K^+ was observed, as compared with concentrations obtained greater than 4 hours after the end of infusion: 0.8 mEq/L (IQR, 0.5–1.1) vs 0.6 mEq/L (IQR, 0.2–0.9) (p < 0.001). Approximately 45.8% of the IV KCl administrations in this study had a follow-up K^+ concentration drawn within 4 hours. Most patients were either on concomitant IV fluids containing K^+ (241 administrations, 83.7%) or loop diuretics (50.3%). Of the 241 administrations that received additional K-containing fluids (e.g., maintenance

fluids, total parenteral nutrition), the median amount of additional K^+ received outside of the 0.5 or 1 mEq/kg supplementation was 1.1 mEq/kg (IQR, 0.5–2.0) in 24 hours. Additional details of K^+ supplementation are outlined in Table 3.

Despite the range in follow-up times to next K^+ concentration, most administrations resulted in an overall positive change in K^+. Nonetheless, 153 administrations (67%) were associated with refractory hypokalemia requiring a second dose of KCl. This occurred with 72 administrations of the 0.5 mEq/kg dose and 81 administrations of 1 mEq/kg dose. Of these administrations, 107 (70%) received concomitant K^+-lowering therapies, which was similar to the overall incidence rate of 70.8%. The median follow-up K^+ concentration after additional supplementation was 3.1 mEq/L regardless of dosing strategy.

A goal potassium of 3.5 to 5 mEq/L was achieved with 129 IV KCl (129/288, 45%) doses administered. Upon multivariate analysis, IV KCl doses of 1 mEq/kg (OR, 2.3; 95% CI, 1.36–3.95; p = 0.002), a baseline K^+ of 2.6 mEq/L or larger (OR, 5.2; 95% CI, 2.82–9.66; p = 0.005), and patients with a follow-up K + concentration checked within 1 to 4 hours of the end of the infusion (OR, 2.4; 95% CI, 1.44–4.00; p = 0.001) were predictors for achieving a K^+ concentration of 3.5 to 5 mEq/L.

Hyperkalemia within 24 hours of parenteral KCl administration occurred after one KCl administration (0.3%). The K^+ concentration for this administration was 5.6 mEq/L and was obtained 21 hours after the end of KCl administration. This event occurred after administration of a 1 mEq/kg dose in a patient who had a baseline K + concentration of 3.4 mEq/L and had also received 0.2 mEq/kg/day of KCl from basal K^+–containing fluids. The patient did not require any K^+-lowering therapy and did not experience any arrhythmias because of hyperkalemia.

Discussion

Hypokalemia is a common occurrence in the pediatric population, with a reported incidence of up to 40% in hospitalized patients.[13] Published literature[8–10] regarding response to KCl supplementation is limited to the pediatric CICU population. There are 2 retrospective reviews[8,9] that directly assessed the effect of K^+ supplementation on serum K^+ concentrations in the pediatric CICU population. Knudson et al[8] found that an average K^+ dose of 0.97 ± 0.006 mEq/kg resulted in an average increase in K^+ concentration of 0.8 ± 0.02 mEq/L. Moffett et al[9] found that IV K^+ doses of 1 mEq/kg resulted in a 0.89 mEq/L increase in serum K^+. A more recent study[10] that examined a protocolized K^+ dosing strategy in a CICU in a tertiary children's hospital did not directly assess the relationship between K^+ dosing and serum K^+ response. These results may not apply to patients outside of the pediatric CICU setting. Pediatric CICU patients may have altered potassium clearance because of altered physiology or postsurgical interventions and may have increased fluid shifts and diuretic usage compared with other pediatric populations.[11,12] Furthermore, the cardiac population is at higher risk for morbidity from arrhythmias and often has customized K^+ goals, which may affect supplementation strategies.

We observed median changes in the K^+ concentration of 0.8 and 0.5 mEq/L with IV KCl supplemental doses of 1 and 0.5 mEq/kg, respectively. Although similar rates of K^+ change have been identified in published pediatric cardiac intensive care supplemental studies,[8,9] we believe that our study is the first to assess supplemental KCl response in a broader pediatric population and the first to evaluate 2 dosing approaches. Our findings suggest that 1 and 0.5 mEq/kg supplemental doses may be safe in the pediatric inpatient population, although a larger sample size would be needed to confirm our finding. It is important to note that most patients included in this study were between 0.4 and 3.9 years of age, weighed between 4.9 and 14.2 kg, and were admitted to an ICU, suggesting that these findings may be more applicable to critically ill young children. This is consistent with typical practice, wherein this population is more likely to receive weight-based KCl doses, while older children and adolescents are more likely to receive non–weight-based doses of potassium repletion.

This study identified 3 predictors for achieving goal potassium concentration (3.5–5 mEq/L): a dose of 1 mEq/kg, mild to moderate hypokalemia (baseline $K^+ \geq 2.6$ mEq/L), and obtaining a follow-up potassium concentration within 1 to 4 hours from the end of the IV KCl infusion. In comparison to a dose of 0.5 mEq/kg, the 1 mEq/kg dose may be more likely to achieve a goal potassium concentration with a low possibility of hyperkalemia (0.6% vs 0%). In addition, the 1 mEq/kg dose was more commonly given for moderate to severe hypokalemia (65%). Together, these findings suggest that IV KCl doses of 1 mEq/kg should be considered for the treatment of moderate to severe hypokalemia. Close monitoring should be considered for patients with severe hypokalemia ($K^+ < 2.6$ mEq/L) because of the increased likelihood of persistent hypokalemia requiring additional supplementation.

Data are needed to understand K^+ distribution characteristics and the true post-distribution peak after supplemental dosing. Our study analyzed the timing of follow-up K^+ and change in K^+ concentrations. We observed that IV KCl doses with follow-up K^+ concentrations obtained within 1 to 4 hours from the end of the infusion administration were more likely to achieve a goal K^+ concentration of 3.5 to 5 mEq/L. Follow-up concentrations were obtained within 1 to 4 hours for 45.8% of the doses administered in this study. This observance may reflect the ability to detect a true peak when concentrations are checked soon after the distribution phase is complete. Follow-up K concentrations drawn within the first hour after the end of an infusion were excluded in this study because of the risk of inaccurately representing

whole body potassium stores via concentrations drawn during the distribution phase. In previous pediatric KCl supplementation studies, the median time from the end of infusion to repeat K^+ concentration was often not reported. Knudson et al[8] included patients with a follow-up K^+ concentration obtained 2 to 4 hours after administration, while Moffett et al[9] included patients with a follow-up serum K^+ concentration obtained within 6 hours of administration. However, neither study reported the median time to follow-up concentrations. Ideal timing to repeat K^+ concentration may be within 1 to 4 hours after the end of an infusion to capture the peak post-distribution effect of supplementation.

Knudson et al[8] reported one incidence of hyperkalemia (7.3 mEq/L) in their study; however, no adverse events were reported, and the serum K^+ returned to normal range after administration of furosemide. Moffett et al[9] reported no incidence of hyperkalemia in their study. Amirnovin et al[10] reported a 28% incidence rate for hyperkalemia among all K^+ samples drawn during a patient's stay. However, these investigators defined hyperkalemia as a K^+ concentration greater than 4.8 mEq/L, and they acknowledged that 24% of hyperkalemic samples were hemolyzed. The incidence of hyperkalemia in our study was low (0.3%), despite the lack of a protocolized dosing strategy. Overall, our rate of hyperkalemia was comparable to those documented in studies by Knudson et al[8] and Moffett et al.[9]

There are several limitations to this study. First, an institutional protocol did not exist at the time of our study. For this reason, KCl dosing was not consistently driven by degree of hypokalemia, and the timing of routine K^+ concentration monitoring was variable. Follow-up K^+ concentrations within 24 hours of KCl administration were included, which may not have captured the peak concentration and true effect of a K^+ dose. Our relatively small sample size limited our analyses of several pertinent factors that may have affected K^+ handling and response to supplementation. Moreover, additional factors may influence the ability to achieve goal potassium concentrations that were not reflected in our population. We were also unable to exclude the net effect of basal K^+ from maintenance IV fluids or total parenteral nutrition, since this is a common requirement in the pediatric population.

Conclusion

Our study demonstrated an association between KCl supplementation doses of 1 and 0.5 mEq/kg and median changes in K^+ concentrations of 0.8 and 0.5 mEq/L, respectively. Doses of 1 mEq/kg in patients with baseline K^+ concentrations of ≥2.6 mEq/L and follow-up K^+ concentrations obtained within 1 to 4 hours of the end of the infusion were more likely to affect the ability to achieve a goal potassium of 3.5 to 5 mEq/L, with an overall low incidence of hyperkalemia. These findings suggest that 1 mEq/kg doses infused over 1 to 2 hours are likely safe and effective for the treatment of mild to moderate hypokalemia in young children admitted to the ICU. To assess the true peak K^+ concentration after supplementation, follow-up concentrations should be obtained within 1 to 4 hours of an administration, particularly for patients with severe hypokalemia who are more likely to need additional supplementation. A trial with protocolized dosing, peak determination, and controls for basal K^+ sources or other K^+-affecting therapies would help determine an optimal K^+ dosing strategy in pediatric patients with identified hypokalemia.

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