Safety of a Nurse-Driven **Standardized Potassium Replacement Protocol** in Critically Ill Patients With Renal Insufficiency

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Background In critically ill patients, maintaining appropriate serum potassium concentrations requires careful supplementation to correct hypokalemia but avoid hyperkalemia. At the study institution, an institution-based, nurse-driven standardized electrolyte replacement protocol is used in critically ill patients with a serum creatinine concentration of 2 mg/dL or less. If the serum creatinine concentration is greater than 2 mg/dL, electrolyte replacement requires a physician order.

Objective To determine if standardized potassium supplementation is safe in critically ill patients with renal insufficiency not requiring renal replacement therapy.

Methods This study was an institutional review board–approved, single-center, retrospective evaluation of critically ill patients receiving intravenous potassium replacement per protocol. Patients were grouped according to serum creatinine concentration (≤ 2 mg/dL or > 2 mg/dL) at the time of replacement. The primary outcome was the incidence of hyperkalemia (potassium concentration ≥ 5 mEq/L) following potassium replacement. Secondary outcomes were the incidence of hyperkalemia, change in serum potassium concentration, and need for hyperkalemia treatment. Outcomes were analyzed using χ^2 and *t* tests.

Results Of 814 patients screened, 145 were included (99 with serum creatinine ≤ 2 mg/dL and 46 with serum creatinine > 2 mg/dL). The incidence of hyperkalemia was not different between groups ($P = .57$). Five patients experienced hyperkalemia; none received hyperkalemia treatment. Change in serum potassium was similar for patients in the 2 groups ($P = .33$).

Conclusions A standardized, nurse-driven electrolyte replacement protocol can be used safely in critically ill patients with renal insufficiency not requiring renal replacement therapy. (*Critical Care Nurse*. 2021;41[2]:e10-e16)

CE 1.0 hour, CERP A, Pharma 0.5

This article has been designated for CE contact hour(s). The evaluation tests your knowledge of the following objectives:
1. Identify the importance of maintaining a normal concentration of serum potassium, including the risk associated with hypokalemia and hyperkalemia.
2. Describe the incidence of hyperkalemia with standardized potassium replacement in patients with serum creatinine ≤ 2 mg/dL and serum creatinine > 2 mg/dL.
3. Analyze the limitations associated with applying nurse-driven standardized potassium replacement to critically ill patients.

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Potassium, an intracellular cation, is responsible for helping create energy for cellular function throughout the cardiovascular, skeletal, and nervous systems.[1-3] The reference range for serum potassium is 3.5 to 4.5 mEq/L. In an otherwise healthy patient, the serum concentration is representative of potassium concentration across the intracellular and extracellular compartments, with 98% being intracellular.[3,4] Intracellular potassium controls cellular metabolism and regulates the resting potential across cell membranes, especially within the myocardium.[3] In patients who are not critically ill, potassium homeostasis is maintained through the balance of oral intake with urinary excretion (80%) and gastrointestinal excretion (15%).[4] Although electrolyte disturbances of all variations can be seen in critically ill patients, maintaining a normal potassium concentration is of great importance because of the risks associated with hypokalemia and hyperkalemia.[3]

Hypokalemia can be divided into categories based on severity and likelihood of adverse events: mild (3-3.4 mEq/L), moderate (2.5-2.9 mEq/L), and severe (< 2.5 mEq/L).[5] Moderate to severe hypokalemia results in membrane hyperpolarization that can induce life-threatening conditions such as dysrhythmias and muscle weakness leading to respiratory or cardiac failure.[3,5-7] However, the incidence of clinically significant hypokalemia in hospitalized patients is low, reportedly ranging from 4% to 5%, and severe hypokalemia is uncommon.[5] Hyperkalemia can also pose a great risk to patients. Although potassium concentrations greater than 5 mEq/L are termed *hyperkalemia,* clinically significant or symptomatic hyperkalemia may not occur until higher concentrations are reached.[7,8] Maintaining adequate potassium homeostasis may be challenging in critically ill patients because of the severity of illness and compromised cellular function.[1,7]

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Potassium dysregulation can occur through many mechanisms that affect the function of the sodium-potassium adenosine triphosphatase pumps that maintain the potassium gradient. Increased catecholamine activity, acid-base imbalances, and metabolic disorders can all alter potassium transport and therefore distribution.[2] A function of the kidney is to aid in regulation of serum potassium.[6] In acute kidney injury or chronic kidney disease, both of which are common in the critically ill population, this regulation of potassium may be compromised, leading to further dyskalemia.[6] Renal dysfunction is one of the main contributing factors associated with serum potassium dysregulation. Other contributory factors include the use of potassium-containing products (fluids and blood); disease states that alter absorption, distribution, and/or clearance (heart failure, gastrointestinal disorders, and diabetes); and medications (renin-angiotensin-aldosterone system inhibitors and diuretics).[6] Avoiding insult related to hypokalemia is important given the availability and proven efficacy of supplementation but can be difficult when renal function is compromised.[6]

Electrolyte replacement protocols have been established to allow consistent and automatic nurse-driven supplementation of electrolytes as soon as laboratory results become available. Various institutions exclude patients with renal insufficiency or adapt replacement protocols on the basis of serum creatinine (SCr) concentrations or creatinine clearance cutoffs because of the perceived risk of hyperkalemia with standardized replacement. For instance, the electrolyte replacement protocol at the study institution excludes patients with a SCr concentration greater than 2 mg/dL, requiring nurses to obtain an order for electrolyte replacement from the clinician. Because electrolyte replacement protocols provide 1-time supplementation of abnormally low serum electrolytes, and therefore should not be affected by renal elimination, the exclusion of this patient population has been called into question. The purpose of this study was to determine if a standardized nurse-driven potassium replacement protocol was safe in critically ill patients with a SCr concentration greater than 2 mg/dL, as compared with patients with a SCr concentration of 2 mg/dL or less.

Methods

This study was an institutional review board–approved, single-center, retrospective cohort evaluation of critically ill patients receiving intravenous potassium replacement. All data were collected from the electronic health database.

Table 1 Evaluated electrolyte replacement protocol for potassium chloride

Serum potassium, mEq/dL	Potassium dose	
	Central catheter	Peripheral catheter
3.6 to 3.9	20 mEq/100 mL over 1 h	20 mEq/250 mL over 1 h
3.1 to 3.5	40 mEq/100 mL over 2 h	40 mEq/500 mL over 2 h
2.6 to 3	60 mEq/250 mL over 3 h	Contact physician
≤ 2.5	80 mEq/250 mL over 4 h	Contact physician

Table 2 Evaluated electrolyte replacement protocol for potassium phosphate[a]

Serum phosphate, mg/dL	Phosphate dose		Potassium received
	Central catheter	Peripheral catheter	
1.6 to 2.5	20 mmol/100 mL over 3 h	20 mmol/250 mL over 5 h	30 mEq
1 to 1.5	40 mmol/250 mL over 5 h	40 mmol/500 mL over 5 h	60 mEq
<1	60 mmol/500 mL over 6 h		90 mEq

[a] Potassium phosphate is used for phosphate replacement when serum potassium level is less than 4 mEq/dL.

Intensive care unit patients admitted between February 1, 2018, and July 31, 2018, were screened and assigned to 1 of 2 groups (SCr ≤ 2 mg/dL or SCr > 2 mg/dL) at the time of potassium replacement. Patients included in the study were adults who received intravenous potassium replacement per the Pharmacy and Therapeutics Committee–approved Critical Care Medicine Electrolyte Replacement Therapy Protocol and were cared for by the critical care medicine service (Tables 1 and 2). All intensive care unit patients at the study site receive continuous cardiac monitoring. Patients were excluded if they received hyperkalemia treatment within 24 hours before potassium replacement. Additionally, patients were excluded if they had clinician- or disease-led electrolyte replacement (eg, electrolyte replacement per nephrology consult for electrolyte management, diabetic ketoacidosis, continuous renal replacement therapy, or hemodialysis).

The Critical Care Medicine Electrolyte Replacement Therapy Protocol allows for nurse-driven replacement of potassium, magnesium, and phosphate on the basis of laboratory results for patients with a SCr concentration of 2 mg/dL or less. Potassium replacement is chosen according to route of administration, including appropriate concentrations for central and peripheral access. The protocol prompts the nurse to obtain samples for repeat laboratory tests at predetermined intervals to assess efficacy and potential need for further electrolyte replacement. Because of concerns for accumulation of electrolytes, especially potassium, in patients with renal insufficiency, the nurse must contact the clinician for electrolyte replacement orders for all patients with a SCr concentration greater than 2 mg/dL. Often clinicians choose to use the protocol as written for these patients instead of writing individual orders daily for electrolyte replacement during the period of kidney injury. The continued use of the protocol in these patients allowed us to create a comparator group of patients with a SCr concentration greater than 2 mg/dL.

The primary outcome was the incidence of hyperkalemia (serum potassium ≥ 5 mEq/L) following potassium replacement in patients with a SCr concentration of 2 mg/dL or less and in those with a SCr concentration greater than 2 mg/dL. Secondary outcomes included an evaluation of patients experiencing hyperkalemia, change in serum potassium concentration, and need for hyperkalemia treatment following potassium replacement.

Nominal data were assessed for statistical differences with χ^2 analyses; continuous data were analyzed with *t* tests. *P* values less than .05 were considered significant.

Results

Of 814 patients screened, 145 were included in the study in a 2:1 ratio (99 patients with SCr ≤ 2 mg/dL and 46 patients with SCr > 2 mg/dL; see Figure). The most common reasons for exclusion were lack of a critical care medicine consult and protocol noncompliance.

The median age in both groups was 65 years. The proportion of men was higher in the group with SCr concentrations greater than 2 mg/dL (Table 3). A quarter of the patients with a SCr concentration of 2 mg/dL or less had kidney dysfunction. Of the patients with a SCr concentration greater than 2 mg/dL, acute kidney injury was the most prevalent form of kidney dysfunction. Baseline serum electrolytes were similar among the 2 groups, with a slightly higher serum phosphate concentration in those with increased SCr.

The primary outcome, incidence of hyperkalemia, was not different between the 2 groups (Table 4). Change in serum potassium was similar for patients with a SCr concentration of 2 mg/dL or less and those with a SCr concentration greater than 2 mg/dL (0.3 mEq/L and 0.4 mEq/L, respectively). Of the total population, 5 patients experienced hyperkalemia; none received hyperkalemia treatment (Table 5). Of the patients who experienced hyperkalemia, 3 had acute-on-chronic renal insufficiency. These patients received potassium replacement doses of 20 mEq (n = 2) and 90 mEq (n = 1). The 2 patients without renal impairment received potassium replacement doses of 40 mEq; 1 of these patients had the highest serum potassium concentration following replacement (6.5 mEq/L).

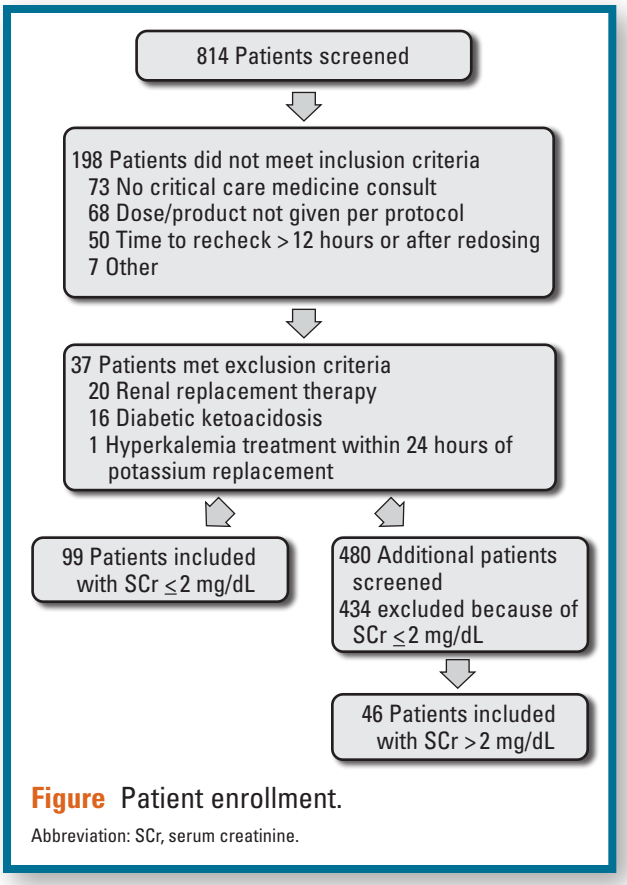

Figure Patient enrollment.

Abbreviation: SCr, serum creatinine.

Discussion

According to the study results, a standardized potassium replacement protocol can be used safely in critically ill patients with renal insufficiency not requiring renal replacement therapy. Hyperkalemia was observed in only 5 patients (3.4% of the total study population), and 4 of these patients had a SCr concentration of 2 mg/dL or less. No interventions were required for any cases of hyperkalemia.

The results of our study are in contrast with recommendations to decrease potassium replacement by 50% or greater in patients with impaired renal function.[4] However, a paucity of data supports such recommendations. To our knowledge, this is the first study to evaluate the safety of a nurse-driven potassium replacement protocol in critically ill patients with renal insufficiency. Hamill et al[9] similarly demonstrated that regardless of renal function or potassium dose, patients with renal insufficiency tolerated a single potassium infusion without difficulty. However, the total number of patients with renal dysfunction was low (n = 15).[9]

Table 3 Baseline characteristics of patients included in the study

Characteristic	Patients with SCr ≤2 mg/dL (n=99)	Patients with SCr >2 mg/dL (n=46)
Age, median (IQR), y	65 (55-74)	65 (56-73)
Male sex, No. (%)	39 (39)	25 (54)
Medical history, No. (%)		
Diabetes	27 (27)	23 (50)
Congestive heart failure	26 (26)	14 (30)
Kidney dysfunction, No. (%)	29 (29)	46 (100)
Acute kidney injury	19 (19)	22 (48)
Chronic kidney disease	4 (4)	4 (9)
Acute-on-chronic kidney disease	6 (6)	20 (43)
Laboratory values at replacement, median (IQR)		
Creatinine, mg/dL	0.8 (0.6-1.2)	2.9 (2.4-3.7)
Magnesium, mg/dL	2.1 (1.9-2.3)	2.0 (1.9-2.3)
Phosphate, mg/dL	2.8 (2.0-3.5)	3.6 (3.2-4.9)
Potassium, mEq/L	3.7 (3.4-3.8)	3.6 (3.3-3.7)

Abbreviations: IQR, interquartile range; SCr, serum creatinine.

Table 4 Primary and secondary outcomes of patients in study

Outcome	Patients with SCr ≤2 mg/dL (n = 99)	Patients with SCr >2 mg/dL (n = 46)	*P*
Incidence of hyperkalemia, No. (%)	4 (4)	1 (2)	.57
Absolute change in serum potassium, mEq/dL, median (IQR)	0.3 (0.1-0.7)	0.4 (0.03-0.8)	.33
Change in serum potassium for every 10 mEq of potassium received, mEq/dL, median (IQR)	0.1 (0.03-0.25)	0.1 (0.03-0.22)	.83
Patients receiving treatment for hyperkalemia, No.	0	0	

Abbreviation: IQR, interquartile range; SCr, serum creatinine.

Table 5 Patients who experienced hyperkalemia

Age, y, and sex of patient	Renal impairment	SCr, mg/dL	Before potassium replacement: serum potassium, mEq/L	Potassium dose, mEq	After potassium replacement: serum potassium, mEq/L	Change in serum potassium, mEq/L
87, male	None	0.8	3.2	40	6.3	3.1
37, female	None	0.9	3.4	40	6.5	3.1
58, female	AoCKD	1.5	3.8	20	5.6	1.8
73, male	AoCKD	1.8	2.9	90	5.1	2.2
66, female	AoCKD	3.5	3.9	20	5.1	1.2

Abbreviation: AoCKD, acute-on-chronic kidney disease; SCr, serum creatinine.

Nurse-driven assessment and replacement of electrolytes in critically ill patients allows for prompt supplementation and appropriate timing of follow-up laboratory tests for verifying efficacy of electrolyte replacement.[10-13] Use of a formalized electrolyte replacement protocol that pairs serum electrolyte concentration with a predetermined drug, dose, and route of administration promotes standardized electrolyte replacement for all critically ill patients.[14] Allowing the bedside nurse autonomy to oversee electrolyte supplementation creates greater shared responsibility for patient care and relieves the clinician of direct oversight.

Protocol-based, 1-time potassium replacement can be safely applied to patients with and without kidney dysfunction, not requring renal replacement therapy.

Our study results support modifying our institution's electrolyte replacement protocol to exclude only patients currently receiving renal replacement therapy and patients with diabetic ketoacidosis. The protocol can be safely applied to patients with and without kidney dysfunction because it directs nurses to recheck serum laboratory tests following a 1-time dose of potassium, mitigating the risk for accumulation and therefore hyperkalemia. The limited exclusion criteria allow the results to be applied to a diverse group of critically ill patients with a variety of disease states. Additionally, because protocol compliance was ensured, the findings accurately reflect the protocol.

Limitations

A few limitations may have affected the findings. The small sample size might not allow for adequate detection of a difference in hyperkalemia incidence. Many patients with a SCr concentration greater than 2 mg/dL did not have documentation of a baseline SCr concentration. These patients may have been diagnosed with acute-on-chronic kidney disease without direct evidence of acute kidney injury other than an elevated SCr concentration. The study design did not include evaluation of confounders such as medications, fluids, and disease

Table 6 Revised electrolyte replacement protocol for potassium chloride

	Potassium dose (NS is the preferred diluent)				
Serum potassium, mEq/L	Enteral		Central catheter	Peripheral catheter	Preferred route
3.1 to 3.5	40 mEq	–	40 mEq/100 mL over 2 h	40 mEq/150 mL over 4 h	Enteral
2.6 to 3.0	–	60 mEq	60 mEq/250 mL over 3 h	60 mEq/250 mL over 6 h	IV
<2.6	–	80 mEq	80 mEq/250 mL over 4 h	80 mEq/500 mL over 8 h	IV
Recheck level	Morning laboratory values	4 hours after administering dose	2 hours after end of infusion		

Abbreviations: IV, intravenous; NS, normal saline.

Table 7 Revised electrolyte replacement protocol for potassium phosphate

	Potassium phosphate dose (NS is the preferred diluent)			
Serum phosphate, mEq/L	Central catheter	Peripheral catheter	Potassium received, mEq	Preferred route
1.6 to 2.5	20 mmol/100 mL over 3 h	20 mmol/250 mL over 3 h	30[a]	Enteral
1.0 to 1.5	40 mmol/250 mL over 3 h	40 mmol/500 mL over 6 h	60	IV
< 1.0	60 mmol/500 mL over 5 h	60 mmol/500 mL over 9 h	90	IV
Recheck level	2 hours after end of infusion (phosphate and potassium)			

Abbreviations: IV, intravenous; NS, normal saline.

[a] If potassium level is 2.5 mEq/L or less, give an additional 40 mEq of IV potassium chloride with 20 mmol of potassium phosphate for a total potassium replacement of 70 mEq. For all other potassium phosphate replacements, do not give additional potassium chloride.

states that may have contributed to electrolyte abnormalities. Exclusion of patients with clinician- or disease-led electrolyte replacement may have limited the patient population evaluated, but only 4.5% of all patients screened fell into this category.

In addition to expanding the institution's electrolyte replacement protocol to include patients with increased SCr, the protocol was revised to align with current recommendations. Revisions included adjustment of the serum potassium concentration at which to initiate potassium replacement (eg, the protocol now starts potassium replacement at a serum potassium concentration of 3.5 mEq/L instead of 3.9 mEq/L), changes in electrolyte concentrations for peripheral administration, and changes in infusion times (Tables 6 and 7).[6,7,15,16] Follow-up assessment of the revised protocol and evaluation of the additional electrolytes (magnesium and phosphate) included in the protocol will be completed. Other plans include nursing staff education pertaining to protocol adherence, including the correct product and dose selection, in addition to the timing of laboratory test rechecks. Implementation of an electrolyte replacement protocol in intensive care unit patients receiving intermittent hemodialysis should be investigated because this population was excluded from the study.

Conclusions

An increase in serum potassium following potassium replacement in this critically ill population did not differ according to renal function at the time of supplementation. According to the study results, the protocol can be safely applied to all critically ill patients not requiring renal replacement therapy. CCN

Financial Disclosures
This research was conducted without funding through a postgraduate year 2 critical care pharmacy residency program at Lakeland Regional Health Medical Center in Lakeland, Florida.

See also

To learn more about caring for patients with renal insufficiency, read "Continuous Renal Replacement Therapy Update: An Emphasis on Safe and High-Quality Care" by Schell-Chaple in *AACN Advanced Critical Care,* 2017;28(1):31-40. Available at **www.aacnacconline.org**.

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