

# Effectiveness and Safety of Potassium Replacement in Critically Ill Patients: A Retrospective Cohort Study

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**BACKGROUND** Rules of thumb for potassium replacement are used in intensive care units despite minimal empirical validation.

**OBJECTIVE** To evaluate the effectiveness and safety of rule-of-thumb potassium replacement in critically ill patients with mild and moderate hypokalemia.

**METHODS** A retrospective, observational study was done of patients with mild (potassium, 3-3.9 mEq/L) and moderate (potassium, 2-2.9 mEq/L) hypokalemia admitted to a medical intensive care unit who received potassium replacement. Expected and actual frequencies of replacement that achieved target potassium concentrations ( $\geq 4$  mEq/L) were compared by using a  $\chi^2$  test. Logistic regression analysis was used to assess whether rule-of-thumb administration affected the probability of target attainment within 24 hours of replacement.

**RESULTS** Serum potassium concentrations were checked within 24 hours after potassium replacement on 354 of 577 days (61.4%) when replacement was provided. Concentrations were within target range in 82 instances (23.2%). Of 62 episodes of replacement expected to achieve the target according to the rule-of-thumb estimation, 22 did (35%). Rule-of-thumb administration was associated with greater likelihood of target attainment (odds ratio, 2.12; 95% CI, 1.18-3.85;  $P = .01$ ). This difference in likelihood remained significant after adjustment for covariates (odds ratio, 2.18; 95% CI, 1.04-4.56;  $P = .04$ ).

**CONCLUSION** In critically ill patients given potassium replacement without regard to a formal protocol, the target serum potassium concentration was achieved more often than expected according to the rule-of-thumb estimation but less than one-third of the time. (*Critical Care Nurse*. 2019;39[1]:e13-e18)

**E**lectrolyte disturbances may develop in patients during normal care. When intravascular depletion of an electrolyte or electrolytes occurs, replacement should be provided safely and efficaciously. Unfortunately, replacement may not meet these standards for many reasons, including unnecessary measurements of serum electrolyte concentrations, incomplete or overzealous replacement, and excessive administration of carrier fluids.<sup>1</sup>

Potassium has a role in many physiological functions, including cellular metabolism, protein and glycogen synthesis, and regulation of electrical action potential across cell membranes.<sup>1</sup> Hypokalemia results in membrane hyperpolarization and impaired muscular contraction. Signs and symptoms of hypokalemia can be mild, including nausea, vomiting, and weakness. More severe signs and symptoms include paralysis, respiratory compromise, electrocardiographic changes, cardiac arrhythmias, and sudden death.<sup>2</sup>

Rules of thumb exist for replacing electrolytes in critically and noncritically ill patients; however, these rules are empirically derived from marginal evidence and are not individualized to each patient. For example, the rule that every 10 mEq of potassium increases the serum potassium concentration by 0.1 mEq/L if the concentration already is greater than 3 mEq/L is a commonly held

but minimally supported belief.<sup>2,3</sup>

### Hypokalemia results in membrane hyperpolarization and impaired muscular contraction.

Our objective was to evaluate the effectiveness and safety of rule-of-thumb potassium replacement in critically ill patients with mild and moderate hypokalemia.

## Methods

The study was approved by the institutional review board at the University of Arkansas for Medical Sciences, Little Rock, Arkansas.

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## Study Design and Setting

We did a retrospective, observational study at a single tertiary care hospital. The institution has 332 beds for adults; 28 of these are in the medical intensive care unit (MICU). Data were collected from electronic health records. During the study period, the hospital had no formal protocol for electrolyte replacement. Standard practice in the MICU included monitoring serum electrolyte concentrations in samples obtained during morning laboratory collection (approximately 4 AM) and ordering potassium replacement if a serum concentration was less than 4 mEq/L.

## Patients

Patients were eligible for the study if they were at least 18 years old, had had at least 1 episode of hypokalemia for which oral and/or intravenous potassium was ordered for replacement, and were cared for in the MICU during the period May 2014 through April 2016. Each day on which a patient received potassium replacement was treated as an individual instance of replacement; thus, an individual patient could have more than 1 instance of potassium replacement included in the analysis. For example, a patient who received potassium replacement on 4 different hospital days was eligible to have each day's replacement included in the analysis. Patient days on which replacement could have occurred were excluded if the patient received renal replacement therapy; infusion of bicarbonate, a loop diuretic, or insulin; parenteral nutrition; or administration of amphotericin B or digoxin on that day. Data on patients admitted to the MICU during the study period were included in the sample until the desired sample size was reached.

## Data Collection and Study Outcomes

The primary effectiveness outcome was the actual percentage of target serum potassium concentrations ( $\geq 4$  mEq/L) achieved at 24 ( $\pm 6$ ) hours after completion of replacement compared with the expected percentage of target serum potassium concentrations achieved on the basis of a rule-of-thumb estimation. The rule of thumb for critical care patients with mild hypokalemia (serum potassium level 3-3.9 mEq/L) was that every 10 mEq of a potassium salt (ie, potassium chloride) would increase the serum potassium concentration by 0.1 mEq/L.<sup>2,3</sup> For example, a patient with a serum potassium concentration of 3.5 mEq/L who received 60 mEq intravenous potassium

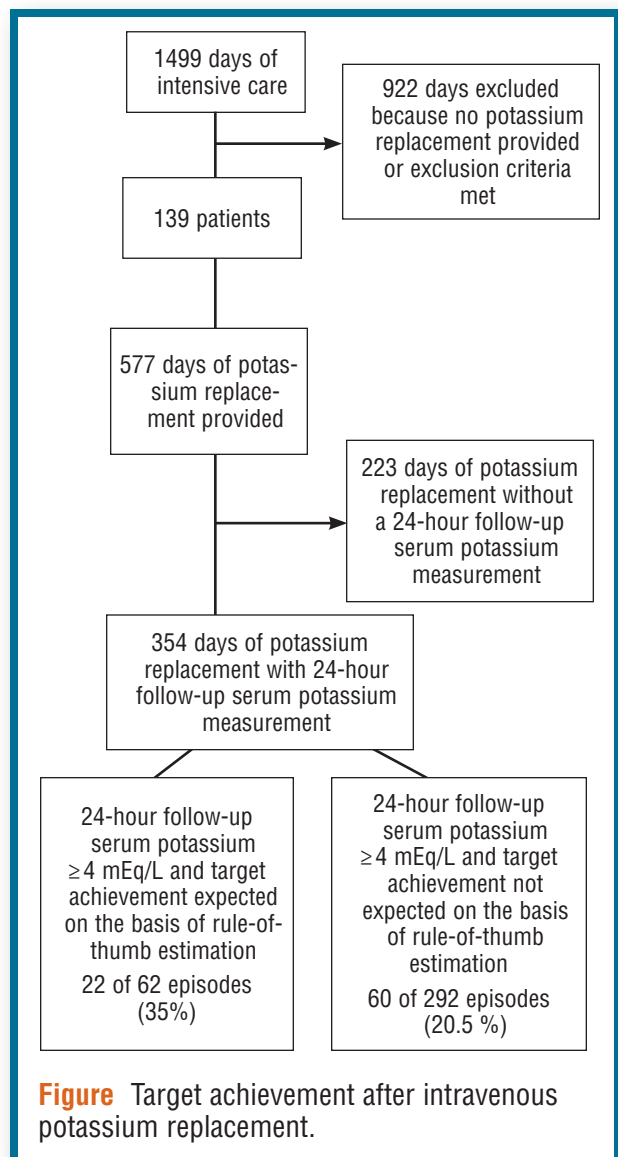
chloride would be expected to achieve a serum concentration of 4.1 mEq/L, thereby reaching the target.

The rule of thumb for critically ill patients with moderate hypokalemia (serum potassium 2-2.9 mEq/L) was that every 10 mEq of a potassium salt would be expected to increase the serum potassium concentration by 0.05 mEq/L.<sup>2,3</sup> For example, a patient with a serum potassium concentration of 2.8 mEq/L who received 100 mEq intravenous potassium chloride would be expected to achieve a serum concentration of 3.3 mEq/L, thereby not reaching the target. If a patient received more than 1 order for potassium replacement during a 24-hour period, the amounts of all replacements were summed and recorded as the total replacement provided for that episode of hypokalemia. The primary safety outcome was measurement of serum potassium within the 24 (± 6) hours after completion of replacement.

The amount and time of oral and intravenous potassium replacement ordered were collected. Additional data collected included demographic and clinical characteristics such as sex; age; weight; height; medical history; and serum levels of other electrolytes, creatinine, urea nitrogen, glucose, and albumin. Data on concomitant use of insulin, loop diuretics, other non-potassium-sparing diuretics, and intravenous fluids were collected.

### Statistical Analysis

The primary outcome was evaluated in patients with mild and moderate hypokalemia and measured as a binary variable: achievement or no achievement of the target serum potassium concentration within 24 hours of replacement. The primary effectiveness outcome could only be evaluated in patients for whom a follow-up serum potassium concentration within 24 hours of replacement was recorded. We used logistic regression analysis to assess whether the rule-of-thumb administration had any effect on the probability of attaining the target concentration within 24 hours of potassium replacement compared with replacement given without using the rule of thumb. Additionally, we used logistic regression analysis to assess whether the effect was consistent across mild and moderate hypokalemia by using baseline serum potassium concentration, baseline magnesium concentration, presence of chronic kidney disease, and body mass index. Baseline demographics and clinical characteristics were described by using descriptive statistics. We determined that a sample size of 272 days of replacement would have



**Figure** Target achievement after intravenous potassium replacement.

90% power to detect a 15.5% absolute difference (actual 28% vs expected 12.5%) in the percentage of hypokalemic events with adequate replacement at  $\alpha = .05$ .<sup>3-7</sup>

### Results

In total, 139 patients with 1499 days in the MICU were considered for inclusion in the study; 922 of the 1499 days were excluded from analyses because no potassium replacement was provided. Of the remaining 577 days, potassium replacement was provided and serum potassium concentration was checked within 24 hours after replacement in 354 instances (see Figure). Of these 354 instances, 172 (48.6%) days were accounted for by patients 45 to 64 years old, and the median day of hospitalization on which replacement was provided was day

**Table** Breakdown of days of potassium replacement with 24-hour follow-up measurement of serum level of potassium by characteristics of patients

Characteristic	No. (%) of days <sup>a</sup> (n=354)
Age, y	
18-44	92 (26)
45-64	172 (48.6)
≥65	90 (25.4)
Male sex	222 (62.7)
Body mass index <sup>b</sup>	
<25	160 (45.2)
25-30	59 (16.7)
>30	135 (38.1)
Medication use	
Intravenous fluid bolus	20 (5.6)
Potassium-sparing diuretic	2 (0.6)
Loop diuretic	61 (17.2)
Insulin, intravenous bolus or oral	80 (22.6)
Comorbid disease state	
Alcohol abuse	41 (11.6)
Diabetes	51 (14.4)
Chronic kidney disease	37 (10.5)
Received magnesium replacement	46 (13.0)

<sup>a</sup> No. of days of potassium replacement with 24-hour follow-up measurement of serum level of potassium.

<sup>b</sup> Calculated as the weight in kilograms divided by height in meters squared.

13.6 (SD, 13.1). Comorbid disease states that could have affected serum potassium concentrations were a history of alcohol abuse on 41 days (11.6%), diabetes mellitus on 51 days (14.4%), and chronic kidney disease on 37 days (10.5%). On days when patients received potassium replacement, many patients were receiving medications that could have affected serum potassium concentrations: 61 (17.2%) days accounted for intravenous bolus or oral loop diuretic, 2 (0.6%) days for oral non-potassium-sparing diuretic, 80 (22.6%) days for subcutaneous insulin, and 20 (5.6%) for intravenous fluid bolus (see Table).

### Achievement of Target Serum Potassium Concentration

The final sample consisted of 354 days of potassium administration for which a 24-hour follow-up serum potassium concentration was measured. Mean potassium concentration was 3.22 mEq/L (SD, 0.30) before replacement and 3.57 mEq/L (SD, 0.45) after replacement. Potassium concentration after replacement met the target level ( $\geq 4$  mEq/L) in 82 episodes of replacement

(23.2%). Of 62 episodes of replacement that were expected to meet the target on the basis of the rule-of-thumb estimation, only 22 (35%) did. Of 292 episodes of replacement that were not expected to meet the target on the basis of the rule-of-thumb estimation, 60 (20.5%) of these replacements did (see Figure). Magnesium was replaced on 46 (13.0%) of the 354 days. Mean serum concentration of magnesium before potassium replacement on these days was 1.92 mEq/L (SD, 0.31).

### Subgroup and Regression Analyses

Results from logistic regression analysis suggested that compared with potassium replacement supplied without use of a protocol, rule-of-thumb administration was associated with a greater likelihood of attaining the target serum concentration (odds ratio [OR], 2.12; 95% CI, 1.18-3.85;  $P = .01$ ). This difference remained significant after adjustments for other covariates (OR, 2.18; 95% CI, 1.04-4.56;  $P = .04$ ). Patients with a serum potassium concentration of 2 to 2.9 mEq/L received 52 days (14.7%) of potassium replacement. After adjustments for other covariates, baseline serum concentration did not significantly affect the likelihood of attainment of the target serum potassium concentration (OR, 0.80; 95% CI, 0.32-2.00;  $P = .63$ ). No replacements resulted in a measured serum potassium concentration greater than 5 mEq/L.

### Discussion

Only one-third of MICU patients who had potassium replacement based on the rule-of-thumb method achieved a serum potassium concentration within the target range within 24 hours of replacement. This proportion was significantly greater than that of patients who had potassium replacement without use of a rule-of-thumb estimation. This finding remained true after adjustments for patient characteristics.

The small percentage (23.2% overall and 35% when rule-of-thumb estimation was provided) of potassium replacements in our study that resulted in attainment of the target serum concentration is within the range reported for other cohorts of critically ill patients in whom replacement was determined by using or not using a replacement protocol.<sup>4,9</sup> Before beginning use of a nurse-initiated, evidence-based order form in an MICU, Owen et al<sup>5</sup> observed achievement of the target serum potassium concentration in 18% of cases. After implementation, the



percentage of target attainment increased to 72%. In a population of surgical ICU patients, Todd et al<sup>9</sup> found a comparably large increase (28%-66%) in the effectiveness in attaining a target serum potassium concentration. Couture et al<sup>8</sup> observed a smaller but significant difference (66.1% vs 56.8%) in achieving a target serum potassium concentration in surgical ICU patients when a replacement protocol was followed rather than traditional practice. The potassium replacement orders that originate from rule-of-thumb recommendations are unsuccessful in achieving the target serum potassium concentration in 43% to 82% of patients.

Although no potassium replacements resulted in hyperkalemia in our study, more than three-quarters of replacements did not resolve a patient's hypokalemia. Of more concern, more than one-third of potassium replacement orders were not paired with a follow-up order to assess the serum potassium concentration after replacement. In a study<sup>10</sup> in critically ill patients, hyperkalemia, hypokalemia, and variability in serum potassium concentrations were associated with increased in-hospital mortality. Laboratory tests to determine serum potassium concentration after potassium replacement were part of the protocol in studies in which a protocol was used.<sup>4-6,8</sup> Hoekstra et al<sup>4</sup> reported that use of a nurse-centered, computerized potassium replacement protocol was associated with reduced rates of hyperkalemia and hypokalemia and ensured that all patients had serum levels of potassium determined after potassium replacement. Serum potassium concentrations should be monitored at least every 4 hours after potassium replacement if indications of abnormal potassium levels are present and every day or other day if patients are asymptomatic.<sup>1</sup>

In our study, magnesium was replaced in less than one-fifth of the patients despite a baseline serum concentration less than 2 mEq/L in more than half of the patients. Hamill-Ruth and McGory<sup>11</sup> found a significant improvement in potassium homeostasis when serum magnesium was maintained at high-normal values in critically ill patients. In their study,<sup>11</sup> the placebo group, maintained at a low-normal magnesium concentration, had a persistently negative potassium balance, higher urine potassium losses, and a trend toward greater potassium replacement. Inadequate replacement of magnesium may have affected attainment of target serum potassium concentrations in our sample; however, achievement of a safe, target magnesium concentration of at least 2 mEq/L may

occur less often than previously thought after magnesium replacement.<sup>12</sup> In a cohort of critically ill patients with hypomagnesemia who had magnesium replacement, less than 60% of the patients achieved a serum magnesium concentration of at least 2 mEq/L.

The treatment teams in our study were aware of the target serum potassium concentrations; however, we had no protocols to guide replacement of electrolytes. Patients in the protocol arms of studies in critically ill patients that used protocols had a higher rate of appropriate replacement than we did. However, the replacement targets that we obtained were within the wide range of appropriate replacement targets attained among patients in the studies for whom no protocol was followed.

Because some patients received potassium replacement on consecutive days and because multiple rounds of replacement could have been provided throughout the day in response to concerns that overly aggressive replacement might lead to hyperkalemia, 24 hours after potassium replacement was the most sensible time to evaluate achievement of target goals in our study. In patients who are asymptomatic, measuring serum potassium concentration less frequently than every 24 hours may be appropriate. We might have increased the percentage of unmeasured serum potassium levels if we had obtained measurements less frequently than we did. The percentage of episodes in which the target serum concentration was achieved might have remained the same or increased if these values were measured.

We used values of serum potassium concentrations obtained 24 hours after replacement because most patients did not have data on the level of serum potassium present within 4 hours after replacement. Data on the concentration of potassium in serum 4 hours or less after potassium replacement would have been better than the data obtained 24 hours after replacement that we used to evaluate the effect of replacement on serum potassium concentrations. Most likely the values we used yielded underestimates of target achievement in all analyses. The effect of using values determined at 24 hours compared with those obtained at an earlier time point is difficult to estimate but may have allowed other variables

**Inadequate replacement of magnesium may have affected attainment of target serum potassium concentrations in our sample.**

to affect the follow-up serum potassium concentration. Other MICUs may have a target serum concentration that differs from our target (4-5 mEq/L), a situation that could affect the generalizability of our results; however, a serum potassium level of 4 to 5 mEq/L is a commonly used target for reducing hypokalemia in critically ill patients.<sup>1,2</sup> Additionally, we did not assess the route of potassium administration. The route used might have affected target attainment for patients with lower baseline serum potassium concentrations before replacement but most likely did not affect target attainment when baseline concentrations were closer to 4 mEq/L.<sup>13</sup>

We also did not incorporate patient-specific factors that may affect a patient's response to potassium replacement into our assessment of attainment of target concentrations of serum potassium. These factors should be evaluated with a larger sample of critically ill patients to develop an algorithm to guide replacement in MICU patients, a step that was beyond the intended scope of our study.

## Conclusion

Critically ill MICU patients who received potassium replacement without regard to a protocol achieved the target serum potassium concentration more frequently than the rule-of-thumb estimations predicted. However, target attainment occurred in only one-third of patients, suggesting development and institution of a patient-specific algorithm for potassium replacement that is not based on rule-of-thumb estimations may be necessary to improve the effectiveness of potassium replacement. Critical care nurses should be aware that potassium replacement based on rule-of-thumb estimations often will not yield the targeted serum potassium concentration. [CCN](#)

### Acknowledgment

This research was approved by the University of Arkansas for Medical Sciences institutional review board (205528).

### Financial Disclosures

None reported.

### References

1. Kraft M, Btaiche I, Sacks G, Kudsk K. Treatment of electrolyte disorders in adult patients in the intensive care unit. *Am J Health Syst Pharm.* 2005; 62(16):1663-1682.
2. Weiner ID, Wingo CS. Hypokalemia—consequences, causes, and correction. *J Am Soc Nephrol.* 1997;8(7):1179-1188.
3. Kruse IA, Carlson RW. Rapid correction of hypokalemia using concentrated intravenous potassium chloride infusions. *Arch Intern Med.* 1990;150(3): 613-617.
4. Hoekstra M, Vogelzang M, Drost JT, et al. Implementation and evaluation of a nurse-centered computerized potassium regulation protocol in the intensive care unit—a before and after analysis. *BMC Med Inform Decis Mak.* 2010;10:5.
5. Owen P, Monahan MF, MacLaren R. Implementing and assessing an evidence-based electrolyte dosing order form in the medical ICU. *Intensive Crit Care Nurs.* 2008;24(1):8-19.
6. Kanji Z, Jung K. Evaluation of an electrolyte replacement protocol in an adult intensive care unit: a retrospective before and after analysis. *Intensive Crit Care Nurs.* 2009;25(4):181-189.
7. Hijazi M, Al-Ansari M. Protocol-driven vs physician-driven electrolyte replacement in adult critically ill patients. *Ann Saudi Med.* 2005;25(2): 105-110.
8. Couture J, Létourneau A, Dubuc A, Williamson D. Evaluation of an electrolyte repletion protocol for cardiac surgery intensive care patients. *Can J Hosp Pharm.* 2013;66(2):96-103.
9. Todd SR, Sucher JF, Moore LJ, Turner KL, Hall JB, Moore FA. A multidisciplinary protocol improves electrolyte replacement and its effectiveness. *Am J Surg.* 2009;198(6):911-915.
10. Hessels L, Hoekstra M, Mijzen LJ, et al. The relationship between serum potassium, potassium variability and in-hospital mortality in critically ill patients and a before-after analysis on the impact of computer-assisted potassium control. *Crit Care.* 2015;19:4.
11. Hamill-Ruth RJ, McGory R. Magnesium repletion and its effect on potassium homeostasis in critically ill adults: results of a double-blind, randomized, controlled trial. *Crit Care Med.* 1996;24(1):38-45.
12. Hammond DA, Stojakovic J, Kathe N, et al. Effectiveness and safety of magnesium replacement in critically ill patients admitted to the medical intensive care unit in an academic medical center: a retrospective, cohort study [published online ahead of print January 1, 2017]. *J Intensive Care Med.* doi:10.1177/0885066617720631
13. DeCarolis DD, Kim GM, Rector TS, Ishani A. Comparative dose response using the intravenous versus enteral route of administration for potassium replenishment. *Intensive Crit Care Nurs.* 2016;36:17-23.