Management of Hyperkalemia in Hospitalized Patients

Kristy N. Fordjour, PharmD, Ted Walton, PharmD and John J. Doran, MD

Abstract: *Purpose:* The aim of this study was to determine the incidence of treatment of hyperkalemia in hospitalized patients. *Methods:* This is a prospective chart review of adults in a tertiary care hospital with hyperkalemia (serum potassium [K^+] ≥5.1 mEq/L) over a 6-month period. The treatments and their effectiveness, causative factors and associated electrocardiographic (ECG) changes were examined. *Results:* There were 154 hyperkalemic episodes, 32 with K^+ ≥6.5 mEq/L and 122 with K^+<6.5 mEq/L. Overall, 97% received treatment for an average K^+ of 5.9 mEq/L. Sodium polystyrene sulfonate (SPS) was included in 95% of the regimens. Incremental doses of SPS monotherapy yielded potassium reductions between 0.7 and 1.1 mEq/L, and inadequate responses (K^+ <0.5 mEq/L) were less frequent with higher doses. There were no differences in the effectiveness of SPS among dialysis-dependent, chronic kidney disease, or nonchronic kidney disease patients. Greater reductions in potassium were observed using a combination of treatments. ECGs were performed in 44% of patients, and 50% showed no ECG changes despite K^+ being ≥6.5 mEq/L. The most common abnormality, peaked T waves, was associated with a higher frequency of calcium administration but not with the number of K+-lowering therapies. *Conclusions:* Almost all the patients were treated for hyperkalemia. Oral SPS monotherapy was the predominant treatment with the best response at the highest dose. Some combination therapies had greater K^+ reductions but were used infrequently. An ECG was obtained in about 50% of the cases, but two thirds showed no K^+-related changes. Reduced kidney function was associated with 70% of hyperkalemic episodes. Angiotensin-converting enzyme inhibitors and trimethoprim were the most commonly implicated medications.

Key Indexing Terms: Hyperkalemia; Electrocardiography; Sodium polystyrene sulfonate; Angiotensin-converting enzyme inhibitors; Kidney failure. **[Am J Med Sci 2014;347(2):93–100.]**

Hyperkalemia, defined as serum potassium (K^+) ≥5.1 mEq/L, occurs in 1.4% to 10% of hospitalized patients[1–4] and is caused by decreased kidney function (from acute or chronic kidney disease [CKD]), medications, exogenous or endogenous potassium sources and inadequate or missed dialysis.[1,5–7] It has been more than a decade since the last hospital study of treatment practices for hyperkalemia,[5] and although no new therapies have been developed, the safety of one agent, sodium polystyrene sulfonate (SPS), has been questioned[8] due to reports associating it with colonic necrosis.[9] Most but not all[10] cases involved rectal administration in combination with the osmotic laxative, sorbitol. Despite this potential complication, SPS remains the only Food and Drug Administration–approved medication for treatment of hyperkalemia.[11]

K^+ can be lowered by 2 general mechanisms: The first is by shifting potassium intracellularly using insulin,[12] albuterol[13] or sodium bicarbonate.[14] The second is by excreting it from the body using 1 of 4 routes: the stool with binding resins,[15] the urine with diuretics, the blood with hemodialysis or the peritoneal fluid with peritoneal dialysis. Other than SPS, the medications that treat hyperkalemia, such as insulin,[12] diuretics, beta agonists[13] and sodium bicarbonate,[14] simply cause hypokalemia as a side effect. These alternatives to SPS may cause undesirable effects resulting in hypoglycemia, volume depletion and tachycardia, respectively.

All the current therapies for hyperkalemia have been available for many years. Some form of SPS has been in use in the United States for >50 years.[8] Intravenous bicarbonate has been used to correct hyperkalemia in acidotic patients since the late 1950s.[16] Loop diuretics such as furosemide and bumetanide were Food and Drug Administration approved in 1966 and 1967,[17] and although their hypokalemic effects are well known, neither has been studied as a treatment for hyperkalemia. The "newest" therapy for hyperkalemia, beta agonists, were first used intravenously in the late 1970s[18] and via a nebulizer in the early 1980s.[13] Dialysis therapies have also been available since the 1950s, although hemodialysis and peritoneal dialysis were not routinely available until decades later.

Practitioners have the option of using one or a combination of K^+-lowering therapies, but there remains little data to guide which treatments should be administered. Since the 1950s, the electrocardiogram (ECG) has been used to judge the severity of hyperkalemia and hence how aggressively it should be treated. Generally, if ECG changes are seen, intravenous calcium salts are given to stabilize the myocardium in order to prevent life-threatening arrhythmias. The earliest sign, peaked T waves, occur at K^+ concentrations of approximately 5.6 mEq/L.[19,20] It has been reported that as the concentration further increases, the PR interval becomes prolonged and finally the QRS widens. The clinical problem is that these changes may not occur even with severe hyperkalemia.[21] In fact, studies have reported ECG abnormalities in only 25% to 50% of patients with hyperkalemia.[5,22] Overall, management of hyperkalemia has traditionally been based on the physician's personal judgment[8,23] or institutional protocols.[5]

In this article, we report how the physicians at our hospital managed patients with hyperkalemia. We examined the K^+ concentration that prompted treatment, treatments for hyperkalemia (medications and dialysis) and their effectiveness and the potential precipitating factors such as medications and reduced kidney function. We also looked at the frequency of ordering ECGs and the changes observed according to the K^+ concentration.

METHODS

Study Design

This was a prospective chart review conducted in hospitalized patients at Grady Memorial Hospital, a public, academically affiliated teaching hospital staffed by 2 medical

From the Department of Pharmaceutical Services (KNF), Emory University Hospital Midtown, Atlanta, Georgia; Department of Pharmacy and Drug Information (TW), Grady Health System, Atlanta, Georgia; and Renal Division (JJD), Emory University School of Medicine, Grady Memorial Hospital, Atlanta, Georgia.

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Correspondence: Kristy N. Fordjour, PharmD, Department of Pharmaceutical Services, Emory University Hospital Midtown, 550 Peachtree Street, NE, Atlanta, GA 30308 (E-mail: kristy.fordjour@emoryhealthcare.org).

schools, that became hyperkalemic during August 1, 2008, through January 31, 2009. All data were gathered during each patient's hospitalization. The patients were included if they were 18 years of age or older and had hyperkalemia (defined as $K^+ \geq 5.1$ mEq/L). The subjects were excluded for a diagnosis of diabetic ketoacidosis (DKA), previous evaluation within the study period, or the presence of pseudohyperkalemia (hemolyzed sample reported per the laboratory). The patients receiving treatment for hyperkalemia were identified by medication utilization reports for calcium salts, sodium bicarbonate and SPS. A daily report of patients with $K^+ \geq 6.5$ mEq/L was generated by the institution's laboratory to identify patients with critical laboratory values who did not receive treatment for hyperkalemia. Treatments for hyperkalemia included the administration of the following medications: calcium salts, regular insulin plus dextrose, albuterol (excluding metered dose inhalers), SPS and/or hemodialysis. Data collection included the following: (1) demographics (age, sex, race, weight); (2) serum creatinine; (3) frequency and dosage of medications given for treatment of hyperkalemia; (4) pretreatment and post-treatment K^+ concentrations and the times each were obtained; (5) causative factors; (6) 12-lead ECGs, noting the K^+ immediately prior to obtaining the ECG. Medications (angiotensin-converting enzyme inhibitors [ACEI], angiotensin receptor blockers, digoxin, total parenteral nutrition, spironolactone, trimethoprim, triamterene, penicillin G potassium and potassium containing fluids) administered 24 to 72 hours before the hyperkalemic episode were considered to be causative factors, except in dialysis-dependent patients. Neither heparin, because of its ubiquitous use for thromboembolism prophylaxis, nor beta blockers, because large clinical trials have shown that they do not cause clinically significant hyperkalemia[24] were included. ECG tracings were collected and reviewed by a physician for changes including peaked T waves, prolonged PR interval (>0.20 seconds) and widened QRS (>0.12 seconds). Potential confounding variables were noted for each ECG interpretation. To maintain patient confidentiality, the patients were assigned a unique patient identifier that was used on all study documents. Data collection forms were anonymous and securely stored when not in use. All the identifiers were destroyed after the completion of the study analysis. This study was approved by the hospital's research oversight committee and was conducted in compliance with Institutional Review Board Research Committee requirements.

Statistical Analyses

A paired *t*-test was used to compare therapy combinations; SPS failure rate and calcium usage was analyzed with Fisher's exact probability test.

RESULTS

A total of 330 patients had hyperkalemic episodes. Ten patients were excluded for DKA and 166 patients had pseudohyperkalemia. Baseline characteristics of the 154 study patients are presented in Table 1. The demographics of the study population were predominantly African American and between 18 and 95 years of age. The mean and median serum creatinine were 3.2 and 2.0 mg/dL, respectively. Seventy percent of the population had chronic kidney disease (CKD), defined as the following: documented kidney disease, estimated glomerular filtration rate (GFR) <30 mL/min or receiving dialysis. Twenty of these patients were dialysis dependent.

The distribution of pretreatment K^+ concentrations is shown in Figure 1. K^+ concentrations ranged from 5.1 to 9.5 mEq/L, and the mean and median concentrations prompting treatment were 5.9 and 5.8 mEq/L, respectively. One hundred twenty-two patients (79%) had $K^+ < 6.5$ mEq/L and 120 (98%) of them received treatment. Thirty-two patients (21%) had $K^+ \geq 6.5$ mEq/L, and all but 2 received treatment. The untreated patients had K^+ concentrations of 6.7 and 6.6 mEq/L, normal renal function, no ECG changes and repeat K^+ concentrations were within normal range.

TABLE 1. Demographics for 154 patients with hyperkalemia

Baseline characteristics	N = 154
Age, mean (range; yr)	52 (18–95)
Gender, n (%) male	104 (68)
Race, n (%)	
African American	136 (88)
White	10 (6)
Hispanic	6 (4)
Other	2 (1)
Serum creatinine, mean (range), mg/dL	3.2 (0.2–16.5)
Median (mg/dL)	2.0
Chronic kidney disease, n (%) (documented renal disease or estimated GFR <30 mL/min, or on dialysis)	108 (70)
Hemodialysis, n (%)	20 (13)

The SPS was the most commonly used therapy as part of treatment regimens and was administered to 95% of the patients (Figure 2). Insulin ranked second at 21%, while bicarbonate, hemodialysis and albuterol were utilized infrequently. Most patients who received insulin also received IV dextrose (94%), so they are herein grouped together. Twenty-three percent of hyperkalemic episodes were treated with >1 K^+-lowering therapy. Most patients (74%) were treated with monotherapy (Figure 3, columns). The patients with higher average pretreatment K^+ concentrations received greater number of therapies (Figure 3, line). All the treatments in this study were given as 1 time doses except for 3 occurrences. In these cases, the SPS dose was repeated once, and the post-treatment K^+ concentrations were always drawn after the repeat dose.

All the patients had post-treatment K^+ concentrations. The elapsed time between the pretreatment and post-treatment K^+ concentrations versus the cumulative number of patients is shown in Figure 4. Eighty-eight percent of patients had post-treatment K^+ concentrations drawn within 24 hours, which is an appropriate time to expect K^+-lowering effects from SPS. SPS was the most frequently used monotherapy for hyperkalemia, and the patients were grouped according to the dose ranges they received (Table 2). Only 2 patients received doses above the manufacturer's recommended maximal oral dose of 60 g/d.[11] The highest doses of SPS were given for the highest K^+($P < 0.05$) and produced a significantly greater K^+ reduction compared with the 10- to 20-g doses but not the 30- to 40-g doses (Table 2). None of the subsets (presence or absence of CKD or dialysis dependent) had significant differences in K^+ reduction for any SPS dose. There were no cases of hypokalemia ($K^+ < 3.5$ mEq/L) at any dose of SPS monotherapy.

Some patients had an inadequate response (K^+ reduction <0.5 mEq/L) to SPS therapy as shown in the rightmost column of Table 2. There was a trend toward fewer inadequate responders as the SPS dose increased, but it did not reach statistical