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Potassium Abnormalities in Current Clinical Practice: Frequency, Causes, Severity and Management

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Key Words
Hyperkalemia · Hypokalemia · Potassium

Abstract
Objective: We aimed to investigate the prevalence and etiology of potassium abnormalities (hypokalemia and hyperkalemia) and management approaches for hospitalized patients. ***Subjects and Methods:*** Over a 4-month period, all hospitalized patients at Hacettepe University Medical Faculty Hospitals who underwent at least one measurement of serum potassium during hospitalization were included. Data on serum levels of electrolytes, demographic characteristics, cause(s) of hospitalization, medications, etiology of potassium abnormality and treatment approaches were obtained from the hospital records. ***Results:*** Of the 9,045 hospitalized patients, 1,265 (14.0%) had a serum potassium abnormality; 604 (6.7%) patients had hypokalemia and 661 (7.30%) had hyperkalemia. In the hypokalemic patients, the most important reasons were gastrointestinal losses in 555 (91.8%) patients and renal losses in 252 (41.7%) patients. The most frequent treatment strategies were correcting the underlying cause and replacing the potassium deficit. Of the 604 hypokalemic patients, 319 (52.8%) were normokalemic at hospital discharge. The most common reason for hyperkalemia was treatment with renin-angiotensin-aldosterone system blockers in 228 (34.4%) patients, followed by renal failure in 191 (28.8%). Two hundred and ninety-eight (45.0%) patients were followed without any specific treatment. Of the 661 hyperkalemic patients, 324 (49.0%) were normokalemic at hospital discharge. ***Conclusion:*** This study showed a high prevalence of potassium imbalance among hospitalized patients. Although most of the potassium abnormalities were mild/moderate, approximately half of the patients treated for hypokalemia or hyperkalemia were discharged from the hospital with ongoing dyskalemia.

Introduction

Potassium is a critical electrolyte for cellular functions and its serum concentration must be precisely maintained between 3.5 and 5.5 mEq/l [1]. The kidneys, gastrointestinal organs, several hormones and cellular transport mechanisms are important in the regulation of potassium homeostasis [2–5]. Disturbance of one or more of these mechanisms results in dyskalemia, which may range from a mild asymptomatic disorder to a life-threatening emergency hospitalization. Abnormalities in po-

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tassium balance are frequently encountered in clinical practice and have been investigated in several studies [6–8]. However, changes in demographics, due to increased life expectancy, increased rates of multiple drug use and changes in dietary habits, demand a continuous surveillance for potassium disorders among different patient populations in clinical practice. The aim of this study was to investigate the prevalence of hypokalemia and hyperkalemia, the etiology of potassium abnormalities and the management approaches for hospitalized patients in a tertiary medical center.

Subjects and Methods

Patients

All hospitalized patients (n = 9,045) in Hacettepe University Medical Faculty Hospitals during a 4-month study period, who underwent at least one serum measurement of potassium during hospitalization, were included in this study. Records were taken of those with potassium abnormalities. The potassium values were followed throughout the hospitalization period. This study was conducted in accordance with the Declaration of Helsinki and approved by the Hacettepe University Medical Faculty local ethics committee.

Methods

A total of 21,435 potassium measurements were performed in 9,045 patients during the study period. Serum potassium levels were taken from the electronic health records system of the hospital. All of the measurements were performed using an ion-selective electrode method with a Roche modular system as soon as the samples were received. Samples with hemolysis were excluded. The results were grouped as normokalemia (serum K^+ = 3.5–5.0 mEq/l), hypokalemia (serum K^+ <3.5 mEq/l) and hyperkalemia (serum K^+ >5.0 mEq/l). If the patients had hypokalemic and hyperkalemic measurements during hospitalization, the first abnormal potassium result was considered as the present potassium abnormality. Demographic characteristics and laboratory parameters of the patients including age, gender, cause(s) of hospitalization, comorbidities, medications, levels of serum creatinine, sodium, calcium, phosphorus, magnesium and albumin and the results of arterial or venous blood gas analysis, urinalysis and 24-hour urine tests were recorded. The causes of hypokalemia were investigated and classified as impaired oral intake, redistribution, gastrointestinal or renal loss. Impaired oral intake is defined as consuming nothing by mouth or a clear-liquid diet only. In hyperkalemic patients, pseudohyperkalemia, redistribution, aldosterone deficiency or resistance and decreased renal excretion were investigated as potential causes. Management approaches for the patients with potassium abnormalities and the results of the treatment were also recorded. All treatments were conducted by the patients' own physicians with no intervention by the investigators.

Statistical Methods

All statistical analyses were performed using the Statistical Package for Social Sciences version 18, (SPSS Inc., Chicago, Ill., USA). Descriptive statistics were used to define demographics and the frequency of dyskalemia. Categorical variables were compared by means of the χ^2 test. $p < 0.05$ was considered statistically significant.

Table 1. Distribution of potassium levels in all measurements

Potassium levels, mEq/l	Patients, n (%)
<2.5	71 (0.3)
2.5 – 3.0	556 (2.6)
3.01 – 3.5	2,142 (10.0)
3.51 – 5.0	16,219 (75.7)
5.01 – 5.5	1,316 (6.1)
5.51 – 6.0	521 (2.4)
>6.0	610 (2.9)
Total	21,435 (100)

Table 2. Serum potassium levels at the time of discharge after treatment for hypokalemia

Potassium level	Patients, n (%)
Hypokalemia	233 (38.6)
Normokalemia	319 (52.8)
Hyperkalemia	52 (8.6)

Results

Prevalence of Dyskalemia

Distribution of the results of the serum potassium measurements are shown in table 1. Of the 21,435 measurements, 5,216 (24.3%) were abnormal. Of the 9,045 hospitalized patients, 1,265 (14.0%) had potassium abnormalities: hypokalemia in 604 (47.7%) and hyperkalemia in 661 (52.3%). Of the 661 hyperkalemic patients, 451 were male (68.2%) and 358 of the 604 hypokalemic patients were female (59.2%).

Hypokalemia

The mean age of the hypokalemic patients was 54.4 ± 16.3 years and the mean serum potassium level was 3.25 ± 0.24 mEq/l. Of the 604 hypokalemic patients, 371 (61.4%) were hospitalized in surgical wards. The extent of the severity of hypokalemia was as follows: severe (K^+ <2.5 mEq/l) in 8 patients (1.3%), moderate (K^+ 2.5–2.99 mEq/l) in 68 (11.3%) and mild (K^+ 3.0–3.49 mEq/l) in 528 (87.4%). The etiology of hypokalemia included im-

paired oral intake or evidence of gastrointestinal potassium loss (mainly due to vomiting and diarrhea) in 555 patients (91.8%) or renal loss (mainly due to diuretic treatment) in 252 (41.7%). Other less common etiologies were catecholamine excess, insulin treatment, intravenous hydration without potassium replacement and hypomagnesemia. The major options used for managing hypokalemia were: correcting the underlying causes by ensuring an adequate oral intake and the cessation of diuretics in 401 patients (66.4%), and intravenous or oral potassium replacement in 255 (42.2%) and 144 (23.8%) patients, respectively. Other less commonly used approaches were administering aldosterone receptor blockers or magnesium supplementation. No specific treatment was given to 36 hypokalemic patients (6.0%). Serum potassium levels at the time of discharge following treatment were as follows: severe hypokalemia (K^+ <2.5 mEq/l) in 4 patients (1.7%), severe hyperkalemia (K^+ ≥6 mEq/l) in 7 (13.5%) and normokalemia in 319 (52.8%) (table 2).

Hyperkalemia

The mean age of the hyperkalemic patients was 56.8 ± 17.0 years and the mean serum potassium level was 5.4 ± 0.4 mEq/l. Of the 661 hyperkalemic patients, 397 (60.1%) were hospitalized in surgical wards. Distribution of the severity of hyperkalemia was as follows: mild (K^+ 5–5.49 mEq/l) in 483 (73.0%), moderate (K^+ 5.5–5.99 mEq/l) in 124 (8.8%) and severe (K^+ ≥6.0 mEq/l) in 54 (8.2%). The etiology of hyperkalemia included the use of renin-angiotensin system (RAS) blockers or nonsteroidal anti-inflammatory drugs (NSAIDs) in 225 (34.4%) patients and impaired renal function in 178 (27%). The most commonly used therapeutic approaches were diuretics, intravenous dextrose-insulin and inhaled salbutamol. Hemodialysis was performed in 52 hyperkalemic patients (7.9%). No specific treatment was recorded for 298 (45.0%) hyperkalemic patients. Serum potassium levels at the time of discharge after the treatment of hyperkalemia were as follows: hypokalemia in 43 patients (6.5%), normokalemia in 324 (49.0%) and hyperkalemia in 294 (44.5%). Hence, at discharge 337 patients (51.0%) had abnormal potassium levels.

Discussion

This study indicated a high prevalence (24.3%) of serum potassium abnormalities in the hospitalized patients and this was within the 13.7–48.0% of prevalence of serum potassium abnormalities reported previously [3, 7, 9, 10]; this wide range could be due to the different cut-off points and patient characteristics used in these studies.

The 6.7% prevalence of hypokalemia in hospitalized patients in this study was lower than in previous studies [9, 11] indicating 12–20%; these differences could be due to the different cut-off points used in the studies and the patient characteristics. The main etiologies of hypokalemia were decreased oral intake and gastrointestinal and renal loss. Another important cause was intravenous saline administration without potassium supplementation in patients with no oral intake; this is an iatrogenic cause of hypokalemia that can easily be prevented. This study confirmed that diuretic use was the main cause of the renal loss of potassium (41.7% of the cases). In a previous study performed on a geriatric population, diuretics were observed as an important cause of hypokalemia (39.0%) [12]. There were no follow-up data in our study, but it is well known that diuretic-induced hypokalemia increases the risk of arrhythmia. When the serum potassium levels are <3 mEq/l, the prevalence of malignant ventricular arrhythmias increases 2-fold in patients on diuretic treatment [13]. Hypokalemia also increases the duration of hospitalization [14]. The main treatments for hypokalemia in this study were oral or intravenous potassium replacement. For some patients with insufficient oral intake, total parenteral nutrition was given. Total parenteral nutrition was previously defined as one of the causes of iatrogenic hyperkalemia [9]. In this study, more than half of the patients treated for hypokalemia were discharged with abnormal potassium levels and 8.6% were discharged with iatrogenic, overshoot hyperkalemia. These findings highlight the need for the careful scrutiny of hospital practices (e.g. the excessive use of diuretics or intravenous fluid replacement without any additional potassium as potential causes of hypokalemia or the inadvertent use of total parenteral nutrition as a cause of overshoot hyperkalemia) in the evaluation and management of hypokalemia.

The prevalence of hyperkalemia was 7.3% in the hospitalized patients in this study. There was a finding of severe hyperkalemia in 8.2% of the patients, similar to previous reports [15, 16]. The main etiologies of hyperkalemia in these patients were medications (NSAIDs, RAS blockers, beta-blockers, spironolactone and heparin), chronic kidney disease, insulin deficiency and hemolysis. RAS blockers were the most common cause of hyperkalemia, as in previous studies. Hyperkalemia risk due to RAS blockers increases in patients with a serum creatinine level >1.5 mg/dl [17]. RAS blockers cause hyperka-

lemia in 10–38% of hospitalized patients and in 10% of outpatients after 1 year of treatment. The risk of hyperkalemia is especially high in patients with diabetes and chronic kidney disease [10, 18–21]. Previous studies indicated that 22–25% of hyperkalemic hospitalized patients were receiving iatrogenic potassium replacement [22], and most of these patients received this together with diuretic treatment to prevent hypokalemia [16]. The use of diuretics and beta-blockers was more common in this study than in previous ones, due to the higher proportion of patients with congestive heart failure. The causes of hyperkalemia were different for patients in the medical or surgical wards, with the main causes being the use of RAS blockers and postoperative NSAIDs, respectively. Some rare causes of hyperkalemia should also be considered in appropriate clinical circumstances, such as accidental potassium ingestion [23]. In this study, almost 8% of the patients needed hemodialysis treatment for ameliorating hyperkalemia. This treatment obviously increases the burden of hyperkalemia, both for the patient and for hospital resources. Mortality in patients with hyperkalemia was found to be 17.0% in a previous study, although the definite relation between hyperkalemia and mortality was not clear [24]. The reason for high mortality may be the more common prescription of RAS blockers in patients with congestive heart failure and chronic kidney disease. The contribution of hyperkalemia to mortality in such cases needs further study.

Almost 45.0% of the hyperkalemic patients were followed up with no treatment. In most of these patients, potassium levels were generally between 5.0 and 5.5 mEq/l. We demonstrated that among patients treated for hyperkalemia, 6.5% were discharged with a serum potassium level <3.5 mEq/l and 44.5% were discharged with a level >5 mEq/l. Although most of the serum potassium abnormalities at the time of discharge were mild, there were cases >6.0 mEq/l. Discharging more than half of the patients with a potassium level outside the normal range not only indicates that the treatment of hyperkalemia was inadequate, but also carries a potential risk for increased morbidity and mortality.

This study had several limitations: deficiencies in determining the exact cause of potassium abnormality treatment approaches as well as the absence of data on long-term morbidity, follow-up and use of dyskalemia-attributed hospital resources.

Conclusion

This study showed a high prevalence of potassium abnormalities among hospitalized patients. Although most of the potassium abnormalities were mild to moderate, there were many severe cases for whom simple hospital surveillance measures could hinder serious morbidity and mortality. Beyond this, almost half of the patients treated for either hypokalemia or hyperkalemia were discharged from the hospital with an ongoing dyskalemia. Further studies are warranted in order to determine morbidity and mortality as well as the risks associated with dyskalemia-attributed length of hospital stay and being discharged with a potassium abnormality.

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