How to Cite:
Mohamed, S. A. M. (2022). Settings for hyperkalemic patients in emergency department: A prospective study. *International Journal of Health Sciences*, *6*(S8), 2681–2689.
https://doi.org/10.53730/ijhs.v6nS8.12547

Settings for hyperkalemic patients in emergency department: A prospective study

Sameh Ahmed Mahmoud Mohamed
Emergency Medicine Specialist, MCME - UAE
Corresponding author email: Saa4ever@yahoo.com

***Abstract*---**Background: Hyperkalemia is a common electrolyte disorder observed in the emergency department. It is often associated with underlying predisposing conditions, such as moderate or severe kidney disease, heart failure, diabetes mellitus, or significant tissue trauma. Additionally, medications, such as inhibitors of the renin-angiotensin-aldosterone system, potassium-sparing diuretics, nonsteroidal anti-inflammatory drugs, succinylcholine, and digitalis, are associated with hyperkalemia. To this end, Kidney Disease: Improving Global Outcomes (KDIGO) convened a conference in 2018 to identify evidence and address controversies on potassium management in kidney disease. This review aimed to summarize the deliberations and clinical guidance for the evaluation and management of acute hyperkalemia in this setting. The toxic effects of hyperkalemia on the cardiac conduction system are potentially lethal. The ECG is a mainstay in managing hyperkalemia. Membrane stabilization by calcium salts and potassium-shifting agents, such as insulin and salbutamol, is the cornerstone in the acute management of hyperkalemia. However, only dialysis, potassium-binding agents, and loop diuretics remove potassium from the body. Frequent reevaluation of potassium concentrations is recommended to assess treatment success and to monitor for recurrence of hyperkalemia.

***Keywords*---**acute, electrolytes, emergency, hyperkalemia, potassium.

Introduction

Hyperkalemia is a common clinical problem that is most often a result of impaired urinary potassium excretion due to acute or chronic kidney disease (CKD) and/or disorders or drugs that inhibit the renin-angiotensin-aldosterone system (RAAS). Therapy for hyperkalemia due to potassium retention is ultimately aimed at inducing potassium loss (1). In some cases, the primary problem is movement of potassium out of the cells, even though the total body potassium may be reduced. Redistributive hyperkalemia most commonly occurs in uncontrolled

hyperglycemia (eg, diabetic ketoacidosis or hyperosmolar hyperglycemic state). In these disorders, hyperosmolality and insulin deficiency are primarily responsible for the transcellular shift of potassium from the cells into the extracellular fluid, which can be reversed by the administration of fluids and insulin. Many of these patients have a significant deficit in whole body potassium and must be monitored carefully for the development of hypokalemia during therapy (2).

Elevated serum potassium level above the upper limit of normal is a common electrolyte imbalance in adults that might be a life-threatening condition causing lethal cardiac arrhythmias; thereby, this condition requires immediate management. The incidence rates of hyperkalemia vary among studies, with estimates ranging between 1.1 and 10% among hospitalized patients. Emergency department (ED)-based studies reported incidence rates between 0.36 and 3.6% of hyperkalemia. The development of new oral therapies for hyperkalemia has led to renewed interest in hyperkalemia. Also, the increased use of hyperkalemia-inducing drugs, such as antihypertensive drugs including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin-receptor blockers (ARBs), and beta-blockers, as well as spironolactone has led to increasing the incidence rates of hyperkalemia among ED patients. Besides, as more patients live with chronic kidney disease, renal failure, hemodialysis, and congestive heart failure (CHF), hyperkalemia cases will trend to increase (3).

The recognition of patients with hyperkalemia in ED is challenging. Even though severe hyperkalemia might be associated with cardiac arrest or muscle paralysis, the symptoms in most hyperkalemia cases are non-specific. These symptoms may include chest pain, palpitations, weakness, muscle spasm, numbness, tingling, trouble breathing, dysphagia, abdominal pain, fatigue, nausea, or vomiting. Also, the physical findings of absent or depressed deep reflexes, hypotension, or dysrhythmia are not specific for hyperkalemia diagnosis. Thus, history and physical examination in patients with high potassium levels could not be enough to diagnose hyperkalemia, and the initiation of appropriate treatment for hyperkalemia might be delayed due to the non-specificity of presentation (4).

Pathophysiology

Potassium is the primary intracellular cation; 95-98% of the total body potassium is found in the intracellular space, primarily in muscle. Total body potassium stores amount to approximately 50 mEq/kg (3500 mEq in a 70-kg person) (5). Normal homeostatic mechanisms precisely maintain the serum potassium level within a narrow range (3.5-5.0 mEq/L). The primary mechanisms for maintaining this balance are the buffering of extracellular potassium against a large intracellular potassium pool (via the sodium-potassium pump), which provides minute-to-minute control, and urinary excretion of potassium, which determines total body potassium balance (6). Potassium is obtained through the diet. Common potassium-rich foods include meats, beans, tomatoes, potatoes, and fruits such as bananas. Gastrointestinal (GI) absorption is complete, resulting in daily excess intake of about 1 mEq/kg (60-100 mEq) (7).

Under normal conditions, approximately 90% of potassium excretion occurs in the urine, with less than 10% excreted through sweat or stool. Within the

kidneys, potassium excretion occurs mostly in the principal cells of the cortical collecting duct (CCD). Urinary potassium excretion depends on adequate luminal sodium delivery to the distal convoluted tubule (DCT) and the CCD, as well as the effect of aldosterone and other adrenal corticosteroids with mineralocorticoid activity (8).

Etiology

Hyperkalemia can result from increased potassium intake, decreased potassium excretion, or a shift of potassium from the intracellular to the extracellular space. The most common causes involve decreased excretion. Alone, excessive intake or an extracellular shift is distinctly uncommon. Often, several disorders are present simultaneously (5).

Increased potassium intake

Alone, increased intake of potassium is a rare cause of hyperkalemia, because the mechanisms for renal excretion and intracellular disposition are very efficient. In general, a relatively high potassium intake contributes to hyperkalemia in individuals who have impaired renal excretion or intracellular-to-extracellular shift (2).

Decreased potassium excretion

Almost all patients who present with persistent hyperkalemia have impaired renal excretion of potassium. Mild degrees of renal failure generally do not result in resting hyperkalemia, because of compensation by adaptive mechanisms in the kidneys and GI tract. However, once the GFR falls below 15-20 mL/min, significant hyperkalemia can occur, even in the absence of an abnormally large potassium load. The simple lack of nephron mass prevents normal potassium homeostasis (9). Other mechanisms, such as drug effects or renal tubular acidosis, can decrease renal potassium excretion and cause hyperkalemia even in individuals with normal or only mildly decreased kidney function. Two other causes of decreased excretion of potassium are reduced distal sodium delivery and reduced tubular fluid flow rate (8).

History

Many individuals with hyperkalemia are asymptomatic. When present, the symptoms of hyperkalemia are nonspecific and predominantly related to muscular or cardiac function. The most common complaints are weakness and fatigue. Occasionally, a patient may complain of frank muscle paralysis or shortness of breath. Patients also may complain of palpitations or chest pain. Patients may report nausea, vomiting, and paresthesias. The history is most valuable in identifying conditions that may predispose to hyperkalemia (10).

When hyperkalemia is discovered, investigate potential pathophysiologic mechanisms. For excessive potassium intake, query patients about the following: Eating disorders - Very unusual diets consisting almost exclusively of high-potassium foods, such as fruits (eg, bananas, oranges, or melons), dried fruits,

raisins, fruit juices, nuts, and vegetables with little to no sodium, heart-healthy diets - Very low–sodium and high-potassium diets recommended for patients with cardiac disease, hypertension, and diabetes mellitus and use of potassium supplements in over-the-counter herbal supplements, sports drinks, dietary supplements such as noni (*Morinda citrifolia*) juice, salt substitutes, or prescribed pharmacologic agents (8).

Physical Examination

In patients with hyperkalemia, vital signs generally are normal. Nonspecific findings can include muscle weakness, fatigue, and depression. Occasionally, cardiac examination may reveal extrasystoles, pauses, or bradycardia resulting from heart block or tachypnea resulting from respiratory muscle weakness. Skeletal muscle weakness and flaccid paralysis may be present, along with depressed or absent deep tendon reflexes. Patients with ileus may have hypoactive or absent bowel sounds (2).

In general, the results of the physical examination alone do not alert the physician to the diagnosis, except when severe bradycardia is present or muscle tenderness accompanies muscle weakness, suggesting rhabdomyolysis. However, when hyperkalemia has been recognized, evaluation of vital signs is essential for determining hemodynamic stability and identifying the presence of cardiac arrhythmias related to the hyperkalemia (9).

Electrocardiography

ECG is vital for assessing the physiologic significance of hyperkalemia. ECG findings generally correlate with the potassium level, but potentially life-threatening arrhythmias can occur without warning at almost any level of hyperkalemia. In patients with organic heart disease and an abnormal baseline ECG, bradycardia may be the only new ECG abnormality (3). ECG changes have a sequential progression, which roughly correlate with the potassium level. Early changes of hyperkalemia include tall, peaked T waves with a narrow base, best seen in precordial leads; shortened QT interval; and ST-segment depression. These changes are typically seen at a serum potassium level of 5.5-6.5 mEq/L (1). The electrocardiogram (ECG) is an inexpensive, non-invasive, highly compliant, broadly available, and readily accessible test. Theoretically, abnormally elevated serum potassium levels above 6.0mmol/L may be associated with apparent changes in ECG, including peaked T waves, prolonged intraventricular and atrioventricular conductions, the disappearance of the P waves, QRS prolongation, depression, and obliteration of the ST segments, and shortening of QT corrected (QTc) interval (8).

Thus, ECG was suggested by some clinicians and researchers as a good indicator of hyperkalemia, especially in critical situations and among unstable patients. Also, it has been reported that the ECG changes became more evident with severely increased serum potassium levels, and a better prediction of hyperkalemia using ECG was noted as the hyperkalemia severity increases. The reliability of ECG changes in diagnosing hyperkalemia is clinically unclear. There is no clear evidence to demonstrate high sensitivity or specificity of the ECG

changes in predicting severe hyperkalemia incidents with more than 6.0 mmol/L potassium levels. Moreover, ECG changes could hardly be observed when the concentrations of serum potassium levels are slightly elevated above the normal level (5).

A previous experiment conducted by Porter et al. and aimed to predict hyperkalemia in dogs using ECG parameters incorporated with an artificial neural network. This neural network had a high sensitivity (89%), specificity (77%), and accuracy (86%) with a positive likelihood ratio of 3.9. However, these results have not been reproduced in human clinical settings. Multiple investigators extensively studied the ECG alterations suggestive of hyperkalemia clinically and indicated that ECG findings were variable, unreliable, and had poor sensitivity clinically (6). Wrenn et al., (11) in their retrospective study, asked two independent emergency physicians to predict the presence or absence of hyperkalemia and its severity based on the interpretation of ECGs solely. They were blinded to the laboratory serum potassium values, patients' clinical diagnoses, and each other's reading. Their sensitivities in the ECG diagnosis of hyperkalemia were low to be estimated as 34 to 43%. While the specificities were higher and ranged between 85 and 86%, with a high degree (90%) of agreement between the readers

Interestingly, Wrenn et al. observed improvements in the readers' sensitivities to become between 55 and 62% when the readers were limited to interpret ECGs with serum potassium levels of more than 6.5 mmol/L. Thus, most missed hyperkalemia diagnoses occurred with serum potassium levels lower than 6.5mmol/L. Also, the authors suggested that hyperkalemia management in the ED could be initiated solely based on ECG abnormalities in unstable patients, while it could be delayed among stable patients until laboratory confirmation of high potassium levels (3).

Although the recommendations of immediate therapy for any patient with high serum potassium level and the initial management of hyperkalemia involves few maneuvers, previous studies reported an average delay of 2 h before initiation of treatment of severe hyperkalemia. Given these uncertainties and the necessity for rapid management of hyperkalemia to decrease its life-threatening associated risks, it is crucial to understand the fastest diagnostic tool for hyperkalemia (8). It was hypothesized that clinical and ECG findings would be associated with early diagnosis and initiation of hyperkalemia management. Thus, the primary goal of this study was to describe the presenting symptoms, clinical features, and initial ECG parameters associated with laboratory diagnosis of hyperkalemia among ED patients. Also, we investigated the ability of two experienced independent physicians to predict hyperkalemia based on initial ECG alterations and presenting symptoms. Thus, investigating the ECG alterations suggestive of hyperkalemia and clinical presentation as a possible screening tool for the purpose of early diagnosis and management of hyperkalemia. Besides, we aimed to identify the determinants of time from triage to the initiation of hyperkalemia management in ED (4).

Hyperkalemia is a common electrolyte imbalance in adults with a potentially peri-arrest risk, but of reversible possibility when diagnosed and managed in time. This study highlights the challenges associated with the diagnosis and

management of hyperkalemia. Hyperkalemic patients in our study tend to be older adults and elderly and suffer from several comorbidities, such as HTN, DM, and chronic kidney disease. Besides, drugs inducing hyperkalemia were common, including analgesics, beta-blockers, CCBs, ACEIs, and ARBs (8).

Given the non-specific clinical presentations of hyperkalemia, and about one-quarter of our patients were asymptomatic, it was evaluated ECG as an attainable test to raise the possibility of hyperkalemia. The results indicated a poor sensitivity of initial ECG and presenting symptoms in detecting hyperkalemia as it ranged between 0.28 and 0.36 and improved minimally when potassium ≥6.5 mmol/L with peaked T wave was significantly more observed than in mild and moderate hyperkalemia. Thus, the absence of ECG alterations suggestive of hyperkalemia should not lower the physician's suspicion of the presence of hyperkalemia in high-risk patients. Also, a mean delay of 1 h from triage to initial hyperkalemia treatment was observed, which is an alarming finding (7).

ECGs had abnormalities consistent with hyperkalemia among around two third of the studied patients with hyperkalemia, and the most common alterations were elevations of T wave amplitude and QRS duration. As well, increased PR interval and QRS duration and presence of peaked T wave were correlated with serum potassium levels. These findings align with previous reports of a higher frequency of ECG alterations suggestive of hyperkalemia with elevated serum potassium levels. Trail has found that ECG disturbances, including peaked T waves and an increase in the duration of the QRS complex, were associated with hyperkalemia and more evident with a serum potassium level of ≥7.8 mEq/L (1).

T wave in ECG occurs due to repolarization of ventricles, whereas QRS duration represents the time for ventricular depolarization, and PR interval represents the time between atrial depolarization and ventricular depolarization. Hyperkalemia causes an increase in the velocity of phase 3 of the action potential, which is associated with the peaking of the T wave. Also, hyperkalemia causes a decrease in the resting membrane potential of myocardial cells with less negativity which causes conduction defects and prolongation of the PR intervals and QRS complexes

Varga et al., (12) reported the QRS widening, peaked T waves, first-degree heart block, and bradycardia as the most frequent ECG alterations suggestive of hyperkalemia in severely hyperkalemic patients with serum potassium levels of >7 mmol/L (31.6%, 18.4%, 18.4%, 18.4%, respectively). These ECG alterations were significantly more common among severely hyperkalemic patients than in normokalemia patients (8.2, 4.7, 7.1, and 6.5%, respectively). Hicks, in his case report, assessed hyperkalemia-associated ECG findings in a 34-year-old female with DM, abnormal cardiac rhythm, and no known history of renal failure presented to the ED. The most significant findings were peaked T waves and widening QRS complex with a potassium level of 7.6 mmol/L. Peaked T waves could be considered one of the typical and earliest ECG signs of elevated serum potassium levels (7).

Other ECG alterations suggestive of hyperkalemia in our study included flattening and disappearance of P waves, RBBB, and ST elevations were observed. Similarly,

in a clinical review, a woman presented to the ED with respiratory distress and altered mental status and had an elevated serum potassium level of 9.6 mmol/L; her ECG recorded ST elevations, RBBB, and loss of P wave amplitude. ST segment is the state of the ventricles between repolarization and depolarization. ST elevation had been previously linked to hyperkalemia and called “pseudo-infarction”; therefore, hyperkalemia is a potential differential diagnosis for the cause of elevations in the ST segments. However, the mechanism of ST segment elevation due to hyperkalemia is not already known. Also, ST depression and shortening of the QTc interval had been reported in several investigations as manifestations of hyperkalemia (5).

Most studies suggested an association between lower potassium levels and a higher risk of atrial fibrillation. However, it was reported that atrial fibrillation as the most common arrhythmia observed among hyperkalemic patients. This finding is concordant with Varga et al.’s findings that aThe trail fibrillation was more prevalent in severely hyperkalemic patients than normokalemia patients. they attribute these results to the synergistic effect of CHF and CKD, which often present in patients with high serum potassium levels. Hyperkalemia and CHF are common in chronic kidney disease, and CHF could cause atrial fibrillation. Thus, atrial fibrillation occurs not as the result of hyperkalemia but rather as the consequence of illnesses often associated with hyperkalemia (6).

ECG is an inexpensive, broadly available, and easily attainable test. There have been conflicting reports about its sensitivity and specificity to capture elevated serum potassium levels. It was found tha poor sensitivity of initial ECG and clinical presentation in detecting hyperkalemia as ranged between 0.28 and 0.36. These results are concordant with previous studies showing that physicians’ ability to predict hyperkalemia from the ECG was low with sensitivities between 0.43 and 0.34, and experienced readers’ ability to predict the severity of hyperkalemia was likewise poor. Similarly, Rafique et al. reported a mean sensitivity of 0.19 (± 0.16) for the emergency physicians detecting hyperkalemia based on the ECG, and this sensitivity improved to 0.29 (± 0.20) in severe hyperkalemia (1).

Varga et al., (12) captured ECG alterations suggestive of hyperkalemia among 46% of the hyperkalemic patients, and surprisingly 24% of normokalemia patients exhibited such ECG alterations. Thus, based on ECG analysis and with or without presenting symptoms knowledge, the physician could not confirm or exclude hyperkalemia, and serum laboratory tests should be conducted for accurate hyperkalemia diagnosis. Montague et al. had conducted a study on ninety patients diagnosed with hyperkalemia as serum potassium of ≥6 mmol/L.

The authors reported that the probability of ECG changes increased with increasing potassium levels, but the sensitivity and specificity of ECG changes in diagnosing hyperkalemia were poor. It could be concluded that the management of hyperkalemia should be guided by the clinical scenario and serial laboratory potassium measurements, and the absence of ECG alterations suggestive of hyperkalemia should not lower the physician’s concern for the presence of hyperkalemia in high-risk patients (6).

Although the lack of sensitivity in detecting hyperkalemia based on ECGs ultimately depends on physicians' interpretations, other confounding factors could not be excluded. First, the possible effects of other electrolytes, such as calcium and magnesium, in mitigating the ECG changes suggestive of hyperkalemia as proposed by prior investigators. Second, 64% of our patients suffered from CKD, and about one third of participants were on regular dialysis, which could cause the non-specificity of ECG abnormalities (10).

It was reported that hemodialysis patients with hyperkalemia were less likely to show ECG changes despite the risk of suddenly developing arrhythmias as the myocytes were less sensitive to electrolyte changes in these patients; therefore, hyperkalemia did not manifest in them its typical forms. Third, the rate of increase in serum potassium levels could affect the development of ECG changes. As the velocity of serum potassium concentrations risen was unknown to the readers, their insensitivity could be attributed to the slowly rising potassium levels, especially in the setting of CKD. Fourth, patients' medications such as digitalis could have interacted with the effects of electrolytes on myocytes and masked the effects of hyperkalemia. Lastly, metabolic acidosis and ischemia could be associated with arrhythmias and ST and T wave alterations in the patterns suggestive of hyperkalemia (3).

Although including serum markers of cardiac ischemic injury and ABGs for acidosis detection, the absence of abnormalities in these serum markers does not exclude them as confounding factors. There is also the potential that elevated serum potassium levels may potentiate arrhythmias that could be attributable to other causes. However, these possibilities could not be ruled out as they are part of clinical practice (2).

One of our most striking findings was that the meantime from triage to initial hyperkalemia treatment of more than one hour. Freeman et al. investigated the possible effects of presentations and ECGs on triage time to the initial hyperkalemia management. The authors found that most hyperkalemic patients waited for a median of 2 h from triage to initial treatment, even though ECG was performed before the laboratory serum potassium measurement. Also, the delay in hyperkalemia treatment was reported among hospitalized patients, with approximately 2 h delays from laboratory notification of potassium to initiation of treatment (4).

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