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**Case Report**

# Refractory hypokalemia: a case report

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## ABSTRACT

Hypokalemia is a common electrolyte disturbance in hospitalized patients, which prompts appropriate identification of hypokalemia symptoms and signs. As many as 20% of hospitalized patients are found to have hypokalemia. Many hypokalemia patients could also have systemic disease. A 55-year-old woman was presented with weakness, nausea, and vomiting for 2 days before admission. Vomit consisted of water; there was no blood in the vomit. Defecation was normal; consistency and odor of feces were normal. Patient had diabetes and was already on insulin regiment. Insulin was discontinued during hospitalization since blood sugar was close to lower limit. Electrocardiography (ECG) was within normal limit. Symptoms and signs of hypokalemia may not be readily apparent, as seen in this case. Treatment of hypokalemia should intend not to only replenish potassium, but also to identify underlying cause. Causes include gastrointestinal losses, intracellular shift, renal potassium losses, and inadequate intake.

**Keywords:** Hypokalemia, Potassium, Electrolyte disturbance

## INTRODUCTION

Hypokalemia is a condition where serum potassium level falls below normal (<3.5 mEq/l). It is a common electrolyte disturbance in hospitalized patients. As many as 20% of hospitalized patients are found to have hypokalemia. Approximately 80% of patients who receive diuretics become hypokalemic, whereas many hypokalemia patients could also have systemic disease.[1] Sometimes hypokalemia requires immediate medical care, especially when severe hypokalemia is present. Severe hypokalemia is defined when serum potassium level falls below 2.5 mEq/l.

Signs and symptoms of hypokalemia tends to be proportional to the degree and duration of serum potassium reduction. Symptoms usually don't appear until serum potassium level is below 3.0 mEq/l, unless serum potassium level falls rapidly or the patient has potentiating factor (such as use of digitalis, in which the patient has predisposition to arrhythmia). Symptoms can vary from absent to lethal arrhythmias. Hypokalemia symptoms can be categorized according to affected organ systems, as shown in below.[1]

Further investigation of a suspected hypokalemia patient includes laboratory panel; which comprises of serum sodium, potassium, chloride, glucose, urea, and creatinine. As difference between serum potassium level in arterial and vein blood sample isn't clinically significant, measurement of potassium level in vein blood sample isn't contraindicated. Serum digoxin level should be measured if patient is on digitalis.[1]

Tests and imaging of endocrine glands are relevant, but these should not be first line tests unless clinical index suspicion of such disorder is high. Computerized tomography (CT) or magnetic resonance imaging (MRI) may be done if there is suspicion of mineralocorticoid, glucocorticoid, or cathecholamine excess. MRI of pituitary gland is useful to diagnose Cushing's disease.[1]

Electrocardiography (ECG) is recommended for all hypokalemia patients. ECG findings may include ST

segment suppression, T wave amplitude decrease, and U wave amplitude increase. Various arrhythmias may be associated with hypokalemia, which include sinus bradycardia, premature atrial contraction (PAC), premature ventricular contraction (PVC), paroxysmal atrial tachycardia, paroxysmal junctional tachycardia, atrioventricular (AV) block, ventricular tachycardia (VT), and ventricular fibrillation (VF).[2]

Underlying cause of hypokalemia is usually evident after a careful history taking and physical examination. Hypokalemia usually results from increased potassium excretion through urine or gastrointestinal tract.[3] Reduced potassium intake could also cause hypokalemia, although it is less common. Reduced potassium intake is seen in the case of starvation, dementia, or anorexia.[4] Excessive potassium excretion through urine (kaliuresis) may result from use of drugs, endocrine disease (such as primary hyperaldosteronism), kidney disorders, or genetic diseases.[5] Common drugs which can induce hypokalemia include diuretics and penicillin.[6] Loop or thiazide diuretic therapy is associated with hypokalemia.[1] Congenital adrenal hyperplasia is an example of genetic disease which causes excessive mineralocorticoid secretion, resulting in hypokalemia. Gastrointestinal loss of potassium can be caused by prolonged diarrhea, chronic laxative use, intestinal obstruction or infections.

Other hypokalemia cause includes intracellular shift. It is commonly caused by insulin administration, sympathetic nervous system stimulation, thyrotoxicosis, and familial periodic paralysis.[1,7] Intracellular shift causes transient hypokalemia.[4]

**Table 1: Symptoms and signs of hypokalemia.[1]**

| Hypokalemia | Symptoms and signs |
|---|---|
| **Mild to moderate hypokalemia** | Asymptomatic or with mild symptomatology, especially in elderly people or in people suffering from heart or kidney disease |
| **Severe hypokalemia** | Renal system: metabolic acidosis; rhabdomyolysis; hypokalemic kidney disease (tubular interstitial nephritis, nephrogenic diabetes insipidus) |
| | Nervous system: leg cramps; weakness and paralysis; ascending paralysis |
| | Gastrointestinal system: constipation or intestinal paralysis |
| | Respiratory system: respiratory failure |
| | Cardiovascular system: ECG changes (U waves, T waves flattening, ST segment changes); cardiac arrhythmias; heart failure |

**Table 2: Causes of hypokalemia.[1]**

| Parameters | Causes |
|---|---|
| **Gastrointestinal tract losses** | Chronic diarrhea, including chronic laxative abuse and bowel diversion; clay (bentonite) ingestion, which binds potassium and greatly decreases absorption; villous adenoma of the colon, which causes massive potassium secretion (rarely) |
| **Intracellular shift** | Glycogenesis during total parenteral nutrition of enteral hyperalimentation (stimulating insulin release); insulin administration; stimulation of the symphatetic nervous system, particularly with beta-2 agonists (albuterol, terbutaline); thyrotoxicosis (occasionally) due to excessive beta symphatetic stimulation (hypokalemic thyrotoxic periodic paralysis); familial periodic paralysis |
| **Renal potassium losses** | Adrenal steroid excess (Cushing's syndrome); primary hyperaldosteronism; rare renin secreting tumors; glucocorticoid remediable congenital adrenal hyperplasia; ingestion of substances such as glycyrrhizin; Bartter syndrome; Gitelman syndrome; Liddle syndrome; renal tubular acidosis; Fanconi syndrome; hypomagnesemia |
| **Drugs** | Thiazides; loop diuretics; osmotic diuretics; laxatives; amphotericin B; antipseudomonal penicillins (carbencillin); penicillin in high doses; theophylline (both acute and chronic intoxication) |

## CASE REPORT

A 55-year-old woman was presented with weakness, nausea, and vomiting for 2 days before admission. Vomit consisted of water, and a little food. She had decreased appetite. There was no blood in the vomit. Defecation was normal, once every 2 days. Consistency and odor of feces were normal. The feces didn't contain any mucus or blood. Urine color was light yellow with normal urine volume, and there was no pain during urination.

She was hospitalized 3 weeks before admission, with diabetic foot on both right and left side. Debridement was done on both sides, and the right foot underwent amputation on 2nd and 4th finger. Blood test showed anemia, and 3 units of packed red blood cells were given. Albumin was decreased; albumin infusion and tablet were given as treatments.

Patient had a long history of diabetes mellitus for 10 years. Insulin was given to treat the condition; oral diabetic

agents were no longer given. Patient also had hypertension, but didn't take daily medication.

During admission, she was fully conscious without any neurological disturbance. Initial vital signs revealed blood pressure of 131/71 mmHg, heart rate 80 beats/ minute, respiratory rate 20 breaths/ minute, and body temperature of 36ºC.

Both conjuctiva appeared pale. Sclera wasn't icteric. There wasn't lymph node enlargement at facial, coli, supraclavicular, and axillary areas. Physical examination of lung, heart, and abdomen was not remarkable. No edema was found on the extremity. Right and left feet were covered in gauze. Wound care was adequate; no blood, pus, or foul odor was found.

Initial laboratory test showed leucocytosis with neutrophil predominance, anemia, hyponatremia, hypokalemia, and hypochloremia. ECG was within normal limit. Initial laboratory test result can be seen in Table 3.

Based on history taking, physical examination, and initial laboratory test, patient was given intravenous levofloxacin 1×750 mg, intravenous NaCl 3% (12 drops per minute), and intravenous KCl 50 mEq in 500 ml NaCl 0.9% (20 drops per minute). Oral lisinopril 1×10 mg was given to treat hypertension. Other medications include intravenous omeprazole 2×40 mg and intravenous ondansetron 3×4 mg to treat nausea and vomiting. Vomiting stopped after omeprazole and ondansetron administration, although nausea persisted. Transfusion was ordered to treat anemia. 1 unit of packed red blood cells was given.

Patient was on insulin treatment during admission (10 units of basal insulin daily and 10 units of bolus insulin with every meal). However, both insulins were stopped during hospitalization because blood sugar was close to lower limit. No hyperglycemia was found, despite discontinuation of insulin.

**Table 3: Initial laboratory test result.**

| Lab tests | Findings |
|---|---|
| **Complete blood count** | |
| Erythrocyte count ($10^6$/µl) | 3.49 |
| Hb (g/dl) | 9.4 |
| Hct (%) | 28.0 |
| MCV (fL) | 80.2 |
| MCH (pg) | 26.9 |
| MCHC (g/l) | 33.6 |
| Leucocyte count ($10^3$/µl) | 16.59 |
| Neutrophil (%) | 79.1 |
| Lymphocyte (%) | 9.2 |
| Monocyte (%) | 11.1 |
| Eosinophil (%) | 0.3 |
| Basophil (%) | 0.3 |
| Platelet count ($10^3$/µl) | 413 |
| **Blood chemistry** | |
| Random blood sugar (mg/dl) | 85 |
| Urea (mg/dl) | 14 |
| Creatinine (mg/dl) | 1.2 |
| **Electrolyte** | |
| Natrium (mEq/l) | 120 |
| Kalium (mEq/l) | 2.5 |
| Chloride (mEq/l) | 70 |

Patient was febrile (38.3ºC) on the 3rd day of hospitalization. Intravenous paracetamol 3×500 mg and intravenous metronidazole 3×500 mg were given. Albumin was checked on the 3rd day, result indicated hypoalbuminemia and patient was given intravenous albumin 25% and oral albumin.

Fever resolved quickly after intravenous paracetamol administration, but came back after a few hours. This continued until 5th day, which prompts additional laboratory tests. Result of these additional tests can be seen in Table 4.

**Table 4: Additional laboratory test result.**

| Lab tests | Findings |
|---|---|
| **Complete blood count** | |
| Erythrocyte count ($10^6$/µl) | 8.77 |
| Hb (g/dl) | 10.2 |
| Hct (%) | 30.6 |
| MCV (fL) | 83.6 |
| MCH (pg) | 27.9 |
| MCHC (g/l) | 33.3 |
| Leucocyte count ($10^3$/µl) | 8.77 |
| Neutrophil (%) | 67.0 |
| Lymphocyte (%) | 18.4 |
| Monocyte (%) | 11.9 |
| Eosinophil (%) | 2.1 |
| Basophil (%) | 0.6 |
| Platelet count ($10^3$/µl) | 385 |

Continued.

| Lab tests | Findings |
|---|---|
| **Urinalysis** | |
| Color | Yellow |
| Clarity | A bit cloudy |
| Specific gravity | <1.005 |
| pH | 7.5 |
| Leucocyte esterase (Leu/µl) | 75 |
| Nitrites | Negative |
| Protein | Negative |
| Glucose | Negative |
| Keton | Negative |
| Urobilinogen | Normal |
| Bilirubin | Negative |
| Blood | Negative |
| RBCs (/hpf) | 0-1 |
| WBCs (/hpf) | 3-4 |
| Casts | Negative |
| Squamous epithelial cells (/lpf) | 1-2 |
| Crystal | Negative |
| Bacteria | (+) |

Culture testing- location: base of wound on right foot, culture result: growth of specific pathogenic bacteria, and bacteria identification: *Serratia liquefaciens*. Sensitivity testing- sensitive: amikacin, piperacilin/tazobactam, trimetrophim/ sulfamethoxazole; intermediate; and resistant: ampicillin, cefazolin, ceftazidime, gentamicin, ciprofloxacin

Culture and sensitivity testing was ordered on 5$^{th}$ day, and result came back on 12$^{th}$ day. Intravenous levofloxacin 1×750 mg (which was given since admission) was switched to oral cotrimoxazole 2×960 mg as sensitivity testing suggested. Cotrimoxazole was given for 5 days.

Intravenous NaCl 3% was stopped on 3rd day as severe hyponatremia had been resolved (126 mEq/l). On the other hand, hypokalemia persisted after 8 rounds of intravenous KCl 50 mEq administration, and KCl was switched to oral preparation (3×600 mg). Electrolyte was checked after 3 days of oral KCl administration. Result indicated severe hypokalemia, and patient was given another 2 rounds of intravenous KCl. After 2 rounds of intravenous KCl, patient's kalium level improved (3.5 mEq/l) and patient was discharged.

## DISCUSSION

Hypokalemia is a common electrolyte disturbance in hospitalized patients. Therefore, it is important to recognize symptoms and signs of hypokalemia appropriately. Symptoms and signs of hypokalemia can be seen in Table 1. Hypokalemia symptoms and signs in this case weren't readily apparent. This poses a challenge to identify hypokalemia patient correctly. Patient had only general weakness. No cramps, paresis, or paralysis were identified. Neurological disturbances were absent. Patient had no episodes of constipation or other suspected intestinal paralysis. Respiratory and cardiovascular findings weren't remarkable. No respiratory failure, ECG changes, arrhythmia, or heart failure were identified.

Treatment of hypokalemia should aim not to only replenish potassium stores, but also to identify underlying cause. Elimination of causative factor is critical in hypokalemia management. This includes discontinuation of laxatives, use of potassium neutral or potassium sparing diuretics, treatment of diarrhea, and control of hyperglycemia.[1] Among hypokalemia causes mentioned in Table 2, hypokalemia in this case report appears to be caused by intracellular shift and reduced potassium intake. Intracellular shift happened with the use of insulin, although insulin was swiftly discontinued because blood sugar was close to lower limit. Decreased insulin clearance may occur in chronic kidney disease patients, but insulin clearance seems to be normal in this case.[7] Patient creatinine level was within normal range. Inadequate intake (including inadequate potassium intake) occurred because patient was nauseous. Inadequate intake was also reflected on blood sugar level, which close to lower limit throughout hospitalization despite insulin discontinuation.

Gastrointestinal loss and renal potassium loss through drugs weren't suggested as hypokalemia since patient didn't have any history of laxative abuse or diuretics use. However, gastrointestinal loss and renal potassium loss may occur in this setting since patient has diabetes. Gastrointestinal tract losses in diabetic patients occur due to malabsorption syndrome (diabetic induced motility disorders and bacterial overgrowth). Chronic diarrheal state in diabetic patients may occur, but diarrheal state wasn't found in this case. Renal potassium losses in diabetic patients occur due to osmotic diuresis.[8]

Other patient's condition that may trigger hypokalemia include urinary tract infection. Patient had fever, and bacteria was identified in patient's urine. A case control study describes that urinary tract infection is associated with hypokalemia among inpatients. The association is independent of patients' medication and comorbidities.[9] Blood transfusion doesn't appear to be cause of hypokalemia since common potassium disturbance that is linked to it is hyperkalemia, and not hypokalemia.[10]

Every 1 mEq/l decrease in serum potassium represents potassium deficit of approximately 200-400 mEq. Patient had potassium level of 2.5 mEq/l during admission, which means patient had potassium deficit of approximately 200-400 mEq. Hypokalemia persisted after 8 rounds of intravenous KCl 50 mEq administration and 3 days of oral KCl (3 times a day). Hypokalemia improved with 2 additional rounds of KCl administration.

Patients with potassium levels of 2.5-3.5 mEq/l may only need oral potassium replenishment. Intravenous potassium should be given when potassium falls below 2.5 mEq/l, alongside continuous ECG monitoring and serial potassium level measurements. Normal saline is the preferred infusion fluid, as 5% glucose may cause transcellular shift of potassium into cells. Potassium should be very carefully replaced in patients with renal impairment, and renal team should be contacted. Oral potassium form is taken with plenty of fluid (between 100 and 250 mL of water), and is better taken with or after meals.[1] Severity of hypokalemia dictates whether oral or intravenous potassium should be administered.

## CONCLUSION

We presented a case report of a patient with refractory hypokalemia. Symptoms and signs of hypokalemia may not be readily apparent, as seen in this case. Treatment of hypokalemia should intend not to only replenish potassium, but also to identify underlying cause. Causes include gastrointestinal losses, intracellular shift, renal potassium losses, and inadequate intake. Diabetes mellitus may provoke further potassium loss through gastrointestinal and renal routes.

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