CLINICAL RESEARCH STUDY

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# Etiologic and Therapeutic Analysis in Patients with Hypokalemic Nonperiodic Paralysis

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## ABSTRACT

**BACKGROUND:** Hypokalemic nonperiodic paralysis represents a group of heterogeneous disorders with a large potassium ($K^+$) deficit. Rapid diagnosis of curable causes with appropriate treatment is challenging to avoid the sequelae of hypokalemia. We prospectively analyzed the etiologies and therapeutic characteristics of hypokalemic nonperiodic paralysis.

**METHODS:** Over an 8-year period, patients with hypokalemic nonperiodic paralysis were enrolled by excluding those with hypokalemic periodic paralysis due to acute shift of $K^+$ into cells. Blood and spot urine samples were collected for the measurements of electrolytes, pH, and biochemistries. Intravenous potassium chloride (KCl) at a rate of 10-20 mmol/h was administered until muscle strength recovered.

**RESULTS:** We had identified 58 patients with hypokalemic nonperiodic paralysis from 208 consecutive patients with hypokalemic paralysis, and their average $K^+$ concentration was 1.8 ± 0.2 mmol/L. Among patients with low urinary $K^+$ excretion (n = 17), chronic alcoholism, remote diuretic use, and anorexia/bulimia nervosa were the most common causes. Among patients with high urinary $K^+$ excretion (n = 41) and metabolic acidosis, renal tubular acidosis and chronic toluene abuse were the main causes, while primary aldosteronism, Gitelman syndrome, and diuretics were the leading diagnoses with metabolic alkalosis. The average KCl dose needed to restore muscle strength was 3.8 ± 0.8 mmol/kg. Initial lower plasma $K^+$, volume depletion, and high urinary $K^+$ excretion were associated with higher recovery KCl dosage. During therapy, patients with paradoxical hypokalemia (n = 32) who required more KCl supplementation than patients without (4.1 ± 0.7 vs 3.4 ± 0.7 mmol/kg, $P < 0.001$) often exhibited significantly higher plasma renin activity and received a higher volume of normal saline before its appearance.

**CONCLUSIONS:** Understanding the common etiologies of hypokalemic nonperiodic paralysis may aid in early diagnosis. Patients with initial lower plasma $K^+$, renal $K^+$ wasting, and hypovolemia required higher recovery $K^+$ dosage. Paradoxical hypokalemia is prone to develop in hypovolemic patients even during $K^+$ supplementation with volume repletion.

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**KEYWORDS:** Etiology; Hypokalemia; Paralysis; Treatment

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Hypokalemia is a laboratory finding but can cause morbidity and mortality due to critical complications such as cardiac arrhythmias and respiratory failure.[1,2] In some circumstances, severe hypokalemia can cause neuromuscular paralysis (so-called hypokalemic paralysis), a potentially reversible medical emergency with unique diagnostic

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and therapeutic challenges.[3,4] Based on the pathophysiology, it can be divided into 2 groups: hypokalemic periodic paralysis due to an acute shift of potassium ($K^+$) into cells, and hypokalemic nonperiodic paralysis resulting from a large deficit of $K^+$.[5,6] Due to often indistinguishable clinical features, we had shown previously that an assessment of urinary $K^+$ excretion and blood acid-base status coupled with a detailed history and physical examination help separate the 2 groups.[7] Among the etiologies of hypokalemic periodic paralysis, the most common are thyrotoxic periodic paralysis[8-13] and sporadic periodic paralysis[14] in Asia and familial periodic paralysis in Western countries.[15,16] Within hypokalemic nonperiodic paralysis, the etiologies are complex and challenging to the clinician hoping to make an early diagnosis. The correct diagnosis of the underlying hypokalemia avoids recurrence and missing any potentially curable and treatable disorders.

The strategy and dosage of $K^+$ supplementation should be guided by the early and correct diagnosis of hypokalemic nonperiodic paralysis. For patients with hypokalemic periodic paralysis, potassium chloride (KCl) should be infused intravenously to quickly reverse hypokalemia, but should be minimized to avoid rebound hyperkalemia in the recovery phase. In hypokalemic nonperiodic paralysis patients, intravenous KCl infusion is usually followed by chronic oral KCl tablets to replete the large deficit of total body $K^+$. However, the therapeutic course and factors that influence the effectiveness of $K^+$ supplementation in patients with hypokalemic nonperiodic paralysis have not been well characterized. In this study, we analyzed the etiologies and therapeutic courses of 58 consecutive patients with hypokalemic nonperiodic paralysis over an 8-year span at a single medical center to improve our ability to diagnose and optimize treatment for these critical patients.

**CLINICAL SIGNIFICANCE**

- Approximately 25% of cases of hypokalemic paralysis were secondary to hypokalemic nonperiodic paralysis with chronic alcoholism, recent/remote diuretic use, anorexia/bulimia nervosa, renal tubular acidosis, primary aldosteronism, and Gitelman syndrome being the most common.
- Hypokalemic patients with initial lower plasma potassium ($K^+$), volume depletion, and renal $K^+$ wasting required much higher recovery $K^+$ dosage.
- Hypokalemic patients with hypovolemia are often prone to develop paradoxical hypokalemia during $K^+$ supplementation with aggressive volume repletion.

## MATERIALS AND METHODS

### Study Subjects

The study protocol was approved by the Ethics Committee on Human Studies at Tri-Service General Hospital. As part of this study, the history, urine and plasma samples, and hospital course of patients admitted with hypokalemia (plasma $K^+$ level $<3.5$ mmol/L) and muscle paralysis (Medical Research Council grade $\leq 3$) have been collected prospectively from January 2005 through December 2012. Patients who had had previous hypokalemic attacks or currently were receiving KCl treatment or been diagnosed as hypokalemic periodic paralysis were excluded.

### Definitions

Hypokalemic periodic paralysis was diagnosed by acute muscle weakness with inability to ambulate accompanied by hypokalemia, low urinary $K^+$ excretion, and the presence of thyrotoxic periodic paralysis, familial periodic paralysis, or sporadic periodic paralysis. The rest were hypokalemic nonperiodic paralysis, which is a more appropriate term than non-hypokalemic periodic paralysis published previously. We distinguish hypokalemic periodic paralysis from hypokalemic nonperiodic paralysis based on history such as a positive family history, clinical course, urinary $K^+$ excretion, and acid-base status.[7]

## METHODS

All patients received a standard 12-lead electrocardiogram. Blood pressure and electrocardiogram monitoring were recorded. Muscle strength graded on a 5-point scale, venous blood and spot urine samples were obtained at the first visit in the emergency department, and then every 1-2 hours before recovery. Blood gases were measured by ABL 510 (Radiometer, Copenhagen, Denmark). Plasma and urine biochemical studies were determined by automated methods (AU 5000 chemistry analyzer; Olympus, Tokyo, Japan) and supine plasma renin activity and aldosterone level were also measured.

Intravenous KCl supplementation was initiated at a rate of 10-20 mmol/h, but infused rate could be increased to 30 mmol/h through a central venous catheter if the patient developed ventricular arrhythmias, respiratory failures, or a fall in plasma $K^+$ concentration during therapy. The rate of KCl supplementation was lowered to $<10$ mmol/h when muscle strength recovered enough for the patient to ambulate. Patients with coexisting hypomagnesemia received intravenous elemental magnesium 400-600 mg. The total amount of KCl administered up to the time of recovery was recorded. The recovery time was defined as the time period from the start of KCl therapy to the recovery of muscle strength. Nadir plasma $K^+$ was the lowest plasma $K^+$ concentration during KCl therapy. Paradoxical hypokalemia was defined as a fall of plasma $K^+$ concentration $\geq 0.1$ mmol/L during KCl therapy.[17]

### Statistical Analysis

Results are expressed as mean $\pm$ standard deviation. The nonparametric Mann-Whitney *U* rank-sum test was used for continuous data to compare the differences in variables between 2 subgroups were not distributed normally.