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Original Research Article

A Hospital Based Clinical-Etiological Spectrum of Hypokalaemia Periodic Paralysis

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Abstract

Aim: To determine the etiological spectrum of hypokalaemia periodic paralysis.

Material and methods: This study was conducted in the department of Medicine, JNKTMCH, Madhepura, Bihar, India for one year. All patients admitted in the neurology ward with acute flaccid paralysis with hypokalaemia (serum potassium <3.5) involving two or more limbs without sphincter and sensory disturbances were included in the study. Medical history, previous episodes of similar weakness, hyperthyroidism, diarrhoea, vomiting, renal disease, and drug intake were noted. Any history of similar illness in the family and precipitating factors were enquired about and noted.

Results: Off these patients, 15 (83.33%) patients had primary HPP, while three (16.67%) cases had secondary HPP [2/3 with thyrotoxic periodic paralysis and 1/3 cases was secondary to gastroenteritis. The reduction in serum potassium was moderate (2.5-3.5 mmol/L) in primary and severe (<2.5 mmol/L) in secondary HPP. Those with quadriparesis had severe hypokalaemia with a mean serum potassium of 2.1 mmol/L. Concomitant magnesium deficiency was observed in 3/18 (17%) patients. These patients were treated with intravenous potassium replacement with dramatic recovery. The mean recovery time was 38.6±20.3 hours. Recovery time in patients with quadriparesis was about 24 hours and in those with paraparesis was around 12 hours. Only one patient with thyrotoxic periodic paralysis (TPP) and with severe serum potassium deficiency (0.9 meq/L) died due to cardiac arrhythmia. No atypical presentation was seen in the present study.

Conclusion: Hypokalaemia paralysis should always be kept in mind when making a differential diagnosis for acute flaccid paralysis. In all patients, serum electrolytes panel, ECG, and thyroid profile should be done at admission in the intensive care unit (ICU).

Keywords: hypokalaemia periodic paralysis, hypokalaemia paralysis,

Introduction

Hypokalaemia periodic paralysis (HPP) is a rare neuromuscular disorder characterized by episodic muscle weakness associated with a decrease in serum potassium levels. The aetiology of HPP is diverse, encompassing genetic mutations, endocrine disorders, and various other conditions. Understanding the etiological spectrum of HPP is crucial for accurate diagnosis, effective management, and the prevention of recurrent episodes. The primary aetiology of HPP is often genetic, with mutations in specific ion channels. Mutations in the CACNA1S gene, which encodes the alpha-1 subunit of the dihydropyridine-sensitive calcium channel, and the SCN4A gene, encoding the alpha subunit of the sodium channel, are the most common genetic causes. These mutations lead to impaired ion transport, resulting in muscle cell depolarization and subsequent weakness [1,2]. Genetic HPP typically manifests in the second decade of life and follows an autosomal dominant inheritance pattern. Secondary HPP can be caused by endocrine disorders such as thyrotoxicosis, where increased thyroid hormone levels enhance the activity of the sodium-potassium ATPase pump, leading to an intracellular shift of potassium and hypokalaemia. Thyrotoxic periodic paralysis (TPP) is most commonly observed in Asian males and presents with acute episodes of muscle weakness similar to primary HPP [3]. Additionally, conditions like hyperaldosteronism, characterized by excessive aldosterone production, can cause renal potassium wasting and lead to HPP [4]. Hypokalaemia in HPP

can also result from gastrointestinal or renal losses. Gastrointestinal causes include chronic diarrhoea and vomiting, which deplete body potassium stores. Renal causes encompass conditions like Bartter syndrome and Gitelman syndrome, which are inherited disorders of the renal tubules leading to excessive urinary potassium excretion [5]. These conditions often require a detailed history and laboratory evaluation for diagnosis. Certain medications can induce hypokalaemia and trigger HPP episodes. Diuretics, particularly thiazides and loop diuretics, are known to cause significant potassium loss through the urine [6]. Beta-adrenergic agonists, commonly used in asthma treatment, can also shift potassium intracellularly, precipitating hypokalaemia. Recognizing drug-induced hypokalaemia is essential for preventing recurrent HPP episodes through medication adjustments. Other less common causes of HPP include dietary deficiencies, particularly in potassium and magnesium, which are essential for maintaining normal muscle function. Paraneoplastic syndromes, where malignancies produce hormones or other substances affecting potassium metabolism, can also lead to HPP [7-10]. Identifying these rare causes requires a comprehensive diagnostic approach, including imaging and specialized testing.

Material and methods

This study was conducted in the department of Medicine, JNKTMCH, Madhepura, Bihar, India for one year. All patients admitted in the neurology ward with acute flaccid paralysis with hypokalaemia (serum potassium <3.5) involving two or more limbs without sphincter and sensory disturbances were included in the study. Patients with other causes of acute flaccid weakness, e.g. Guillain-Barré Syndrome (GBS), myasthenia crisis, and on diuretic therapy were precluded from the study. Medical history, previous episodes of similar weakness, hyperthyroidism, diarrhoea, vomiting, renal disease, and drug intake were noted. Any history of similar illness in the family and precipitating factors were enquired about and noted. Complete neurological examination scores including muscle tone, assessment of power using Medical Research Council (MRC) scale, and deep tendon reflexes were noted. Any atypical presentation was also noted, e.g. facial, bulbar, or respiratory muscle involvement. Labs including complete blood count (CBC), serum potassium, serum sodium, serum calcium, serum bicarbonate, thyroid profile (T3, T4, thyroid-stimulating hormone (TSH)), and electrocardiogram (ECG) were obtained on the day of admission. All patients were treated with potassium supplements—oral (500 mg at eight-hour intervals) or intravenous (IV) (10 meq/hour) depending upon their serum potassium levels and severity of clinical manifestations (extreme weakness). Patients with idiopathic periodic paralysis were started on acetazolamide (250 mg tid) and the dose was titrated according to the response. Patients were divided into groups: the first group was patients with primary idiopathic hypokalemic periodic paralysis and the second group was patients with secondary hypokalemic periodic paralysis (thyrotoxic periodic paralysis, renal tubular acidosis, and gastroenteritis).

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation. A p-value < 0.05 was considered statistically significant and a p-value < 0.01 was considered statistically highly significant. All statistical analysis was conducted using SPSS Version 20.0 (IBM Corp., Armonk, NY)

Results

We enrolled 18 patients (mean age 35±15) and 14 patients (77.78%) were males, [male: female ratio: 3.5:1]. The mean age of onset of HPP in males was (29.5±10.14 yrs.) as compared to females (41±10.8 yrs); however, this difference was statistically not significant (p<0.066). Off these patients, 15 (83.33%) patients had primary HPP, while three (16.67%) cases had secondary HPP [2/3 with thyrotoxic periodic paralysis and 1/3 cases was secondary to gastroenteritis]. Out of total 18 patients, symmetrical weakness was found in 12 (66.66%) patients with predominance in male patients (five cases of paraparesis and all were male; seven cases of quadriparesis: six males and one female). Six (33.33%) patients had asymmetrical weakness (two paraparesis: one male, one female; four quadriparesis: two males, two females). Statistically, no significant difference (p<0.709) was seen in those with symmetrical vs. asymmetrical weakness. Deep tendon reflexes were absent in seven (38.89%) patients, diminished in one patient (5.55%), and intact in the remaining 10 (55.55%). None of the cases had cranial, bulbar, or respiratory involvement. The mean serum potassium of sample was 3.18±0.5 SD. The reduction in serum potassium was moderate (2.5-3.5 mmol/L) in primary and severe (<2.5 mmol/L) in secondary HPP. Those with quadriparesis had severe hypokalaemia with a mean serum potassium of 2.1 mmol/L. Concomitant magnesium deficiency was observed in 3/18 (17%) patients. These patients were treated with intravenous potassium replacement with dramatic recovery. The mean recovery time was 38.6±20.3 hours. Recovery time in patients with quadriparesis was about 24 hours and in those with paraparesis was around 12 hours. Only one patient with thyrotoxic periodic paralysis (TPP) and with severe serum potassium deficiency (0.9 meq/L) died due to cardiac arrhythmia. No atypical presentation was seen in the present study.

Table 1: Patient Demographics and Characteristics

Parameter	Value
Total Patients Enrolled	18
Mean Age (years)	35 ± 15
Male Patients	14 (77.78%)
Female Patients	4 (22.22%)
Male: Female Ratio	3.5:1
Mean Age of Onset (Males) (years)	29.5 ± 10.14
Mean Age of Onset (Females) (years)	41 ± 10.8
Primary HPP	15 (83.33%)
Secondary HPP	3 (16.67%)
Secondary HPP Causes	2 thyrotoxic periodic paralysis, 1 gastroenteritis

Table 2: Weakness Characteristics

Parameter	Symmetrical Weakness (n=12)	Asymmetrical Weakness (n=6)	p-value
Total Patients	12 (66.66%)	6 (33.33%)	0.709
Paraparesis	5 males	1 male, 1 female	
Quadriparesis	6 males, 1 female	2 males, 2 females	
Deep Tendon Reflexes Absent	7 (38.89%)		
Deep Tendon Reflexes Diminished	1 (5.55%)		
Deep Tendon Reflexes Intact	10 (55.55%)		
Cranial/Bulbar/Respiratory Involvement	0	0	

Table 3: Serum Potassium and Recovery

Parameter	Value
Mean Serum Potassium (mmol/L)	3.18 ± 0.5
Moderate Reduction (2.5-3.5 mmol/L)	Primary HPP
Severe Reduction (<2.5 mmol/L)	Secondary HPP
Mean Serum Potassium in Quadriparesis (mmol/L)	2.1
Concomitant Magnesium Deficiency	3/18 (17%)
Treatment	Intravenous potassium replacement
Mean Recovery Time (hours)	38.6 ± 20.3
Recovery Time in Quadriparesis	24 hours
Recovery Time in Paraparesis	12 hours
Mortality	1 patient with TPP and severe hypokalemia (0.9 meq/L) died due to cardiac arrhythmia
Atypical Presentation	None

Discussion

The hypokalaemia paralysis of 15 patients in our study was primary idiopathic hypokalaemia periodic paralysis. Secondary hypokalaemia paralysis occurred in three (16.67%) patients, thyrotoxic periodic paralysis (11.5%), and diarrhoea (5.6%). The aetiology of hypokalaemia paralysis is varied across different ethnicities and geographical areas [1,3]. There was a significant difference in serum potassium levels in the two groups; patients with secondary hypokalaemia paralysis had more severe hypokalaemia than primary hypokalaemia periodic paralysis. Despite the higher incidence of thyrotoxic periodic paralysis in males [11], in our study there was one male and one female with TPP. Male preponderance of thyroid periodic paralysis is hypothesized to be due to testosterone levels in blood [4,6]. TPP is curable once acute thyrotoxicosis is resolved. Overall, the mean recovery time was 38.6±20.3 hours. Recovery time in patients with quadriparesis was about 24 hours and those with paraparesis was around 12 hours. Rarely does the thyrotoxic or hypokalaemia periodic paralysis affect bulbar, ocular muscles, or cranial nerves [2,3,7,11]. In previous studies, the need for ventilator support in hypokalaemia and thyrotoxic periodic paralysis has been reported [11]. None of our patients had any involvement of eye muscles or cranial nerves, neither did they need ventilator support. Other electrolyte abnormalities in thyrotoxic periodic paralysis have been reported, e.g. transient hypomagnesemia and hypophosphatemia, which tend to resolve once acute thyrotoxicosis settles [4,7]. In our study, one female patient with TPP had concomitant magnesium deficiency that was documented to be 0.9 meq/L and that patient died of cardiac

arrhythmia. There were increased occurrences of recurrent attacks in hypokalaemia periodic paralysis than in thyrotoxic periodic paralysis. Treatment depends upon the severity of attack. Minor attacks with mild hypokalaemia tend to resolve spontaneously. Management of hypokalaemia periodic paralysis includes accurate diagnosis, optimum potassium replacement, choice of diuretic prophylaxis, identification of triggering factors, and managing the issues in pregnancy [12]. Potassium chloride is the preferred salt given at 0.5-1 mEq/kg for acute attacks [13]. In the hypokalaemia periodic paralysis group, 43% (7/16) had paraparesis, and 56% (9/16) had quadriparesis. Typical hypokalaemia periodic paralysis causes paraparesis. The sensory system, bowel, and bladder remain intact [10]. Acetazolamide or potassium sparing diuretics decrease the frequency of attacks and severity of attacks in future but are of no use during acute attack hypokalaemia paralysis [10]. Oral potassium in the form of solution, powder dissolved in water, or sustained release tablets have a role in its management [13]. In cases where patients suffer from recurring morning attacks of paralysis, a trial of sustained release tablet taken at the time of sleep is warranted [10]. In this study all patients responded well to intravenous potassium. Patients with moderate to severe hypokalaemia require intravenous potassium [14]. There was only one patient in the primary group in whom there was a spontaneous recovery. Potassium can be given orally for prophylaxis as well before strenuous exercise or carbohydrate load [10]. During an acute attack, quicker results can be obtained by giving an oral solution of potassium; response is seen within 30 minutes after administration [14], and total dose of potassium given should not exceed 240 meq/l in 24 hours. Glucose or dextrose should not be used as the solvent for oral solution, instead mannitol is considered a preferred solvent [13]. Chronic administration of potassium supplements can lead to gastric irritation from locally high salt concentration. This can be counteracted with concomitant proton pump inhibitors. Acetazolamide is given as maintenance therapy. Carbonic anhydrase inhibitors are potassium wasting; occasional potassium supplements, even in the absence of attack, is warranted. If carbonic anhydrase inhibitors are not available, then spironolactone is an option [15]. Management of thyrotoxic periodic paralysis depends on the adequate management of hyperthyroid state and correction of electrolyte abnormalities associated with it [16]. All three patients in the secondary group were also given intravenous potassium, and there was one mortality due to cardiac arrhythmia in the TPP group. Intravenous (IV) replacement of potassium is done in TPP patients to prevent cardiopulmonary disturbances. However, with potassium replacement there is a danger of rebound hyperkalaemia, usually after recovery of muscle weakness. Beta adrenergic blockers, e.g. propranolol, are given to prevent rebound hyperkalaemia and hasten recovery [16]. Myopathy develops in at least 25% of the affected individuals and may lead to permanent muscle weakness later in life [10]. No fixed, progressive proximal myopathy was found in our patients.

Conclusion

Hypokalaemia paralysis should always be kept in mind when making a differential diagnosis for acute flaccid paralysis. In all patients, serum electrolytes panel, ECG, and thyroid profile should be done at admission in the intensive care unit (ICU). Immediate treatment should be started either orally or intravenously on the diagnosis of hypokalaemia paralysis. Monitoring for cardiac arrhythmias should be done vigilantly.

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