

Original Research Article

Study of incidence and prevalence of hypokalemic periodic paralysis

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ABSTRACT

Background: Hypokalemic periodic paralysis (HPP) is a rare autosomal dominant channelopathy characterised by muscle weakness or paralysis when there is a fall of potassium level in the blood. In individuals with mutation, attack begins during adolescents and most commonly occurs after sleep on awakening, rest after strenuous exercise, high carbohydrate diet and meal with high sodium content. This study was conducted to analyse the age of incidence and prevalence of HPP with various clinical presentations, diagnosis and its effective treatment.

Methods: A retrospective analysis of 50 patients of Hypokalemic periodic paralysis was analysed in tertiary care centre "Rajendra institute of medical science" Ranchi, Jharkhand, India, with reference to its clinical presentation, age of incidence and prevalence with laboratory parameters and treatment outcomes.

Results: Incidence of attack is more common in men between 26-35 years of age. Sudden onset of flaccid quadriplegia was the most common presentation with history of high carbohydrate diet on the background of strenuous work during summer season. Around 60% had similar history of attacks in the past and most of the patients had serum potassium levels between 2.1-3.0mEq/L. Electrocardiography (ECG) abnormalities associated with hypokalemia had been observed in 90% of patients, and also significant clinical, biochemical changes have been observed as well.

Conclusions: Early diagnosis not only helps in definitive management with potassium replacement, but also prevents patient going for life threatening respiratory failure. Patients recover completely without any clinical sequelae. Therefore, it is imperative for physicians, particularly those working in acute care settings, to be aware of this condition. Further management depends on the cause, frequency of attacks, severity of symptoms and the duration of the illness.

Keywords: Hypokalemic periodic paralysis (HPP), Quadriplegia, Serum potassium

INTRODUCTION

Hypokalemic periodic paralysis (HPP) is a rare autosomal dominant channelopathy characterized by muscle weakness or paralysis when there is a fall in potassium level in the blood. There are several types of Periodic Paralysis associated with metabolic and electrolyte abnormalities. Of these, hypokalemic periodic paralysis (HPP) is the most common with a prevalence of 1 in 100,000.¹

Plasma potassium is normally kept at 3.5 to 5.0mEq per liter by multiple mechanisms. Levels outside this range are associated with an increasing rate of death from multiple causes.² Hypokalemia is defined as a deficiency of potassium below 3.5mEq/L³ in the plasma and increased gastrointestinal and renal losses are the common culprits.⁴ Homeostasis of this cation is tightly regulated and achieved mainly via alteration in renal

excretion.^{5,6} Autosomal dominant mutations are of two types HPP1 with CACNA1S gene codes for a voltage gated calcium channel Cav1.1 found in transverse tubules of skeletal muscle and HPP2 is with SCN4 A gene mutation encoding a voltage gated sodium channel Nav1. found at neuromuscular junction.⁷ The clinical features of the syndrome vary somewhat depending on the underlying aetiology but the most striking feature is the sudden onset of weakness ranging in severity from mild, transient weakness to severe disability resulting in life threatening respiratory failure. There are a multitude of factors that can trigger weakness or paralysis including acute stress, pain, anaesthesia, surgery, alcohol, strenuous exercise, heavy carbohydrate diet, or certain medications such as beta-agonists, insulin and steroids etc.^{8,9} A perturbation of sodium and calcium ion channels results in low potassium levels and muscle dysfunction.¹⁰ As this is primarily a problem with muscle contraction rather than nerve conduction, tendon reflexes may be decreased or absent but sensation is generally intact. Although the serum potassium level is often alarmingly low, other electrolytes are usually normal. Indeed, total body potassium is actually normal with the change in the serum level reflecting a shift of potassium into cells.¹¹

Although the pathogenesis of HPP remains incompletely understood, alterations in potassium regulation have been well documented. Total body potassium stores remain adequate, but serum potassium decreases due to potassium migration into muscle cells which causes the muscles to become electrically in excitable. The exact method of potassium translocation is not known but is possibly secondary to an abnormality in muscle membrane. Recent electrophysiologic studies have suggested that the fundamental defect in hyperkalaemic periodic paralysis may involve an increase in muscle membrane sodium permeability but the problem with hypokalaemic periodic paralysis is possibly a calcium channel problem.^{7,12} Genetic linkage data have suggested that the defect in hypokalaemic periodic paralysis may be within a dihydropteridine binding, voltage-sensitive, skeletal muscle calcium channel.¹³

Therefore, aim of this study was to evaluate cases of Hypokalemic periodic paralysis in RIMS Ranchi Jharkhand state, with reference to its clinical presentations, age of incidence and prevalence, with various diagnostic and treatment modalities.

METHODS

A retrospective study was done from January 2017 to December 2017 with the sample size of 50 patients with Hpp were analysed. The analysis of 50 patients of hypokalemic periodic paralysis was carried out in tertiary care centre Rajendra Institute of medical science Ranchi, Jharkhand between January 2017 to December 2017 with reference to its clinical presentation, age of incidence and prevalence with laboratory parameters and treatment

outcomes. The informed consent was obtained from the patients before enrolling them for clinical examination.

Inclusion criteria

- Cases admitted in medicine ward with history of acute flaccid paralysis of limbs with low potassium levels or electrocardiographic changes suggestive of hypokalemia
- Patients with Progressive muscle weakness and 1st degree relatives with hypokalemic periodic paralysis
- Referral cases of hypokalemic paralysis to find out secondary causes of hypokalemia.

Exclusion criteria

- Patients with history suggestive of Diabetes mellitus, chronic kidney disease
- Patients with history of vomiting and diarrhea
- Patients on drugs such as steroids, insulin, diuretics, salbutamol, laxatives etc.
- Patients with abnormal thyroid function tests
- Patients with abnormal arterial blood gas analysis.

A thorough clinical examination of the patient was done after taking detailed history and blood was sent for biochemical analysis such as urea, sugar, thyroid function test, and serum creatinine, serum electrolytes like sodium, potassium and magnesium. Electrocardiography was also taken simultaneously to observe changes at various levels of potassium. Finally, the different parameters like age, sex, past and family history of similar complaints, serum potassium levels and electrocardiographic changes were analysed with treatment outcomes of the patients.

RESULTS

Table 1 shows out of 50 patients, HPP is more common in men 22 (44%) between 26-35 years of age group 28(56%) most of them have family history of HPP 24 (48%) and fast history as well 22 (44%) that suggest HPP is genetic.

Table 2 is showing that when serum potassium level was between 1-2mEq/L maximum number (28%) of patients responded to both oral syrup and IV potassium preparations, 6% of people were responded to IV potassium as well as oral acetazolamide. When serum potassium was between 2.1-3mEq/L no one was responded for oral syrup preparations, but when added IV potassium along with oral syrup around 36% patients regains their muscle power and around 8% of patients regains power after IV potassium and acetazolamide. Similarly, when serum potassium was between 3.1-3.5mEq/L, 6% of patients responded only to oral syrup and 4% regains their power after oral syrup as well as IV Kcl. When serum potassium was > 3.6mEq/L maximum number of patients responded only to oral syrup. Based on above findings we can observe that both oral syrup

and IV potassium preparations under strict monitoring of serum potassium improved the muscle power very early.

Table 1: Observations are presented in tabular form.

Age in years	N= 50 (%)	Gender		Family history		Past history		Clinical presentation		Potassium levels In mili equivalents/Litres(mEq/L)				ECG	
		Male (%)	Female (%)	Absent (%)	Present (%)	Absent (%)	Present (%)	Quadri paresis (%)	Paraparesis (%)	1 - 2 mEq /L (%)	2.1 - 3.0 mEq /L (%)	3.1 - 3.5 mEq /L (%)	3.6 - 4.0 mEq /L (%)	Abnormal (%)	Normal (%)
15-25	12(24)	10 (20)	2 (4)	4 (8)	8 (16)	6 (12)	6 (12)	11 (22)	1 (2)	9 (18)	2 (4)	1 (2)	0	12 (24)	0
26 - 35*	28 (56)*	22 (44)*	6 (12)	4 (8)	24 (48)*	6 (12)	22 (44)*	26 (52)*	2 (4)	4 (8)	18 (36)*	2 (4)	4 (8)	27 (54)*	1 (2)
36 - 45	6 (12)	3 (6)	(6)	2 (4)	4 (8)	2 (4)	4 (8)	6 (12)	0	2 (4)	1 (2)	1 (2)	2 (4)	6 (12)	0
> 46	4 (8)	3 (6)	1 (2)	0	4 (8)	2 (4)	2 (4)	4 (8)	0	2 (4)	1 (2)	1 (2)	0	3 (6)	1 (2)

Serum potassium levels in mEq/L=mili equivalents, ECG=Electrocardiogram,*= Significant findings

Most common clinical presentation was quadripareisis-26 (52%) when serum potassium level between 2.1-

3.0mEq/L and around 27(54%) people had abnormal ECG findings that consistent with hypokalemia.

Table 2: Treatment received at various potassium levels.

Treatment	Serum potassium levels in mEq/L				Total
	1-2mEq/L	2.1 - 3.0mEq/L	3.1-3.5mEq/L	> 3.6mEq/L	
Oral Kcl	0	0	3 (6%)	6 (12%)	9 (18%)
Oral Kcl	14 (28%)	18 (36%)	2 (4%)	0	34 (68%)
IV Kcl					
Acetazolamide	3 (6%)	4 (8%)	0	0	7 (14%)
Total	17 (34%)	22 (44%)	5 (10%)	6 (12%)	50 (100%)

DISCUSSION

Weakness is a common, yet nonspecific presentation of various neurological and non-neurological conditions. While hypokalemic paralysis is an important cause of acute flaccid paralysis, there are many clinical differentials like Guillain Barré syndrome, acute transverse myelitis, polymyositis, poliomyelitis, and porphyria; that should be considered. Of the differentials, the immediate life-threatening causes like stroke and space occupying lesions (SOLs) should be ruled out at the earliest. Most cases of periodic paralysis are familial or primary hypokalemic periodic paralysis. Sporadic cases are associated with numerous other conditions including barium poisoning, hyperthyroidism, renal disorders, certain endocrinopathies and gastrointestinal potassium losses. Hypokalemic paralysis presents as acute flaccid weakness with hypokalemia (serum potassium <3.5 mmol/l), without sensory signs, facial,

bulbar, autonomic, bladder and bowel involvement, normal creatine kinase, and NCV.

There are several types of periodic paralysis associated with metabolic and electrolyte abnormalities. Of these, hypokalemic periodic paralysis (HPP) is the most common with a prevalence of 1 in 100,000.¹ The clinical features of the syndrome vary somewhat depending on the underlying etiology, but the most striking feature is the sudden onset of weakness ranging in severity from mild, transient weakness to severe disability resulting in life threatening respiratory failure. Patients remain alert during the attacks. Patients often report additional symptoms either before, during, or after attacks. These include paresthesia, sweating, myalgia, extreme fatigue, thirst, shortness of breath (either due to anxiety or to the episode itself), palpitations, clumsiness, irritability, and mental dullness.¹⁴

Plasma potassium is normally kept at 3.5 to 5.0mEq/L by multiple mechanisms. Levels outside this range are associated with an increasing rate of death from multiple causes.² Hypokalemia is defined as a deficiency of potassium below 3.5mEq/L³ in the plasma and increased gastrointestinal and renal losses are the common culprits.⁴ Homeostasis of this cation is tightly regulated and achieved mainly via alteration in renal excretion.^{5,6} Autosomal dominant mutations are of two types HPP1 with CACNA1S gene codes for a voltage gated calcium channel Cav1.1 found in transverse tubules of skeletal muscle and HPP2 is with SCN4A gene mutation encoding a voltage gated sodium channel Nav1.4 found at neuromuscular junction.⁷ Attacks may be provoked by acute stress, pain, anaesthesia, surgery, alcohol, strenuous exercise, heavy carbohydrate diet, or certain medications such as beta-agonists, insulin and steroids etc.^{8,9} A perturbation of sodium and calcium ion channels results in low potassium levels and muscle dysfunction.¹⁰ Although the pathogenesis of HPP remains incompletely understood, alterations in potassium regulation have been well documented. Total body potassium stores remain adequate, but serum potassium decreases due to potassium migration into muscle cells which causes the muscles to become electrically inexcitable. The exact method of potassium translocation is not known but is possibly secondary to an abnormality in muscle membrane. Recent electrophysiologic studies have suggested that the fundamental defect in hyperkalaemic periodic paralysis may involve an increase in muscle membrane sodium permeability, but the problem with hypokalaemic periodic paralysis is possibly a calcium channel problem.^{7,12} Genetic linkage data have suggested that the defect in hypokalaemic periodic paralysis may be within a dihydropteridine binding, voltage-sensitive, skeletal muscle calcium channel.¹³

Serum electrolytes like potassium, sodium, magnesium including ECG, TSH, free T3 and T4 are the minimum indicated laboratory investigations, with renal and adrenal function also recommended. Management of HPP mainly includes potassium supplementation through oral or parental route repeated at 15-30minute intervals depending on the response of the ECG, serum potassium level, and muscle strength followed by treatment of underlying cause if present. Prophylaxis against recurrent periodic attacks has been successful with a wide variety of treatment modalities including spironolactone and acetazolamide. It is important to note that this disorder is autosomal dominant in two-thirds of cases; with male preponderance when providing genetic counselling.¹⁵ The basic guidelines to follow when caring for the patient include control of plasma potassium, avoidance of large glucose and salt loads (which promote intracellular shift), maintenance of body temperature, acid-base balance, and cautious use of neuromuscular blocking agents.^{16,17} Failure to properly diagnose and treat periodic paralysis can be fatal, but early correction of potassium abnormalities can resolve the symptoms quickly and completely.

When possible, the underlying cause must be adequately addressed to prevent the persistence or recurrence of paralysis.

CONCLUSION

Incidence of attack is more common in men between 25-40 years of age. Sudden onset of flaccid quadriplegia is the common presentation with history of high carbohydrate diet on the background of strenuous work during summer season. Around 60% had similar history of attacks in the past and most of the patients had serum potassium levels between 2-3mEq/L. ECG abnormalities associated with hypokalemia had been observed in 90% of patients, and also significant clinical and biochemical changes have been observed as well. Early diagnosis not only helps in definitive management with potassium replacement, but also prevents patient going for life threatening respiratory failure. Patients recover completely without any clinical sequelae. Therefore, it is imperative for physicians, particularly those working in acute care settings, to be aware of this condition. Further management depends on the cause, frequency of attacks, severity of symptoms and the duration of the illness.

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