Hypokalemic Periodic Paralysis as a Manifestation of Thyrotoxicosis

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Objective: *To study the clinical characteristics of patients who suffer from hypokalemic periodic paralysis, as the presenting symptoms of thyrotoxicosis.*

Material and Method: *A retrospective review of 29 patients who presented with the syndrome of hypokalemic periodic paralysis as the symptom of thyrotoxicosis at Ratchaburi Hospital between January 1,1995 and December 31, 2007. Patients' data, diagnosis, blood chemistry, and thyroid function test were collected from medical records.*

Results: *All patients exhibited muscle weakness for a duration of one to two days, while all patients with hypokalemic periodic paralysis were determined to have high serum thyroid hormone and diagnosed with thyrotoxicosis. Patients with hypokalemic periodic paralysis were the first symptom leading to diagnosis of thyrotoxicosis. The attack of weakness occurred during the night in all patients. The patients, 96.6% being male, showed improvement of their symptoms through potassium replacement and thyrotoxicosis treatment using propylthiouracil and non selective beta adrenergic blocker. All patients recovered and did not demonstrate reoccurring hypokalemic periodic paralysis. The degree of muscle weakness was found to correlate significantly ($p < 0.05$) with level of serum potassium, magnesium, and duration of weakness.*

Conclusion: *It is important to determine blood thyroid hormone in all patients with hypokalemic periodic paralysis.*

Keywords: *Hypokalemic periodic paralysis, Thyrotoxicosis*

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Hypokalemic periodic paralysis is characterized as a rare disorder that causes episodes of muscle weakness with hypokalemia. The condition has the potential to be life threatening and can appear in a range of different settings. Supportive measures are particularly of respiratory and cardiovascular status. Early detection and rapid diagnosis is crucial, as some of the underlying causes are correctable. The source of the disorder could have originated from heterogeneous disorders, including familial hypokalemic periodic paralysis and thyrotoxicosis. Familial hypokalemic periodic paralysis is differentiated through a positive family history and earlier onset. It is an autosomal dominant disorder, found to be more widespread in Caucasian populations[1-5]. Others include hyperthyroidism, a rare presentation of hyperthyroidism, more common in Asian men between the second and fourth decades of life[6-19]. The aim of the present study was to describe the clinical characteristics of the patients who suffer from hypokalemic periodic paralysis, as primary indicators and symptoms of thyrotoxicosis.

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Material and Method

The author reviewed the medical records of the patients (14 years of age or older) who presented with hypokalemic periodic paralysis and were admitted to Ratchaburi Hospital in Thailand. The diagnostic criteria for diagnosis of hypokalemic periodic paralysis with thyrotoxicosis consisted of recording the patient's history, complete physical and neurological examinations, and routine laboratory investigations. All data was collected from patients between January 1, 1995 and December 31, 2007 at the Ratchaburi Hospital

referral center. The criteria for diagnosis of hypokalemic periodic paralysis with thyrotoxicosis was determined by clinical diagnosis and laboratory findings. Patients with acute hypokalemic paralysis from renal tubular acidosis, familial hypokalemic paralysis were excluded. Cases were collected from the medical records, and all patients underwent detailed physical and neurological examination, blood chemistry analysis, thyroid function test, and electrocardiography.

Statistical analysis used the SPSS package. Comparison to the degree of muscle weakness and different variables were assessed by Kruskal-Wallis test. A p-value of < 0.05 was considered statistically significant.

Results

Twenty-nine patients (28 male (96.6%) and 1 female) with hypokalemic periodic paralysis and thyrotoxicosis were studied. Age range was 26 to 46 years, with a mean age of 33.62 years.

The average duration of hypokalemic periodic paralysis prior to admission to the hospital was 1.5 days (range 0.4 to 2 days). In 29 patients, muscle weakness was more symmetrical than asymmetrical proximal muscle weakness. None of the patients had bulbar involvement. The attack of weakness occurred during the night in all patients. The majority had symptoms of thyrotoxicosis. Seventy five percent of the patients had precipitating factors. At the time of hospitalization, not all patients exhibited respiratory failure. None of the patients was known to have thyrotoxicosis. The first symptom that lead to the diagnosis of thyrotoxicosis for each patient was hypokalemic periodic paralysis. Their muscle weakness improved by correction of hypokalemia. All the patients received both intravenous and oral potassium chloride. The serum magnesium levels were low and low normal in all patients. Seven patients received supplemental magnesium sulfate because they showed low serum magnesium levels. Upon hospital admission, the symptoms of thyrotoxicosis included weight loss and palpitation for 20 patients. Precipitating factors, such as high carbohydrate diet before the episode of acute paralysis, were apparent in 75.9 per cent of the patients. The majority of the patients had one episode of hypokalemic periodic paralysis. All patients recovered after treatment and did not have serious complications (Table 1).

The mean serum potassium level was 2.05 mEq/L (range 1.45 to 2.85 mEq/L), serum magnesium level of 1.75 mEq/L (range 1.65 to 2.03 mEq/L), serum free T4 3.8 ng/dL (range 2.8 to 4.5 ng/dL), serum TSH 0.05 ulU/ml (range < 0.05 to 0.4 ulU/ml), T3 6.64 pg/ml (range 3.6 to 9.85 pg/ml).

Table 1. Clinical manifestation (n = 29)

Clinical manifestation	n = 29	Percentage
Proximal muscle weakness		
Symmetrical	21	72.4
Asymmetrical	8	27.6
Weight loss	20	69.0
Palpitation	20	69.0
Muscular pain	18	62.1
Cramp	11	38.0
Precipitating factors		
High carbohydrate diet	22	75.9
Unknown	7	24.1
Duration of weakness		
< 1 day	6	20.7
1-2 days	23	79.3
Episode of periodic paralysis		
1	25	86.2
2	3	10.3
3	1	3.4

Table 2. Electrocardiogram findings (EKG)

EKG	n = 29	Percentage
Sinus tachycardia	26	89.7
Non specific ST-T change	4	13.8
Prominent U wave	2	6.9
Second degree AV block	3	10.3

The electrocardiograms were obtained during weakness in all patients, with the majority having sinus tachycardia. Other findings included non-specific ST-T change, prominent U wave, and second degree AV block (Table 2).

For statistical analysis, the correlation of degree of muscle weakness and serum potassium, magnesium, serum thyroid, and duration of weakness were analyzed by the Kruskal-Wallis Test. The serum potassium, magnesium, and duration of weakness was significantly lower in patients with more muscle weakness ($p < 0.05$) (Table 3).

Discussion

Hypokalemic periodic paralysis with thyrotoxicosis is a rare condition. According to the literature, the prevalence for Asian men is approximately 2% in patients with thyrotoxicosis, but has been reported to

Table 3. Comparison of data in relation to degree of muscle weakness by Kruskal-Wallis Test

Determinations	Chi-square	p-value
Serum potassium (mEq/L)	20.738	0.000
Serum magnesium (mEq/L)	9.267	0.010
Serum FT4 (ng/dl)	0.349	0.840
Serum T3 (pg/ml)	0.306	0.858
Serum TSH (uIU/ml)	1.901	0.387
Duration of weakness (day)	18.895	0.000

be only 0.1-0.2% in other races. Males are more predominantly affected than females, with a male to female ratio of 20:1, despite the higher incidence of thyrotoxicosis in females[6-11]. Patients with hypokalemic periodic paralysis with thyrotoxicosis usually experience the attack during the night, after heavy exercise and with a high carbohydrate diet. The severity of muscle weakness correlated with serum potassium levels. Mild hypomagnesemia was noted in most patients during paralysis, which has also been observed in several previous reports[6-18]. These findings are supported by the present study.

During an attack of muscle weakness in hypokalemic periodic paralysis, respiratory and bulbar involvement are usually spared, although a severe attack can cause respiratory and cardiovascular arrest[13]. In the present study, none of the patients had respiratory and bulbar involvement.

The pathophysiology of hypokalemic periodic paralysis with thyrotoxicosis is not completely understood. The high incidences of hypokalemic periodic paralysis in the Asian population suggests that the basic defect may be genetically determined[15]. In animal models, the Na-K-ATPase activity has been noted as being significantly greater in males than in females,and testosterone tends to induce an increase in the Na-K-ATPase activity. The effect of sex hormones on the Na-K pump may contribute to the predisposition of hypokalemic periodic paralysis with thyrotoxicosis in men[19]. The episode of paralysis that occurred during the night for patients with hypokalemic periodic paralysis with thyrotoxicosis, have shown that plasma glucose and insulin responses to meals are markedly higher in the evening than in the morning in controlled subjects. This phenomenon suggests a mechanism for the nocturnal attack of paralysis. Another explanation could be that the circadian rhythmicity of some hormones reach their peak levels during sleep[20]. Hypokalemia and muscle weakness resulted from intracellular shift of potassium into muscle cell and not as a result of potassium loss. It has been proposed that the direct effect of the thyroid hormone in stimulating membrane of Na-K - ATPase activity and indirect effect of thyroid hormone in stimulating insulin hyper secretion may involve an intracellular potassium shift[9,13]. It has been observed that beta adrenergic blocker with propanolol prevents paralysis, which suggests that the development of paralysis is partly influenced by the hyperadrenergic state characteristic of thyrotoxicosis[21].

Currently, due to migration of populations worldwide the incidence of hypokalemic periodic paralysis with thyrotoxicosis is increasingly found in Western countries[10-18].

Management of the underlying hyperthyroidism is the goal to prevent recurrence of hypokalemic periodic paralysis. Anti-thyroid drug and non-selective beta-adrenergic blockers have been used successfully. Although rare, some patients with hypokalemic periodic paralysis and thyrotoxicosis relapse during the euthyroid state[22,23]. In the present study, the recurrence of attacks no longer occurred.

Practically, all patients who present with hypokalemic periodic paralysis should be examined to determine their serum thyroid hormone level. This suggestion may not only help in diagnosis of previously unsuspected thyrotoxicosis, but also in the appropriate management of hypokalemic periodic paralysis and prevention of complications.

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อาการกล้ามเนื้ออ่อนแรงเป็นช่วงเวลา จากระดับเกลือแร่โพแทสเซียมในเลือดต่ำ เป็นอาการนำของโรคต่อมไทรอยด์เป็นพิษ

ศุภชัย ไพบูลย์ผล

วัตถุประสงค์: *เพื่อศึกษาอาการทางคลินิกของผู้ป่วยที่มาด้วยอาการกล้ามเนื้ออ่อนแรงเป็นช่วงเวลา จากระดับเกลือแร่โพแทสเซียมในเลือดต่ำซึ่งเป็นอาการนำอย่างหนึ่งของโรคต่อมไทรอยด์เป็นพิษ*

วัสดุและวิธีการศึกษา: *เป็นการศึกษาย้อนหลังจากเวชระเบียนผู้ป่วย 29 ราย ที่มาด้วยอาการกล้ามเนื้ออ่อนแรงเป็นช่วงเวลา จากระดับเกลือแร่โพแทสเซียมในเลือดต่ำซึ่งเป็นอาการนำอย่างหนึ่งของโรคต่อมไทรอยด์เป็นพิษ ในระหว่างวันที่ 1 มกราคม พ.ศ. 2538 ถึง วันที่ 31 ธันวาคม พ.ศ. 2550 ในโรงพยาบาลราชบุรี โดยศึกษาอาการทางคลินิก การวินิจฉัย ระดับเกลือแร่ และระดับไทรอยด์ฮอร์โมนในเลือด*

ผลการศึกษา: *จากการศึกษาผู้ป่วย ซึ่งมีอาการกล้ามเนื้ออ่อนแรงเป็นช่วงเวลา จากระดับแกลือแร่โพแทสเซียมในเลือดต่ำ ซึ่งเป็นอาการนำอย่างหนึ่งของโรคต่อมไทรอยด์เป็นพิษ ผู้ป่วยมีอาการกล้ามเนื้ออ่อนแรงหนึ่งถึงสองวัน ผู้ป่วยทุกรายที่มีอาการกล้ามเนื้ออ่อนแรง เป็นช่วงเวลาจากระดับเกลือแร่โพแทสเซียมในเลือดต่ำ มีระดับของไทรอยด์ฮอร์โมนในเลือดสูง ซึ่งได้รับการวินิจฉัยเป็นครั้งแรกว่า เป็นโรคต่อมไทรอยด์เป็นพิษ ผู้ป่วยทุกรายเริ่มมี อาการกล้ามเนื้ออ่อนแรงตอนกลางคืน ส่วนใหญ่เป็นเพศชายร้อยละ 96.6 อาการกล้ามเนื้ออ่อนแรงดีขึ้นหลังได้รับเกลือแร่โพแทสเซียม และให้การรักษาโรคต่อมไทรอยด์เป็นพิษด้วยยาต้านไทรอยด์ ไม่มีผู้ป่วยรายใดเสียชีวิต และไม่มีอาการกล้ามเนื้ออ่อนแรงเป็นช่วงเวลา จากระดับเกลือแร่โพแทสเซียมในเลือดต่ำอีก ระดับอาการอ่อนแรงของกล้ามเนื้อ มีความสัมพันธ์กับระดับเกลือแร่โพแทสเซียม แมกนีเซียมในเลือด และระยะเวลาที่ผู้ป่วยอ่อนแรงอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$)*

สรุป: *ผู้ป่วยทุกรายที่มาด้วยอาการกล้ามเนื้ออ่อนแรง เป็นช่วงเวลาจากระดับเกลือแร่โพแทสเซียมในเลือดต่ำ ควรตรวจหาระดับของไทรอยด์ฮอร์โมนในเลือด*