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CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS PRESENTING WITH HYPOKALEMIC PERIODIC PARALYSIS – A SINGLE CENTRE STUDY FROM SOUTH INDIA

Medical Science

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ABSTRACT

Background: Hypokalemic periodic paralysis is an important cause of acute muscular weakness, but it has several underlying etiologies and can at times be potentially life-threatening. Recognition of the underlying causes is essential for the appropriate management of patients.
Objectives: To study the clinical profile, etiology, and outcome of patients with hypokalemic paralysis in a tertiary care teaching hospital in South India.
Materials & Methods: Consecutive patients presented with acute muscle weakness and hypokalemia from June 2012 to November 2013 were included in the study. Patients with GuillaineBarre´ syndrome, porphyria, polio and non-polio enterovirus infection and myositis were excluded. Detailed clinical examination, urinalysis, renal function tests, arterial blood gas analysis, thyroid hormones, and electrocardiogram were carried out. Patients were Investigated for possible secondary causes of hypokalemia.
Results: Forty-six patients participated in this study, of which 26 (57%) were males and 20 (43%) were females. Most of our patients belong to age group between 20-30 years . There were 23 (50%) cases of Distal Renal Tubular Acidosis, 13 (28.2%) cases of Acute Gastroenteritis, 3 (6.5%) patients of Gitelman's syndrome and 2 (4.3%) patients of Bartter's syndrome, 2 (4.3%) patients of Proximal Renal Tubular Acidosis in our study.
Conclusion: A significant number of patients in this study had secondary and potentially reversible causes of hypokalemic periodic paralysis. We strongly recommend urine spot potassium and Arterial Blood Gas (ABG) to be the first line investigation in working up a case of hypokalemic paralysis. A detailed work-up for secondary causes should be undertaken in patients with hypokalemic periodic paralysis .

KEYWORDS

Hypokalemic Periodic Paralysis, Hypokalemic Paralysis

INTRODUCTION:

Hypokalemic periodic paralysis (HPP) constitutes a heterogeneous group of disorders that present with acute muscular weakness and can at times be potentially life-threatening. The underlying etiologies of hypokalemia can be classified in two major categories: acute conditions that cause the intracellular shifting of potassium without total body potassium depletion; and total body potassium loss via excessive renal potassium excretion or extra-renal potassium loss due to vomiting or diarrhea. [1]

When properly diagnosed and treated appropriately, patients recover without much clinical sequelae. Although a number of these cases may be associated with ion channel mutations, some are due to potentially reversible causes. Since definitive therapy can be offered to some of these patients, identifying causes that are reversible is important. [2]

There are only a few earlier studies of hypokalemic paralysis reported in literature and focus on renal dysfunction is very minimal, further they cover only cases of hypokalemic paralysis and did not include the entire spectrum of symptomatic hypokalemia and renal dysfunction.

The current study was planned with the below objectives
- To study the clinical profile of patients presenting with hypokalemic paralysis to a tertiary care medical college hospital in Chennai, Tamil Nadu.
- To correlate serum Potassium concentration with severity and distribution of muscle weakness.
- To correlate ECG changes with serum potassium concentrations in hypokalemia.
- Etiological work up in finding out the cause of hypokalemia in patients presenting with hypokalemic paralysis.

MATERIALS AND METHODS

This observational cross-sectional study was conducted in Stanley Medical College Hospital, Chennai, Tamil Nadu, India from June 2012 to November 2013. A total of forty-six patients who presented with hypokalemic muscle weakness were included in this study. A written informed consent was obtained from all the participants. The study was conducted according to Good Clinical Practice.

Patient identity was always kept confidential and the study was approved by the Human Ethics Committee. All patients were admitted and all relevant investigations for finding out the etiology of hypokalemia were sent as inpatient basis.

Inclusion Criteria:
Patient presenting with muscle weakness with documented hypokalemia.

Exclusion Criteria:
Patients who are not willing to get investigated in complete, Pediatric patients, Muscle weakness due to causes other than hypokalemia (GuillaineBarre´ syndrome, porphyria, polio and non-polio enterovirus infection and myositis)

Data were collected from the patient or the attendants by personal interview, structured physical examination and a predetermined protocol of biochemical and radiological investigations were done. A detailed information proforma was filled out for every patient in the study.

Specific information collected using the proforma:
Socio-economic and demographic data, hospital admissions details, occupation, with mention of the involvement of excessive sweating.

Diet:
Source of drinking water, oil used for cooking and the source of the same-market/ration shop, Material with which the cooking utensils are made of: mud/aluminum/iron/alloy, Diet diary of the patient's family on a typical week with special mention of plant products

***Clinical Features*:**
Presenting complaints in chronological order with the exact duration of each of them, history of muscle weakness: duration, distribution, severity, respiratory involvement, myalgias, nocturia, polyuria, salt craving.

History of Ureteric colic/renal stone disease, Loose stools/ constipation/ urinary retention, Drug intake:β2 agonists/α agonists, diuretics, analgesics, Tobacco chewing, usage of betel nut, Diabetes mellitus, hypertension and drug intake for them, Dry mouth/ dry eyes/ dental caries, Number of similar episodes in the past, the nature of symptoms of each episode, hypokalemia documented or not, treatment received, response to treatment, Similar illness in the family/ neighborhood.

***Examination* -**
Patients coming to Govt Stanley Medical College Hospital, Chennai for skeletal muscle weakness were admitted to the General Medicine

ward and were subjected to ECG as a part of evaluation of paralysis. If hypokalemic changes were seen in the ECG, then serum electrolyte values were sought to confirm hypokalemia.

After confirming hypokalemic paralysis, urine spot potassium was estimated to check for renal or non- renal causes of potassium loss. If the urine spot potassium values were>20mEq/d then it suggests renal loss of potassium. If the urine spot potassium values were <20mEq/d then they were grouped as non- renal loss of potassium. An Arterial blood gas test was done for both sets of patients and according to the results were classified into patients who have metabolic acidosis, metabolic alkalosis and normal acid base.

Patients with renal loss of potassium and normal anion gap metabolic acidosis were evaluated for Distal RTA, Proximal RTA, Diabetic Keto Acidosis(DKA), or use of acetazolamide or amphotericin B. Early morning urine pH is done to differentiate between the two RTAs. If the pH was >5.5 then Distal RTA was diagnosed, and patient subjected to USG abdomen for ruling out urolithiasis. If it was <5.5 then Proximal RTA was diagnosed. Serum ketone levels helped in the diagnosis of Diabetic Keto Acidosis. A detailed history was taken to rule out hypokalemia induced by use of drugs like acetazolamide and amphotericin B.

Patients with renal loss of potassium and with normal acid base were evaluated for post ATN diuresis, post obstructive diuresis, osmotic diuresis or other gentle diuretic usage, hypomagnesemia, usage of high dose of penicillin or polydipsia due to diabetes insipidus. Diabetes insipidus can be confirmed with the voiding of large volumes of hypotonic urine. History can reveal the usage of penicillin or any gentle diuretics by the patient. Serum electrolyte levels can be checked to find out hypomagnesemia. Osmotic diuresis can be checked by investigating the food intake of the patient for osmotically active materials.

In patients with renal loss of potassium, those who have metabolic alkalosis, urine chloride is assayed. If the urine chloride levels are <20mEq/L, then the hypokalemic paralysis is probably due to vomiting and naso gastric suction. If the urine chloride levels are >20mEq/L and the patient is hypotensive or normotensive, then Bartter's syndrome or Gitelman's syndrome is suspected. In Bartter's syndrome, patients will have normal serum magnesium and the urine Calcium: Creatinine ratio will be >0.2 due to hypercalciuria . In Gitelman's syndrome patients will have hypomagnesemia and their urine Calcium: Creatinine ratio will be <0.2.

In the hypertensive patients who have metabolic alkalosis, aldosterone levels were checked. If the aldosterone levels were high, then the possibilities point to Conn's syndrome or secondary hyperaldosteronism. In Conn's syndrome, the renin levels will be lower or normal. In patients with secondary hyperaldosteronism, the renin levels will be elevated. In the hypertensive patients, if the aldosterone levels are normal or low then the following conditions can be suspected: Cushing's syndrome, Liddle's syndrome, apparent mineralocorticoid excess or Congenital Adrenal Hyperplasia(CAH).

For patients with non-renal loss of potassium, their ABG is seen for further management. Patients showing metabolic acidosis in ABG mostly have potassium lost through lower GI tract as in diarrhea. If the patients have normal acid base then they could have been the result of decreased intake of potassium, diuretic usage, profuse sweating, naso-gastric suctioning, or vomiting.

Thyroid function tests were done on all patients to rule out thyrotoxic periodic paralysis. Renal function tests including serum urea and creatinine were performed on all patients to find out any background Chronic Kidney Disease(CKD).All the patients, especially those diagnosed with Distal RTA, were subjected to USG abdomen to study the kidney size and morphology and to rule out nephrolithiasis.

RESULTS

This study includes a total of 46 patients presenting with apparently spontaneous, symptomatic hypokalemia. Of which 26 were males and 20 were females (Fig1).

The mean age of presentation was 37 years , the youngest was 14 years and the oldest was 85 years. Most of the patients was in age group between 20-30 years – 18 patients. (Table1)

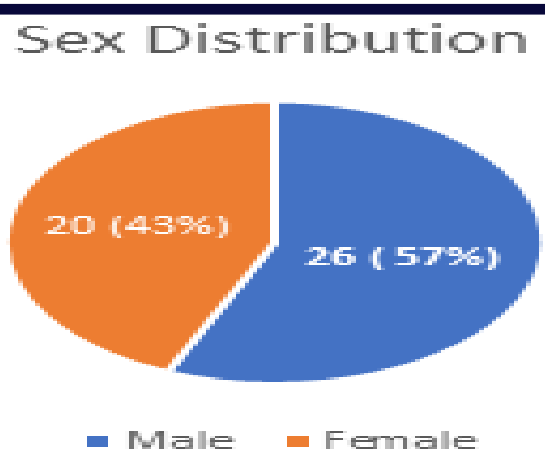

Fig 1 Sex Distribution

Table 1: Age Distribution

Age Distribution	Male	Female	Total	%
10-20	3	1	4	8.69
20-30	8	10	18	39.13
30-40	7	1	8	17.39
40-50	3	0	3	6.52
50-60	3	2	5	10.87
60-70	2	5	7	15.21
70-80	-	-	-	-
80-90	-	1	1	2.17

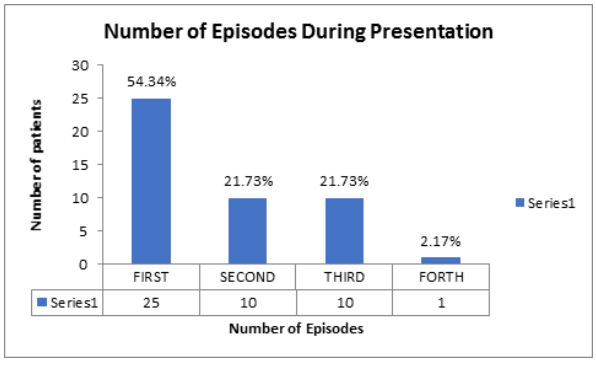

Fig 2: Number Of Episodes During Presentation

Table 2: ECG Changes And Its Relation With Potassium Concentration

ECG Changes	No. Of Patients	%	Mean K Value	SD
T Flattening	46	100	1.92	0.20
U shorter than T	24	52.17	2.06	0.24
U taller than T	22	48.88	1.76	0.18
PR Prolongation	8	14.28	1.57	0.11

Table 3: Distribution Of Weakness And Mean Potassium Values

Distribution Of Weakness	No. Of Patients	Percentage	Mean K+ Vaues	SD
Muscle Cramps	20	43.4	2.07	0.26
UL,LL	25	54.3	1.82	0.22
Neck	9	19.5	1.74	0.17
Respiratory Muscle Weakness	2	4.3	1.4	0

Table 4: Urine Spot Potassium

Urine K	No. Of Patients	Percentage	Mean K^+	SD
<20	15	32.60	7.14	5.25
>20	31	67.39	23.99	3.13

Table 5: Arterial Bloog Gas Results

ABG Results	Number Of Patients	Percentage
Normal	6	13
NAGMA	30	65.21
Metabolic Alkalosis	10	21.74

(NAGMA: Non-anion-gap metabolic acidosis)

Table 6: Final Diagnosis And Clinical Profile Of Patients

Diagnosis	No. Of Cases	Percentage
Distal RTA	23	50
Acute Gastroenteritis	13	28.2
Gitelman's Syndrome	3	6.5
Bartter's Syndrome	2	4.3
Proximal RTA	2	4.3
CKD-Diuretic Induced	2	4.3
ADPKD-CKD	1	2.1

(RTA- renal tubular acidosis; CKD - Chronic kidney disease; ADPKD - Autosomal dominant polycystic kidney disease)

DISCUSSION

In our study, out of total 46 patients with symptomatic hypokalemia, 26 were males which constitutes 56.52% and 20 were females which constitutes 43.47%. Most of our patients belong to age group between 20-30, Totally 18 patients which constitutes 39.13%. Most of our patients presented with cramps and muscle weakness, and in our results, we found the distribution of muscle weakness correlates well with the severity of hypokalemia.

The earliest neuro-muscular manifestation of hypokalemia is muscle cramps that occurred in patients with mean serum potassium levels of 2.07 mEq/L. The next sign of hypokalemia will be muscle weakness involving lower limb followed by upper limb leading to quadriparesis. The mean serum potassium level of patients presenting with quadriparesis in hypokalemia was 1.82mEq/L in our study. The severe form of hypokalemia manifests as axial and neck muscle weakness. In our study we had 9 patients presented with neck muscle weakness and we found the mean serum potassium levels in those patients were 1.74mEq/L.

Involvement of respiratory muscles occurs in serum potassium levels of less than 1.5mEq/L leading to respiratory arrest. In our study we had 2 patients who presented with respiratory muscle weakness and we found their mean serum potassium values of 1.4mEq/L. Invasive mechanical ventilation was provided, and the patients were revived. 54.34% of our patients presented with muscle weakness due to hypokalemia for the first time. Second and third episodes of weakness was documented in 21.73% patients respectively. 2.17% of the patients presented with muscle weakness for the fourth time.

We found the etiology behind recurrent episodes of hypokalemic paralysis had renal loss of potassium as the cause. The most common being Distal RTA, Gitelman's syndrome, Bartter's syndrome, Proximal RTA, CKD and diuretic induced. Most of the patients presenting with single episode of hypokalemic paralysis had gastrointestinal loss of potassium. Older age group patients with history of loose stools, exertion who presented with first episode of weakness had gastrointestinal loss of potassium.

ECG remains one of the most valuable tools in bedside diagnosis of hypokalemia even before we get serum potassium values. ECG changes correlates well with the severity of hypokalemia. In our study the earliest ECG change what we noted is T wave flattening which was present in 100% of the patients and their mean serum potassium value was 1.92mEq/L. The next change in ECG what we noted was the appearance of U wave(shorter than T wave) that occurred in 52.17% of patients whose mean serum potassium value was 2.06mEq/L. Still severe form of hypokalemia had U waves(taller than T wave), that we saw in 48.88% of patients and their mean serum potassium values was 1.76mEq/L. PR prolongation in ECG was seen in most severe form of hypokalemia that was documented in 14.28% of patients and their mean serum potassium values was 1.57mEq/L. In our study ECG held good in predicting the severity of hypokalemia.

Urine spot potassium remains the first step in approaching a patient with hypokalemic paralysis. Urine potassium of >20mEq/L indicates renal loss of potassium. Urine spot potassium of <20mEq/L indicates non renal loss of potassium.

In our study we had 67.39% of patients having urine spot potassium of >20mEq/L coming under renal potassium loss etiology and 32.60% having urine spot potassium of <20mEq/L coming under non renal potassium loss etiology. Approximately two-thirds of the patients had renal loss of potassium as etiology and one-thirds of the patients had non renal loss of potassium as etiology.

Among non-renal loss, gastrointestinal loss of potassium due to gastroenteritis constitutes 86.66% of cases who had significant loose stools.

Arterial blood gas remains the second most useful investigation in finding the etiology of the hypokalemia. A total of 65.21% of patients in our study had normal anion gap metabolic acidosis(NAGMA). Most of them had early morning urine pH values of >5.5 and was diagnosed as Distal RTA. A total of 21.7% of patients had metabolic alkalosis. Out of that we had 3 patients with Gitelman's syndrome and 2 patients with Bartter's syndrome. A total of 13% of patients had normal arterial blood gas values. Renal function tests were done to all patients. We found elevated urea and creatinine values in 3 patients and who had CKD as background. Pre-renal pattern of renal function tests was found in patients with severe AGE.

Ultrasound abdomen was done for all patients to look for kidney size and morphology. We had 1 patient with autosomal dominant polycystic kidney disease(ADPKD) and 2 patients with CKD who presented with hypokalemic paralysis.

Thyroid function test was done to all patients to rule out thyrotoxic periodic paralysis. TFT was normal in all the patients in our study. Serum magnesium levels was checked to patients who had metabolic alkalosis and was found low in 3 patients who were diagnosed as Gitelman's syndrome. Urine spot Calcium/Creatinine ratio was calculated for patients who had renal loss of potassium and metabolic alkalosis. Urine spot Ca/Cr ratio <0.2 was found in 3 patients who had Gitelman's syndrome and the diagnosis was confirmed. Urine spot Ca/Cr ratio >0.2 was found in 2 patients who had renal loss of potassium and metabolic alkalosis and was diagnosed as Bartter's syndrome.

In a study from South India, Rao N et al [3] reported 31 patients of hypokalemic paralysis over a period of 6 years. In another study from North India, Maurya PK et al [4] did a study of clinical profile of patients with hypokalemic periodic paralysis, reported 30 patients over a period of 3 years. Garg RK et al study [5] included 29 patients with hypokalemic periodic paralysis. Wi JK et al [6] study done in Korea which included 34 patients with hypokalemic paralysis. Table 7 explains on the comparison of various available studies comparing the etiology of hypokalemic Paralysis with our current study.

Table 7. Etiology Of Hypokalemic Paralysis From Various Published Studies.

Diagnosis	Rao N et al [3]	Maurya PK et al [4]	Garg RK et al [5]	Wi JK et al [6]	Our study
Distal RTA	3	3	3	2	23
Proximal RTA	10	1	-	-	2
Gitelman's syndrome	2	4	1	2	3
Bartter's syndrome	-	-	-	-	2
TPP	2	5	6	16	-
Acute Gastroenteritis	-	-	-	-	13
Primary hyperaldosteronism	13	-	1	1	-
Diuretic induced	-	-		4	3

[RTA- renal tubular acidosis; TPP- thyrotoxic periodic paralysis]

CONCLUSION

A significant number of patients in our study had secondary and potentially reversible causes of hypokalemic periodic paralysis We strongly recommend urine spot potassium and ABG to be the first line investigation in working up a case of hypokalemic paralysis. We noted the distribution and severity of muscle weakness correlates well with serum potassium levels. The milder form of hypokalemia presenting as muscle cramps occurred in patients with mean serum potassium levels of 2.07 mEq/L. The mean serum potassium level of patients presenting with quadriparesis in hypokalemia was 1.82mEq/L in our study. Involvement of respiratory muscles occurs in serum potassium levels of 1.4 mEq/L leading to respiratory arrest. ECG changes correlates well with severity of hypokalemia, ECG remains the best bed side tool to diagnose hypokalemia. A detailed work-up for secondary causes should be undertaken in patients with hypokalemic periodic paralysis.

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