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CLINICAL AND ETIOLOGICAL PROFILE OF PATIENTS WITH PERIODIC PARALYSIS - A STUDY FROM A RURAL TERTIARY CENTRE ,WEST BENGAL.

Neurology

Dr Debal Laha* Assistant Professor, Department of Neurology, Burdwan Medical College, Baburbag, P.O.Rajbati Burdwan - 713104 West Bengal, India. *Corresponding Author

Prasenjit Sengupta Professor, Department of Neurology, Burdwan Medical College, Baburbag, P.O.Rajbati Burdwan - 713104 West Bengal,India.

ABSTRACT

Periodic Paralysis is a disease of skeletal muscle in which patients experience episodic attacks of muscle weakness .The present study has been undertaken to determine the various etiologies of hypokalemic paralysis, its varied presentations, and the clinical outcome after potassium replacement therapy. The present study is a prospective single centre observational study of 40 patients done over a period of one year. Extensively clinically and biochemically evaluated. Hypokalemia seen in 90%.There was a seasonal variation , maximum during the summer season. Atypical presentation included hemiparesis and early neck muscle weakness. Primary hypokalemic periodic paralysis occurred in 60%, Secondary in 40%. Variety of secondary cases were evaluated extensively. Among the studies, our study showed the detection of maximum mumber of cases within a short period which reflect possibly the cases in the community may be high and need to be validated through survey.

KEYWORDS

Periodic paralysis, HOPP/HPP, primary, secondary

INTRODUCTION

Periodic Paralysis is a disease of skeletal muscle in which patients experience episodic attacks of muscle weakness of variable duration and severity.[1,2] Periodic paralysis is classified according to serum potassium during attacks into hypokalemic, normokalemic and hyperkalemic periodic paralysis. This has now been supplemented by the newer molecular genetic classification[4,8]

Hypokalemia is defined as serum Potassium concentration of less than 3.5mmol/litre (normal 3.6-5.0mmol/ litre).[3] Most of the cases are due to familial or primary hypokalemic periodic paralysis (HOPP) with underlying genetic basis. Two genes are known to be associated with HOPP, calcium channel gene (CACNA1S) accounting for approximately 55-70% of HOPP type 1 and sodium channel gene (SCN4A) accounting for 8-10% of HOPP type 2.[2,4]

Symptoms of idiopathic primary hypokalemic paralysis typically begin in the first or second decade with attacks of flaccid paralysis usually occurring on awakening in the night or in the early morning. Weakness is usually generalized, rarely being focal, usually sparing facial and respiratory muscles, and lasting for hours(occasionally days) with gradual resolution. Frequency of individual attacks can vary from daily to few episodes in a lifetime. Attacks often decrease spontaneously or resolute in frequency after age of 40.[6]It is now known that in both genetic and acquired forms of periodic paralysis,is the dysfunction of voltage- gated ion channels which is the underlying pathophysiology.[5,7]

Although the clinical manifestation may be similar in both primary and secondary hypokalemic paralysis, the long term management of different types of hypokalemic paralysis. The treatment of acute attacks is aimed at restoring serum potassium levels to normal. Long term management differs in secondary hypokalemic paralysis depending on the underlying cause.The present study has been undertaken to determine the various etiologies of hypokalemic paralysis, its varied presentations, and the clinical outcome after potassium replacement therapy of this fairly treatable but potentially fatal metabolic disease.

MATERIALAND METHODS

This present study had been conducted in Burdwan Medical College, Burdwan in the Department of Neurology. The present study is a prospective single centre observational study of 40 (Forty) patients done over a period of one year from January 2019 to December 2019. Those patients that presented with acute onset generalized or focal weakness were evaluated. Patients with upper motor weakness have been excluded.

The clinical data collected for HPP were age, sex, ethnic origin, duration of illness, number of episodes of acute muscular weakness, time to improve, precipitating factor, and family history. For secondary causes, history of renal stone, bone pain, dry eye, fracture, thyroid disease, parotid and lacrimal gland enlargement. Clinical examination with special emphasis on blood pressure and detailed neurological examination were done including muscle power evaluation based on MRC scale.

The following biochemical parameters were estimated: Serum sodium, potassium, bicarbonate, chloride, creatinine, calcium, phosphate, magnesium, albumin, and globulin. 24 hour urinary calcium, phosphate, potassium and creatinine were also carried out in selected patients. All the patients underwent thyroid function test, arterial blood gas analysis and 12 lead Electrocardiogram (ECG).Serum aldosterone, plasma rennin levels and CT of the adrenal gland were done in selected group of patients . The clinical and laboratory data of these patients were analyzed after taking proper consent.

STATISTICALANALYSIS:

Results were analyzed by SPSS 17 statistical software SPSS (version 17) for Microsoft software. (IBM, Illinois, Chicago, USA). Mean and standard deviations were done and analyzed by Chi-square test.

RESULTS

Total Forty cases presented with periodic paralysis (mean age 31.2,range 12-58).Out of the 40 patients, 28 were men. Out of 40 patients, 36 had hypokalemia and 4 had normokalemia. This Normokalemic patients presented with acute onset LMN type Quadriparesis which recovers very quickly and spontaneously. There is varied clinical presentation, out of forty(40), 30 presented with sudden onset quadriparesis (Lower limb followed by upper limbs),four (4) cases had sudden onset paraplegia,4 cases had hemiparetic presentation and Two(2) case presented with isolated neck muscle weakness without any limb weakness. Six (6) patients were tribal, Eight(8) were alcoholic, most of them manual worker (n=30) and all were habituated with large amount of carbohydrate diet. Among them, average duration of illness was sixteen months (2-48months) and most of the primary cases improved quickly as compared to secondary. Patients were further investigated for possible secondary causes of hypokalemia.

A total of 24/40 (60%) cases diagnosed as idiopathic HOPP. Primary (Idiopathic) HOPP cases had symptoms onset in late childhood or adolescence and rarely after age of 25 years with male preponderance and 8 cases had positive family history. They are frequently precipitated after vigorous physical activity and carbohydrate rich diet (n=20). The limb muscles are affected earlier than trunk muscles, proximal muscles are more susceptible than distal ones.

A total of Sixteen (16) patients (40%) in this study had secondary potentially reversible causes of HOPP. Out of 16 patients 8 cases Renal tubular Acidosis, 4 cases Primary Hyperaldosteronism, 2 cases of

Thyrotoxic Peiodic Paralysis and 2 cases of Gitleman Syndrome. A detailed workup for secondary cause should be undertaken for these patients. Of the patients(20%) with Renal Tubular Acidosis which had significantly lower serum bicarbonate and higher levels of chloride as compared with those who had primary Hyperaldosteronism (n=4) although potassium levels were similar. All patients with primary Hyperaldosteronism had hypertension at presentation.

Two cases of Gitelman Syndrome who presented with severe hypokalemia, hypomagnesemia, hypophosphataemia and hypocalciuria was detected.

All patients had recovery with potassium replacement therapy or spontaneously. The secondary group needed significantly longer time to recover compared to patients with primary hypokalemic paralysis. Treatment with acetazolamide with no further recurrence of symptoms were seen during this period.

DISCUSSION

Thus this study shows a group of 40 patients of periodic paralysis presented with predominantly hypokalemic type in 36 cases (90%).The largest study on HOPP was from Taiwan by Lin et al reported a total of 97 cases over a period of 10years.[9] Agarwal et al. has reported 40 cases of HOPP in a period of 23 years[10] . In an earlier series reported by Arya et al. a total of 22 cases of HPP were reported over 30 years[11]. Various Series of HOPP cases have been reported from different parts of India.

Table:1 showing clinical features and underlying causes in different regions of India

Author's Name	Region	Period of study	No of case	Mean age (Years) (Range)	Gender	Idiopathic	Secondary	Causes of secondary
Kayalet al [14]	North East India	Oct2009 to Sept. 2011 (24m)	56	(36.76+/- 13.72) (15- 92)	41:15	32(57.1%) (5 pt had family history)	24 (42.9%)	RTA -4 ,Gitelman syndrome-4, TPP-3 Hypothyroidism , gastroenteritis, Liddlesyndrome -2 each,primary hypothyroidism, alcoholism, dengue fever-1 each
Maurya et al.[13]	Central India	2008 -2010 (24m)	32	17-52	27:3	17 (56.6%)	13 (43.3%)	RTA -4, Gitelman syndrome -4, TPP-5, (secondary group has greater severe hypokalemia): respiratory paralysis was present in 20%
Rao N et al. [12]	Southern	1995 to 2001 (6 years)	31	34.5	19:12	1	30 (96.7%)	RTA-13 pt, Primary hyperaldosteronism (13, all adrenal adenomas), TPP (2), Gitelman Synd (1)
Our study	Eastern	Jan, 2019 to December 2019 (12 months)	40	31.2 (12.58)	14:6	24 (60%) Familial – 8 cases	16 (40%)	RTA -8, primary hyperaldosteronism -4, Gitelman syndrome-2, TPP-2

Among the studies, our study showed the detection of maximum mumber of cases within a short period. The underlying reasons may be due to quick recognition of cases by doctors, availability of neurological services and rapid hospitalization facilities.

There was a seasonal variation in the frequency of hypokalemic attacks; highest numbers of cases were during the summer season. In this study, most of the cases were found in the summer months. Rice is the major food of the region, which is rich in carbohydrate content and thus can be a precipitating factor for HPP.During summer, excessive sweating caused excess potassium loss which may precipitate HPP in genetically susceptible subjects. This is similar to an earlier Indian study, which had also shown higher number of cases of HPP in the summer season.[15]

Male preponderance was observed in the present study, which has earlier been documented in all previous studies and may be related to high manual labour and large consumption of carbohydrate food as compared to women.[12,13]

In our study primary hypokalemic periodic paralysis occurred in 60% of patients, out of which 66.6 % of total cases were sporadic while 33.3% where familial. In this study, 40% of patients with HPP had a secondary cause for their condition. An earlier study from Kashmir has reported 21 cases of HPP secondary to distal RTA over a period of 8 years.[16] Gitelman syndrome which we diagnosed in 5% of cases, was one of the rare causes of secondary HPP. Gitelman syndrome has been reported in earlier Indian studies with a varying frequency rate ranging from 3.2% to 13.3%.[12,13] In our study, Gitelman syndrome presented with tetany, which may be attributed to exacerbation of alkalosis and consequent low ionized plasma calcium in presence of hypomagnesaemia.

In this study thyrotoxic periodic paralysis (TPP) was the cause in 5% of the cases of HPP and the underlying cause of low incidence may be related to genetic reason, since it is common among Polynesians. The earlier Indian studies has shown variable incidence of TPP, ranging from 6.4%[12] to 16.7%.[13]

In our series, 4 patients (10%) had primary hyperaldosteronism as the secondary cause of HPP. The patient presented with isolated episodic, asymmetric weakness (1 case presented with paraparesis) and was finally diagnosed as primary hyperaldosteronism. Periodic paralysis as a presentation of primary hyperaldosteronism is commonly reported among the oriental races.[18] In a series of 50 patients with primary hyperaldosteronism from Taiwan, 42% presented with periodic paralysis, although all 50 had hypokalemia indicating possible role of modifier gene.[18]

Six patients had hypokalemic paralysis with heavy alcohol intake, 2 of them having past history of recurrent episodes of weakness on repeated alcohol intake. All the 6 patients had severe myalgia, and they took longer time to recover in comparison to other secondary disorders. Occurrence of recurrent attacks was more in secondary hypokalemic periodic paralysis as compared to primary hypokalemic periodic paralysis.

Atypical presentation included hemiparesis and early neck muscle weakness in our study, though these have also been reported in earlier Indian studies.[15] It is likely that these atypical manifestations are a result of failure of transmission of nerve impulses at the synaptic junctions as a result of hypokalemia to susceptible muscle.[19]In our study the serum potassium concentrations were lower in patients with secondary hypokalemic paralysis than in those with primary hypokalemic paralysis. The same observation has been made by another study from India in the study by Maurya and colleagues,[13] the serum potassium concentrations were significantly lower in patients of secondary hypokalemic paralysis than in those with primary hypokalemic paralysis probably due to acid base imbalance and associated other electrolyte deficiency. This may explain delayed recovery in secondary HPP.

The elevation of serum CPK is an indirect evidence of damage to muscle membrane. This has also been infrequently reported in earlier Indian studies.[15] In our study serum CPK was also significantly higher in the secondary group compared to the primary group. It is postulated that hypokalemia causes muscle ischemia, resulting in a rise in serum CPK. In contrast to the primary group patients, an acid base disorder was present only in the secondary group due to associated renal dysfunction. Distal RTA was the diagnosis in cases with metabolic acidosis, while cases with metabolic alkalosis had Gitelman syndrome, or primary hyperaldosteronism as the final diagnosis. This has been reported in earlier studies also.[9] So in cases with an acid-base disorder, a secondary cause of HPP should be suspected and investigated.

In this study, four patients recovered spontaneously and in other cases potassium replacement was necessary. The secondary group needed longer time to recover compared to the patients with primary HPP. Among the secondary group the recovery time was longer in

alcoholics. This delay in recovery can be because of co-existent hypomagnesaemia with hypokalemia in alcoholics as reported in earlier case reports[20]. Two patients of RTA as secondary causes expired due to late presentation and delay in diagnosis during entire period of this study. This suggests that timely intervention can be life-saving in this easily treatable but potentially fatal disease.

CONCLUSION

In this series of periodic paralysis from Burdwan Medical College, West Bengal forty (40) cases of periodic paralysis were detected in a short period of time (twelve months) which reflect possibly the cases in the community may be high and need to be validated through survey. We have also seen varied clinical presentation and wide variety of secondary causes in comparison to previous study. Our study also highlights acute onset recurrent LMN type quadriparesis inspite of normal potassium level which recovers very quickly and spontaneously. In this study 60% of the cases are idiopathic periodic paralysis. This is the first study from West Bengal and second study from eastern India. Predominant cases are idiopathic and emphasize the needs of genetic study to determine any underlying abnormalities.

Limitation of article

Epidemiological studies required community based study for unbiased estimate. Since predominant cases are idiopathic and it needs further genetic study to determine any genetic abnormalities.

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