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Study of clinical profile in patients presenting with Hypokalemic Paralysis

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Abstract

Background: Hypokalaemic paralysis is a clinical syndrome characterised by severe muscular weakness but in cases with severe hypokalaemia may lead to virtually total paralysis including respiratory, bulbar and cranial musculature. Hypokalaemic paralysis can occur as a result of either an alteration in the transcellular distribution of potassium or true potassium depletion as a result of renal or extra renal losses. **Methodology**- The study was carried out on patients admitted in wards and ICU presenting with Hypokalemic Paralysis at a Tertiary health centre, Solapur. The duration of the study was from September 2019 to August 2021. Total 24 patients were included in the study. Predesigned and pretested case record form was used as tool for data collection. **Results**- Sporadic periodic paralysis was most common etiology contributing 58.3%, followed by thyrotoxic periodic paralysis (16.6%), familial hypokalemic periodic paralysis (12.5%), excess insulin induce (8.3%), diuretic induce (4.16%). Quadriparesis was most common clinical presentation contributing 83.3%, followed by paraparesis 16.6%. Majority of patients treated with oral plus iv potassium chloride (87.5%), 12.5% treated with oral potassium chloride only and 3 patients (12.5%) required iv magnesium with potassium correction. **Conclusion**- The commonest causes for hypokalemic paralysis (HP) in our study were sporadic periodic paralysis (SPP) and TPP. Spot urine K^+/Cr ratio helps to distinguish the diagnostic categories of HPP and TPP**.** Sporadic periodic paralysis (SPP) was more common than familial periodic paralysis (FPP) in this study.

Keywords- Hypokalemic, paralysis, familial, quadriparesis, SPP, TPP

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Introduction

Hypokalaemic paralysis is a clinical syndrome characterised by severe muscular weakness but, in cases with severe hypokalaemia may lead to virtually total paralysis including respiratory, bulbar and cranial musculature. In addition to diminished motor power, the patient may also have decreased or non-existent tendon reflexes on physical examination. It is a rare, but treatable, cause of severe acute weakness. Hypokalaemic paralysis can occur as a result of either an alteration in the transcellular distribution of potassium or true potassium depletion as a result of renal or extrarenal losses. The majority of instances are caused by a transcellular shift in potassium.[1]

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Sporadic periodic paralysis (SPP), has a presentation similar to that of familial periodic paralysis (FPP) and is caused by gene mutations in the calcium (Ca(2+)) (CACNA1S) and sodium (Na(+)) (SCN4A) channels of skeletal muscles.[2] Whereas channels responsible for familial periodic paralysis include mutations in the skeletal muscle dihydropyridine receptor calcium channel (CACNL1A3), tetrodoxin sensitive voltage sensitive sodium channel (SCN4A), and potassium channel have been discovered (Kir2.1).[3]

K (+) homeostasis depends on external balance (dietary intake [typically 100 mmol per day] versus excretion [95% via the kidney; 5% via the colon]) and internal balance (the distribution of K (+) between intracellular and extracellular fluid compartments). The uneven distribution of K (+) across cell membranes means that a mere 1% shift in its distribution can cause a 50% change in plasma K (+) concentration. Extra renal K (+) losses from the body are usually small, but can be marked in individuals with chronic diarrhea, severe burns or prolonged sweating. Under normal circumstances, the kidney's distal nephron secretes K (+) and determines final urinary excretion. In patients with hypokalemia (plasma K (+) concentration <3.5 mmol/l), after the exclusion of extrarenal causes, alterations in sodium ion delivery to the distal nephron, mineralocorticoid status, or a specific inherited or acquired defect in distal nephron function (each of which affects distal nephron K (+) secretion), should be considered. Clinical management of hypokalemia depends on underlying cause.[4]

Hence, the study was carried out to investigate the several etiologies, varied presentations and outcome of therapy in Hypokalemic Paralysis patients admitted to tertiary care centre, Solapur.

Materials And Methodology

Study place- The study was carried out on all patients presenting with hypokalemic paralysis at Tertiary health care center, Solapur from September 2019 to August 2021.

Study Design- It was an observational study. Predesigned and pretested case record form was used as tool for data collection.

Inclusion criteria- All patient presenting with clinical feature of Hypokalemic paralysis, Acute flaccid paralysis and muscle weakness were included in the study.

Exclusion criteria- Patients with acute paralysis secondary to other causes other than hypokalemia like GBS, stroke, traumatic brain injury, multiple sclerosis were excluded from the study.

Sample size- 24 patients were taken into consideration for the study**.**

Data analysis- Consecutive sampling method was used to include subjects as per inclusion criteria. Predesigned and pretested case record form was used as tool for data collection.

Ethical Considerations- Institutional Ethical Clearance was obtained before starting the study.

Clinical data was collected. Any history of similar disease in the family was enquired about, and reports of weakness, thyroid disease, diarrhea, vomiting, hypertension, bone pain, fractures, dry mouth, dry eyes, and kidney disease were recorded. Intake of drugs like diuretics, β2 agonists, decongestants, insulin, laxatives and antipsychotics were noted. The examination included anthropometry, pulse, blood pressure, anemia, thyroid status. Complete neurological examination was performed. Schirmer's test was performed in selected patients. Patients with urinary K+ loss and hyperchloraemic metabolic acidosis with normal anion gap underwent: SSA, SSB antibody ANA Urinary aminoacid. Patients with urinary K+ loss and metabolic alkalosis underwent: 24-hours urinary calcium. Patients with Urinary K+ loss with normal acid base status underwent an ammonium chloride loading test (0.1 g/kg). TTKG was done when there was doubt in diagnosis of hypokalemia due to transcellular shifts or due to renal

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loss.

Result

Table 1: Age-distribution

Age (years)	Frequency	Percentage
< 20	3	12.5%
21-30	13	54.16%
31-40	6	25%
>40	2	8.33%
Total	24	100%

Above table shows majority of patients were from age group 21-30 years (54.16%), followed by 31-40 years (25%), <20 years (12.5%), >40 years (8.33%).

Table 2: Sub groups based on Etiology

Etiology	Frequency	Percentage
SPP	14	58.3%
TPP	4	16.6%
Familial HPP	3	12.5%
Excess insulin	2	8.3%
Diuretics induced	1	4.16%
Total	24	100%

Above table shows sporadic periodic paralysis is most common etiology in our patients contributing 58.3% followed by Thyrotoxic periodic paralysis contributing 16.6%.

Table 3: Potassium levels in serum

Levels (meq/L)	Frequency	Percentage
1.1-2.0	8	33.3%
2.1-3.0	14	58.3%
3.1-3.5	2	8.3%
Total	24	100%

Above table shows majority of patients have serum potassium levels between 2.1-3.0 meq/L contributing 58.3%

Table 4: Clinical presentation

Clinical features	Frequency	Percentage
Quadriparesis	20	83.3%
Paraparesis	4	16.6%
Total	24	100%

Above table shows majority of patients presented with quadriparesis (83.3%).

Table 5: Complications

Complications	Frequency	Percentage
Respiratory paralysis	2	8.3%
Cardiac complications	4	16.6%

Above table shows 4 patients had cardiac complications in form of arrhythmias & premature ventricular complex, 2 patients landed in respiratory paralysis which were intubated.

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Table 6: Comparison of various parameters between sub-diagnosis (ANOVA test)

	SPP	**TPP**	**Familial HPP**	**Excess insulin**	**Diuretics induced**	**F-value**	**p-value**
Sr.k+	2.23 ±0.49	2.45 ±0.59	1.97±0.86	2.35±0.21	2.40 ± 0.0	0.37	0.82
Sr.Na	137.36±2.7	137.25±2.22	134.67±3.21	137±1.41	130 ± 0.0	2.28	0.09
Sr. Cl	96.36±3.9	101.5±2.1	98.33±3.0	100 ± 2.8	92 ± 0.0	2.44	0.08
B. urea	25.86±5.0	25.50±6.9	30.67±5.1	33.0±1.4	38.0 ± 0.0	2.30	0.09
Sr. creatinine	1.06±0.6	1.18±0.1	1.37 ± 0.7	0.95±0.2	1.5 ± 0.0	0.34	0.85
Sr.PO4	3.5 ± 0.4	3.0 ± 0.2	3.4 ± 0.7	3.3 ± 0.7	3.1 ± 0.0	0.98	0.44
Sr.Ca	9.0 ± 0.3	9.1 ± 0.4	8.9 ± 0.1	8.8 ± 0.5	9.5 ± 0.0	0.88	0.49
Sr.Mg	2.06±0.2	1.95±0.1	1.67 ± 0.5	2.10±0.1	0.8 ± 0.0	7.42	**0.001**
PH	7.39±0.04	7.36±0.02	7.37±0.04	7.40±0.03	7.50 ± 0.0	3.77	**0.02**
Urine K+	11.13±2.6	14.75±1.9	11.67±0.6	15.0±1.4	31 ± 0.0	18.37	**<0.0001**
Urine Cr.	6.77±1.0	7.15±1.2	7.63 ± 0.9	6.40±0.3	5.80 ± 0.0	0.93	0.47
U K+/ U Cr	1.65±0.4	2.08±0.3	1.55 ± 0.3	2.34±0.1	5.34 ± 0.0	28.5	**<0.0001**
T4	10.65±1.0	26.25±1.7	10.27±0.6	10.95±0.8	9.5 ± 0.0	167.43	**<0.0001**
TSH	1.56± 0.3	0.41±0.37	1.73 ± 0.5	1.80±0.1	1.5 ± 0.0	10.8	**<0.0001**
Hospital Stay	7.21± 2.8	5.50± 1.3	10 ± 4.6	6.50±0.7	7.0 ± 0.0	1.13	0.37

Further analysis was performed by post hoc Bonferroni Multiple comparison for those statistical significant observed in ANOVA test. In the present study, there was significant difference between diagnosis for Sr.Mg (p=0.001), PH (p=0.02), Urine K+ (p<0.0001), U K+/U Cr (p<0.0001), T4 (p<0.0001), TSH (p<0.0001). Further post hoc analysis for Sr.Mg. found that, there was no significant difference of multiple comparison between sub-diagnosis (p>0.05). Further post hoc analysis for PH found that, there was no significant difference of multiple comparison between sub-diagnosis (p>0.05). Further post hoc analysis for Urine K+ found that, there was no significant difference of multiple comparison between sub-diagnosis (p>0.05). Further post hoc analysis for U K+/U Cr found that, there was no significant difference of multiple comparison between sub-diagnosis (p>0.05). Further post hoc analysis for T4 found that, there was significant difference of SPP with TPP (Mean difference=15.6, p<0.0001), TPP with Familial HPP (Mean difference=15.98, p<0.0001), TPP with Excess insulin (Mean difference=15.30, p<0.0001). Further post hoc analysis for TSH found that, there was significant difference of SPP with TPP (Mean difference=1.14, p<0.0001), TPP with Familial HPP (Mean difference=1.32, p<0.0001), TPP with Excess insulin (Mean difference=1.4, p=0.001). Further post hoc analysis for hospital stay found

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that, there was no significant difference of multiple comparison between sub-diagnosis ($p>0.05$).

Table 7: Association of Serum potassium level and clinical features

Clinical features	Serum potassium level			χ^2 value	p-value
	<2	2-3	3-4		
Quadriparesi	8 (40)	11 (55)	1 (5)	0.94	0.33
Paraparesis	0	3 (75)	1 (25)	0.94	0.33

Table 8: Association of Sub-diagnosis and response to treatment

Response to treatment	**Sub-diagnosis**					**χ^2 value**	**p-value**
	SPP	TPP	FamilialHPP	Excess insulin	Diuretics induced		
IV kesol	13	3	2	2	1	0.88	0.35
Oral kcl	14	4	3	2	1	0.0	1.0
IV mg	1	0	1	0	1	0.88	0.35

Table 9: Association of Serum potassium level and response to treatment

Response to treatment	**Serum potassium level**			**χ^2 value**	**p-value**
	<2	2-3	3-4		
IV kesol	8	13	0	0.43	0.51
Oral kcl	8	14	2	0.0	1.0
IV mg	2	1	0	0.43	0.51

DISCUSSION

Large study was conducted by G Chandra Mohan, T Dinesh Kumar, R Arul, M Seenivasan, J Dhanapriya, R Sakthirajan, T Balasubramaniyan, N Gopalakrishnan1(2018) [5] on 206 patients in tertiary care centre in India.

Table 10

Variable	SPP	TPP	dRTA	pRTA	GS	ALDO
N	70	8	75	6	39	7
Mean age (year)	34.7	37.62	37.86	40	41.82	41.71
Mean episodes	2.9±2	1.5±0.5	3.3±1.7	3.1±1.5	1.5±0.7	4.1±2.1
Mean porassium at presentation(mEq/L)	2.64	2.75	2.67	3.1	2.5	2.34
Urine potassium (mEq/L)	12.24	13.67	25.27	33.67	25.79	36.87
Recovery time (h)	22.1±5	23.7±4	31.3±6	30±7.2	37.5±6	34.2±4
Mean KCL requirement(mEq/L)	58±23	47.5±21	101±18	89±24	90±16	112±24

SPP: Sporadic periodic paralysis. dRTA: Dosta; renal tubular acidosis, pRTA: Proximal renal tubular acidosis, TPP: Thyrotoxic paralysis, GS: Gitelman syndrome, ALDO: Hyperaldosteronism, KCL: Potassium chloride, HKP: hypokalemic paralysis

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In the given table below table, distal-RTA is most common followed by SPP, in our study SPP was most common cause. In another study from North India, **Maurya et al (2010)** reported HP in 30 patients, 17 (56.7%) had primary idiopathic hypokalemic paralysis or SPP, 5 (16.7%) had TPP, 4 (13.3%) had RTAand 4 (13.3%) had Gitelman's syndrome.[6]

In our study 14 patients (43%) had Sporadic Periodic Paralysis(SPP) and 3 patients had family history of periodic paralysis. The mean age of onset was 27.9±2.7 years. None had urinary loss of potassium in this group. Two patients had respiratory paralysis in this group and 3 patients had cardiac complications in form of arrhythmias. Twelve patients noticed weakness while getting up from bed in the morning, 1 patient noticed weakness after recovering from alcohol binge. Limb muscles were more affected than the trunk muscles. Those who had respiratory paralysis and muscle power ≤2/5 where treated with intravenous potassium chloride and others were treated with oral potassium supplementation. We had 4 patients with TPP with a mean age of 41.5±3.2 years, the incidence of TPP is highest in Asian population according to study in Taiwan by Lin SH et al [7,] another study by Annie W. C. Kung et al [8] but TPP is not the most common causes in our study and other Indian studies by Chandra mohan, Dinesh kumar, R Arul, M Seenivasan, J Dhanapriya, R Sakthirajan, T Balasubramaniyan. [5] All the four patients in our study had tachycardia without any overt thyrotoxic symptoms. These findings in our study are in conformity with studies by Phillip wing et al[9], other study by Karen M O'Neil et al[10], which states that TPP affects males more than females although thyrotoxicosis is common in females and most patients have only mild or no symptoms of thyrotoxicosis. These patients were managed with oral potassium and propranolol followed by definitive therapy for thyrotoxicosis. We did not see recurrences in this group of patients. Hypokalemia is a recognized complication during treatment of diabetic ketoacidosis and also hyperosmolar hyperglycemic state or accidental insulin excess according to study of Amalnath, Deepak S, Dutta, Tarun Kumar.[11] In our study we had two patients secondary to insulin excess. One patient was known case of type one diabetics on fixed dose of 40 unit of insulin mixtard , he presented with quadriparesis with serum potassium 2.5 meq/L and was treated with intravenous and oral potassium chloride. Other patient presented with hyperosmolar hyperglycaemic state with random BSL of 650 mg/dl, newly diagnosed. Presented with quadriparesis with serum potassium of 2.2 meq/L. was treated with intravenous and oral potassium chloride, insulin Therapy was given under close supervision. Our study agrees with study by T Johnson et al on Endogenous insulin fluctuations during glucose-induced paralysis in patients with familial periodic hypokalemia.[12]

Overall, hypokalemia is more frequent with thiazide diuretics than with loop diuretics, despite having a less potent natriuretic effect. One potential explanation is the differential effect on calcium excretion. Whereas thiazide diuretics decrease calcium excretion , loop diuretics lead to a significant increase in calcium excretion. The higher luminal calcium concentration in the distal nephron produced by loop diuretics reduces the lumen-negative driving force for potassium excretion, there by blunting their kaliuretic effect of loop diuretics. [14] In our study 52- year female know case of Copd and newly diagnosed hypertension was treated with Nifedpine 20mg and Chlorthalidone 12.5mg OD 3 weeks prior to admission, presented with quadriparesis. thiazide diuretic where stop and treated with IV plus oral potassium chloride, our study agrees with study conducted by Richard L Tannen et al.[13]

Conclusion

The commonest causes for hypokalemic paralysis (HP) in our study were sporadic periodic paralysis (SPP) and TPP. Spot urine K^+/Cr ratio helps to distinguish the diagnostic categories of HPP (Hypokalemic paralysis due to K^+ shifts) with non-HPP (Hypokalemic paralysis due to K^+ deficits). Sporadic periodic paralysis (SPP) was more common than familial periodic

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paralysis (FPP) in this study. Absence of history of thyroid disease or clinical thyrotoxicosis does not exclude the diagnosis of TPP. So thyroid function tests should be done in all patients with HP. Most patients were treated with IV potassium during therapy of HPP (SPP, TPP), thereis still a danger of rebound hyperkalemia.

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