SHORT REPORT

Arterial blood gas analysis aids early differential diagnosis and treatment of primary and secondary hypokalaemic periodic paralysis

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Abstract

This study aimed to examine changes in electrolytes and acid-base status in primary and secondary hypokalaemic periodic paralysis (HypoPP), which will help early differential diagnosis of HypoPP. A total of 64 HypoPP patients were enrolled and relevant data from clinical records was collected. Overall, 64 patients (mean age 28.2±7.3 years) of which 58(91%) were males, with 39, 11 and 14 patients, respectively, diagnosed as primary HypoPP, thyrotoxic HypoPP, and other secondary HypoPPs at discharge, were assessed. Those with HypoPP secondary to conditions other than hyperthyroidism were more likely to develop acid-base imbalance ($p<0.001$); they had higher pH ($p=0.046$) and HCO_3 levels ($p=0.014$) at baseline, and needed a higher dose of potassium supplement before the serum potassium level returned to normal ($p=0.007$) and a longer time to regain full muscle strength ($p=0.004$), compared with those with primary or thyrotoxic HypoPP. Emergent arterial blood gas analysis may aid early differential diagnosis of patients with primary and secondary HypoPP.

Keywords: Hypokalaemic periodic paralysis, arterial blood gas, acid-base balance.

DOI: https://doi.org/10.47391/JPMA.949

Introduction

Early diagnosis of hypokalaemic periodic paralysis (HypoPP) is usually based on the history of episodes of paralysis and ictal serum potassium levels. The management involves oral and/or intravenous potassium administration. This may cause rebound hyperkalaemia in certain cases, especially in patients with primary HypoPP and thyrotoxic HypoPP when there is acute shift of potassium into the cells instead of the body that is deficient in potassium.[1-4] However, it is difficult to differentiate primary and secondary HypoPP based on the clinical features alone in the early stage of presentation, particularly in patients with few episodes without a history of potential primary causes for HypoPP. Previous case reports or small studies had indicated that electrolytes and acid-base status might be different in patients with HypoPP of different aetiologies.[5-7] Therefore, the current study aimed to examine the changes in acid-base status and electrolytes in patients with primary and secondary HypoPP, to help early differential diagnosis in affected patients.

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Methods

This was a retrospective, observational study, with no additional intervention against routine clinical practice among the patients involved. Sixty-four patients admitted to a tertiary hospital (the Houjie Hospital) in Dongguan, Guangdong Province, China, in 2018 were retrospectively enrolled by using the following criteria: 1) those who presented to the hospital within 10 hours of ictal muscle weakness; 2) serum potassium level ≤3.5 mmol/L as tested at the emergency department; 3) those who were diagnosed as primary or secondary HypoPP at the time of discharge. Those with acid-base imbalance diagnosed before the index episode of muscle weakness as well as those with other previously diagnosed severe systemic diseases that may cause electrolyte disturbance and acid-base imbalance, such as end-stage renal disease and severe digestive disorders, were excluded. The study was approved by the Ethics Committee of the Houjie Hospital, and informed consent was waived due to its retrospective nature. All data was collected by reviewing the clinical records.

Medical history, physical examination, and electrocardiogram of all patients had been performed, and the following lab tests were conducted as early as possible: serum potassium level test, arterial blood gas (ABG) test for electrolytes and acid-base status, and thyroid function tests. Oral and intravenous potassium administrations were started as soon as reduced serum potassium level was detected. All patients received routine potassium supplemental treatment for HypoPP at the hospital, decided by the neurologist in charge, which included oral potassium chloride solution (10%), 20 ml, administered every two hours, and continuous intravenous potassium

chloride solution (0.03%). Tests for serum potassium level were repeated every two hours after initiation of treatment with potassium supplement, which was stopped as soon as the serum potassium level returned within the normal range. The doses of oral and intravenous potassium administration were recorded every two hours, and the total dose of potassium administration was recorded after normalisation of the serum potassium level. The intervals between initiation of potassium administration and normalisation of serum potassium, and then recovery of full muscle power, were recorded. Rebound hyperkalaemia was defined as serum potassium level of higher than 5.3 mmol/l, in any of the repeated tests.

In addition, all patients underwent relevant tests to determine the aetiologies of HypoPP. Primary or secondary HypoPP, and the potential primary causes, were diagnosed accordingly before discharge. Patients were divided into three groups according to the final diagnosis at discharge: primary HypoPP, thyrotoxic HypoPP, and other secondary HypoPPs. Patients with thyrotoxic HypoPP were separated from those with secondary HypoPP of other causes, since there was no potassium deficiency in the body in thyrotoxic HypoPP unlike other secondary HypoPPs.

Statistical Analyses: Demographics, serum potassium levels, and results of ABG analysis before treatment with potassium supplement, doses of potassium administration, and time from initiation of potassium administration to recovery of muscle power, were compared among the three groups of patients with the final diagnosis of primary HypoPP, thyrotoxic HypoPP, and other secondary HypoPPs. Pearson chi-square tests and analysis of variance (ANOVA) tests were respectively performed for comparison of categorical and continuous variables. The Student-Newman-Keuls method was used for pairwise comparison of continuous variables. Two-sided p values of <0.05 were considered statistically significant. SPSS (version 16.0) software was used for all statistical analyses.

Results

Overall, 64 patients (mean age 28.2±7.3 years) of which 58(91%) were males, with HypoPP were retrospectively enrolled in the current study, with a mean baseline serum potassium level of 2.2±0.6 mmol/L. Among these patients, 39 (61%) and 25 (39%) patients, respectively, were diagnosed as primary and secondary HypoPP. Of those with secondary HypoPP, 11 were thyrotoxic HypoPP, and others had HypoPP secondary to the following conditions: hyperaldosteronism in 2 patients, renal tubular acidosis in 2 patients, excessive sweating in 5 patients, severe vomiting and diarrhoea in 3 patients, and long-term use of potassium-sparing diuretics in 2 patients. There was no

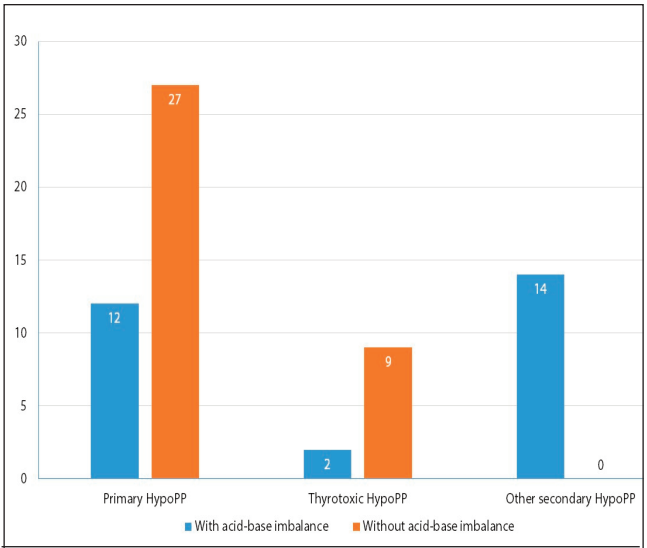

Figure-1: Numbers of patients with and without acid-base imbalance at baseline. HypoPP, hypokalaemic periodic paralysis.

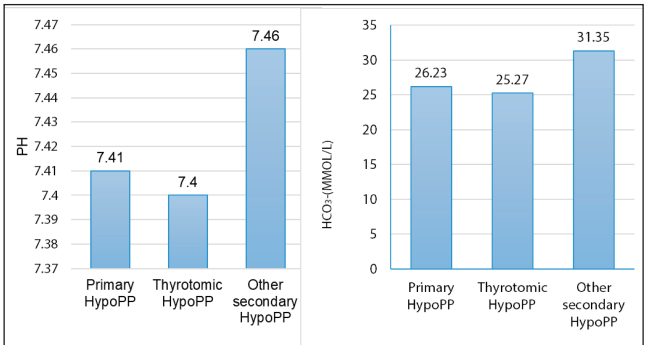

Figure-2: Mean pH (left panel) and HCO_3^- (right panel) levels of patients with primary HypoPP, thyrotoxic HypoPP, and other secondary HypoPPs. P values in the figure were for Student-Newman-Keuls tests. HypoPP, hypokalaemic periodic paralysis.

significant difference in baseline serum potassium levels among those with primary HypoPP (1.99±0.59 mmol/L), thyrotoxic HypoPP (2.07±0.66 mmol/L), and other secondary HypoPPs (2.19±0.64 mmol/L) (p=0.575).

ABG analysis: Baseline ABG analysis was performed within 10 hours after the onset of symptoms. Among those with primary HypoPP, 12 (30.8%) patients had acid-base imbalance, of which 10 and 2 patients, respectively, had metabolic alkalosis and metabolic acidosis. Only 2 (18.2%) of the 11 patients with thyrotoxic HypoPP had acid-base imbalance, with one being metabolic alkalosis and the other being metabolic acidosis. While all the 14 patients with secondary HypoPP due to other causes had acid-base imbalance, with 12 and 2, respectively, being metabolic alkalosis and metabolic acidosis. Patients with HypoPP secondary to conditions other than hyperthyroidism were more likely to develop acid-base imbalance than those with

primary HypoPP or thyrotoxic HypoPP (p<0.001; Figure 1). In addition, there were significant differences in pH and HCO3 levels at baseline among the three groups of patients (p=0.046 and 0.014, respectively). Pairwise comparisons showed no significant differences in pH and HCO_3 levels between patients with primary HypoPP and patients with thyrotoxic HypoPP, while those with HypoPP secondary to conditions other than hyperthyroidism had significantly higher pH and HCO_3-levels than the other two groups of patients (Figure 2).

Treatment and prognosis: Mean doses of oral and intravenous potassium were 11.76±4.28g, 12.13±4.29g, and 16.49±5.98g (p=0.007), and mean time from initiation of potassium administration to recovery of muscle power was 9.10±3.63, 9.64±3.78, and 13.43±4.99 hours (p=0.004), respectively, in patients with primary HypoPP, thyrotoxic HypoPP, and other secondary HypoPPs. Overall, rebound hyperkalaemia occurred in 3 patients (2 patients with primary HypoPP and 1 with thyrotoxic HypoPP). All the patients had normal serum potassium levels and regained muscle power upon discharge. No patient presented with severe arrhythmia or other critical clinical manifestations that could be caused by hyperkalaemia.

Discussion

In the current study, the baseline electrolytes and acid-base status of patients presenting with suspected HypoPP at the emergency department and diagnosed as primary or secondary HypoPP at discharge were reviewed. It was observed that patients with HypoPP secondary to conditions other than hyperthyroidism were more likely to develop acid-base imbalance, mostly metabolic alkalosis, and had higher pH and HCO_3 levels at baseline, than those with primary or thyrotoxic HypoPP. Moreover, those with primary or thyrotoxic HypoPP may need lower dose of supplemental potassium to retain normal serum potassium level, who could be at higher risk of rebound hyperkalaemia.

Although serum potassium level decreases in patients with either primary or secondary HypoPP, the mechanisms of lowered potassium level differed among those with primary HypoPP, thyrotoxic HypoPP, and other secondary HypoPPs. In brief, it is the shift of potassium into cells that causes decreased serum potassium level in primary and thyrotoxic HypoPP, while there is potassium loss in most of the patients with secondary HypoPP due to conditions other than hyperthyroidism. For instance, hyperaldosteronism, renal tubular acidosis, and long-term use of potassium-sparing diuretics caused HypoPP in 25 cases in the current study, due to excessive potassium loss.

Those with primary or thyrotoxic HypoPP are at higher risk of rebound hyperkalaemia, which could be as high as 40% in patients with thyrotoxic HypoPP.[1,4,8,9] In the current study, all of the three patients presenting with rebound hyperkalaemia were those with primary or thyrotoxic HypoPP. Acute treatment strategies for HypoPP of different mechanisms are different. For primary HypoPP, potassium supplement via oral or intravenous administration is needed to restore the balance of intra- and extracellular potassium, in which case serum potassium level and electrocardiogram should be closely monitored to avoid rebound hyperkalaemia and cardiac arrhythmia.[1,8] In patients with thyrotoxic HypoPP, treatment with potassium supplement should be cautious[4,9] and adjuvant non-specific beta-adrenergic blockers could be used to alleviate weakness. While in most cases of secondary HypoPP due to other causes, active potassium supplemental therapy and timely identification of the primary causes are important to maintain serum potassium levels and correction of excessive potassium loss.[10]

Optimal treatment of HypoPP patients in the acute phase relies on accurate differential diagnosis of HypoPP of different aetiologies, which is difficult in the emergent scenarios, especially in cases with first occurrence. Simple and fast tests to differentiate primary and secondary HypoPP would be helpful in guiding acute treatment strategies in such patients. According to the results of the current study, emergent ABG test for electrolytes and acid-base status may help differentiate potassium deficit and disturbed intra- and extracellular potassium distribution in patients presenting with ictal muscle weakness and decreased serum potassium level who were suspected of HypoPP.

The limitations of the current study include its retrospective nature, and the relatively small sample size that did not allow multivariate analysis to adjust for potentially confounding factors, and to explore for cut-points of baseline pH and HCO_3 values and the corresponding sensitivity and specificity to predict the final diagnosis of primary or secondary HypoPP.

Conclusion

Emergent arterial blood gas analysis may help early differential diagnosis of patients with primary and secondary HypoPP, which may help avoid rebound hyperkalaemia in such patients. Further prospective and larger studies are needed to validate findings of the current study, and to conduct multivariate analyses to verify the independent correlations between baseline ABG test results and the final diagnosis of patients presenting with suspicious HypoPP. Moreover, studies are needed to explore the role of baseline ABG analysis results in guiding

acute treatment strategy and avoiding rebound hyperkalaemia in such patients.

Disclaimer: None

Conflict of Interest: None

Funding Sources: This study was supported by Grants to Xiao-yun HUANG from the Social Development Foundation of Dongguan City (No.2018507150231644/ 20211800904952).

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