A Study on Occurrence of Hypomagnesemia in Hypokalemia in a Tertiary Care Center

Authors
Dr Deborah D’silva, Dr Manjunath J, Dr Jayaprakash Alva

Introduction
Hypokalemia is a common electrolyte abnormality encountered in clinical practice. It has been found in up to 21% of hospitalized patients according to reports from studies done mainly among Caucasians.\(^1,2\) The concentration of potassium (K) in the serum is a balance among intake, excretion, and distribution between the extra- and intracellular spaces.\(^3\) Hypokalemia is associated with alterations in the function of several organs systems, especially neuromuscular and cardiovascular systems, with resultant increase in morbidity and mortality in affected patients.\(^4\)

The effective treatment of hypokalemia requires the identification of its cause. Hypokalemia has been found to be frequently associated with hypomagnesemia in hospitalized patients according to previous reports mainly from studies done among Caucasians.\(^5\) Magnesium deficiency, when present, worsens hypokalemia by aggravating renal wasting of potassium and enhances the adverse effects of hypokalemia. Because both hypokalemia and hypomagnesemia can be induced by the same mechanisms (e.g., diuretic administration, primary hyperaldosteronism, renal tubular acidosis) attention in recent years has been focused on their co-occurrence.\(^6\)

Clinically, combined potassium and magnesium deficiency is most frequently observed in individuals receiving loop orthiazide diuretic therapy. Other causes include diarrhea; alcoholism; intrinsic renal tubular transport disorders such as Bartter and Gitelman syndromes; and tubular injuries from nephrotoxic drugs, including amino glycosides, amphotericin B, cisplatin, etc. Concomitant magnesium deficiency has long been appreciated to aggravate hypokalemia.\(^10\)

An observational study supported the view that uncorrected magnesium (Mg) deficiency impairs repletion of cellular potassium (K). Concomitant Mg deficiency in K-depleted patients ranged from 38% to 42%. Hypokalemia associated with magnesium deficiency is often refractory to treatment with K. Co-administration of magnesium is essential for correcting the hypokalemia.\(^7\)

Detection of coexisting hypomagnesemia and early intervention is crucial for effective treatment and prevention of complications hypokalemia on target tissues.\(^12\)

Indian Data on the frequency of hypomagnesemia among hospitalized patients with hypokalemia in are limited, as most hospitals do not routinely measure plasma magnesium.
Aim
The aim of this study was to determine the occurrence of hypomagnesemia in hospitalized patients with hypokalemia and to suggest or otherwise, the routine measurement of plasma magnesium in patients with hypokalemia in our setting.

Background
When magnesium deficiency coexists with hypokalemia, it aggravates the hypokalemia, potentiates its adverse effects, and also renders it refractory to treatment. Despite the impact of magnesium deficiency on the clinical effects of hypokalemia, plasma magnesium is not routinely measured in patients with hypokalemia in our setting.

Objectives
The objective of this study was to find out the occurrence of hypomagnesemia among hospitalized patients with hypokalemia at a tertiary hospital in Mangalore.

Subjects and Methods
Source of Data: Patients attending OPD services and in-patients admitted in Father Muller Medical College Hospital, Mangalore were included in the study.

Study Type: Cross-sectional Descriptive study
Methodology: In all the patients above the age of 18 years with hypokalemia (serum potassium levels <3.5 meq), serum magnesium was sent and hypomagnesaeemia was defined as any value <1.7 mg/dl.

Study Period: It was conducted over two months from September 2019-October 2019.

The study protocol was approved by the Ethics Committee. Informed consent for participation in the study was obtained from each of the study participants. The study did not interfere with the management of the study participants throughout their hospital stay in any way. Data collection, demographic and clinical data of all the study participants were obtained from patients folders.

The data collected then was analysed using t-test, chi-square test, Pearson correlation and statistical correlation was studied.

Results
In this study the total number of subjects included were 93 out of which females were 47 and males were 46 in number.

| Gender | Hypomagnesemia | Total |
|--------|----------------|-------|
|        | No  | Yes |       |
| F      | 20  | 27  | 47    |
| M      | 15  | 31  | 46    |
| Total  | 35  | 58  | 93    |

The mean age of the patients included in the study was 43 +/- 10 years. In patients with hypokalemia serum magnesium levels were sent and the data was as follows.

In the above graph the mean value of magnesium was 1.6916 and mean value of potassium was 2.9174.
In this study patients with hypokalemia were subjected to magnesium levels. It was found that the patients with normal magnesium was and patients with hypomagnesemia was 62%.

In patients with hypokalemia, subjects with hypomagnesemia had a mean of 3.0069 and the subjects with normal magnesium had a mean of 2.86. An independent sample t-test and pearson test was performed to find out correlation between hypokalemia and hypomagnesemia. There was no correlation found between the two as p value was 0.103.

Discussion
In a Nigerian study the mean plasma magnesium level in patients with hypokalemia was significantly lower than in patients with normokalemia. It was also observed that the frequency of hypomagnesemia was higher among patients with hypokalemia, occurring in 1 in 2 participants (52.5%) when compared with the normokalemic patients (22.5%).

Similar findings of frequent association between hypokalemia and hypomagnesemia were reported in previous studies.

Furthermore, in support of the results of this study concomitant Mg deficiency in K-depleted patients ranged from 38% to 42%, which was demonstrated by Whang et al. reported that 42% of patients on admission with hypokalemia also have concomitant hypomagnesemia. However, the findings of Deheinzelin et al. and Watson and O’Kell did not show a significant association between serum magnesium and potassium which was comparable to our study results. The differences in the reported findings between different studies might be explained by the heterogeneity of the study population.

Patients with conditions that are associated with increase in renal distal sodium delivery and/or hyperaldosteronism (e.g., diuretics therapy, diarrhea, and congestive cardiac failure), which are required for the enhanced renal wasting of potassium, in magnesium deficiency state, are more likely to develop hypokalemia than patients with isolated magnesium deficiency.

Magnesium plays a critical role in potassium metabolism. Na⁺ /K⁺ ATPase pump which facilitates the cellular uptake of potassium requires magnesium for its activation. Hypomagnesemia is, therefore, associated with impairment or decreased activity of the pump with the resultant leakage of potassium into the extracellular fluid and its subsequent excretion through the kidneys and gut.

Magnesium deficiency also enhances renal potassium wasting by increasing renal distal tubular potassium secretion because low intracellular magnesium releases the magnesium-mediated inhibition of the renal outer medullary potassium channel in the renal distal tubules, thereby increasing potassium secretion.

Magnesium deficiency may, therefore, have contributed to the occurrence of hypokalemia in hospitalized patients in our setting. Magnesium deficiency should, therefore, be suspected and treated in patients with hypokalemia, as failure to recognize and treat coexistent hypomagnesemia may lead to refractory hypokalemia.
Limitation
The relatively small sample size could also be a limitation for the analysis of data.

Conclusions
Hypomagnesemia is a common finding among hospitalized patients with hypokalemia. We recommend further studies, using larger sample size, to find out the associated occurrence of these two disturbances and determine the clinical value of routine measurement of magnesium in patients with hypokalemia in our setting.

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Conflicts of Interest: Nil

Keywords- Hypokalemia, Hypomagnesemia

References
1. Lippi G, Favaloro EJ, Montagnana M, Guidi GC. Prevalence of hypokalaemia: The experience of a large academic hospital. Intern Med J 2010;40:315-6.
2. Eliacik E, Yildirim T, Sahin U, Kizilarslanoglu C, Tapan U, Aybal-Kutlugun A, et al. Potassium abnormalities in current clinical practice: Frequency, causes, severity and management. Med Princ Pract 2015;24:271-5.
3. Weiner ID, Wingo CS: Hypokalemia: Consequences, causes, and correction. J Am Soc Nephrol8: 1179 –1188, 19972.
4. Viera AJ, Wouk N. Potassium disorders: Hypokalemia and hyperkalemia. Am Fam Physician 2015;92:487-95.
5. Djagbletey R, Phillips B, Boni F, Owoo C, Owusu- Darkwa E, deGraft-Johnson PK, et al. Relationship between serum total magnesium and serum potassium in emergency surgical patients in a tertiary hospital in Ghana. Ghana Med J 2016;50: 78-83.
6. Boyd JC, Bruns DE, Wills MR. Frequency of hypomagnesemia in hypokalemic states. Clin Chem 1983;29:178-9.
7. Whang R, Oei TO, Aikawa JK, Ryan MP, Watanabe A, Chrysant SG, et al. Magnesium and potassium interrelationships, experimental and clinical. Acta Med Scand Suppl 1981;647:139-44.
8. Whang R, Oei TO, Aikawa JK, Watanabe A, Vannatta J, Fryer A, et al. Predictors of clinical hypomagnesemia. Hypokalemia, hypophosphatemia, hyponatremia, and hypocalcemia. Arch Intern Med 1984;144:1794-6.
9. Deheinzelin D, Negri EM, Tucci MR, Salem MZ, da Cruz VM, Oliveira RM, et al. Hypomagnesemia in critically ill cancer patients: A prospective study of predictive factors. Braz J Med Biol Res 2000;33:1443-10.
10. Solomon R: The relationship between disorders of Kand Mg2 homeostasis. SeminNephrol7: 253–262, 19873.
11. Whang R, Whang DD, Ryan MP. Refractory potassium repletion. A consequence of magnesium deficiency. Arch Intern Med 1992;152:40-5.
12. Chakraborti S, Chakraborti T, Mandal M, Mandal A, Das S, Ghosh S. Protective role of magnesium in cardiovascular diseases: A review. Mol Cell Biochem 2002; 238:163-79.
13. Mohammed A, Bello IM, Hassan A. Magnesium deficiency in hospitalized patients with hypokalemia. The Nigerian Journal of General Practice. 2019 Jan 1;17(1):8., Magnesium metabolism and its disorders. Clin Biochem Rev 2003;24:47-66.
14. Costello RB, Elin RJ, Rosanoff A, Wallace TC, Guerrero-Romero F, Hruby A, et al. Perspective: The case for an evidence-based reference interval for serum magnesium: The time has come. Adv Nutr 2016;7:977-93.
15. Watson KR, O’Kell RT. Lack of relationship between Mg2+ and K+ concentrations in serum. Clin Chem 1980;26:520-1.

16. Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. J Am Soc Nephrol 2007;18:2649-52.