Research Article

IJCRR
Section: Healthcare
Sci. Journal
Impact Factor
4.016

SERUM MAGNESIUM IN RELATION TO APACHE IV SCORE AND OUTCOME IN CRITICALLY ILL PATIENTS

R. Sudha[1], S. Bharanidharan[2]

[1]Department of Biochemistry, Vinayaka Mission's Kirupananda Variyar Medical College and Hospitals, Salem, Tamilnadu, India;
[2]Department of Paediatrics, Annapoorna Medical College and Hospitals, Salem, Tamilnadu, India.

ABSTRACT

Introduction: Hypomagnesemia is a common but less frequently monitored electrolyte abnormality in hospitalized patients, especially in the critically ill. Accumulating evidence suggests a potential association between magnesium levels and the morbidity and mortality of critically ill patients. Assessment of electrolytes upon admission to the ICU is necessary to identify patients at risk and to guide the appropriate management during ICU stay.

Aims and Objectives:

1. To assess the levels of serum magnesium in critically ill patients on admission.

2. To evaluate its relationship with APACHE IV (Acute Physiology and Chronic Health Evaluation) score, ventilator support and its duration, length of stay, and mortality.

Materials and Methods: 80 patients admitted to the Medical intensive care unit (MICU) were taken for the study. The subjects studied were monitored for serum magnesium levels on Day 1 of intensive care unit (ICU) admission and were followed to assess duration of ventilator support, length of ICU stay and mortality.

Results: At admission, 45% patients had hypomagnesemia, 6% patients had hypermagnesemia and 49% patients had normomagnesemia. Patients with lower magnesium levels had higher need and longer duration of mechanical ventilation, more frequently had hypokalemia, hypocalcemia, hyponatremia and a higher mortality rate (39% vs 25%). APACHE IV score and length of stay did not significantly vary in hypomagnesemic patients.

Conclusion: Since the presence of hypomagnesemia at admission in the ICU patients is associated with a worse prognosis, recognition and treatment of hypomagnesemia in patients entering the ICU are important.

Key Words: Critically ill patients, Serum magnesium, Mortality, APACHE IV, Hypomagnesemia

INTRODUCTION

Magnesium (Mg) once considered as the "fifth forgotten ion" is arousing interest in clinicians as there is a high incidence of hypomagnesemia in critically ill patients. Mg plays an essential role as a cofactor in countless enzymatic reactions and cellular functions. Magnesium deficiency is a common but underdiagnosed electrolyte abnormality in hospitalized patients, especially in the critically ill. Studies across the world have shown varying incidences of hypomagnesemia ranging from 20% to 65% [1,2,3] whereas Indian studies have shown 25% [4] and 52% [5]. Hypomagnesemia has been directly implicated with a higher mortality rate and worse clinical outcome in the ICU patients[5, 6]. It is also associated with hypokalemia[7], hypocalcemia and dysrhythmia [8] ultimately increasing the mortality. Multiple factors contribute to the low Mg levels in ICU patients like impaired GI absorption, nasogastric suction, usage of drugs like diuretics, aminoglycosides which cause renal wasting of magnesium[9, 10]. Hypermagnesemia is not as frequent as hypomagnesemia and is mostly due to renal failure or iatrogenic[11]. Based on this background, this study was undertaken to assess the magnesium deficiency in critically ill patients upon admission to the ICU and its influence on the outcome of those patients.

Corresponding Author:
Dr. R. Sudha, MD, Assistant Professor, Department of Biochemistry, Vinayaka Missions Kirupanda Variyar Medical College and Hospital;
Ph: 9894401792; Email: sudhabharani76@yahoo.in

Received: 08.05.2015 **Revised:** 05.06.2015 **Accepted:** 29.06.2015

MATERIALS AND METHODS

A prospective observational study was conducted on 80 patients admitted to the Intensive Care Unit of Vinayaka Missions Kirupananda Variyar Medical College and Hospitals. The subjects included were 48 males and 32 females in the age group of 16 – 70 years. The study was started after the approval of the Institutional Ethical Committee. Informed consent was obtained from the nearest kin of the patient.

There were no specific exclusion criteria for the patient except for treatment with magnesium products. The subjects enrolled into the study were monitored for serum magnesium levels within 24 hours of admission, 2ml of venous blood sample was taken and processed for magnesium analysis. Serum magnesium levels were estimated by Xylidyl blue method using a semiautomated analyser. Reference range for magnesium concentrations were set by drawing blood from healthy staff of our college (1.7 to 2.4 mg/dl). Serum magnesium level of < 1.7 mg/dl was regarded as hypomagnesemia and > 2.4 mg/dl as hypermagnesemia.

Other laboratory investigations included were arterial blood gas analysis, sodium, potassium, calcium, bilirubin, urea, creatinine and glucose.

Details collected from the patients were need for ventilator, duration of ventilator support, length of stay, general patient demographics and mortality in the ICU. Patients were followed until their discharge from the ICU.

The APACHE IV score was determined on the first day. APACHE scoring system takes into consideration various parameters like physiological variables, vital signs, urine output, neurological score, along with age related parameters and comorbid conditions, which may have a significant impact on the outcome of these critically ill patients[12]. APACHE IV is the newest standardized scoring metrics to assess the severity of illness and prognosis among critically ill adults in the ICU. APACHE IV, an improved and updated model for predicting mortality among critically ill patients includes new variables like mechanical ventilation, rescaled Glascow coma scale, PaO2/FiO2 ratio, ICU admission diagnosis and source etc[13, 14]. APACHE IV is probably a more reliable prediction of high risk of death in patients with stroke than APACHE II, which has been widely used in ICU studies[15]. APACHE IV score was calculated using an online calculator.

Statistical analysis: Data was analysed using the SPSS program. All the data were expressed as Mean ± Standard deviation. Pearson's correlation analysis was done for assessing the relationship between variables. Differences were considered as statistically significant if p-value was less than 0.05.

RESULTS

Totally, 80 patients admitted to the MICU were considered for the study. At admission, 45% (36/80) patients had hypomagnesemia, 6% (5/80) patients had hypermagnesemia and 49% (39/80) patients had normomagnesemia. The serum magnesium values were ranging from 1mg/dl to 3mg/dl. When the variables were compared between patients with low and normal magnesium levels, a statistically significant difference was observed in need for ventilator support and duration of mechanical ventilation. Length of stay in the ICU did not vary significantly between the two groups.

The mean APACHE IV score on admission was 43.43 ± 17.67 for the hypomagnesemic group and 42.29 ± 19.02 for the normomagnesemic patients. Mean APACHE IV score of patients in the two groups also did not significantly differ. Hypomagnesemic patients had more incidences of electrolyte abnormalities such as hypokalemia (20% vs 6.25%), hyponatremia (40% vs 12.5%) and hypocalcemia (33% vs 3%). Hypomagnesemic patients had a higher rate of mortality (39% vs 25%) when compared to the normomagnesemic patients. [Table 1]

There was a significant positive correlation between serum magnesium and serum potassium levels. 47% of hypomagnesemic patients had diabetes mellitus, whereas 33% in normomagnesemic group had diabetes.

DISCUSSION

Magnesium is the second most abundant intracellular cation after potassium and is a required cofactor in hundreds of enzyme systems. Magnesium deficiency commonly occurs in critical illness and correlates with a higher mortality and worse clinical outcome in the intensive care unit. A wide range of incidences of magnesium deficiency has been reported in patients of ICU. Moreover, patients who develop magnesium deficiency in the ICU have mortality rates 2 to 3 times higher[16, 17, 18] and prolonged hospitalization when compared with those who are not magnesium deficient. Although RBC magnesium is a better index of intracellular magnesium when compared to serum magnesium, clinicians rely on serum magnesium as it is easier to measure.

In the present study of 80 critically ill patients, a significant number of patients had hypomagnesemia (45%). Similar incidences were observed by Deheinzelin et al (45.6%)[3] and Guerin et al (44%)[20]. Studies carried out throughout the world in critically ill patients have shown varying incidences of Mg deficiency ranging from 14% to 66% [5]. The causes of magnesium deficiency in critically ill patients are multiple, the major ones being GI losses and renal losses. Other common risk factors associated

with magnesium deficiency are alcoholism and poorly controlled diabetes mellitus. It is important to address the cause of Mg deficiency while treating hypomagnesemia, to prevent future recurrences[19].

Hypomagnesemia has long been known to be associated with insulin resistance and diabetes mellitus. In this study, patients with higher blood glucose levels had more incidence of hypomagnesemia. Epidemiologic studies have shown a high prevalence of hypomagnesaemia and lower intracellular Mg concentrations in diabetic subjects. Reduced intracellular Mg concentrations result in a defective tyrosine-kinase activity, post-receptorial impairment in insulin action, and worsening of insulin resistance in diabetic patients[21].

Other electrolyte abnormalities are frequently encountered in patients with hypomagnesemia. Our study results have shown a greater incidence of electrolyte disturbances in hypomagnesemic patients than normomagnesemic patients. These results are consistent with Safavi et al[8] and CS Limaye et al[5]. However, only potassium had a significant positive correlation with magnesium levels (r-value – 0.48, p-value <0.001) [Table 2]. This could be due to underlying disorders which cause both magnesium and potassium loss like diuretic therapy.

Patients with lower total serum magnesium level had higher need for ventilator support and were on mechanical ventilation for a longer period of time. This finding may be because of the muscle weakness and respiratory failure caused by hypomagnesemia.

Length of stay in the ICU and APACHE IV score did not vary in the patients with hypomagnesemia. Few other studies have observed a longer duration of ICU stay in patients with low magnesium (Subhraprakashpramanik et al[23] and Safavi et al[8]). Our observation was in line with Soliman et al[17] and Limaye et al[5] where there was no difference in the length of ICU stay among the three groups.

Soliman et al[17] observed that there was no significant difference in the length of stay as well as the mortality rate in patients with ionized hypomagnesemia, normomagnesemia and hypermagnesemia at admission. But they found that those patients who developed ionized hypomagnesemia during their ICU stay had higher APACHE II score, a longer ICU stay and a higher mortality rate than the other patients.

A higher mortality rate was observed in hypomagnesemic patients when compared to normomagnesemic patients in this study (39% vs 25%). Other studies have demonstrated increased mortality in hypomagnesemia, but only with a variation in the mortality rate. Studies which have shown significantly increased mortality rates are Chernow et al [22] (41% vs 13%), Safavi et al (55% vs 35%), Subhraprakashpramanik et al [23] (47.2% vs 23.4%) and Limaye et al (57.7% vs 31.7%). However Guerin et al[20] observed no difference in mortality rates among hypomagnesemic and normomagnesemic groups (18% vs 17%).

The higher mortality rates in patients with low magnesium levels can be due to various reasons like increased incidence of electrolyte abnormalities such as hypokalemia and hypocalcemia, association of sepsis and diabetes and frequent need of ventilator support.

Hypermagnesemia is a less frequently encountered problem in ICU patients than hypomagnesemia. In our study it was 6%, whereas the literature shows a range of 4 to 14%[20, 17]. Also, we did not find any mortality in patients with high magnesium levels. In contrast, Escuela MP et al had observed a higher mortality rate in patients with ionized hypermagnesemia[24].

CONCLUSION

Hypomagnesemia is a frequent finding in critically ill patients and is significantly associated with a higher mortality rate, more frequent need for mechanical ventilation and other electrolyte abnormalities like hypokalemia, hypocalcemia and hyponatremia when compared to patients with normal magnesium levels. These findings may help in monitoring magnesium levels as an indicator of mortality in critically ill patients.

Limitations: Smaller sample size and lack of measurement of magnesium levels serially during the ICU stay are potential limitations of this study.

ACKNOWLEDGEMENT

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

REFERENCES

1. Reinhart RA, Desbiens NA. Hypomagnesemia in patients entering the ICU. Crit Care Med. 1985:13:506-507.
2. Ryzen E, Wagers PW, Singer FR, Rude RK. Magnesium deficiency in a medical ICU population. Crit Care Med. 1985:13:19-21.
3. 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;33:1443-1448.
4. Zafar MH, Wani JI, Karim R, Mir MM, Koul PA. Significance of serum magnesium levels in critically ill patients. Int J App Basic Med Res 2014;4:34-7.

5. CS Limaye, VA Londhey, MY Nadkar, NE Borges. Hypomagnesemia in critically ill medical patients. JAPI.Jan 2011;59:19-22.
6. Tong GM, Rude RK,. Magnesium deficiency in critical illness. J.Intensiv Care Med 2005;20(1):3-17.
7. 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;144:1794-96.
8. Safavi.M, Honarmand A. Admission hypomagnesemia- Impact on mortality and morbidity in critically ill patients. M.E.J.ANESTH. 2007;19(3):645-660.
9. Salem M, Munoz R, Chernow B. Hypomagnesemia in critical illness. Critical care clinics.1991;7:225-252.
10. Michael JD. Hypomagnesemic disorders. Critical care clinics.2001;17:155-173.
11. James W. Van Hook. Hypermagnesemia. Critical care clinics.1991;7:215-223.
12. Burtin P, Bollaert PE, Feldmann L, Lelarge P, Bauer P, Larcan A. Prognosis of patients with stroke undergoing mechanical ventilation. Intensive care Med. 1994;20:32-36.
13. Zimmerman JE, Kramer AA, McNair DS, Malila FM. Acute Physiology and Chronic Health Evaluation (APACHE) IV:ICU length of stay benchmarks for today's critically ill patients. Crit Care med 2006;34:2517-29.
14. Zimmermann JE, Kramer AA, McNair DS, Malila FM. Acute physiology and chronic health evaluation (APACHE) IV: Hospital mortality assessment for today's critically ill patients. Crit Care Med 2006;34(5):1297-310.
15. Tulin Akarsu Ayazoglu. A comparison of APACHE II and APACHE IV scoring systems in predicting outcome in patients admitted with stroke to an intensive care unit. Anaesth, Pain & Intensive care.2011;15(1):7-12.
16. Rubeiz GJ, Thill Baharozian M, Hardie D, Carlson RW. Association of hypomagnesemia and mortality in acutely ill medical patients. Crit care med. 1993;21:203-209.
17. Soliman HM, Mercan D, Lobo SS, Melot C, Vincent JL. Development of ionized hypomagnesemia is associated with higher mortality rates. Crit care med.2003;31:1082- 1087.
18. Cohen N, Almoznino-Sarafian D, Zaidenstein R, Alon I, Gorelik O, Shteinshnaider M et al. Serum magnesium aberrations in furosemide treated patients with congestive heart failure; pathophysiological correlates and prognostic evaluation. Heart.2003;89:411-416.
19. Kevin J.Martin, Esther A. Gonsalez, Eduardo Slatopolsky. Clinical consequences and management of hypomagnesemia. J Am soc Nephrol.2009;20:2291-2295.
20. Guerin C, Cousin C. Serum and erythrocyte magnesium in critically ill patients. Intensive Care Med.1996;22:724-727.
21. Mario barbagallo, Ligia J Dominguez. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. Archives of Biochemistry and Biophysics.2007 Feb 1;458(1):40-7
22. Chernow B, Bamberger S, Stoiko M, Vadnais M, Mills S, Hoellerich V et al. Hypomagnesemia in patients in postoperative intensive care unit. Chest 1989;95:391-397.
23. Subhraprakashpramanik, Arpan kumar Dey, Pijushkantimandal,Shovan Kumar Das, Debashishghosh, Arpan Bhattacharya, Milan Chakroborty, Somnathdasgupta. Prevalence of hypomagnesemia and its predictive prognostic value in critically ill medical patients. IOSR Journal of Pharmacy.2014;4(1):1-5.
24. Escuela MP, Guerra M, Anon JM, Martinez-Vizcaino V, Zapatero MD, Garcia-Jalon A et al. Total and ionized serum magnesium in critically ill patients. Intensive care med.2005;31(1):151-6.

Table 1: Comparison of variables among patients with low and normal magnesium levels (M ± SD)

Variable	Low magnesium	Normal magnesium	Significance
No. of patients (%)	36 (45%)	39 (49%)	-
Serum Mg (mg/dl)	1.26 ± 0.17	2.05 ± 0.13	Yes ($p < 0.05$)
Age (Yrs)	52.93 ± 20.6	48.53 ± 13.7	-
Mortality rate	14/36 (39%)	10/39 (25%)	Yes ($p < 0.05$)
APACHE IV score	43.43 ± 17.67	42.29 ± 19.02	No ($p > 0.05$)
Need for ventilator	60%	43.8%	Yes ($p < 0.05$)
Duration of ventilator (days)	4.39 ± 3.41	2.24 ± 3.47	Yes ($p < 0.05$)
ICU stay (days)	6.65	7.79	No ($p > 0.05$)
Hypocalcemia	33%	3%	Yes ($p < 0.05$)
Hypokalemia	20%	6.25%	Yes ($p < 0.05$)
Hyponatremia	40%	12.5%	Yes ($p < 0.05$)
Hypoalbuminemia	50%	31%	Yes ($p < 0.05$)
Diabetes mellitus	47%	33%	Yes ($p < 0.05$)

Table 2: Correlation of variables with serum magnesium levels

Variable	r-value	p-value
Sodium	0.06	0.66
Potassium	0.48	0.0001
Calcium	0.154	0.279
Albumin	-0.125	0.384