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Serum Magnesium Level Impact on the Outcome of Patients Admitted to the Intensive Care Unit

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ABSTRACT

Background: *Magnesium deficiency is a common, yet under-diagnosed problem in the intensive Care Unit (ICU). Our aim was to determine the prevalence of abnormalities in serum magnesium concentrations in critically ill patients upon admission to the ICU. The association of serum magnesium level with prognosis was also studied.*

Materials and Methods: *This historical cohort study was conducted in the medical ICU of Hazrat-e-Rasool Hospital and 273 critically ill patients were enrolled in this study during a one-year period. Binary logistic regression analyses were performed to identify significant independent risk factors of mortality in the ICU.*

Results: *The mortality rate was 53.8% in the understudy subjects. One-hundred forty-seven subjects (53.8%) had normal serum magnesium levels, whereas, 126 subjects (46.2%) had abnormal values (hyper- or hypomagnesemia). Patients with lower total serum magnesium level had longer length of mechanical ventilation and ICU stay. The mortality rate was higher in patients who had abnormal magnesium levels. Age, serum Mg and mechanical ventilation were three risk factors that independently predicted probability of mortality in the ICU patients.*

Conclusion: *Monitoring of serum magnesium levels may have prognostic, and perhaps therapeutic, implications and physicians should be alert to the high incidence of magnesium deficiency in critically ill patients.* ***(Tanaffos2010; 9(4): 28-33)***

Key words: *Magnesium, Hypomagnesemia, Intensive Care Unit, Mortality*

INTRODUCTION

Malnutrition in the intensive care unit (ICU) patients is a widely acknowledged problem that may intensify underlying illnesses and increase the risk of complications (1,2). Nutritional assessment upon admission to the ICU is necessary to identify patients at risk and to guide nutritional support during ICU stay (3).

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Magnesium (Mg) is essential for normal cellular functions and is the second most abundant intracellular cation (4). It serves as a co-factor for several enzymes required for electrolyte homeostasis and is also necessary for membrane stability, cell division, and generation of action potentials (5).

Magnesium deficiency commonly occurs in critical illnesses (6, 7) and correlates with higher mortality rate and worse clinical outcome in the intensive care unit patients (7, 8).

Magnesium has been directly implicated in hypokalemia, hypocalcemia, tetany, and dysrhythmia. Moreover, Mg may play a role in acute coronary syndromes, acute cerebral ischemia, and asthma. Magnesium regulates hundreds of enzyme systems. By regulating enzymes controlling intracellular calcium, Mg affects smooth muscle vasoconstriction, important to the underlying pathophysiology of several critical illnesses (7). Its deficiency results primarily from gastrointestinal or urinary Mg losses, but malnutrition and decreased dietary Mg intake may hasten the development of Mg depletion (6). Magnesium therapy is supported by clinical trials in the treatment of symptomatic hypomagnesemia and preeclampsia and is recommended for torsade de pointes (7).

Hypomagnesemia occurs in 40% of hospitalized patients, (9) approximately 60% of postoperative patients, (5) 65% of medical ICU patients, (10) and up to 90% of surgical ICU patients (11). Hypomagnesemia has been implicated in the development of cardiovascular dysfunction and the systemic inflammatory response syndrome in ICU patients (4).

This study was conducted to determine the prevalence of abnormalities in serum magnesium levels in critically ill patients upon admission to the ICU, to study the association of these values with patient's prognosis and to investigate their usefulness in identifying patients at higher risks of morbidity and mortality.

MATERIALS AND METHODS

This study was approved by the Research Committee of Iran University of Medical Sciences and was conducted in the medical ICU of Hazrat-e-Rasool Hospital. A total of 273 critically ill patients who met the inclusion criteria were enrolled in this study during a one-year period. Subjects were excluded from the study if they had a hemoglobin level of less than 10 g/dl, were receiving blood products, magnesium (before sampling), or calcium infusions. Inclusion in the study did not change the routine patient management in the ICU. Samples of venous blood (4.5 ml) were collected from every patient during the first 24 h of admission. Samples showing hemolysis after centrifugation were discarded. Serum magnesium level was assayed in our hospital laboratory. Moreover, the following data were recorded: age, gender, length of stay, use of mechanical ventilation and its duration and mortality in the ICU. Patients were followed until they were discharged from ICU. Normal values for Mg ranged from 1.8 to 2.5 mg/dl. The serum Mg levels were determined via Xylidyl blue method using Pars Azmun kit.

Quantitative data were represented as mean ±standard deviation. To assess the association among qualitative variables the Chi-square test was used. Mann Whitney U test was also used to examine the differences among the means of quantitative variables. Spearman correlation coefficients were computed to examine the association among quantitative study variables. Binary logistic regression analyses were also performed to identify significant independent risk factors for mortality in the ICU. Differences were considered statistically significant if P-value was less than 0.05. Statistical analysis was performed using the "Statistical Package for the Social Sciences Software" (version 16.0) for Windows (SPSS, Chicago Ill., USA).

RESULTS

Totally, 273 critically ill patients who admitted to medical ICU were enrolled in this study during a one year period. The mean age of patients was 60.54±2.06 yrs. (range, 15-97 yrs). There were 252 males (55.7%) and 121 (44.3%) females. The mean length of ICU stay was 13.2±15.75 days. Mechanical ventilation was applied for 76.2% (n=208) of patients. The length of mechanical ventilation for those attached to ventilator was 11.05±15.25 days. The mortality rate was 53.8% in the understudy subjects (n=147).

The mean serum Magnesium level measured during the first 24 hours of admission was 2.01±0.49 mg/dl. According to the normal values mentioned above, 147 subjects (53.8%) had normal serum magnesium level, while 126 subjects (46.2%) had abnormal values (hyper- or hypomagnesemia).

There were 90 hypomagnesemic (33%) and 36 hypermagnesemic patients (13.2%).

The length of ICU stay was inversely correlated with serum magnesium level (Spearman's rho; p=0.003, r= - 0.182). This negative correlation is shown in the scatter plot (Figure 1). The mortality rate was higher in patients who had lower magnesium levels (Mann-Whitney; p=0.000). In subjects with normal ranges of serum magnesium, the mortality rate was 34% but this rate was 77% in hypomagnesemic patients. (Figure 2). The serum magnesium level in mechanically ventilated patients in the ICU, was lower at admission (2.14±0.47 vs. 1.97±0.49 mg/dl, Mann-Whitney; p=0.001) and the duration of ventilation was also negatively correlated with serum magnesium concentration. (Spearman's rho; p=0.000, r= - 0.316)

The serum magnesium level was similar in men and women (Mann-Whitney; p=0.055). The mean age was inversely correlated with serum magnesium. (Spearman's rho; p=0.004, r= - 0.172) The patients were divided into three groups based on the serum magnesium level and the variables were compared among these groups. The results are presented in Table 1.

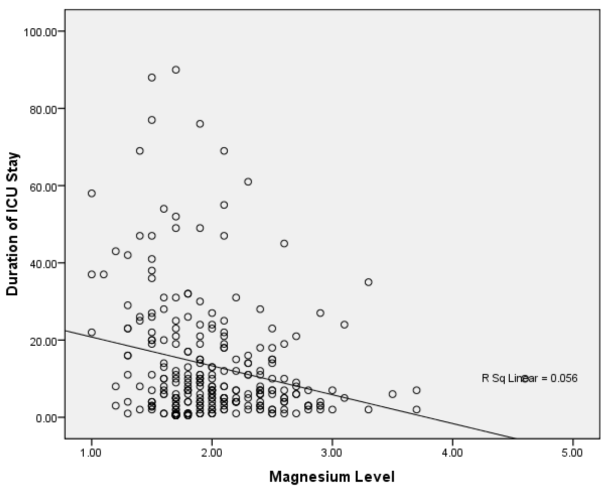
To identify significant independent risk factors for mortality in the ICU, the logistic regression analyses were performed. Age, high levels of serum magnesium and mechanical ventilation were the three risk factors that independently predicted probability of mortality in the ICU patients (Table 2).

Table 1. Comparison of certain variables among three Mg concentration groups

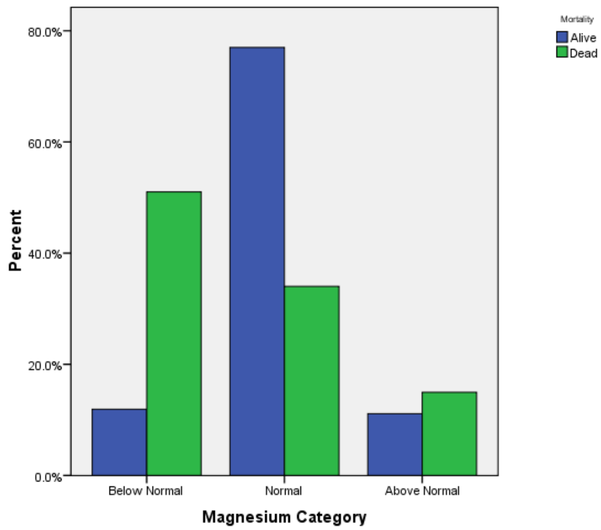
	Hypomagnesemia	Normal range	Hypermagnesemia	P-value
Length of ICU stay	18.41±2.03 days	11.13±1.26 days	8.61±1.00 days	P=0.037
Mortality	83.3%	34%	61/1%	P=0.000
Use of mechanical ventilation	91.1%	66.7%	77.8%	P=0.000
Length of ventilation	16.79±1.83 days	7.96±1.22 days	5.03±7.61	P=0.000
Age	66.57±1.78 years	56.59±2.15 years	61.63±2.01 years	P=0.002

Table 2. Results of binary logistic regression of mortality independent risk factors

	B	S.E.	Sig. (p_{value})	Exp (B)	95%CI, Lower	95%CI, Upper
Serum Magnesium	-0.720	0.309	0.020	0.487	0.266	0.893
Age	0.19	0.007	0.010	1.019	1.005	1.034
Use of mechanical ventilation	-3.466	0.548	0.000	0.031	0.011	0.092



Graph 1. Correlation between total serum Mg level and length of ICU stay in our patients.



Graph 2. Relationship between total serum Mg level and mortality in medical ICU

DISCUSSION

Magnesium is the 4th most abundant cation in the body (12). Its deficiency is a common, yet under-diagnosed problem in the ICU. Magnesium depletion has been shown to be present in about one half of all ICU patients. These patients have significantly higher morbidity and mortality rates than Mg-replete patients. Accurate identification of patients with Mg depletion requires knowledge of the risk factors associated with Mg deficiency. These factors include poorly controlled diabetes mellitus, alcohol ingestion, severe diarrhea and steatorrhea, (13), the use of a number of pharmacologic agents that induce renal Mg wasting (such as diuretics and aminoglycosides) and sepsis (4,14). Manifestations of Mg deficiency include hypokalemia, hypocalcemia, neuromuscular hyperexcitability, respiratory muscle weakness, and intractable arrhythmias. Mg deficiency may also play a role in the genesis of myocardial ischemia (4,13).

We found that 33% of our patients had hypomagnesemia and 13.2% had hypermagnesemia. The patients with lower serum magnesium levels had longer length of mechanical ventilation and ICU stay. The mortality rate was higher in patients who had abnormal magnesium levels. Age, high levels of serum Mg and mechanical ventilation were three risk factors that independently predicted probability of mortality in the ICU.

Previous studies on critically ill adults and children also found considerable proportions of abnormal levels of Mg upon admission (15-20). Also, previous studies on critically ill adults and children revealed association in hypomagnesemia (5,14,21,22) with increased likelihood of mortality, morbidity, prolonged ventilator dependence, and prolonged ICU and hospital stay. With regard to the clinical consequences of the abnormal levels, it is obvious that low levels of albumin and magnesium will be treated (3). Ryzen et al. found hypomagnesaemia in 65% of patients with normal serum creatinine concentrations (10). Hulst and colleagues reported 20% abnormal values in their critically ill patients. They found no significant relationship between magnesium levels and the number of days on mechanical ventilation or length of ICU stay (3). In Dabbagh et al. study, approximately 39.4% had hypomagnesemia on admission and the overall mortality rate was 31%.

They demonstrated that magnesium supplementation per se may be beneficial in lowering mortality rates (8). Rubeiz et al. evaluated 381 acutely ill patients who admitted to emergency department and medical ICU. The mortality rates in the hypomagnesemic and medical ICU patients were approximately twice ($p<0.01$) the rate of the normomagnesemic group. They concluded that hypomagnesaemia detected at the time of admission of acutely ill medical patients was associated with an increased mortality rate for both ward and medical ICU patients (21).

A retrospective study was done on 100 patients in Isfahan by Safavi and colleagues. At the time of admission, 51% of patients had hypomagnesaemia. They reported significant differences in mortality rates (55% vs. 35%) and the length of hospital or ICU stay between hypo- and normomagnesemic patients (23). In Escuela et al. study, the frequency of normo-, hyper- and hypomagnesemia was shown in 34%, 13.5% and 52.5% of patients, respectively. Serum Mg concentrations were similar in both deceased and alive subjects. They found no association between mortality and hypo- or hypermagnesemia determined upon admission (24). Huijgen and colleagues tried to explain the high prevalence of hypomagnesemia in the critically ill patients by a possible extracellular Mg flow to intracellular space related to factors leading that exchange (25).

Magnesium released after injury or cell death in acutely ill patients, evidenced by higher severity scores, may explain the correlation between hypermagnesemia and mortality. Another factor influencing this association could be the development of acute renal failure, a major cause of hypermagnesemia and a frequent complication in the critically ill patients (24).

In conclusion, Mg alterations have frequently been observed in critically ill patients and an association between these alterations and mortality has been found. It seemed that correction of hypomagnesemia has decreased hypomagnesaemia-associated morbidity; therefore, early diagnosis and treatment of hypomagnesaemia is necessary. Monitoring of serum magnesium levels may have prognostic, and perhaps therapeutic, implications and physicians should be alert to the high incidence of magnesium deficiency in critically ill patients.

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