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Original Research Article

A Hospital-Based Assessment of the Effect of Serum Magnesium Concentration on Clinical Outcome of Critically Sick Patients: An Observational Study

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Abstract

Aim: To determine the usefulness of admission serum magnesium levels with regards to patient outcome in critically ill patients admitted in ICU.

Methodology: The present prospective observational study was conducted in the Department of General Medicine, AIIMS, Patna, Bihar, India for three months. The patients were selected for study based on inclusion and exclusion criteria. All patients with APACHE 2 score of more than 20 or less than 6 admitted in ICU, and patients aged more than 18 years were included in the study. Demographic data such as age and sex were recorded. Patients were assessed for presenting complaints, history of other diseases and habits through an interview with the patients or care giver. Further these patients underwent a thorough clinical examination for vitals (pulse rate blood pressure and respiratory rate) and other clinical signs including Glasgow coma score (GCS) followed by systemic examination. These findings were recorded on a predesigned proforma. Patients were followed up for the outcomes such as mortality, need of ventilator support, duration of ICU stay and APACHE 2 score. The selected patients underwent the following investigations: haemoglobin, total white blood cell (WBC) count, haematocrit, platelet count, blood urea nitrogen (BUN), serum creatinine, serum sodium, serum potassium, serum calcium, serum bilirubin, serum albumin, arterial blood gases and serum magnesium.

Results: 50 patients admitted in the medical intensive care unit with various critical medical conditions were enrolled for this study. Regarding clinical presentation, fever was common in both group (56% patients in >1.7 mg/dl group and 72% in 1.7 mg/dl group. In present study, 24% patients with magnesium level <1.7 mg/dl were diagnosed to have pneumonia with septicaemia, 8% acute exacerbation of COPD, 4% acute myocardial infarction, 8% have acute pulmonary oedema, 4% patient have RVF, 16% patients have CVA, meningitis and liver abscess was present in 8% patients, urinary tract infection (UTI) with septicaemia, malaria and dengue haemorrhagic fever was present in 4% patients each. Both groups were comparable to each other regarding GCS (p=0.438). Most of the patients in both groups have GCS score was in between 11 to 15 at the time of admission. In present study, 44% patients with magnesium level <1.7 mg/dl have APACHE 2 score between 21 to 25, APACHE 2 score was between 26 to 30 in 8 (32%) and above 30 in 6 (24%) patients. Similarly 68% patients with magnesium level >1.7 mg/dl have APACHE 2 score between 21 to 25, APACHE 2 score was between 26 to 30 in 28% and above 30 in 4% patients. This finding is significant statistically.

Conclusion: From present observational study we can conclude that Hypomagnesemia is a frequent electrolyte deficiency in critically ill-patients. We also have observed that hypomagnesaemia is associated with high APACHE 2 score, poor outcome and more requirement of ventilatory support. Physicians should be alert to the high incidence of hypomagnesemia in critically ill elderly patients and should consider a routine monitoring program, as hypomagensemia may be associated with adverse outcomes.

Keywords: Hypomagnesemia, hypermagnesemia, Glasgow Coma Scale, septicemia.

Introduction

Magnesium is an essential element in maintaining critical functions like cardiac membrane potential, intracellular signaling, and it also serves as a cofactor for several enzymes involved in protein and DNA synthesis. [1] Serum magnesium is currently receiving more attention from the medical community than in the past because of evidence that its deficiency contributes to a number of abnormal perturbations as it influences over 300 enzyme systems, including Na–K–ATPase-mediated transport, and is essential for calcium homeostasis, nerve conduction, skeletal muscle activity, and maintenance of calcium and potassium homeostasis. This is especially apparent in geriatric patients because of their low magnesium intake, diminished intestinal absorption, and increased urinary output (due to frequent use of diuretics and digitalis) [2, 3].

The incidence of hypomagnesemia is reported to be 2% in the general population, 10-20% in hospitalized patients, 50-60% in intensive care unit (ICU) patients, 30-80% in persons with alcoholism, and 25% in outpatients with diabetes [4]. The incidence of hypomagnesemia varies from 20% to 65% in intensive care unit (ICU) patients [5-7]. Various studies have reported the incidence of hypomagnesemia up to 65% in critically ill-patients [8]. Hyper magnesemia is less common and mostly due to renal failure or iatrogenic. Prevalence of hypermagnesemia was reported to be 7.3% [9].

Causes of magnesium deficiencies comprises of gastrointestinal and renal wasting, drug-induced, metabolic diseases, endocrine disorders, redistribution of magnesium stores and several other conditions [10]. Hypomagnesemia can potentially cause fatal complications including ventricular arrhythmia, coronary artery spasm, and sudden death. It also associates with increased mortality and prolonged hospitalization [11, 12]. Serum magnesium monitoring may have prognostic and perhaps therapeutic implications because critically ill-patients are predisposed to both symptomatic or asymptomatic magnesium deficiency that can lead to some important clinical consequences (such as hypokalemia, cardiac arrhythmias, hypocalcemia, neurotoxicity and psychiatric problems), ultimately increasing the morbidity and mortality [13].

Serum magnesium monitoring may have prognostic and perhaps therapeutic implications, because critically ill patients are predisposed to both symptomatic and asymptomatic magnesium deficiency that can lead to some important clinical consequences (such as hypokalaemia, cardiac arrhythmias, hypocalcaemia, neurotoxicity and psychiatric problems), ultimately increasing the morbidity and mortality. Magnesium deficiency induces a systemic stress response through activation of neuroendocrine pathways [14], has been

implicated in the pathophysiology of many diseases, and has been associated with increased mortality in ICU patients [15]. Hence the present study was undertaken to determine the usefulness of admission serum magnesium levels with regards to patient outcome in critically ill patients admitted in ICU.

Materials and Methods

The present prospective observational study was conducted in the Department of General Medicine, AIIMS, Patna, Bihar, India for three months

Inclusion and Exclusion Criteria

The patients were selected for study based on inclusion and exclusion criteria. All patients with APACHE 2 score of more than 20 or less than 6 admitted in ICU, and patients aged more than 18 years were included in the study. Patients who had received magnesium prior to admission, patients receiving magnesium preparations at time of admission, patients who have received blood transfusions prior to ICU admission, patients with chronic alcoholism, patients receiving diuretics, aminoglycosides, pregnant women with eclamptic seizures, receiving MgSO4, and patients receiving cisplatin and amphotericin were excluded.

Methodology

Demographic data such as age and sex were recorded. Patients were assessed for presenting complaints, history of other diseases and habits through an interview with the patients or care giver. Further these patients underwent a thorough clinical examination for vitals (pulse rate blood pressure and respiratory rate) and other clinical signs including Glasgow coma score (GCS) followed by systemic examination. These findings were recorded on a predesigned proforma (Annexure-II) patients was followed up for the outcomes such as mortality, need of ventilator support, duration of ICU stay and APACHE 2 score.

The selected patients underwent the following investigations: haemoglobin, total white blood cell (WBC) count, haematocrit, platelet count, blood urea nitrogen (BUN), serum creatinine, serum sodium, serum potassium, serum calcium, serum bilirubin, serum albumin, arterial blood gases and serum magnesium.

Estimation of serum magnesium: At the time of admission to medical ICU, serum magnesium levels were tested. Calmagite dye method for quantitative estimation of serum magnesium. Subsequently patients were divided into three groups based their serum magnesium concentrations defined as follows: normal 1.7 to 2.4 mg/dl, low <1.7 mg/dl, and high>2.4 mg/dl. Patients were assessed for the following parameters:

APACHE 2 score: APACHE 2 is a severity of disease classification system one of several ICU scoring systems. It is applied within 24 hours of admission of a patient an ICU. An integer score from 0 to 71 is computed based on several measurements. Higher scores correspond to more severe disease and a higher risk of death. APACHE 2 score was calculated for each patient at admission to medical ICU.

Chronic health points: If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows: for non-operative/emergency postoperative patients-5 points, and for elective postoperative patients-2 points.

Ventilator support was assessed as number patients requiring ventilation and duration of ventilation support in days. Length of stay in ICU was also noted. Mortality Patients were evaluated for the outcome and evaluated as improved or expired.

Statistical analysis

Data were recorded in excel sheet and statistical Analysis was done with software statistical package for the social sciences (SPSS)-14 version.

Results:

In present prospective observational study 50 patients admitted in the medical intensive care unit with various critical medical conditions were enrolled for this study. These patients were divided in two groups based on serum magnesium concentration below 1.7 mg/dl and above 1.7 mg/dl.

Regarding clinicodemographic profile of the patients, there were statistically significant differences between two groups regarding age. In hypomagnesaemia group most of the patients were more than 51 years of age and in normomagnesaemia most of the patients were between 26 to 50 years of age. Both groups were comparable to each other regarding sex distribution.

Table 1: Clinicodemographic profile of patients with hypomagnesaemia and normal magnesium level.

Variables	Serum Magnesium Concentration (mg/dl)		
	<1.7	**> 1.7**	**P-value**
Age of the patients			
<25	5	3	0.015
26 to 50	6	13	
More than 51	14	9	
Sex			
Male	15	19	
Female	8	8	0.39
Fever (%)	14 (56)	18 (72)	
Breathlessness (%)	12 (48)	7 (28)	
Altered consciousness (%)	14 (56)	11 (44)	
Decrease urine output (%)	6 (24)	3 (12)	
Pain abdomen (%)	7 (28)	5 (20)	

Regarding clinical presentation, fever was common in both group (56% patients in >1.7 mg/dl group and 72% in 1.7 mg/dl group.

In present study, 24% patients with magnesium level <1.7 mg/dl were diagnosed to have pneumonia with septicaemia, 8% acute exacerbation of COPD, 4% acute myocardial infarction, 8% have acute pulmonary oedema, 4% patient have RVF, 16% patients have CVA, meningitis and liver abscess was present in 8% patients, urinary tract infection (UTI) with septicaemia, malaria and dengue haemorrhagic fever was present in 4% patients each.

Table 2: Relation between diagnosis of patients and magnesium level.

Variables	Serum magnesium concentration (mg/dl) (%)	
	<1.7	**> 1.7**
Pneumonia with septicaemia	6 (24)	5 (20)
Acute exacerbation of COPD	2 (8)	1 (4)
Acute myocardial infarction	1 (4)	1 (4)
Acute pulmonary oedema	2 (8)	2 (8)
RVF	1 (4)	0 (0)
CVA	4 (16)	2 (8)
Meningitis	2 (8)	3 (12)
Liver abscess	2 (8)	3 (12)
UTI with septicaemia	1 (4)	3 (12)

Malaria	1 (4)	3 (12)
Dengue haemorrhagic fever	1 (4)	2 (8)

Similarly, 20% patients with magnesium level >1.7 mg/dl were diagnosed to have pneumonia with septicaemia, 4% acute exacerbation of COPD, 4% acute myocardial infarction, 8% have acute pulmonary oedema, 8% patients have CVA, meningitis was present in 12% patients, liver abscess was present in 12% patients. UTI with septicaemia, malaria was present in 12% patients each. Dengue haemorrhagic fever was present in 8% patients.

Both groups were comparable to each other regarding GCS (p=0.438). Most of the patients in both groups have GCS score was in between 11 to 15 at the time of admission. In present study, 44% patients with magnesium level <1.7 mg/dl have APACHE 2 score between 21 to 25, APACHE 2 score was between 26 to 30 in 8 (32%) and above 30 in 6 (24%) patients. Similarly 68% patients with magnesium level >1.7 mg/dl have APACHE 2 score between 21 to 25, APACHE 2 score was between 26 to 30 in 28% and above 30 in 4% patients. This finding is significant statistically.

Table 3: Relation between clinical outcome of patients and magnesium level.

Variables	Serum Magnesium Concentration (mg/dl) (%)		
	<1.7	**>1.7**	**P value**
Glasgow coma scale			
Less than 5	1 (4)	2 (8)	0.438
5 to 10	8 (32)	6 (24)	
11 to 15	16 (64)	17 (68)	
APACHE II score			
21 to 25	11 (44)	17 (68)	0.020
26 to 30	8 (32)	7 (28)	
More than 30	6 (24)	1 (4)	
Outcome			
Improved	10 (40)	19 (76)	0.0036
Mrotality	15 (60)	6 (24)	
Ventilation			
Required	18 (72)	12 (48)	
Not required	7 (28)	13 (52)	

Regarding comparison between outcome of patients between two groups, 40% patients with magnesium level <1.7 mg/dl have improved and 60% patient didn't improve. 76% patients with magnesium level >1.7 mg/dl have improved and 24% patient didn't improve. This finding is significant statistically.

Regarding comparison between requirement of ventilation between two groups, 72% patients with magnesium level <1.7 mg/dl have required ventilation and 28% patient didn't required ventilation. 48% patients with magnesium level >1.7 mg/dl have required ventilation and 52% patient didn't required ventilation. This finding is significant statistically.

Discussion

Magnesium is essential for human health, and ionized magnesium is involved in the interaction of more than 300 enzyme reactions and is important for electrolyte homeostasis, membrane stability, cell

division, and generation of action potentials [16,17]. Magnesium disturbance is a common problem in both critical care settings and in the general population. Magnesium dysregulation mainly impacts neuromuscular and cardiovascular functions. Hyper magnesemia is less common and mostly due to renal failure or iatrogenic. Prevalence of hypermagnesemia was reported to be 7.3% [18]. It can lead to severe muscle weakness, respiratory depression, hypotension, cardiac arrhythmia and ultimately progress to cardiac arrest [19]. Many studies found that only hypomagnesemia, but not hypermagnesemia is linked with increased mortality [20, 21].

In current study, 46% patients were more than 50 years of age out of which 56% patients had less than 1.7 mg/dl magnesium levels. The three major factors that affect magnesium requirements, particularly in the elderly, are as follows: (1) dietary factors such as poor intake, and intake of refined processed food, excess fiber, and excess sugar; (2) host factors such as anabolism or catabolism, ischemia, chronic disease, decreased intestinal absorption, increased renal excretion, hormonal, enzyme, vitamin imbalance, and alcohol consumption; and (3) environmental factors such as medications (cardiac medications, diuretics, antibiotics, and purgatives) and stress (provoked and psychological diseases) [22].

The mean age of the patient was 59.36±21.63 years with male predominance. This finding is supported by the work of Hansen et al and Velissaris et al [23, 24]. Fever was common in both group (72% patients in >1.7 mg/dl group and 56% in <1.7 mg/dl group. This finding is supported by work of Chernow et al and Upala et al [25,26]. Pneumonia with septicaemia and CVA was commonly associated with hypomagnesaemia. This finding corroborates with study of Bharath et al [27,28].

In present study we have observed that hypomagnesaemia is associated with high APACHE 2 score, poor outcome and more requirement of ventilatory support. Jiang et al from their meta-analysis concluded that collectively, our data indicated that hypomagnesemia appears associated with greater risk of mortality, sepsis, mechanical ventilation, and the length of ICU stay in patients admitted to ICU. The role of magnesium therapy for improving outcomes in critically ill patients is needed to further study, this statement corroborates with our study [29]. Pannem et al has concluded that higher APACHE 2 score is associated with higher mortality and more length of stay in ICU among the cases of hypomagnesaemia this finding corroborates with our study [30].

The relation between hypomagnesaemia and mortality has varied among studies. Chernow et al. [31] reported no difference in mortality between hypomagnesaemia and normomagnesaemic patients (13% vs 11%). Guerin et al. [32] found no difference in ICU mortality between hypomagnesaemia and normomagnesaemic patients (18% vs 17%). Rubeiz et al. [33] reported nearly double the mortality rates (46% vs 25%) in hypomagnesaemia patients compared with those with normomagnesaemia. [34] In the present study, 40% patients with magnesium level <1.7 mg/dl have improved and 60% patient didn't improve. 76% patients with magnesium level >1.7 mg/dl have improved and 24% patient didn't improve.

Guerin et al [32] in a prospective study to evaluate the prevalence of serum magnesium (Mg) abnormalities in patients on admission to the intensive care unit (ICU) and to test the hypothesis that low levels of Mg are associated with a higher mortality. They confirm the high prevalence of Mgs abnormalities as well as Mg deficiency on admission to a medical ICU. Low levels of Mgs are not associated

with higher fatality. Hyper Mgs was associated with patient death.

Conclusion

From present observational study we can conclude that Hypomagnesemia is a frequent electrolyte deficiency in critically ill-patients. We also have observed that hypomagnesaemia is associated with high APACHE 2 score, poor outcome and more requirement of ventilatory support. Physicians should be alert to the high incidence of hypomagnesemia in critically ill elderly patients and should consider a routine monitoring program, as hypomagensemia may be associated with adverse outcomes.

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