A Study on the Effects of Hypomagnesaemia among Critically Ill Patients at a Tertiary Care Hospital of Southern Bihar

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ABSTRACT

BACKGROUND

Hypomagnesaemia is associated with other electrolyte abnormalities like hypokalaemia, hyponatremia, and hypophosphatemia. We wanted to study the serum magnesium levels in critically ill patients, and correlate the serum magnesium levels with patient outcome and other parameters like duration of stay in ICU, ventilator support and APACHE-II (Acute Physiology and Chronic Health Evaluation-II) score.

METHODS

The study included all the cases admitted in the ICU of Narayan Medical College & Hospital, with variable medical conditions within 6 months fulfilling the inclusion criteria. Demographic data (age and sex), medical history, surgical history, medications administrated and length of ICU stay were recorded for each patient. The severity scoring system used was Acute Physiology and Chronic Health Evaluation-II (APACHE-II).

RESULTS

Prevalence of Hypomagnesaemia in the present study was 60.2 %. Mortality and mechanical ventilator support (2.7 % and 28.4 %) in normomagnesemia subjects were significantly lesser than hypomagnesaemia subjects (33.9 % and 54.5 % respectively).

CONCLUSIONS

Hypomagnesaemia is a common electrolyte imbalance in critically ill patients. It is associated with higher mortality and morbidity in critically ill patients and is also associated with more frequent and more prolonged ventilatory support.

KEYWORDS

Critically Ill, Hypomagnesaemia, APACHE-II Score, Mortality, Ventilator Support

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BACKGROUND

Magnesium (Mg) plays a crucial role in several biochemical and physiological processes in the human body. Normal range of magnesium is 1.7 - 2.4 mg / dL.[1] It has many essential physiological role in various functions of the body.[2] It acts as a cofactor and engages in more than 300 enzymatic reactions, mainly in phosphorylation reaction such as formation of ATP.[3] Its functions include neurotransmitters release, energy generation, nitrous oxide production and it also contributes in immune system to fight against infection.[2,4] Other functions include regulating cardiac and smooth muscle tone, stabilizing cell membrane, and supporting the integrity of cytoskeletal system.[5] Many of studies have reported that electrolyte and fluid Imbalance is responsible for poor outcomes and are foremost common abnormality, seen in ICU setup. Hypomagnesaemia is common in hospitalized patients (7 - 11 %) and even more frequent in patients with other coexisting electrolyte abnormalities[6-8] and in critically ill patients.[9,10] Hypomagnesaemia 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]

Magnesium deficiency is the most commonly overlooked condition in critically ill patients and associated with other coexisting electrolyte abnormalities commonly confused with hypokalaemia. Various studies have reported the incidence of hypomagnesaemia as 65 % in critically ill patients. The incidence of hypomagnesaemia is reported as 2 % in general population, 10 - 20 % in hospitalized patients, 50 – 60 % in ICU patients, and 25 % among out patients with diabetes and alcoholism.[13] Although many paradigms have been explored to minimize the mortality in critical care units, magnesium loss has been scarcely addressed; in this respect leading to inconclusive results. Serum magnesium monitoring may have prognostic as well as 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 hypokalaemia, cardiac arrhythmias, hypocalcaemia, neurotoxicity and psychiatric problems), ultimately increasing the morbidity and mortality.[14]

The aetiology of magnesium deficiency is multifactorial and may be related to drugs (diuretics), renal and gastrointestinal loss, co-morbidities like diabetes mellitus, chronic alcoholism and metabolic disorders (Barters syndrome). Hence a high index of suspicion is warranted in critically ill patients to define the cause of hypomagnesaemia. Results of several studies like Leicester Intravenous magnesium intervention trial (LIMIT-2) have stated a reduction in mortality with reduced incidence of heart failure and arrhythmias among critically ill patients with hypomagnesaemia.[15]

There is a paucity of data in Indian literature, addressing this common, but underdiagnosed electrolyte deficiency. The present study was undertaken against this backdrop at a tertiary care teaching hospital to assess the magnitude of magnesium deficiency and its influence on the outcome of critically ill-patients.

METHODS

This study was undertaken in a tertiary care teaching hospital of north India, over a period of 6 months. It was a prospective observational study, which involved patients from both the medical and surgical ICUs. Patients were enrolled at random and the selection bias was avoided by registering those patients who fulfilled the criteria for critical illness and who were newly admitted to ICU.

Sample Size

The sample size was calculated with 80 % of the power and 5 % of the significance level. The sample size was determined to be 186 patients including 10 % as drop-out rate.

Ethical Clearance

The study was started after getting clearance from the Ethical Committee, which is an independently functioning body of this institute. A detailed protocol was presented and discussed with the committee before the start of the study.

Selection of Study Subjects

The selection of the study participants was done as per the inclusion and exclusion criteria:

Inclusion Criteria

- Above 18 years of age irrespective of the sex.
- APACHE-II score above 18

Exclusion Criteria

- Known cases of hypomagnesaemia, who received magnesium supplements.
- Cases on magnesium lowering drugs or calcium infusions.

Study Procedure

5 ml of venous blood was drawn from the cases on the day of admission in ICU and serum magnesium levels will be assayed in the central laboratory of the hospital by calmagite calorimetric method. Magnesium combines with calmagite in an alkaline medium to form a red coloured complex. Interference of proteins and calcium is eliminated by using chelating agents. Intensity of colour formed is directly proportional to the amount of magnesium present in the sample. The laboratory investigations that were carried out were routine biochemical (CBS, KFT, Sr Magnesium etc.), ECG and radiological investigations (CXR, CT, MRI) were performed as per the management protocol.

Parameters

Demographic data (age and sex), medical history, surgical history, medications administrated and length of ICU stay

were recorded for each patient. The severity scoring system used was Acute Physiology and Chronic Health Evaluation-II (APACHE-II). Other investigations such as arterial blood gases, complete blood count, kidney function tests, liver function tests, serum electrolytes, electrocardiography, chest X-ray and ultrasonography were also done. Blood, urine and endotracheal secretions were sent for culture screen in every febrile patient. Computed tomography and magnetic resonance imaging scanning was performed wherever it was required.

Statistical Analysis

The data was entered into the Microsoft excel and analysed using the SPSS version 25.0. The Student's t-test was applied for the comparing the mean values, Chi-square test for the comparison of frequencies and correlation. The p-value was considered to be at the significance level when it was below 0.05.

RESULTS

The data presented in table 1 reveals that majority (51.1 %) of the sample were in the age group of above 50 years and larger proportion (54.8 %) of the sample were females, 27.4 % had history of hypertension and 38.2 % had history of diabetes.

		Number	%
Age in Years	< 25 Years	17	9.1 %
	25 - 50 Years	74	39.8 %
	> 50 Years	95	51.1 %
Gender	Male	84	45.2 %
	Female	102	54.8 %
History of Hypertension	Yes	51	27.4 %
	No	135	72.6 %
History of Diabetes	Yes	71	38.2 %
	No	115	61.8 %

Table 1. Demographic Profile of the Study Population

Age	Normomagnesemia	Hypomagnesaemia	P-Value[a]
< 25 Years	5 (29.4 %)	12 (70.6 %)	0.001*
25 - 50 Years	33 (44.6 %)	41 (55.4 %)	
> 50 Years	36 (37.9 %)	59 (62.1 %)	
Total	**74 (39.8 %)**	**112 (60.2 %)**	

Table 2. Relation of Age with Serum Magnesium Levels

[a]Chi-square test * Significant difference

The data presented in Table 2 reveals that in the age group of < 25 years, 70.6 % had Hypomagnesaemia followed by more than 50 years (62.1 %) and 25 - 50 years (55.4 %) (Table 2).

Mean Serum Magnesium level mg / dL in Subjects with Normomagnesemia was 1.87 ± 0.12 mg / dL and in Subjects with Hypomagnesaemia was 1.37 ± 0.15 mg / dL. The mean duration of stay in ICU in Subjects with Normomagnesemia was 7.40 ± 4.73 days and in Subjects with Hypomagnesaemia was 8.49 ± 5.19 days. The mean duration of Mechanical Ventilator support (days) among subjects with Normomagnesemia was 2.02 ± 3.20 days and Hypomagnesaemia was 3.91 ± 4.09 days with a statistically significant difference between them. The mean APACHE score in subjects with Normomagnesemia was 21.07 ± 2.17 which was significantly lesser than Subjects with Hypomagnesaemia (25.39 ± 3.09) (Table 3).

Variables	Normomagnesemia	Hypomagnesaemia	P-Value
Serum Magnesium Level mg / dL	1.87 ± 0.12	1.37 ± 0.15	0.012*
Length of ICU Stay	7.40 ± 4.73	8.49 ± 5.19	0.025*
Duration of Ventilator Support	2.02 ± 3.20	3.91 ± 4.09	0.001*
APACHE Score	21.07 ± 2.17	25.39 ± 3.09	0.046*

Table 3. Serum Magnesium Levels According to the Duration of Stay in Hospital (Days)

[p]Unpaired t-test * Significant difference

Variables	Normomagnesemia	Hypomagnesaemia	P-Value[a]
Mortality	2 (2.7 %)	38 (33.9 %)	< 0.001*
Mechanical Ventilator Support	21 (28.4 %)	61 (54.5 %)	0.001*

Table 4. Percentage Distribution of Sample Characteristics Based on Serum Magnesium Levels (mg / dL)

[a]Chi-square test * Significant difference

The data presented in table 4 reveals that, the mortality percentage in normomagnesemia subjects was 2.7 % which was significantly lesser than Hypomagnesaemia subjects (33.9 %). Mechanical ventilators support was required significantly more by Hypomagnesaemia subjects (54.5 %) compared to Normomagnesemia subjects (28.4 %).

DISCUSSION

Magnesium is the second most common intracellular cation in the human body. It plays an important role in the homeostasis of the body. Magnesium is the cofactor for most of the adenosine triphosphate (ATP) reactions because it is the ATP magnesium complex that is bound to and hydrolysed by the enzymes.[16] Hypomagnesaemia, as defined by a total plasma concentration less than 0.7 mmol / l, is an underdiagnosed but common electrolyte abnormality in critically ill patients. Estimates of magnesium deficiency range from 20 - 61 %.[17]

In our study, 51.1 % were in the age group of more than 50 years. This was quite similar to the study by Gholyaf et al,[18] the mean age of 68.07 ± 17.73 years, ranged from 15 to 90 years. In current study, majority (54.8 %) of the sample were females. In the study by Gholyaf et al,[18] 51.5 % were male and 48.5 % were females.

Prevalence of Hypomagnesaemia

In our study, 60.2 % of the sample had Hypomagnesaemia. This was quite similar to the study by Pramanik et al,[19] the prevalence of Hypomagnesaemia was 53 %, Safavi and Honarmand[20] (51 %), Chernow et al[21] (61 %), Limaye et al,[22] 52 % patients had hypomagnesaemia and Guerin et al (66 %). This was contrasting to the studies by Huijigen et al[23] and Soliman et al,[12] the prevalence of hypomagnesaemia was much lower (14 % and 18 % respectively) whereas in the studies which have measured RBC magnesium the prevalence of hypomagnesaemia was higher (20 % to 70 %).

Duration of Mechanical Ventilation

The duration of mechanical ventilation among patients with hypomagnesaemia was 3.91 ± 4.09 days which was significantly more than patients with normomagnesemia (2.02 ± 3.20 days). Safavi and Honarmand[20] had found that in patients with hypomagnesaemia the duration of mechanical ventilation was longer i.e. 7 days. Hypomagnesaemia also leads to muscle weakness and respiratory failure, causing difficulty in weaning the patient from the ventilator. In the current study, it has been seen that patients with hypomagnesaemia needed ventilatory support more frequently and for a longer duration. However, no significant difference was found in the duration of ventilation between the two groups (t = 0.8990, p = 0.3697). Fiaccordori et al.,[24] had observed that patients with low muscle Mg were on ventilatory support for a greater number of days.

Length of ICU Stay

In our study, we found that patients admitted with hypomagnesaemia their length of stay in ICU was prolonged compared to normomagnesaemic individuals. In the study carried out by Soliman et al,[12] there was no difference in the length of ICU stay. However, the patients who developed hypomagnesaemia during their ICU stay had longer duration of stay in the ICU. In the study by Elenjickal and Lakra,[25] the length of ICU stay with magnesium levels was found to be significantly higher in subjects with Hypomagnesaemia compared to those with normo and hypermagnesemia. The mean ICU stay was 9.45 days with the shortest stay being 2 days and the longest stay being 16 days.

APACHE II Score

APACHE II Score is one of the various ICU scoring systems available to prognosticate the patient's condition. The mean APACHE score in Subjects with Normomagnesemia was 21.07 ± 2.17 which was significantly lesser than Subjects with Hypomagnesaemia (25.39 ± 3.09). In the study by Kiran et al,[26] the mean APACHE II score was 22.97 ± 4.06, mean APACHE II score in patients recovered and discharged was 21.13 ± 2.88, in those who died 25.00 ± 4.50, in discharged against medical advice 22.84 ± 3.17, in discharged at request cases 19.00 ± 1.41, in hypomagnesaemia cases 24.13 ± 4.14, in hypomagnesaemia cases with death as outcome 25.91 ± 3.82, in hypermagnesemia cases 25.82 ± 12.24. Hypomagnesaemia was associated with a higher APACHE II score.

Comorbid Conditions

In present study, 27.4 % of them had history of hypertension and around 38.2 % of them had history of Diabetes. In the study by Ugaragol et al,[27] patients admitted in ICU with critical illness with history of Hypertension were associated with Hypomagnesaemia 38.3 % and was statistically significant. In this study hypokalaemia was not significantly associated with hypomagnesaemia. Various studies have shown association of hypokalaemia with hypomagnesaemia. In the study by Limaye et al,[22] half of the patients (48 %) with hypokalaemia had low serum magnesium levels. In another study by Soliman et al[12] about 58.8 % had hypokalaemia with low serum Magnesium levels.

The relation of Hypomagnesaemia with DM may be due to increased renal losses of Mg that accompany glycosuria. There is also a strong relationship between hypomagnesaemia and insulin resistance, and Mg supplementation is associated with decreased insulin requirements. [28]

Mortality

Mortality was another important outcome variable that was chosen for this study. In this study, association of mortality with serum magnesium levels was analysed using chi-square test. Significant association was found to exist, indicating a higher frequency of mortality in subjects with Hypomagnesaemia. In the study by Elenjickal and Lakra,[25] amongst the Hypomagnesaemia group, mortality reached to an astounding 80 %, while that in the Hypermagnesemia group had 53.8 % mortality; 36.8 % patients with Normomagnesemia succumbed to their illnesses.

In the study by Ugaragol et al,[27] a total of 85 patients who were critically ill, were admitted in ICU and observed that those with hypomagnesaemia had a poor prognosis and increased mortality. The mortality in patients with hypomagnesaemia was attributed to be secondary to more common causes like electrolyte imbalance, cardiac arrhythmias, sepsis and septicaemia which are more common in ICU.

Limitations

Serum magnesium levels were recorded only on the day of admission to intensive care unit. Follow-up magnesium levels were not done. Secondly, this was a descriptive non-interventional study. A large multicentric, randomised, double-blind, interventional, trial for magnesium supplementation in critically ill patients with Hypomagnesaemia is needed in future to evolve consensus / guidelines for treatment of Hypomagnesaemia in critically ill.

CONCLUSIONS

Hypomagnesaemia is a common electrolyte imbalance in the critically ill patients. It is associated with higher mortality and morbidity in critically ill patients and is also associated with more frequent and more prolonged ventilatory support. It was seen in this study that hypomagnesaemia is frequently associated with diabetes mellitus and cardiovascular diseases. Assessment of serum magnesium concentration is inexpensive and easy to employ and provides important information about magnesium status in the patients. Hypomagnesaemia, when detected, may require correction for the management of those with critical illness for better

outcomes and hence, benefit of magnesium supplementation to prevent or correct hypomagnesaemia in critically ill patients needs further study.

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