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Original Research Article

A Study of hypomagnesemia in critically ill patients and its correlation with patient outcomes

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Abstract

Background: Magnesium (Mg) is essential for life and plays a key role in the human body's various biochemical and physiological processes. Hypomagnesemia is common in all hospitalized patients, especially with co-existing electrolyte abnormalities in critically ill patients. Hypomagnesemia, if not diagnosed on time and appropriately treated, can cause serious and potentially fatal complications and is associated with increased mortality.**Aim and Objectives:** To study hypomagnesemia in critically ill patients and its correlation with patient outcomes considering the following parameters: Age, Sex, Diabetic status, Association with other lab parameters, APACHE II score, Need for ventilator support, Length of stay in ICU, Total stay in the hospital, Mortality.**Materials and Methods:** The study was a prospective study done in the Department of General Medicine (Medical ICU), Sri Ramachandra Medical College and Research Institute from September 2016 to August 2017. A thorough clinical examination was done; clinical data were recorded into the EXCEL case sheet. Serum calcium, serum potassium, ABG, along with other basic labs was sent for all patients. APACHE II score was calculated and all parameters were entered into an excel sheet. The results of the study were analyzed and statistical data was summarized using SPSS 17 software. Pearson Correlation, Kendall Tau B, Student t-test, and ANOVA were done for specific variables.**Results:** A total of 1067 patients admitted in ICU between September 2016 to August 2017 were taken into the study out of which 169 patients had hypomagnesemia (< 1.8 mg/ dl). Various correlations were analyzed for age, sex, diabetic status, APACHE II score, serum calcium, serum potassium, ventilator requirement, ICU stay, hospital stay, and outcome. A total of 169 patients out of 1067 patients had hypomagnesemia in the present study (15.83%). The minimum magnesium value was 0.8 mg/dl and the maximum value was 1.7 mg/dL. The present study highlighted the importance of hypomagnesemia in intensive care unit and its outcome with various parameters. The present study showed that hypomagnesemia is associated with increased APACHE II score, increased incidence of ventilator requirement and higher mortality.**Conclusion:** Magnesium is an unrecognized cation in critically ill patients. The incidence of hypomagnesemia in the present study was less compared to other studies done in medically ill patients. Hypomagnesemia correlated well with APACHE II score, ventilator requirement, and mortality, which was statistically significant.

Keywords: APACHE II score, Magnesium, Intensive care.

Introduction

The second most abundant intracellular cation is magnesium. In many cell functions, it plays a fundamental role, including energy transfer, storage, and metabolism; maintaining the normal function of the cell membrane; and controlling the secretion of parathyroid hormones. In addition to several other nonfatal complications, hypomagnesemia may lead to well-known compli-cations such as ventricular arrhythmias[1,2]including Torsades de pointes, expanded QT interval [2], coronary artery vasospasm, convulsions, neuromuscular weakness, inability to wean off the ventilator, and many metabolic disorders,

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including metabolic acidosis, hypocalcemia, and hypokalemia, etc. Magnesium is also widely used in the treatment of hypertension, acute asthma, muscle spasticity, and constipation during pregnancy. But in critically ill patients, hypomagnesemia frequently remains unrecognized[3], so magnesium has been called the "forgotten cation"[4] Magnesium systemically reduces blood pressure and modifies peripheral vascular resistance. In almost every aspect of biochemical metabolism, magnesium participates, stimulates almost all enzymes involved in phosphorus reactions, and functions as a ribonucleic acid molecular stabilizer. Because it is bound to adenosine triphosphate inside the cell, shifts in its intracellular concentration may help to regulate cellular bioenergetics, such as mitochondrial respiration. Extracellularly, Mg^{+2} ions block neurosynaptic transmission by interfering with the release of acetylcholine. The release of catecholamines from the adrenal medulla may also interact with Mg^{+2} ions and has been suggested as an endogenous endocrine modulator of the physiological stress response component catecholamine[5]. As magnesium is an unrecognized entity in critically ill patients the present study was done to observe hypomagnesemia and its various associations in ICU.

Materials and methods

The study was a prospective study done in the Department of General Medicine (Medical ICU), Sri Ramachandra Medical College and Research Institute during the period from September 2016 to August 2017.

Inclusion criteria

1. All patients admitted to ICU, who had duration of stay for more than 2 days.
2. Patients with low magnesium values (< 1.8 mg/dl) levels during the first 24 hours were taken into the study.

Exclusion criteria

1. Patients less than 18 years of age
2. Patients who stayed in ICU for less than 48 hours

Methodology

Data were collected prospectively between September 2016 to August 2017. A thorough clinical examination was done; clinical data were recorded into the EXCEL case sheet. Serum calcium, serum potassium, ABG, along with other basic labs was sent for all patients. APACHE II score was calculated and all parameters were entered into an excel sheet. The laboratory reference values of the parameters are as follows Normal BUN (5 -21 mg/dl), Normal creatinine (0.9 –1.3 mg/ dl), Normal calcium value (8.6 –9.1mg/dl), Normal potassium value (3.5 -5.0mmol/litre).

Analysis

The results of the study were analyzed and statistical data was summarized using SPSS 17 software. Pearson Correlation, Kendall Tau B, Student t-test, and ANOVA were done for specific variables.

Results

The present study included a total of 1067 critically ill medical patients admitted to ICU between the months of September 2016 to August 2017. A total of 169 patients had low magnesium (< 1.8 mg /dl). The incidence of hypomagnesemia in critically ill patients in this study was 15.83%. The study included 169 patients, 92 males and 77 females. The mean magnesium value in the present study is 1.535 (minimum 0.8 mg/dl and maximum 1.7 mg / dl). 83 patients (49.1 %) were diabetics out of the 169 patients taken into the study.

Table 1: Descriptive Statistics

	N	Min	Max	Mean	Std. Deviation
Age	169	20	85	52.57	15.544
TC	169	2000	111000	12195.27	9922.298
BUN	169	2	101	22.45	16.847
Creatinine	169	0.4	35.0	2.100	3.6146
Calcium	155	4.6	10.0	8.186	0.7519
MG	169	0.8	1.7	1.535	0.1875
Potassium	169	1.4	6.5	3.638	0.9050
Bicarbonate	169	4	36	21.12	5.801
ICU stay	169	2	12	4.85	2.037
APACHE II	169	0	30	12.67	5.786
Hospital stay	169	2	30	8.86	4.837

Above table shows the various parameters taken into the study, minimum value and maximum value and mean value of each of the parameter. (Table 1)

Magnesium in association with Diabetes

The correlation between the ventilator requirement and magnesium levels was calculated using Student T Test.

Table 2: Magnesium in association with Diabetes

Diabetes	N	Mean	P value
YES	83	1.517	0.220
NO	86	1.552	

The results showed that there was no statistically significant correlation between diabetic status and hypomagnesemia. (Table 2)

Magnesium in association with Total count, Calcium, Potassium, serum Bicarbonate, ICU stay, Hospital stay, and APACHE II

Correlation was calculated between Total count, Calcium, Potassium, serum Bicarbonate, ICU stay, Hospital stay, APACHE II and magnesium level in the study group patients using Pearson Correlation. (Table 3)

Table 3: Magnesium in association with Total count, Calcium, Potassium, serum Bicarbonate, ICU stay, Hospital stay, and APACHE II

S. Cal	4.6	10.0	8.186	0.7519	0.065**	0.422	155
S. K^+	1.4	6.5	3.638	0.9050	0.116**	0.132	169
Bicarbonate	4	36	21.12	5.801	- 0.009*	0.903	169
ICU stay	2	12	4.85	2.037	- 0.130*	0.093	169
Hospital stay	2	30	8.86	4.837	- 0.035*	0.647	169
APACHE II	0	30	12.67	5.786	- 0.186***	0.016	169

* Negative correlation and observation was not statistically significant.
** Positive correlation and observation was not statistically significant.
*** Negative correlation and observation was statistically significant (P = 0 .016).

Magnesium in association with Blood urea nitrogen and Creatinine

Correlation was made between blood urea nitrogen, Creatinine and magnesium level in the study group patients using Kendalls Tau B. (Table 4)

Table 4: Magnesium in association with Blood urea nitrogen and Creatinine

	Min	Max	Mean	SD	Kendall's tau B	P value	N
MG	0.8	1.7	1.535	0.1875			
BUN	2	101	22.45	16.847	0.029*	0.615	169
Creatinine	0.4	35.0	35.0	3.6146	0.038*	0.515	169

*Positive correlation and observation was not statistically significant.

Magnesium in association with Ventilator requirement

In the study group 62 patients required ventilator support and 107 patients did not receive mechanical ventilation, the correlation between the ventilator requirement and magnesium levels was calculated using Student T Test.

Table 4: Magnesium in association with Ventilator requirement

Ventilator	N	Mean	Std. Deviation	P value
YES	62	1.474	0 .2318	0 .001
NO	107	1.570	0.1462	

The results showed that there was statistically significant requirement of mechanical ventilation in patients with hypomagnesemia (P = 0.001). (Table 5)

Magnesium in association with Patient outcome

Among the study group 110 patients were discharged from the hospital (incidence 65.08 %) , 31 patients went AMA (incidence 18.35) , death was noticed in 28 patients (incidence 16.56 %) .

Table 6: Magnesium in association with Patient outcome

	N	Mean	SD	P value
Discharged	110	1.548	0.1601	
AMA	31	1.597	0.1354	
Death	28	1.414	0.2731	.000
Total	169	1.535	0.1875	

The correlation between the patient outcome and hypomagnesemia was calculated using ANOVA and there was a statistically significant correlation between death as an end point and low magnesium (P = 0.000). (Table 6)

Discussion

A comprehensive analysis of hypomagnesemia in critically ill patients was made in the present study. Association of hypomagnesemia with various parameters was analyzed and useful observations were made. A total of 1067 patients admitted in ICU between September 2016 to August 2017 were taken into the study out of which 169 patients had hypo-magnesemia (< 1.8 mg/ dl). Various correlations were analyzed for age, sex, diabetic status, APACHE II score, serum calcium, serum potassium, ventilator requirement, ICU stay, hospital stay, and outcome.A total of 169 patients out of 1067 patients had hypomagnesemia in the present study (15.83%). The minimum magnesium value was 0.8 mg/dl and the maximum value was 1.7 mg/dL. The present study included only medical ICU patients which could explain the low incidence of hypomagnesemia. A few studies mentioned above included surgical and medical ICU patients, Limaye et al[5], Sunil kumar et al[6], Sheba et al[16] included patients only in medical ICU while Chernow et al[10] included exclusively surgical ICU patients and reported a higher incidence of hypomagnesemia.

Table 7:Literature study

Study	Total No. of patients	No. of patients with hypomagnesemia	Prevalence	Mean age	Mean APACHE II Score	Mean ICU stay (Days)	Incidence of mortality	Ventilator requirements
Limaye et al[5]	100	52	52 %		14.52	4.27	57.7 %	73 %
Sunil kumar et al[6]	601	153	25.45 %	47.8	21.82	5.46	35.5 %	56 %
Safavi M et al[7]	100	51	51 %		14.16	9.16	55 %	58.6 %
Chen M et al[8]	374	102	27.27%		15.62	12.43	33.88 %	
Soliman et al[9]	422	76	18 %			15.4	35 %	

Chernow et al[10]	193	118	61 %				41 %	
Dabbagh et al[11]	71	43	60%	54	22.6	8.8	31 %	
Huijgen et al[12]	115	59	51.3%					
Escuela et al[13]	712	180	25.35	62.71	13.6	6.4	36 %	
Guerin et al[14]	179	79	44%	62	18		46 %	
HS Kiran et al[15]	150	45	30%			7.15	51.1 %	
Sheba et al[16]	96	23	23.96%			3.8	22 %	52 %
Present study	1067	169	15.83 %	52.57	12.67	4.85	16.56%	36.7 %

Mean age of the patients in the present study is 52.57.Mean magnesium value of the patients taken into the study was 1.535 (SD = 0.1875), Dabbagh et al[11] reported mean magnesium of 0.78. The mean APACHE II score in the present study is 12.67, (SD 5.786), with a minimum = 0, maximum = 30. The correlation between Hypomagnesemia and APACHE II score showed a negative correlation (Pearson Correlation), suggesting that the lower the magnesium level, the higher the APACHE II score and it was statistically significant (p = 0.016). 36.7% percent (62 patients), out of the 169 patients with low magnesium required ventilator, the correlation with the number of patients requiring ventilator and hypomagnesemia in the patients was calculated using the Student t- test, and they were a statistically significant correlation (p = 0.001). Sixty-three patients who had hypomagnesemia (37.27 %) had hypokalaemia (< 3.5 mmol/litre), the mean potassium value of the patients is 3.638, (SD = 0.9050), (Min = 1.4, Max 6.5). The correlation between the potassium levels and low magnesium levels in the patients was evaluated using Pearson's correlation and the results showed a positive correlation but the results were not statistically significant. Limaye et al[5] reported the incidence of hypokalaemia in the study as 23% and Safavi M et al[7]reported the incidence as 28%.Sixty patients had hypocalcaemia (38.70 %), only 155 patients out of 169 patients the serum calcium levels were sent , the mean calcium value = 8.186, SD = 0.7519, Min = 4.6, Max = 10. The correlation between calcium and hypomagnesemia was calculated using Pearson's correlation and it showed a positive correlation, but the results were not statistically significant, Limaye et al[5] reported the incidence of hypocalcemia as 70 %, Safavi M et al[7] reported an incidence of 24%.The mean ICU stay in our study group patients is 4.85, (SD = 2.037), Min = 2 days, Max =12 days, The correlation between hypomagnesemia in patients and duration was calculated using Pearson's correlation and it showed negative correlation meaning that patients with low magnesium have a longer duration of stay in ICU. The mean duration of hospital stay observed in the present study is 8.86 days, (SD 4.837), Min = 2, Max = 30. The correlation between the hospital stay and hypomagnesemia in patients was calculated using Pearson's correlation and it showed a negative correlation meaning that low levels of hypomagnesemia are associated with higher duration of hospital stay and the results were not statistically significant. Safavi M et al[7] reported the mean duration of hospital stay as 15.29 days, Dabbagh et al[11] reported the mean duration of hospital stay as 19.5, H S Kumar et al[15] reported the mean duration of hospital stay as 21.33. The incidence of mortality is 16.56%, and the relation with the mortality and hypomagnesemia in patients was analyzed using multivariate analysis ANOVA and the analysis showed a statistically significant correlation between mortality and hypomagnesemia in patients. The present study highlighted the importance of hypomagnesemia in the intensive care unit and its outcome with various parameters. The present study showed that hypomagnesemia is associated with increased APACHE II score, increased incidence of ventilator requirement, and higher mortality.

Limitations of the Study

The present study measured serum total magnesium but ionized magnesium is a more accurate predictor of magnesium status. In the studies discussed above Escuela et al[13], Huijgen et al[12], and Guerin et al[14] observed ionized magnesium values in their study. Total magnesium levels were analyzed in various other studies. Total magnesium is a simple and cost-effective measurement. Only initial magnesium values were taken for the study and no follow-up values were done for all patients. We included only medical ICU

patients which revealed a lower incidence of hypomagnesemia and mortality outcome. The inclusion of surgical ICU patients could have changed the observations of this study. Nonetheless, the present study observed that the incidence of hypomagnesemia in the medical ICU is low. The present study was observational and we included only patients with hypomagnesemia and no comparison was made for patients with normomagnesemia to have a specific association of parameters with low magnesium. A few studies have made observations concerning hypermagnesemia also.

Conclusion

Magnesium is an unrecognized cation in critically ill patients. The incidence of hypomagnesemia in the present study was less compared to other studies done in medically ill patients. Hypomagnesemia correlated well with the APACHE II score, ventilator requirement, and mortality, which was statistically significant. As hypomagnesemia has a significant association with adverse outcomes, we suggest that measurement of magnesium be done in all critically ill patients. Prompt correction of magnesium could change the outcome. Further studies will be required to ascertain our conclusion.

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