Journal of Clinical Gerontology & Geriatrics 7 (2016) 104–108

Contents lists available at ScienceDirect

Journal of Clinical Gerontology & Geriatrics

journal homepage: www.e-jcgg.com

Original article

Impact of serum magnesium levels in critically ill elderly patients—A study in a rural teaching hospital

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ARTICLE INFO

Article history:
Received 2 November 2015
Received in revised form
31 March 2016
Accepted 12 April 2016
Available online 3 August 2016

Keywords:
critical care
elderly
magnesium
mortality

ABSTRACT

Background/Purpose: Magnesium deficiency has been a common, but easily ignored, electrolyte abnormality. Studies on magnesium deficiency are lacking in India, especially in a rural setting. Here, we have correlated serum magnesium levels with outcomes in elderly patients admitted to the medical intensive care unit with respect to the length of intensive care unit stay, need for mechanical ventilatory support and its duration, and outcome (discharge/death).

Methods: A prospective, observational study was conducted in patients aged 60 years and older, who had been admitted to the intensive care unit of the medicine department for over a year. The chi-square test was applied to correlate hypomagnesemia with the outcome.

Results: In our study, 59.30% of the elderly patients had hypomagnesemia. Compared with patients with a normal magnesium level, hypomagnesemic patients had no correlation with the duration of medical intensive care unit stay (5.57 ± 6.10 days vs. 5.61 ± 5.55 days), but the need for mechanical ventilation (57.84% vs. 45.71%), rate of discharge from the intensive care unit or cure (60.28% vs. 71.42%), rate of death (39.21% vs. 28.57%), and mean duration of ventilation (3.07 ± 5.05 days vs. 2.15 ± 3.46 days) were higher. However, no significant statistical difference was found between these groups.

Conclusion: Hypomagnesemia was associated with a slightly higher mortality rate. Requirement and duration of ventilatory support were also higher, although not statistically significant. Hypomagnesemia was not found to have any impact on the duration of medical intensive care unit stay. Monitoring of serum magnesium levels may have prognostic and perhaps therapeutic implications in the elderly.

1. Introduction

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).[1,2] To make matters worse, many medications taken by the elderly and the stress they often endure also tend to cause magnesium loss, further lowering tissue magnesium levels.

Disorders of magnesium metabolism are among the most common electrolyte disturbances in hospitalized patients, especially in the critically ill elderly, and are frequently unrecognized. The prevalence of hypomagnesemia (measuring total serum magnesium) has a wide range (11–61%), and a considerable controversy exists regarding its effects on morbidity and mortality.[3–8] 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.[2]

No data are available from India as far as critical elderly individuals are concerned. In this study, we have tried to correlate serum Mg levels with outcomes in elderly patients of the medical

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http://dx.doi.org/10.1016/j.jcgg.2016.04.002
2210-8335/

intensive care unit (MICU) with respect to the length of ICU stay, need for mechanical ventilatory support and its duration, and the ultimate outcome (discharge/death).

2. Methods

This prospective observational study was carried out in the MICU of Acharya Binova Bhave Rural Hospital attached with Jawahar Lal Nehru Medical College, Wardha, Maharashtra, in rural central India, from March 2013 to October 2013, after approval by the Institutional Ethics Committee. Among the 202 elderly patients admitted to the MICU, 172 were included in this study. Patients were enrolled at random, and the selection bias was avoided by registering those patients who fulfilled the criteria for critical illness on the basis of a severity scoring system (Acute Physiology and Chronic Health Evaluation-II). Thirty patients, of whom 20 were stable and eight had financial constraints, were excluded from the study, as shown in the flowchart in Figure 1. Patients who had received magnesium prior to admission to the MICU (although there were no such case) or long-term medication with proton pump inhibitors (2 patients with a history of acid peptic disease) were excluded. Demographic data (age and sex), past medical history, medications administrated, and length of ICU stay were recorded for each patient. Blood, urine, and endotracheal secretions of every febrile patient were sent for culture screen. Blood samples were collected for the estimation of serum total magnesium levels on admission to the MICU, which was determined by a colorimetric method. This study did not interfere with patient management in the MICU. Study participants with hypomagnesemia did not receive magnesium replacement in our research. The normal reference value of serum total magnesium was between 1.5 mg/dL and 2.5 mg/dL.[4] Patients with a magnesium level of < 1.5 mg/dL were considered to have hypomagnesemia. Statistical analysis was performed using descriptive and inferential statistics. All data were expressed as mean ± standard deviation. Analysis was performed using the test statistics Student *t* test for the difference of means, Chi-square test, and correlation. The software used in the analysis included SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) and Graph pad Prism 5.0 (IBM Corporation, www.ibm.com/software/analytics/spss/), and a p value of <0.05 was considered significant.

3. Results

A total of 172 elderly patients, aged 60 years and older (mean age, 69.32 ± 7.32 years for male and 64.30 ± 4.11 years for female patients), who were admitted to the MICU were enrolled in this study. Baseline comparison of the characteristics of study patients is shown in Table 1. On admission, 60/102 (58.82%) male elderly patients and 42/102 (42.18%) female elderly patients had hypomagnesemia. The lowest serum magnesium value recorded was 1 mg/dL, while the highest value was 2.5 mg/dL. The mean duration of stay in the MICU was 5.61 ± 5.55 days in patients with a normal magnesium level and 5.57 ± 6. 10 days in patients with hypomagnesemia, while the total duration of stay was 5.59 ± 5.87 days with $t = 0.39$ and $p = 0.5$ (Table 2). Fifty-nine (57.84%) patients with hypomagnesemia needed mechanical ventilatory support, while 43 (42.15%) patients did not require this support; the difference was not statistically significant ($p = 0.18$ and $\chi^2 = 3.37$). The mean duration of ventilatory assistance for the hypomagnesemic group was 3.07 ± 5.05 days and that for the normomagnesemic group was 2.15 ± 3.46 days; the difference was not statistically significant ($p = 0.09$ and $t = 1.32$; Table 2). The cure/discharge rates were 50 (71.42%) for patients with normal magnesium and 62 (60.78%) for those with low magnesium, and the difference was not statistically significant. The mortality rate in the hypomagnesemic group was 39.21% (40), whereas that in the normomagnesemic group was 28.57% (20) {$\chi^2 = 2.07$, $p = 0.15$}. Finding of the association between characteristics of study participants and hypomagnesemia is shown in Table 2. The major groups of patients admitted to the MICU were grouped as patients with cirrhosis, chronic kidney disease (CKD), chronic obstructive pulmonary disease, diabetes mellitus, ischemic heart disease, malaria, sepsis, stroke, and others (Table 2).

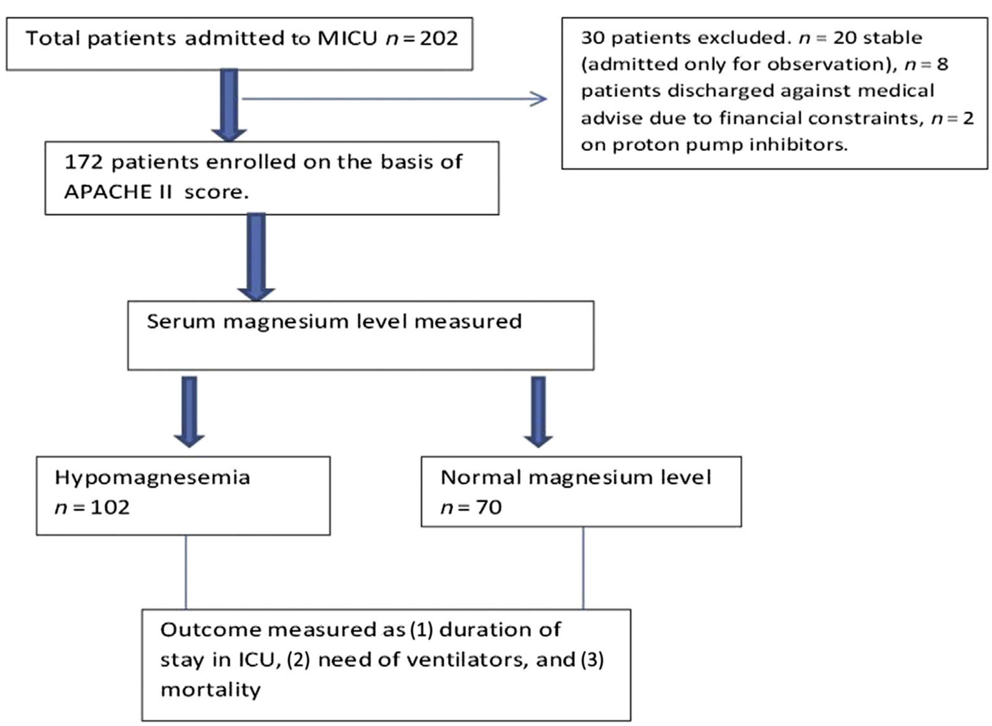

Figure 1. Flowchart showing enrolment of patients. APACHE II = Acute Physiology and Chronic Health Evaluation-II; ICU = intensive care unit.

Table 1
Baseline characteristics of study participants.

Characteristics	Male $N=107$	Female $N=65$	Total $N=172$	Statistical significance
Mean age (SD)	69.32 (7.32)	64.30 (4.11)	67.43 (6.77)	$p<0.01$
Blood pressure				
Normal	94 (87.85)	57 (87.69)	151 (87.79)	$p=0.5770$
Hypertension	13 (12.14)	8 (12.30)	21 (12.20)	
QT				
Normal	78 (60.94)	50 (39.06)	128 (74.42)	$\chi^2=0.165$
Prolonged	29 (65.91)	15 (34.09)	44 (25.58)	$p=0.6844$
Diagnosis				
Cirrhosis	15 (14.01)	1 (01.53)	16 (9.30)	Not applicable
CKD	7 (6.54)	5 (7.69)	12 (6.98)	
IHD	12 (11.21)	9 (13.84)	21 (12.21)	
COPD	3 (2.80)	1 (1.53)	4 (2.33)	
DM	1 (00.90)	2 (3.07)	3 (1.74)	
Malaria	9 (8.41)	9 (13.84)	18 (10.47)	
Sepsis	21 (19.62)	21 (19.62)	42 (24.42)	
Stroke	3 (2.80)	6 (9.23)	9 (5.23)	
Other	36 (33.64)	11 (16.92)	47 (27.33)	

Data are presented as *n* (%), unless otherwise indicated.
QT is electrocardigraphic changes.
CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; IHD = ischemic heart disease; SD = standard deviation.

Table 2
Comparison of patient characteristics between groups with normal magnesium level versus those with hypomagnesemia.

Characteristics	Normal Mg $N=70$ 40.69%	Hypo Mg $N=102$ 59.30%	Total $N=172$	Statistical significance
Mean age (SD)	66.42 (6.75)	68.11 (6.73)	67.43 (6.77)	$t=1.03$ $p=0.30$
Sex				
Male	47 (67.14)	60 (58.82)	107 (62.21)	$\chi^2=1.22$
Female	23 (32.85)	42 (42.17)	65 (37.79)	$p=0.26$
BP				
Normal	61 (87.14)	90 (88.23)	151 (87.79)	$\chi^2=0.04$
Hypertension	9 (12.85)	12 (11.76)	21 (12.21)	$p=0.83$
QT				
Normal	56 (80)	72 (70.58)	61 (35.47)	$\chi^2=1.93$
Prolonged	14 (20)	30 (29.41)	111 (64.53)	$p=0.16$
Diagnosis				
Cirrhosis	4 (5.71)	12 (11.76)	16 (9.30)	Not applicable
CKD	2 (8.33)	10 (9.80)	12 (6.98)	
IHD	7 (9.52)	14 (13.72)	21 (12.21)	
COPD	2 (2.85)	2 (1.9)	4 (2.33)	
DM	2 (2.85)	1 (0)	3 (1.74)	
Malaria	6 (7.14)	12 (11.76)	18 (10.47)	
Sepsis	16 (22.85)	26 (25.49)	42 (24.42)	
Stroke	5 (7.14)	4 (3.9)	9 (5.23)	
Other	26 (37.14)	21 (20.58)	47 (27.33)	
Hypokalemia	0 (0)	74 (72.54)	74(43.02)	
Hyperkalemia	3 (4.28)	0 (0)	3(1.74)	
Hypoalbuminemia	0	86 (84.31)	86(50)	
Outcome				
Discharged/cured	50 (71.42)	62 (60.78)	112 (65.12)	$\chi^2=2.07$
Death	20 (28.57)	40 (39.21)	60 (34.88)	$p=0.15$
ICU stay (d)				
Mean (SD)	5.61 (5.55)	5.57 (6.10)	5.59 (5.87)	$t=0.39$ $p=0.5$
Requirement of ventilator support				
Yes	32 (45.71)	59 (57.84)	91 (52.91)	$\chi^2=3.37$
No	38 (54.28)	43 (42.15)	81 (47.09)	$p=0.18$
Duration of ventilator support (d)				
Mean (SD)	2.15 (3.46)	3.07 (5.05)	2.70 (3.46)	$t=1.32$ $p=0.09$
APACHE II	19.26 ± 4.37	21.82 ± 5.90		$P=0.24$

Data are presented as *n* (%), unless otherwise indicated.
QT is electrocardigraphic changes.
APACHE II = Acute Physiology and Chronic Health Evaluation-II; BP = blood pressure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; IHD = ischemic heart disease; SD = standard deviation.

Table 3
Logistic regression for the correlation between hypomagnesemia and various patient characteristics.

Correlation variable	Standard error	Significance	OR	95% CI for OR	
				Lower bound	Upper bound
Age	0.375	0.225	1.576	0.756	3.288
sex	0.361	0.171	0.610	0.300	1.238
BP	0.396	0.699	1.165	0.536	2.534
ECG QT prolongation	0.394	0.245	1.581	0.730	3.426
Requirement of ventilation	0.411	0.271	1.571	0.702	3.513
Duration of ventilation	0.643	0.424	1.672	0.474	5.898
MICU stay	0.488	0.258	0.576	0.221	1.498
Outcome	0.419	0.966	1.018	0.448	2.312

QT is electrocardigraphic changes.
BP = blood pressure; CI = confidence interval; ECG = electrocardiogram; MICU = medical intensive care unit; OR = odds ratio.

Multiple logistic regression models were applied for the determination of factors associated with hypomagnesemia. Unfortunately, none of the variables had an independent association with serum magnesium levels (Table 3).

4. Discussion

This study points to a possible impact of serum magnesium levels on outcomes in critically ill elderly patients in whom aging itself is a comorbidity. In our study, of the 172 critically ill elderly patients admitted to the MICU, 102 (59.30%) were hypomagnesemic. This suggests frequent occurrence of low Mg in them. In a study by El Said and Aly,[9] 23% of critically ill elderly patients had a low Mg level and 59% of them had a normal Mg level. The primary end points of this study were serum Mg levels and death/discharge rates of critically ill elderly patients. Secondary outcome measures were the associated chronic diseases and length of ICU stay, as well as the need of ventilators.

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).[9] We have not conducted a detailed survey regarding the exact etiology of hypomagnesemia in our study patients, but it may be multifactorial.

There is no doubt that the proportion of macronutrients in the diet can influence magnesium absorption and utilization. The average diet of an elderly individual generally contains more carbohydrates, and less proteins and fats than his/her younger counterpart.[10] The “Western diet” is considered relatively deficient in magnesium, while the “Oriental diet” is traditionally characterized by a greater intake of fruits and vegetables, and is therefore richer in magnesium.[10] In our country, somehow the diet is gradually becoming westernized as the nation has become more affluent. However, no published data of this kind on rural India were available. Excess sugar is associated with magnesiuria, and excess fiber can decrease gastrointestinal absorption of magnesium. Aging is also associated with a high frequency of clinical situations associated with hypomagnesemia. Older patients, because of their proclivity for cardiovascular disorders, are more likely to take digitalis and diuretic preparations. Urinary magnesium excretion increases by 25–400% following digitalis and diuretic therapy.[11] Stress, diabetes, and gastrointestinal disorders, all common in the aged people, frequently have a role in magnesium depletion. Medications to treat infections (aminoglycosides) and constipation (purgatives) can also lead to hypomagnesemia.[11]

Various studies have shown a varying relationship between hypomagnesemia and mortality/morbidity rates. On average, a higher mortality rate was detected in hypomagnesemia patients irrespective of their age when compared with normomagnesemic patients, as reported by Kumar et al[4] (38.56% vs. 14.73%), Limaye et al[5] (57% vs. 31%), Safavi and Honarmand[7] (55% vs. 35%), and Rubeiz et al[8] (46% vs. 25%). This study in critical elderly patients revealed the mortality rate in the hypomagnesemic group to be 39.21% (40), which was higher than the rate of 28.57% (20) in the normomagnesemic group ($\chi^2 = 2.07$, $p = 0.15$).

Hypomagnesemia and sepsis have an important role in increased mortality and morbidity, especially in the aged people. Hypomagnesemia is associated with increased release of endothelin and proinflammatory cytokines.[12,13] This was strongly associated with increased mortality in experimental sepsis, and Mg replacement provided significant protection against endotoxin challenge. This effect was due to the downregulation of the release of inflammatory cytokines (tumor necrosis factor-alpha and interleukin-6).[14–16] Sepsis was an independent risk factor for developing hypomagnesemia during ICU stay, as found by Soliman et al.[13] In the studies conducted by Kumar et al[4] and Limaye et al,[5] the incidence of sepsis was twice as common in hypomagnesemic patients than in normomagnesemic patients. Hypomagnesemia is also associated with diabetes mellitus, which may be due to increased renal losses of Mg that accompany glycosuria, as seen in the studies by Kumar et al[4] and Limaye et al.[5] Hypomagnesemia also leads to muscle weakness and respiratory failure, causing difficulty in weaning the patient from the ventilator. In a study by Kumar et al,[4] it was observed that patients with hypomagnesemia 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 ($p = 0.18$ and $\chi^2 = 3.37$). Fiaccadori et al[17] had observed that patients with low muscle Mg were on ventilatory support for more number of days. Safavi and Honarmand[7] had found that in patients with hypomagnesemia, the duration of mechanical ventilation was longer (7.2 days vs. 4.7 days, $p < 0.01$). Prolonged ventilation is not just due to muscle weakness causing difficulty in weaning. Hypermagnesemia is characteristically associated with neuromuscular blockade and muscle weakness, and therefore also with prolonged ventilation time.[7] Hypermagnesemia were not observed in our patients; the maximum level was 2.5 mg/dL. In the study carried out by Soliman et al,[13] there was no difference in the length of ICU stay between the hypomagnesemic and normomagnesemic groups. However, patients who developed hypomagnesemia during their ICU stay had a longer duration of stay in the ICU. In the study conducted by Limaye et al,[5] there was also no difference in the length of ICU stay between hypomagnesemic and normomagnesemic patients. In a study by Kumar et al,[4] there was a significant difference in the length of ICU stay between the hypomagnesemic and normomagnesemic groups of patients (5.46 ± 5.75 days vs. 3.93 ± 3.88 days, $p = 0.0002$). In this study, the mean duration of stay in the MICU was 5.61 ± 5.55 days for patients with a normal magnesium level and 5.57 ± 6.10 days for patients with hypomagnesemia.

4.1. Limitations

The major flaws of our design and possible biases were confounding factors. For example, electrolyte abnormalities such as hypokalemia are frequently associated with magnesium deficiency due to impairment of Na–K–ATPase activity.[18] As 30% of magnesium is bound to albumin and is therefore inactive, hypoalbuminemic states as in cirrhosis may lead to spuriously low magnesium values. Sepsis and diabetes are independent risk factors for developing hypomagnesemia.[4,5,13] CKD patients possess a higher chance of having a higher magnesium level. In moderate CKD, increases in the fractional excretion of magnesium largely compensate for the loss of glomerular filtration rate to maintain normal serum magnesium levels. However, in more advanced CKD (as creatinine clearance falls below 30 mL/min), this compensatory mechanism becomes inadequate such that overt hypermagnesemia develops frequently in patients with creatinine clearances at <10 mL/min.[19] It is a shortcoming of our design and we were unable to control these possible confounders adequately.

Another limitation is medication, which may be one of the important reasons to result in hypomagnesemia. We have not collected the medication information of our patients.

5. Conclusion

Mg alterations have frequently been observed in critically ill elderly patients, as in this study, who have a high prevalence of hypomagnesemia. 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.

Conflicts of interest

There is no conflict of interest.

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