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Hyopomagnesemia in Critically Ill Children

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Abstract

Objectives: To investigate the incidence of hypomagnesemia, hypomagnesemia-associated risk factors, and the effect of hypomagnesemia effect on prognosis among patients followed at pediatric intensive care unit.
Methods: This study enrolled patients who were admitted to the Pediatric Intensive Care Unit between January and December 2017. Patients' admission serum Mg level was measured, and a level below 1.8 mEq/L was considered hypomagnesemia. Patients with hypomagnesemia were grouped as group 1 and those with normal serum magnesium level as group 2.
Results: A total of 59 (39.9%) of the 148 patients were female and 89 (60.1%) were male; the mean age was 62.82 $\pm$ 72.8 (min: 2 - max: 245) months. Compared with the normomagnesemic patients, those with hypomagnesemia had a greater mean age (P: 0.04), PRISM score (P: 0.015), duration of intensive care unit stay, (P: 0.001), mechanical ventilator need (P: 0.016) and the number of days connected to mechanical ventilator (P: 0.027), having nasogastric drainage (P: 0.02), and mortality rate (P: 0.041). No significant difference was found between the groups with respect to diuretic use. Increase risk of hypomagnesemia by nasogastric drainage was not significant (P: 0.082). The rates of hypokalemia, hypocalcemia, hypophosphatemia, and hypoalbuminemia were significantly greater in group 1 ($P < 0.05$). Hypokalemia increased the risk of hypomagnesemia by 5.13 times, hypophosphatemia by 21.8 times, hypoalbuminemia by 5.12 times, and nasogastric drainage by 3.01 times.
Conclusions: It should be noted that hypomagnesemia might be common and associated with mortality among patients admitted to pediatric intensive care units. Therefore, serum magnesium level should be closely monitored.

Keywords: Magnesium, Critical Illness, Mortality, Risk Factor, Hypomagnesemia

1. Background

Magnesium is the fourth most abundant element in the human body and the second most abundant intracellular element after potassium. A total of 60% of it is bound to calcium and phosphate in bones. However, it does not exert its main function in the bones but in the blood and muscular system, which is where 40% of it is found. It plays an important role for muscle strength, protein synthesis, and enzymatic activity, as well as cellular growth, and regeneration. Magnesium acts as a cofactor of more than 300 enzymes containing adenosine triphosphate, particularly of enzymes responsible for phosphate transfer. Therefore, it is of great importance for electrically excitable tissues. Moreover, it regulates calcium ion movement in smooth muscle cells, which has an important role maintaining cardiac contractility and peripheral vascular tonus (1, 2). Hypomagnesemia is mostly asymptomatic but may present with tetany, tremor, hyperreflexia, nystagmus, ventricular arrhythmia, torsades de pointes, hypertension, coronary vasospasm, hemiparesia, bronchial airway constriction, and generalized tonic-clonic convulsions (3). Previous studies have reported that hypomagnesemia had arate of 44% at pediatric intensive care units (4). The etiology of hypomagnesemia in critical disorders is complex and may include various mechanisms such as inadequate oral intake, renal and gastrointestinal losses, and alterations in intracellular and extracellular distribution (5). Prolonged proton pump inhibitor use is known to inhibit Mg absorption from the intestines (6).

The aim of this study was to investigate the incidence of hypomagnesemia, to identify hypomagnesemia-associated risk factors, and to determine its effect on prognosis among patients admitted to pediatric intensive care unit.

2. Methods

This study was approved by the local Ethics Committee and conducted single center, cross sectional, retrospec-

tively among patients admitted to the 10-bed Pediatric Intensive Care Unit of Umraniye Research and Training Hospital. It included children between the ages of 1 month to 17 years who were admitted to the pediatric intensive care unit and followed at the PICU for more than two days between January 2017 and December 2017. Patients who received magnesium products within the last 24 hours and those with congenital renal magnesium loss were excluded. Age, sex, body weight, admission diagnosis, pediatric risk of mortality score (PRISM), duration of PICU stay, need for ventilatory support, diuretic use, nasogastric drainage, duration of mechanical ventilation, and 28-day mortality were recorded for all patients. Admission serum magnesium, sodium, potassium, phosphorus, calcium, and albumin levels were studied. Serum magnesium level of less than 1.8 mEq/L was termed as hypomagnesemia, serum sodium level of less than 135 mEq/L as hyponatremia, serum potassium level of less than 3.5 mEq/L as hypokalemia, serum phosphorus level of less than 2.5 mg/dL as hypophosphatemia, serum calcium level of less than 8.5 mg/L as hypocalcemia, and serum albumin level of less than 3.5 g/dL as hypoalbuminemia (4). The patients were grouped into two groups as hypomagnesemic and normomagnesemic. Patients with hypomagnesemia were administered intravenous magnesium sulphate (15%) at a dose of 25 mg/kg.

Study data were analyzed using the IBM SPSS Statistics v. 22 (IBM SPSS, Türkiye). Shapiro Wilk test was used to test the normality of distribution of the study data. Descriptive statistics included mean, standard deviation, and frequency. Normally distributed quantitative data were compared using the Student's *t* test and non-normally distributed ones with the Mann Whitney-U test and. Qualitative data were compared with the Chi-Square test, Fisher's Exact Test, and continuity (Yates) correction. Regression analysis was performed with backward 8 step logistic regression analysis. Statistical significance was set at $P < 0.05$.

3. Results

Among the 148 patients included in the study, 59 (39.9%) were female and 89 (60.1%) were male; they had a mean age of 62.82 $\pm$ 72.8 (min: 2 - max: 245) months. The mean body weight was 19.2 $\pm$ 18.3 (3 - 110) kg, mean PRISM score 11.53 $\pm$ 10.11 (1 - 49), mean duration of intensive care unit stay was 11.7 $\pm$ 14.0 (2 - 90) days, and mean duration of mechanical ventilation was 12.03 $\pm$ 14.45 (1 - 70) days. In terms of diagnosis on admission to intensive care, the largest group consisted of respiratory diseases (31 cases), followed by neurological diseases (30 cases) and cardiac diseases (28 cases) (Table 1). A total of 43 (29.1%) patients had hypomagnesemia. An analysis of serum magnesium level according to admission diagnosis revealed that hypomagnesemia was present in 56.3% of the patients with sepsis, 44.4% of the patients with cancer, and 42.9% of the trauma patients (Table 2). The mortality rate was 16.9%. The hypomagnesemic patients had a greater mean age (P: 0.04), PRISM score (P: 0.015), duration of intensive care unit stay (P: 0.001), need for mechanical ventilation (P: 0.016), duration of mechanical ventilation (P: 0.027), rate of having nasogastric drainage (P: 0.02), and mortality rate (P: 0.041). No significant difference was observed between the groups with respect to diuretic use (Table 3). Increase risk of hypomagnesemia by nasogastric drainage was not significant (P: 0.082).

The patients with hypomagnesemia had significantly greater rates of hypokalemia, hypocalcemia, hypophosphatemia, and hypoalbuminemia than the normomagnesemic ones ($P < 0.05$) (Table 4).

The rate of hypomagnesemia was significantly higher in patients with sepsis and postoperative patients (P: 0.01 and P: 0.047).

The risk of hypomagnesemia was increased by hypokalemia by 5.13 times, hypophosphatemia by 21.8 times, hypoalbuminemia by 5.12 times, and nasogastric drainage by 3.01 times (Table 5).

Table 1. Admission Diagnosis

	No. (%)
Pulmonary disease	31 (20.9)
Neurologic disease	30 (20.3)
Cardiac disease	28 (18.9)
Sepsis	16 (10.8)
Trauma	14 (9.5)
Oncologic disease	9 (6.1)
Others	20 (13.5)

Table 2. Serum Magnesium Levels by Diagnosis

Diagnosis	Hypomagnesemic, No. (%)	Normomagnesemic, No. (%)
Sepsis	9 (56.3)	7 (43.8)
Pulmonary disease	4 (12.9)	27 (87.1)
Cardiac disease	7 (25)	21 (75)
Neurologic disease	8 (26.7)	22 (73.3)
Oncologic disease	4 (44.4)	5 (55.6)
Trauma	6 (42.9)	8 (57.1)
Others	5 (25)	15 (75)
P	0.055	

Table 3. Comparison of the Parameters by Magnesium Level[a]

	Group 1	Group 2	P
Age, mo	81.6 ± 78.41	55.12 ± 69.3	0.044[b,c]
Prism score	15.02 ± 11.55	10.1 ± 9.13	0.015[b,c]
Duration of intensive care stay, d	18.37 ± 19.75	9.08 ± 9.88	0.001[b,d]
MV duration, d	16.93 ± 18.64	8.73 ± 9.7	0.027[b,d]
Sex			0.291[e]
Female	20 (46.5)	39 (37.1)	
Male	23 (53.5)	66 (62.9)	
Diuretic use			0.715[f]
Yes	7 (16.3)	13 (12.4)	
No	36 (83.7)	92 (87.6)	
Nasogastric drainage			0.002[b,f]
Yes	18 (41.9)	17 (16.2)	
No	25 (58.1)	88 (83.8)	
MV need			0.016[b,f]
Yes	26 (60.5)	39 (37.1)	
No	17 (39.5)	66 (62.9)	
Prognosis			0.041[b,f]
Alive	31 (72.1)	92 (87.6)	
Died	12 (27.9)	13 (12.4)	

[a] Values are expressed as mean ± SD or No. (%).
[b] P < 0.05.
[c] Student's *t* test.
[d] Mann Whitney-U test.
[e] Chi Square test.
[f] Continuity (Yates) correction.

Table 4. Comparison of the Laboratory Results of the Groups[a]

	Group 1	Group 2	P
Na (< 135 mEq/L)			0.120[c]
< 135	12 (27.9)	16 (15.2)	
≥ 135	31 (72.1)	89 (84.8)	
K (< 3.5 mEq/L)			0.001[b,c]
< 3.5	13 (30.2)	8 (7.6)	
≥ 3.5	30 (69.8)	97 (92.4)	
Ca (< 8.5 mg/L)			0.001[b,c]
< 8.5	19 (44.2)	16 (15.2)	
≥ 8.5	24 (55.8)	89 (84.8)	
P (< 2.5 mg/L)			0.001[b,d]
< 2.5	9 (20.9)	3 (2.9)	
≥ 2.5	34 (79.1)	102 (97.1)	
Albumin (< 3.5 gr/dL)			0.003[b,c]
< 3.5	25 (58.1)	32 (30.5)	
≥ 3.5	18 (41.9)	73 (69.5)	

[a] Values are expressed as No. (%).
[b] P < 0.05.
[c] Continuity (Yates) correction.
[d] Fisher's Exact Test.

4. Discussion

Hypomagnesemia is one of the common metabolic abnormalities in patients followed at the intensive care unit. In this study, we investigated the prognostic role of admission serum magnesium on the outcome of critically ill pediatric patients considering other factors that are expected to affect the outcome. The hypomagnesemic patients had a greater mean age, PRISM score, duration of intensive care unit stay, need for mechanical ventilation, duration of mechanical ventilation, rate of having nasogastric drainage, and mortality rate.

Previous studies have reported that it is seen in 44% of pediatric patients and 20% - 40% in adult patients admitted to intensive care unit (4, 5, 7, 8). In accordance with literature data, we detected hypomagnesemia in 43 (29.1%) of the 148 patients enrolled in our study. Limaye et al. (9) reported that of the 100 intensive care patients, 52% were hypomagnesemic, 7% were hypermagnesemic, and 41% were normomagnesemic. They reported that, as compared to patients with normal magnesium levels, those with hypomagnesemia had a greater need for mechanical ventilation (73% vs 53%), received mechanical ventilatory support for a longer period (4.2 days vs 2.1 days), had a higher incidence of sepsis (38% vs 19%), and suffered a greater mortality (57.7% vs 31.7%). Hypomagnesemia is known to cause muscle weakness and respiratory failure and is causing difficulty in weaning the patient from the ventilator. We similarly detected that the hypomagnesemic patients had a greater need for mechanical ventilation, had a longer duration of MV and PICU stay, and had a greater rate of sepsis.

In another study of 446 ICU patients, 18% of the patients had hypomagnesemia, 14% had hypermagnesemia, and 68% had a normal magnesium level. The authors of this study reported that the hypomagnesemic patients had a greater shock prevalence (57% vs 11%), had a longer duration of ICU stay (5.4 days vs 2.8 days), and a had a greater mortality rate (35% vs 12%) (10). The higher mortality rates in the hypomagnesemic patients can be explained by a greater incidence of electrolyte abnormalities and a strong association of hypomagnesemia with sepsis and septic shock.

Haque and Saleem (4) reported that 44% of pediatric intensive care patients were hypomagnesemic. They identified being older than 1 year of age, sepsis, hypokalemia, hypocalcemia, diuretic and aminoglycoside use, and hos-

Table 5. Risk Factors for Hypomagnesemia[a]

	β	S.E	P	Exp (β)	%95 CI
Nasogastric drainage	1.103	0.634	0.082	3.013	0.869 - 10.438
Hypopotassemia	1.637	0.726	0.024[b]	5.139	1.238 - 21.332
Hypophosphatemia	3.082	1.228	0.012[b]	21.804	1.965 - 242.009
Hypoalbuminemia	1.634	0.66	0.013[b]	5.125	1.406 - 18.68
Constant	-4.853	1.509	0.001[b]	0.008	

[a] Binary Logistic Regression.
[b] $P < 0.05$.

pital stay of more than five days as the important risk factors. They stressed that the combination of hypokalemia and hypomagnesemia may have originated from underlying conditions that may affect the levels of both electrolytes, such as diuretic therapy, diarrhea, vomiting, and nasogastric aspiration. Safavi and Honarmand (11), reported that hypocalcemia, hypokalemia, and hyponatremia were more common among hypomagnesemic ICU patients older than 16 years of age.

Gupta et al. (12), showed that administering hypocalcemia and hypokalemia were not sufficient to correct hypocalcemia and hypokalemia in critical care patients, and stressed that hypomagnesemia should be corrected and serum magnesium level closely monitored in these patients. We also revealed that the rates of hypokalemia, hypocalcemia, hypophosphatemia, and hypoalbuminemia were significantly greater in hypomagnesemic patients than their normomagnesemic counterparts ($P < 0.05$). This is due to defective membrane ATPase activity and also due to the fact that the renal potassium loss is increased in the presence of hypomagnesemia. Hypocalcemia is a well-known manifestation of Mg deficiency. Patients with combined hypocalcemia and hypomagnesemia also show low levels of parathyroid hormone (13).

Previous studies reported that hypomagnesemia was more prevalent among patients using diuretics and aminoglycosides (14). Diuretics exert this effect by inhibiting magnesium absorption. Aminoglycosides cause urinary magnesium excretion by impairing magnesium reabsorption in loop and distal tubules. As the number of our patients using aminoglycosides was so low, we excluded them; we did not detect any difference with regard to diuretic use, either.

Magnesium plays an important role for immunological functions such as macrophage activation, adherence, lymphocyte proliferation, endotoxin binding to monocytes (15). Cojocaru et al. (16), showed that the serum magnesium level was markedly reduced among patients with sepsis due to acute bacterial infection. They stressed that it should be kept in mind that hypomagnesemia occurs at a particularly high rate among patients with bacterial infections in whom serum magnesium levels should be closely followed. We also observed hypomagnesemia at a higher rate in patients with sepsis than those without.

Early recognition of hypomagnesemia and its treatment with magnesium sulphate 25 mg/kg/dose may be associated with less mortality. Patients with malabsorption and a serum magnesium level between 0.5 - 0.7 mmol/L may sometimes need long-term enteral or parenteral nutritional support (17).

The two limitations of the present study were: first, this study was a single center study, second, being a retrospective study.

In conclusion, it should be remembered that hypomagnesemia may be common and associated with increased mortality among patients followed at pediatric intensive care units. Hence, serum Mg level needs to be closely monitored.

Footnote

Authors' Contribution: Seher Erdoğan developed the original idea and the protocol, abstracted and analyzed data, wrote the manuscript, and is guarantor. Tuba Seven Menevşe contributed to the development of the protocol and prepared the manuscript.

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