Hypomagnesaemia in critically ill patients

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ABSTRACT

Background: Hypomagnesaemia is a common electrolyte abnormality in critically ill patients. A lot of controversy exists regarding the optimum method of measuring magnesium and the influence of hypomagnesaemia on the morbidity and mortality of these patients.

Objectives: To study the prevalence of hypomagnesaemia (measured in serum and RBCs) in critically ill patients and its impact on morbidity and mortality.

Patients and methods: Sixty five (65) critically ill patients were studied. Their total serum and erythrocyte Mg (representing intracellular Mg) were measured within 24 hours of intensive care unit (ICU) admission. The patients were followed throughout their ICU stay and assessed regarding the severity of their illness using acute physiology and chronic health evaluation II (APACHE II) score, duration of stay in the ICU and mortality rate.

Results: Serum hypomagnesaemia was present in 84.6% of patients. Only 36.9% of patients were having low erythrocyte Mg. There was a weak positive correlation between serum and erythrocytes Mg levels.

No patient with normal serum Mg died, compared with 22.2% mortality rate in patients with low serum Mg (p=0.000). No significant difference in the mortality rate was noticed between patients with normal and low erythrocyte Mg. Neither low serum nor erythrocyte Mg had been associated with more severe illness or prolonged ICU stay.

Conclusion: Hypomagnesaemia (measured as total serum Mg) is associated with excess ICU mortality, irrespective of the severity of the underlying illness. Intracellular Mg (measured as erythrocyte Mg) does not correlate with ICU morbidity and mortality, and its routine measurement may not be indicated.

نقص المغنيسيوم في مرضى الحالات الحرجة

الخلاصة

الخلفية: نقص المغنيسيوم أحد اضطرابات الكهاريز الشائعة لدى مرضى الحالات الحرجة. يكتنف كثير من التضارب الطريقة المثلى لقياس المغنيسيوم وتاثير نقص المغنيسيوم على مرضية ووفيات هؤلاء المرضى.

الأهداف: دراسة انتشار نقص المغنيسيوم (مقاسا في المصل والكريات الحمراء) في مرضى الحالات الحرجة، وتأثير ذلك على نسبة المرضية والوفيات.

المرضى وطرق العمل: درسنا ٦٥ مريضا من المصابين بحالات حرجة. أجرينا قياس نسبة المغنيسيوم في مصل الدم والكريات الحمراء خلال ٢٤ ساعة من إدخالهم الى وحدة العناية المركزة. تمت متابعة حالة هؤلاء المرضى طيلة فترة رقودهم، وتم إحتساب حرز اباشي (كمؤشر لشدة المرض) وفترة بقائهم في العناية المركزة ونسبة الوفيات.

النتائج: سجل إنخفاض في نسبة المغنيسيوم في مصل الدم لدى ٨٤,٦ ٪ من المرضى، بينما بلغت نسبة المرضى الذين لديهم إنخفاض في نسبة المغنيسوم في الكريات الحمراء ٣٦,٩ ٪. كانت هناك علاقة موجبة ضعيفة بين نسبة المغنيسيوم في مصل الدم والكريات الحمراء. لم يتوف أي مريض من الذين لديهم نسبة مغنيسيوم طبيعية في الدم، بينما بلغت نسبة الوفيات ٢٢,٢٪ لدى المرضى الذين إنخفضت لديهم نسبة المغنيسيوم في مصل الدم عن المدى الطبيعي (ب = ٠,٠٠٠). لم يكن لنقص المغنيسيوم في

الكريات الحمراء تأثير ذو قيمة احصائية على نسبة الوفيات. لم يكن لإنخفاض نسبة المغنيسيوم في المصل أو الكريات اي علاقة بشدة المرض أو فترة البقاء في العناية المركزة.

الإستنتاج: إنخفاض نسبة المغنيسيوم (مقاساً في مصل الدم) متعلق بزيادة نسبة الوفيات عند مرضى الحالات الحرجة، وهذا التأثير لا علاقة له بشدة المرض. لم يكن لنسبة المغنيسيوم داخل الخلايا (متمثلا بنسبة المغنيسيوم في الكريات الحمراء) أي تأثير على مرضية ووفيات حالات العناية المركزة، وقد لا يكون قياسه ضروريا.

Magnesium (Mg) is the second most abundant intracellular cation after potassium. It has a fundamental role as a co-factor in more than 300 enzymatic reactions involving energy metabolism and nucleic acid synthesis. Mg is also involved in several other processes including hormone receptor binding, gating of calcium channels, muscle contraction, neuronal activity and cardiac excitability [(1)]. Mg deficiency is associated with a number of clinical manifestations, such as cardiac arrhythmias, muscle weakness, tetany and electrolyte abnormalities [(2)].

Only 1% of total Mg is in the extracellular compartment. Within the plasma, Mg circulates in three forms; 62% is ionized, and the remainder is bound to protein (mostly albumin), or complexed with anions such as phosphate, bicarbonate and citrate[(1)].

Hypomagnesaemia is one of the most common electrolyte abnormalities in hospitalized patients, especially in those who are critically ill[(3)]. The prevalence of hypomagnesaemia is about 12% in general hospital inpatients, but it varied from 14.3%[(4)] to 61%[(5)], when critically ill patients were studied. Considerable controversy exists regarding the effect of hypomagnesaemia on morbidity and mortality in the intensive care unit (ICU).

Adding to the complexity of the subject, there is a wide disagreement on the optimum method of assessing Mg status in these patients. Most of earlier studies measured total Mg, but with availability of ion selective electrodes, the physiologically active ionized Mg was measured in some recent trials[(6,7)]. At least within normal levels, total and ionized Mg tend to correlate with each other[(6)]. Considering the intracellular predominance of Mg and the role it plays in intracellular reactions, the benefit of measuring extracellular Mg has been questioned, and there was a new trend toward the measurement of intracellular Mg, one of which is erythrocyte Mg[(4,8,9)].

The aim of this study is to assess the prevalence of hypomagnesaemia among critically ill patients on their admission to the ICU. We tried to define the association of serum and erythrocyte Mg with the severity of the illness (defined by APACHE II score), the duration of stay in the ICU and the mortality rate.

PATIENTS AND METHODS

The study was conducted in the ICU of Ibn Sina Teaching Hospital in Mosul. This is a 13-bed-unit that receives patients having acute medical conditions, but it also accepts non-surgical acute obstetric emergencies from the nearby Al-Batool Maternity Hospital. The unit does not admit pure surgical cases, nor does it admit medical cases that are better treated in the coronary care or artificial kidney units that are present in the same hospital.

We included critically ill patients admitted in the period from January to May and from October to December 2008. We excluded women with eclampsia who have received parenteral Mg as part of their management. Sixty five patients met the inclusion criteria and were recruited in the study. For every patient, we defined the cause of admission and the duration of stay in the ICU. Enquiry was made regarding the patient's previous chronic diseases, history of alcohol drinking, and of receiving drugs known to induce hypomagnesaemia. APACHE II score was calculated for every patient in the first 24 hours of admission. This is the most commonly used scoring system which identifies high risk groups of critically ill patients and standardizes the prediction of mortality of these patients[(10)]. Approval was obtained from the scientific committee of the Department of Medicine, College of Medicine, University of Mosul.

Two sets of blood samples were taken within the first 24 hours after ICU admission. The first was a clotted blood; from which serum was obtained for assessment of total serum Mg. the second was EDTA sample; from which whole blood was used for measuring RBC Mg. The patients received the

standard care according to their illness, and were followed throughout their stay in the ICU. The duration of stay and the ultimate outcome was recorded.

Serum and erythrocytes Mg were measured by Gindler, Heth and Khayam-Bashi method [11,12], using kits purchased from Biolabo SA (France). The principle of the method depends on binding of Mg with calmagite, which is a metalochromic indicator, forming a coloured complex which is measured by spectrophotometer at wave length 510 – 550 nm.

Data tabulation and analysis were done by MiniTab version 14.1. Independent T-test of two means and Z-test two proportions were used. Simple Persson's correlation (linear) between serum and erythrocyte Mg was also applied. P-value < 0.05 was considered significant.

RESULTS

The mean age (±SD) of the studied group was 52.6 ± 18.29 years, of whom 33 (50.77%) were males and 32 (49.23%) were females. Their APACHE II score ranged from 0 – 31, with a mean (±SD) of 12.27 ± 7.19.

Pneumonia was the leading cause of ICU admission (14 patients), followed by respiratory failure caused by COPD or advanced tuberculosis (10 patients), and upper gastrointestinal bleeding from duodenal ulcer or oesophageal varices (8 patients) (**Table 1**).

Mean serum Mg of these patients was 0.47 mmol/l (ranging from 0.1- 1 mmol/l). Serum hypomagnesaemia below the reference range of 0.7 – 1 mmol/l was present in 55 of them (84.6%). Intracellular Mg (measured as erythrocyte Mg) was in the range of 0.3 – 4.5 mmol/l (normally 1.5 -2.5 mmol/l), with a mean of 1.46 mmol/l. When erythrocyte Mg was considered, 24 of the 65 patients (36.9%) were having hypomagnesaemia. There was a weak positive correlation between serum and erythrocyte Mg (correlation coefficient (r) = 0.284, p=0.02) (**Figure 1**).

Development of serum or erythrocyte hypomagnesaemia was not related to any particular illness, including patients with a diagnosis of sepsis. Mean APACHE II score was not statistically different between patient with low serum or erythrocyte Mg and those having normal levels (12.6 vs. 10.5 (p=0.291) and 13.3 vs. 11.6 (p=0.362) respectively). Similarly, the mean duration of stay in the ICU was not different weather patients were having low or normal serum or erythrocytes Mg (4.9 vs. 4.6 and 4.5 vs. 5.1 respectively).

The mortality rate of the studied group was 18.8%. All of the 10 patients with the normal serum Mg survived, compared with 22.2% mortality rate among hypomagnesaemic patients; the difference was highly significant (p=0.000, 95% CI: (0.111, 0.333)) (Z-two proportion test).

No significant difference on ICU mortality was noticed between patients with normal erythrocyte Mg (22.5%) and those with low erythrocytes Mg (12.5%) (p=0.290, 95% CI: (-0.285, 0.085)) (Z-two proportion test) (**Table 2**).

Table 1. The underlying diseases of the critically ill patient in the study.

Underlying disease	No. of patients
Pneumonia (including aspiration pneumonia and empyema)	14
Respiratory failure (COPD, bronchiectasis and advanced tuberculosis)	10
Upper gastrointestinal bleeding	8
Diabetic ketoacidosis	5
Sepsis (causes other than pneumonia)	4
Pulmonary embolism	4
Pulmonary oedema and cardiogenic shock)	4
Acute severe asthma	3
Liver failure	3
Meningitis and encephalitis	3
Status epilepticus	3
Guillain Barre syndrome	2
Drug poisoning	1
SLE with lupus nephritis	1

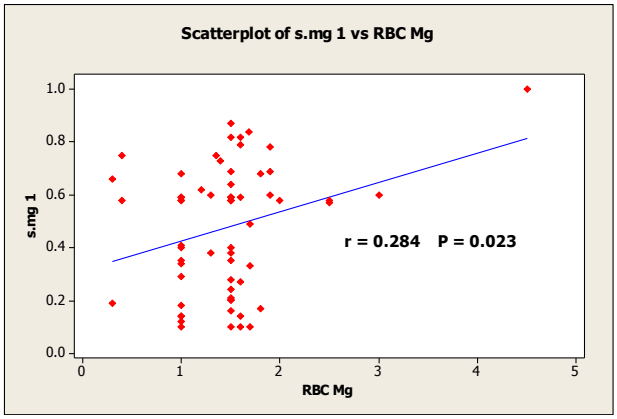

Figure 1. Correlation between serum and RBC Mg.

Table 2. Comparison between patients with normal and low serum and RBC Mg.

	Serum Mg			RBC Mg		
	Normal (15.4%)	**Low (84.6%)**	**P value**	**Normal (63.1%)**	**Low (36.9%)**	**P value**
Mean APACHE II score	10.5	12.6	0.291	11.6	13.3	0.362
Duration of ICU stay (days)	4.6	4.9	0.836	4.5	5.1	0.494
Mortality rate (%)	0	22.2	0.000	22.5	12.5	0.290

DISCUSSION

Hypomagnesaemia was highly prevalent in our ICU patients. In fact, the result of 85.6% was the highest when compared with ten similar studies[3-9,13-15]. However, the percentage of serum hypomagnesaemia was highly variable between these studies (ranging from 14.3%[4] to 61%[5]), probably reflecting the difference in the nature of the underlying diseases of these critically ill patients. Lack of attention to pre-existing hypomagnesaemia before our patients were admitted to the ICU may contribute to the high prevalence of admission hypomagnesaemia in our series.

Hypomagnesaemia assessed by serum Mg level was associated with highly significant increase in ICU mortality rate (22.2%), when compared with those having normal serum Mg who had no mortality. Such dramatic impact of hypomagnesaemia on ICU survival in our study was similarly noticed by Safavi[3], Chernow[5], Soliman[7]and Rubiez[14]. The later found twice more deaths in patients with hypomagnesaemia when compared with patients with normal serum Mg. However, many other researchers did not notice a significant influence of low serum Mg on ICU mortality[8,9,12,13]. Despite this controversy, the result of our study calls for serious consideration of a larger trial to be conducted for better clarification of this issue.

The lack of association between hypomagnesaemia and the severity of the underlying illness as assessed by APACHE II score (similarly noticed by Chernow[5], Koch[13] and Rubiez[14]) suggests a direct contribution of hypomagnesaemia to the excess mortality; perhaps, by predisposing to arrhythmias.

When erythrocyte Mg was considered, fewer patients were shown to have low serum Mg level (35%), with only weak positive correlation between serum and erythrocyte Mg. Huigren[8] found low serum Mg in 51.3% of 150 critically ill patients in a medical ICU, but none of them had low erythrocyte Mg (with no correlation between serum and erythrocyte Mg levels). In contrast to this study, Malon[4] and Guerin[9] in two different studies diagnosed 14.3% and 44% of their patients, respectively, as having hypomagnesaemia when serum Mg was measured, but a higher prevalence of hypomagnesaemia (33.3% and 66%, respectively) was detected when erythrocyte Mg was tested.

Regardless to the true relationship between serum and erythrocyte Mg, no study found any association between erythrocyte Mg and excess ICU mortality[8,9].

In conclusion, low serum Mg in critically ill patients in the ICU seems to increase the inpatient mortality rate. The real value of measuring intracellular Mg is not clear, and its routine measurement may not be indicated.

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