

Magnesium Levels in Critically Ill Patients

What Should We Measure?

Henk J. Huijgen, PhD,^{1,5} Marcel Soesan, MD,² Renata Sanders, PhD,¹ Willem M. Mairuhu, BSc,³ Jozef Kesecioglu, MD, PhD,⁴ and Gerard T. Sanders, PhD¹

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Abstract

We studied the relation between ionized magnesium, total magnesium, and albumin levels in serum of 115 critically ill patients and the role of extracellular and intracellular magnesium in outcome prediction. Levels of serum total and ionized magnesium, serum albumin, and magnesium in mononuclear blood cells and erythrocytes were measured and the APACHE II score and 1-month mortality recorded.

Of all patients, 51.3% had a serum total magnesium concentration below the reference range. In 71% of these hypomagnesemic patients, a normal serum ionized magnesium concentration was measured. None of the patients had an intracellular magnesium concentration below the reference limit. Except for serum total and ionized magnesium, none of the magnesium parameters correlated significantly with each other. A significantly negative correlation was found between serum albumin and the fraction ionized magnesium. There was no association between low extracellular or intracellular magnesium and clinical outcome.

The observation of hypomagnesemia in critically ill patients depends on which magnesium fraction is measured. The lack of correlation with clinical outcome suggests hypomagnesemia to be merely an epiphenomenon. Reliable concentrations of serum ionized magnesium can be obtained only by direct measurement and not by calculation from serum total magnesium and albumin.

For some time, magnesium (Mg) has been considered the “fifth forgotten ion.” However, for several years now, the qualification “forgotten” is no longer relevant. In the Academic Medical Center, Amsterdam, the Netherlands, there is a growing interest among clinicians in the determination of the total Mg concentration in serum (tMg_s). The requests for tMg_s measurements in the Academic Medical Center increased during the period 1990 to 1998 by almost 30%, to a total of 4,450 per year. Toffaletti¹ reported in 1995 that requests for Mg measurement increased faster than any other test at his laboratory.

One of the main reasons for this increased interest among clinicians, especially those working in intensive care units (ICUs), is the reports about a high incidence of hypomagnesemia in patients admitted to an ICU.²⁻⁴

Because the role of Mg is primarily that of a cofactor in intracellular biochemical reactions, and almost 99% of the total body Mg can be found intracellularly, the benefit of the measurement of tMg_s has been questioned.⁵ Based on the assumption that cell and tissue measurements should better reflect the total body magnesium status, studies have been conducted in which serum Mg was compared with Mg measured in bone or muscle biopsy specimens.⁵ As an alternative, the Mg concentration in erythrocytes (Mg_{RBC}) or mononuclear blood cells (Mg_{MBC}) also has been measured.⁶

A new parameter that may help to better establish hypomagnesemia is ionized serum Mg (iMg²⁺_s). In 1988 it was stressed by Fiaccadori and colleagues⁷ that the free ionic form of the cation is the active form and would be the ideal quantity to measure, in both serum and cells. However, practical methods for routine clinical use were not available until recently.⁸ In 1997, Hébert et al⁹ reported their study that measured iMg²⁺_s in the serum of 44 consecutive critically ill

patients and compared the measured concentrations with the results obtained with the Mg loading test as a reference, which was performed in 19 of these patients. They concluded that levels of both iMg^{2+}_s and tMg_s were poor predictors of functional Mg deficiency.

The present study was undertaken to investigate the relation between the levels of iMg^{2+}_s , tMg_s , and albumin (the most important binding protein of magnesium in blood) in the serum of critically ill patients and the role of extracellular and intracellular Mg in outcome prediction, expressed as the Acute Physiology and Chronic Health Evaluation (APACHE II) score,¹⁰ and 1-month mortality of this patient group.

Materials and Methods

Study Design

We conducted a prospective multicenter study for the relationship between Mg parameters and clinical outcome for ICU patients. This study was conducted in the ICUs of the Academic Medical Center (1,000-bed university hospital) and the Slotervaart hospital (400-bed general teaching hospital), Amsterdam. We included 115 consecutively admitted patients who met the inclusion criteria: vital instability for which ICU treatment was necessary and an expected length of stay in the ICU of more than 2 days. There were no exclusion criteria except for treatment with Mg products. Blood for Mg measurements was drawn within 24 hours of admission. The APACHE II score at entry or first 24 hours and the 1-month mortality (1 month was defined as 28 days) for each patient were recorded. Reference ranges were obtained by drawing blood from healthy laboratory workers and had already been established during previous Mg studies in our laboratory.¹¹

Depending on the amount of blood available and blood cells isolated, tMg_s was measured in all 115 patients, iMg^{2+}_s was measured in 111, Mg_{MBC} in 95, and Mg_{RBC} in 105. Based on the 2 serum parameters, iMg^{2+}_s and tMg_s , the fraction iMg^{2+}_s ($friMg^{2+}_s$) was calculated as $iMg^{2+}_s / tMg_s \times 100\%$.

All procedures were in accordance with the Helsinki Declaration of 1975, as revised in 1983.

Methods

Venous blood used for measurements of iMg^{2+}_s and tMg_s was drawn into plain nonsiliconized 4.5-mL tubes (Vacutainer tubes, Becton Dickinson, Leiden, the Netherlands). After clotting (45 minutes) and centrifugation (10 minutes, 1,500g), serum was separated from the cells and stored at -20°C in completely filled rubber-sealed airtight tubes. iMg^{2+}_s was measured in the fresh samples by a Mg

ion-selective electrode (KONE Instruments, Espoo, Finland), and tMg_s was measured batch-wise within 6 months in the stored aliquots by atomic absorption spectroscopy (PE2100, Perkin-Elmer, Überlingen, Germany). Blood for the determination of Mg_{MBC} and Mg_{RBC} was collected in 10-mL heparinized tubes (Vacutainer, Becton Dickinson). Mononuclear blood cells and erythrocytes were isolated by density gradient separation as described earlier.⁶ Isolated cells were lysed by addition of water and the lysate was frozen at -20°C . The Mg concentration in the lysate was determined batch-wise by atomic absorption spectrometry; the concentration in mononuclear blood cells was expressed as micromoles per gram of protein and in erythrocytes as femtomoles per cell. The protein concentration of the mononuclear blood cell lysate was measured colorimetrically, according to the method of Bradford, and the serum albumin concentration with bromocresol green.

Statistical Analysis

Reference ranges for all 5 magnesium parameters were defined as mean \pm 2 SD. Hypomagnesemia was defined as a magnesium concentration below the lower reference limit. Comparison of Mg values measured in ICU patients with the reference values was done by using the Mann-Whitney *U* test. Correlations between the Mg parameters and albumin were calculated by using the Kendall rank correlation. When correlated, the line of equality was calculated by regression analysis. Prediction of iMg^{2+}_s based on the measured tMg_s concentration and albumin was calculated by multiple regression based on two thirds (randomly selected) of the 111 included serum samples. The usefulness of the calculated relation was tested by applying the equation to the remaining one third of the data. The role of Mg in clinical outcome was studied by calculating the positive predictive value of decreased intracellular or extracellular Mg parameters for a high APACHE II score (20 or more) and mortality within 1 month. All statistical analyses were performed with the statistical SPSS 6.1 (SPSS Benelux BV, Gorinchem, The Netherlands). Values of $P < .05$ (2-tailed) were considered significant.

Results

Frequency of Hypomagnesemia

In **Table 1**, an overview of the intracellular and extracellular Mg parameters measured in the ICU population is given, including reference ranges. The mean tMg_s concentration in ICU patients was decreased ($P < .01$), while the mean iMg^{2+}_s concentration did not deviate ($P = .47$). Consequently, the mean $friMg^{2+}_s$ of the ICU population was significantly

Table 1
Intracellular and Extracellular Magnesium Values in Patients in the Intensive Care Unit (ICU)

| | Extracellular Magnesium | | | Intracellular Magnesium | |
|--------------------------|-----------------------------------|---|--------------------------------------|------------------------------------|-----------------------------------|
| | tMg _s , mg/dL (mmol/L) | iMg ²⁺ _s mg/dL (mmol/L) | friMg ²⁺ _s (%) | Mg _{MBC} , μmol/g Protein | Mg _{RBC} , fmol per Cell |
| ICU patients | | | | | |
| n | 115 | 111 | 111 | 95 | 105 |
| Mean ± SD | 1.9 ± 0.4 (0.77 ± 0.17)* | 1.4 ± 0.3 (0.59 ± 0.14) | 76 ± 8* | 59.2 ± 20.2* | 0.18 ± 0.03 |
| Range | 1.1-3.5 (0.44-1.42) | 0.8-2.6 (0.34-1.06) | 54-98 | 28.7-124.6 | 0.13-0.26 |
| Healthy control subjects | | | | | |
| n | 81 | 81 | 81 | 68 | 83 |
| Mean ± SD | 2.1 ± 0.2 (0.88 ± 0.07) | 1.4 ± 0.1 (0.56 ± 0.05) | 64 ± 4 | 47.5 ± 10.3 | 0.18 ± 0.03 |
| Reference range | 1.8-2.5 (0.75-1.01) | 1.1-1.6 (0.47-0.65) | 56-72 | 27.1-67.9 | 0.12-0.24 |

friMg²⁺_s, fraction ionized magnesium (iMg²⁺_s/tMg_s × 100%); iMg²⁺_s, serum ionized magnesium; Mg_{MBC}, magnesium in mononuclear blood cells; Mg_{RBC}, magnesium in erythrocytes; tMg_s, serum total magnesium.

* *P* < .001 for comparison of ICU patients with healthy volunteers, calculated by using the Mann-Whitney *U* test.

Table 2
Frequency of Hypomagnesemia in Patients in the Intensive Care Unit

| Magnesium Parameter | n | Cutoff Value | Mean Magnesium Value | Frequency of Hypomagnesemia, % |
|--|-----|--------------|----------------------|--------------------------------|
| tMg _s , mg/dL (mmol/L) | 115 | 1.8 (0.75) | 1.9 (0.77) | 51.3 |
| Mg ²⁺ _s , mg/dL (mmol/L) | 111 | 1.1 (0.47) | 1.4 (0.59) | 14.4 |
| Mg _{MBC} , μmol/g protein | 95 | 27.1 | 59.2 | 0 |
| Mg _{RBC} , fmol per cell | 105 | 0.12 | 0.18 | 0 |

iMg²⁺_s, serum ionized magnesium; Mg_{MBC}, magnesium in mononuclear blood cells; Mg_{RBC}, magnesium in erythrocytes; tMg_s, serum total magnesium.

higher than the mean reference value (*P* < .01). Of the 2 intracellular Mg parameters, the mean Mg_{MBC} concentration was significantly higher (*P* < .01), while the mean Mg_{RBC} concentration was equal to the mean value of the reference range. The percentage of mononuclear blood cells in the isolated cell suspensions from patients were (mean ± SD) 82.6% ± 9.8% vs 93.3% ± 7.2% isolated from healthy volunteers. The median APACHE II score and 1-month mortality rate of the 115 enrolled patients were 20 and 38%, respectively.

In **Table 2**, the frequencies of hypomagnesemia calculated for the 4 measured Mg parameters are given. Based on tMg_s measurements, 51.3% of the patients admitted to the ICU are hypomagnesemic. However, only in 14.4% of the patients was a decreased iMg²⁺_s measured. Hypomagnesemia based on intracellular Mg parameters was detected in none of the ICU patients studied.

Relations Between the Mg Fractions

Except for the tMg_s and iMg²⁺_s concentrations, no significant correlation was found between the measured Mg parameters, not even between the 2 intracellular Mg parameters. In **Figure 1**, the correlation between the 2 serum markers (tMg_s and iMg²⁺_s) for 111 patients is shown (Kendall rank correlation coefficient [tau], 0.645; *P* < .001). Of the 56 patients with tMg_s less than 1.8 mg/dL (0.75 mmol/L), hypomagnesemia was present in only 16 based on iMg²⁺_s measurements; the other 40 patients had a normal or

elevated level of iMg²⁺_s. In none of the patients with a tMg_s level above the lower reference limit was a decreased iMg²⁺_s found.

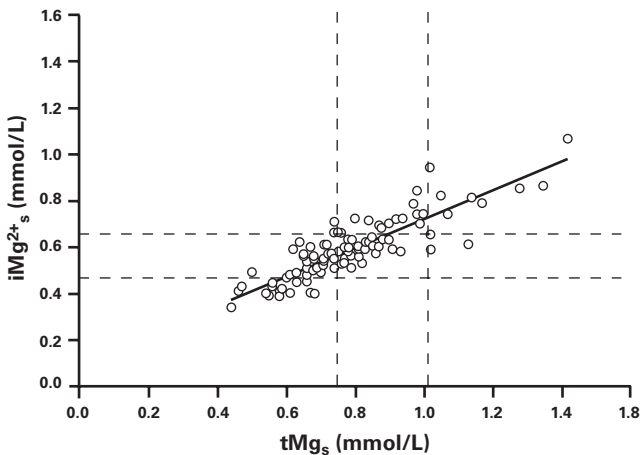


Figure 1 Correlation between the serum total magnesium (tMg_s) and serum ionized magnesium (iMg²⁺_s) in 111 patients in the intensive care unit. The dotted lines represent the lower and upper reference limits. Rank correlation coefficient tau = 0.645; *P* < .001. Equation of the regression line: Y = 0.614X + 0.106; *r*² = 0.753; 95% confidence interval: slope, 0.547 to 0.681; intercept, 0.053 to 0.159. To convert magnesium values to milligrams per deciliter, divide by 0.4114.

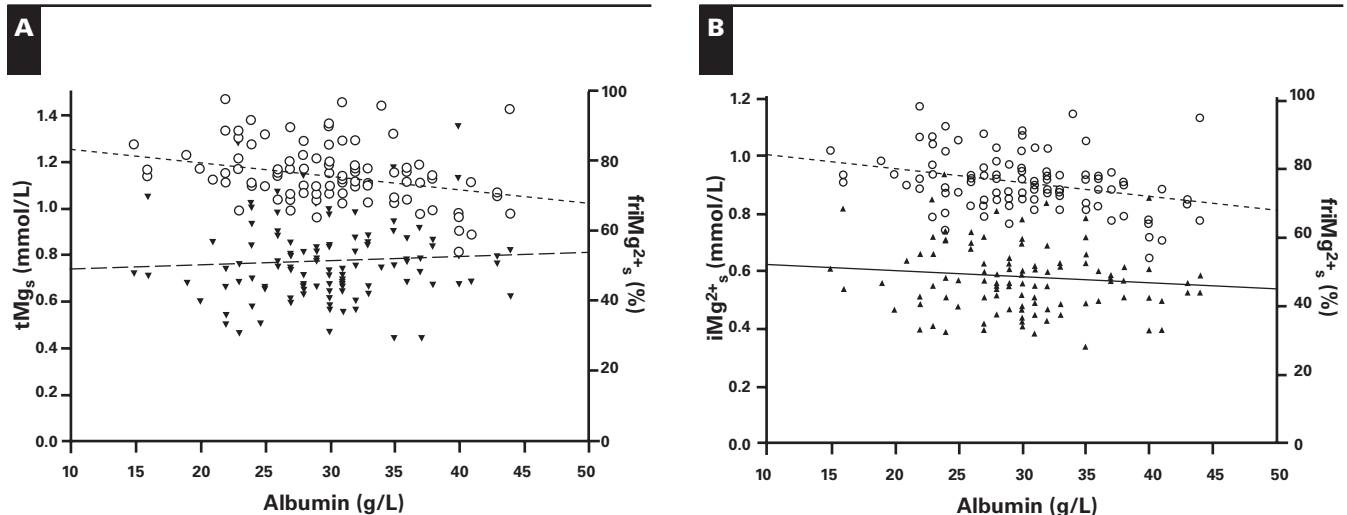


Figure 2 Relation between serum albumin and (A) serum total magnesium (tMg_s; n = 115) and fraction ionized magnesium (friMg_s²⁺; n = 111) and (B) serum ionized magnesium (iMg_s²⁺; n = 111) and friMg_s²⁺ (n = 111) in patients in the intensive care unit. Regression lines are dashed for tMg_s, solid for iMg_s²⁺, and dotted for friMg_s²⁺. Significant correlation was found between albumin and friMg_s²⁺. Kendall rank correlation coefficient tau = −0.195; P = .003. Equation of the regression line: Y = −0.396X + 87.79; r² = 0.086; 95% confidence interval: slope, −0.645 to −0.147; intercept, 80.16 to 95.41. Downward triangles, tMg_s; circles, friMg_s²⁺; upward triangles, iMg_s²⁺. To convert magnesium values to milligrams per deciliter, divide by 0.4114; to convert albumin values to grams per deciliter, divide by 10.

The relation between albumin, tMg_s, iMg_s²⁺, and friMg_s²⁺ is shown in **Figure 2**. No significant correlation was found between serum albumin and tMg_s or serum albumin and iMg_s²⁺. However, between serum albumin and friMg_s²⁺, a significantly negative correlation was detected (tau = −0.195; P = .003).

Multiple regression analysis based on two thirds of the 111 included serum samples resulted in a significant relation between iMg_s²⁺ and a combination of tMg_s and albumin: iMg_s²⁺ = 0.687 × tMg_s − 0.004 × albumin + 0.166. **Figure 3** shows the comparison of the calculated iMg_s²⁺ concentration for the remaining third of the serum samples with the measured iMg_s²⁺ concentration. The solid line represents the line of equality.

Hypomagnesemia and Clinical Outcome

The positive predictive value of hypomagnesemia for a bad clinical outcome (1-month mortality and APACHE II score of 20 or more) was 50% or less for all measured Mg parameters. Only the calculated parameter friMg_s²⁺ had a positive predictive value of more than 50%. The positive predictive value of an increased friMg_s²⁺ (friMg_s²⁺ >72%) for an APACHE II score of 20 or more was 53%, but the combination of a decreased friMg_s²⁺ (friMg_s²⁺ <56%) with an APACHE II score of 20 or less or 1-month mortality was not observed. **Figure 4** shows the comparison of all Mg results for ICU patients who survived the first month

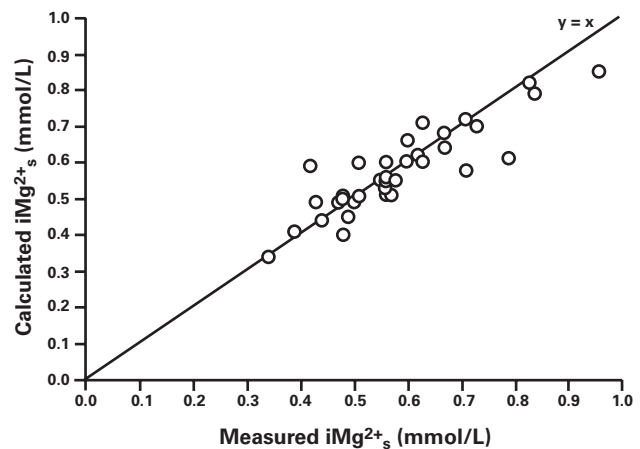


Figure 3 Measured serum ionized magnesium (iMg_s²⁺) vs calculated iMg_s²⁺ based on the equation iMg_s²⁺ (mmol/L) = 0.687X tMg_s (mmol/L) − 0.0038X albumin (g/L) + 0.166; r² = 0.767; 95% confidence intervals, 0.596 to 0.778, −0.00618 to −0.00133, and 0.0730 to 0.260, respectively. tMg_s, serum total magnesium. The solid line represents the line of equality. To convert magnesium values to milligrams per deciliter, divide by 0.4114.

after admission with the Mg results of all patients who died within 1 month. No significant differences between the 2 groups could be detected for any of the tested parameters.

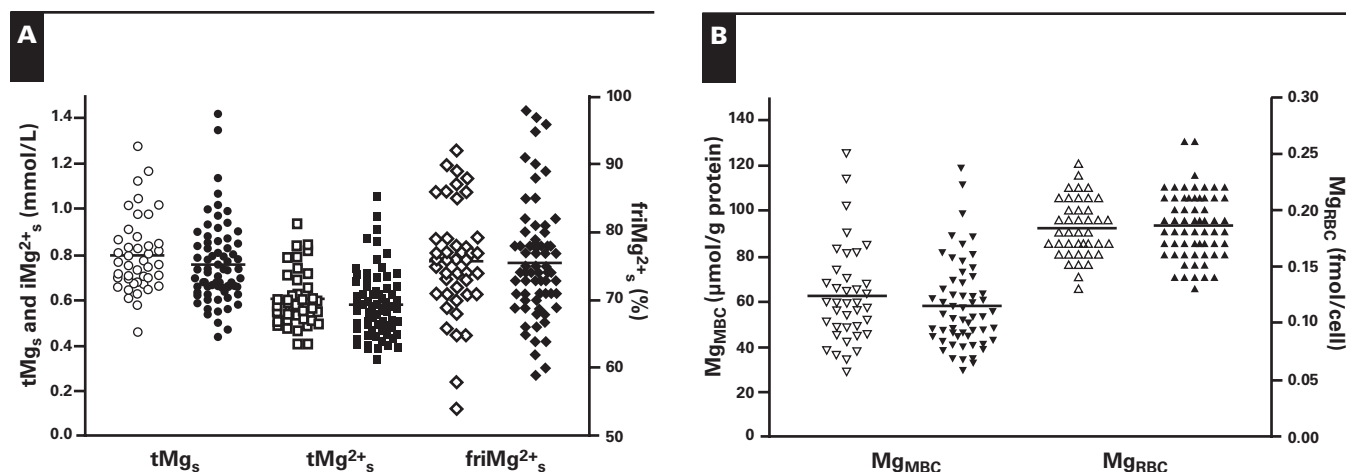


Figure 4 Extracellular (A) and intracellular (B) magnesium concentrations in patients in the intensive care unit in relation to the 1-month mortality. Open symbols, survival of the first month after admission; closed symbols, died within 1 month after admission. friMg^{2+}_s , fraction ionized magnesium in serum; iMg^{2+}_s , serum ionized magnesium; Mg_{MBC} , magnesium in mononuclear blood cells; Mg_{RBC} , magnesium in erythrocytes; tMg_s , serum total magnesium. To convert magnesium values to milligrams per deciliter, divide by 0.4114.

Discussion

Hypomagnesemia is a common finding in ICU patients. However, until now, most studies on this subject dealt with the measurement of the tMg_s concentration.²⁻⁴ In the present study, we compared intracellular and extracellular Mg concentrations in ICU patients. Moreover, we examined whether a significant correlation between Mg parameters and clinical outcome existed.

Frequency of Hypomagnesemia

Measurement of tMg_s resulted in a high prevalence of hypomagnesemia (51.3%). Results reported in preceding studies varied from 9.4% in critically ill patients with chronic obstructive pulmonary disease to 61% in postoperative ICU patients, depending on the population studied and which tMg_s threshold value was chosen.^{7,12} The prevalence of hypomagnesemia based on iMg^{2+}_s (<1.1 mg/dL [<0.46 mmol/L]) was only 14.4%, which concurs with the frequency reported in the solitary other study about iMg^{2+}_s in ICU patients: Hébert et al⁹ found a level of iMg^{2+}_s of less than 1.1 mg/dL (0.44 mmol/L) in 15% of their selected 34 critically ill patients. Owing to lack of a Mg ion-selective analyzer, Zaloga et al¹³ studied ultrafilterable Mg in critically ill patients. They found that 5 (8%) of 64 patients had a low ultrafilterable Mg concentration in serum, which is in agreement with our results obtained with a Mg ion-selective electrode.

None of the ICU patients tested had intracellular Mg concentrations lower than the reference range. Moreover, the mean Mg_{MBC} in the ICU population was significantly higher

than the mean reference value. A possible explanation for the elevated Mg_{MBC} is the decreased percentage (mean \pm SD) of mononuclear blood cells in the cell suspension isolated by gradient separation. The decreased percentage of mononuclear blood cells was accompanied by an increased percentage of granulocytes, which are presumably young cells with a buoyant density similar to that of lymphocytes. These cells have, similar to reticulocytes, a higher Mg content than mature granulocytes.¹⁴

An explanation for the high prevalence of hypomagnesemia, based on tMg_s , is probably a shift from extracellular to intracellular compartments of the body whereby the concentration iMg^{2+}_s , in contrast with tMg_s , usually remains unchanged. More than 99% of the body Mg can be found intracellularly; thus, an increase of the intracellular concentration due to a Mg shift from extracellular fluid remains undetectable. In our opinion, it is unlikely that Mg deficiencies occurred in 51.3% of the patients immediately after their admission to the ICU.

Relation Between the Mg Fractions

The function of Mg is mainly intracellular,⁵ and no correlation was found between the extracellular and the intracellular Mg concentrations. Therefore, for theoretical reasons, intracellular measurements should be considered the method of choice to evaluate the Mg status. However, there is no consensus about which type of cells should be used and which intracellular fraction should be measured: the ionized or the total intracellular Mg concentration.

Fiaccadori et al,⁷ who measured Mg in muscle specimens and serum of 32 pulmonary ICU patients, also were

unable to find a significant correlation between these 2 parameters. The Mg level in blood cells of ICU patients was measured in 1 preceding study.¹⁵ Low levels of Mg_{MBC} and Mg_{RBC} were found in 3 of 12 and none of 13 patients, respectively, while the prevalence of hypomagnesemia measured as tMg_s was surprisingly 0%. According to the literature, a good alternative and probably the “gold standard” for establishing a Mg deficiency might be the Mg loading test.^{16,17} However, normal renal function and adequate urine output are important restrictions to this test. Two reports about applying this test in an ICU population are available.^{9,15} In the study by Arnold et al,¹⁵ mainly based on patients undergoing coronary artery bypass surgery, 10 (62%) of 16 patients retained more than 30% of the Mg infused, indicating a Mg deficiency. In this patient population, tMg_s , Mg_{MBC} , and Mg_{RBC} also were measured, and no correlation could be found with outcome of the loading test. In the study by Hébert et al,⁹ 12 (63%) of 19 ICU patients were found to be hypomagnesemic. However, despite referring to the loading test described by Ryzen et al,¹⁶ a different test was performed without measuring the basal Mg secretion of each patient before the Mg load. Moreover, no reference values for their specific performance of the test were established.

Mg in serum is divided into 3 fractions: Mg bound to protein (27%), in particular to albumin and to a lesser extent to globulins^{18,19}; ionized Mg (65%); and Mg complexed with anions (8%) such as phosphate, bicarbonate, and citrate.²⁰ As is the case with calcium, tMg_s is expected to correlate with iMg^{2+}_s , partly influenced by binding components. In the ICU population, we found a significant correlation between tMg_s and iMg^{2+}_s , but in our opinion, this correlation could not be put into practice. This means that based on measured tMg_s concentrations, no reliable iMg^{2+}_s can be predicted, which is shown in Figure 1. When the 95% confidence interval of the slope and intercept taken into account, a tMg_s concentration of 2.4 mg/dL (1.0 mmol/L) corresponds with an iMg^{2+}_s concentration that varies between 1.4 and 2.0 mg/dL (0.60 and 0.84 mmol/L). The first value is judged as normomagnesemic and the second as hypermagnesemic. However, in our study, one of the conclusions may be that a normal or high tMg_s level always is accompanied by a normal or high level of iMg^{2+}_s . In contrast, the positive predictive value of a low tMg_s for a low iMg^{2+}_s is only 29%.

Because it was not possible to predict reliable iMg^{2+}_s concentrations by the measurement of only tMg_s , we studied the relation between both serum magnesium parameters and serum albumin. However, no significant correlation was found. Broner et al,²¹ who studied tMg_s and calcium in critically ill pediatric patients, found no correlation between tMg_s and albumin, nor did Chernow et al.¹² However, Külpman and Gerlach¹⁹ found that friMg^{2+}_s was dependent on the albumin concentration; an increasing protein concentration

was accompanied by a decreased fraction. In the same study, they found that in paraproteinemic serum samples, friMg^{2+}_s increased (tMg_s decreased) when the albumin concentration decreased. In our population, we found a significant negative correlation between friMg^{2+}_s and albumin and also that serum albumin contributed significantly ($P = .0028$) to the estimation of iMg^{2+}_s based on a combination of tMg_s and serum albumin. However, when applying the calculated formula, a rather large scatter around the line of equality was found (Figure 3), which limits its practical value. A calculated iMg^{2+}_s concentration of 1.4 mg/dL (0.60 mmol/L) corresponded with a range of measured concentrations from 1.0 to 1.9 mg/dL (0.42–0.78 mmol/L), indicating that a reliable iMg^{2+}_s concentration in ICU patients can be obtained only by direct measurement of the cation.

Hypomagnesemia and Clinical Outcome

After potassium, Mg is the second most prevalent intracellular cation, and it has an important role as a cofactor in various enzymatic reactions, including those involving adenosine triphosphatase. Mg is therefore an important element for providing energy and regulating various processes in the cell and cell membrane. It also has a role in protein and DNA synthesis, DNA and RNA transcription, translation of messenger RNA, and the regulation of mitochondrial function. So recognition and treatment of hypomagnesemia in patients entering the ICU may be important and has been discussed several times.^{2,3,22,23} Moreover, it is comprehensible that hypomagnesemia is associated with severity of illness or increased mortality. However, previous studies concerning this subject, all based on serum tMg_s measurements, did not report reproducible results.^{12,21,24} Chernow et al¹² reported that postoperative ICU patients with severe hypomagnesemia (<1.2 mg/dL [<0.5 mmol/L]) had higher mortality than the entire population ($P < .02$), despite the fact that the severity of illness score in both populations was similar. Broner et al,²¹ who studied critically ill pediatric patients, found a mortality rate of 8% in both the hypomagnesemic and normomagnesemic groups, but the mortality rate in the hypermagnesemic patients was significantly higher, a phenomenon that also was found by Chernow et al.¹² As expected, more of these patients with hypermagnesemia had renal failure than those with normo- or hypomagnesemia. In 1993, Rubeiz et al²⁴ reported their measurement of tMg_s in 184 medical ICU patients. Although APACHE II scores of the hypomagnesemic patients ($\text{tMg}_s < 1.5$ mg/dL [0.62 mmol/L]) were similar to those of normomagnesemic patients (the few hypermagnesemic patients were excluded), in hypomagnesemic patients, the mortality rate was significantly higher than in normomagnesemic patients. Based on our tMg_s data, we were unable to confirm the increased mortality rate in hypomagnesemic ICU

patients. Hypomagnesemia based on iMg^{2+}_s or intracellular measurements did not correlate with an increased mortality rate or increased APACHE II score either. Only an increased $friMg^{2+}_s$ had a positive predictive value for an increased APACHE II score, but it was too low for reliable application. However, in the present study, we also found that the $friMg^{2+}_s$ was negatively correlated with the serum albumin level, which is known to be negatively correlated with increased mortality.²⁵ Some possible explanations for the lack of correlation between the Mg parameters and clinical outcome can be hypothesized: (1) the heterogeneous patient population in every ICU study or (2) the fact that all serum and intracellular Mg measurements are not a reliable reflection of the real Mg status of the body. A study among ICU patients comprising the measurement of extracellular and intracellular ionized and total Mg, the Mg loading test, and recording clinical outcome can possibly clarify this dilemma. Because the Mg loading test is rather laborious and impractical, the short-time version, recently developed for outpatients,²⁶ perhaps offers new opportunities.

Our results confirm that hypomagnesemia measured as tMg_s is a common finding in critically ill patients, but when measured as iMg^{2+}_s , about 70% of these patients are no longer shown to be hypomagnesemic. This finding implies that in a situation of suspected hypomagnesemia combined with an abnormal protein concentration, the measurement of iMg^{2+}_s is preferred above the routinely measured tMg_s . The Mg result obtained with an ion-selective electrode is independent of any variability due to protein binding: it measures the active fraction only. Moreover, reliable iMg^{2+}_s concentrations can be obtained only by direct measurements and not deduced arithmetically from tMg_s and serum albumin concentrations. For the measured Mg_{MBC} and Mg_{RBC} , none of the ICU patients had a Mg concentration below the lower reference limit. No association between low extracellular or intracellular Mg and clinical outcome was found.

Therefore, in our opinion it does not make sense to request one of these parameters routinely. Mg measurements, preferably iMg^{2+}_s , should be performed only when a patient is suspected of having hypomagnesemia. The only test that possibly can be used to confirm supposition of hypomagnesemia or Mg deficiency is the Mg loading test. Unfortunately, until now there is no experience with this test in a large heterogeneous group of medical ICU patients.

From the Departments of ¹Clinical Chemistry and ⁴Intensive Care, Academic Medical Center, University of Amsterdam; ²Internal Medicine and ³Clinical Chemistry, Slotervaart Hospital; and ⁵Clinical Chemistry, Boven IJ Hospital, Amsterdam, The Netherlands.

Address reprint requests to Dr Huijgen: Boven IJ Hospital, Dept of Clinical Chemistry, PO Box 37610, Amsterdam, 1030 BD, The Netherlands.

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