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Research Article

Investigating the Agreement of Hypomagnesemia Diagnosis in Three Perimeter of Serum, Urine, and Red Blood Cell in Intensive Care Unit: Pilot Study

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ABSTRACT

Background: Magnesium is a vital element in the body involved in biochemical and physiological processes. Magnesium deficiency can lead to serious consequences including cardiac, neurological, muscular disorders, and other clinical manifestations. In our country, commonly, magnesium measurement is done by measuring serum magnesium levels. This paper discusses the prevalence and consequences of magnesium deficiency in patients hospitalized in the ICU and emphasizes the importance of diagnosis and treating hypomagnesemia.

Methods: Diagnosis of hypomagnesemia is done by measuring serum magnesium, urine magnesium, and magnesium in RBCs. We conducted a prospective study on 30 critically ill patients (14 male, and 16 female) who were admitted to the ICU to examine the prevalence of magnesium deficiency. In eligible patients, after measuring serum and RBC magnesium levels, 7.5 grams of magnesium sulfate in 1000 ml isotonic saline was infused over 8 hours at a rate of 125 ml/hour and urine was collected for 24 hours from the start of the infusion.

Results: The mean age was 71. There was a significant difference between the levels of serum Mg and RBC Mg (U statistic = 266 and P<0.05). The results showed a significant difference between the levels of serum Mg and urinary Mg (U statistic was almost 0 and P<0.05). The results indicated a significant difference between the levels of urinary Mg and RBC Mg (U statistic was almost 0 and P<0.05).

Conclusion: There is no correlation between serum magnesium and the body's magnesium requirement in patients, and serum magnesium does not reflect the actual status of patients in the ICU. Therefore, measuring the level of magnesium in red blood cells is preferable to urinary magnesium and serum magnesium to investigate hypomagnesemia in the ICU. Additionally, there is no correlation between age, gender, APACHE II score, and the percentage of infused magnesium absorption in patients.

The authors declare no conflicts of interest.

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Introduction

Hypomagnesemia is prevalent among patients in the ICU, especially those who are critically ill. With studied reporting occurrence of up to 65% [1-3]. Magnesium is commonly administered intravenously in intensive care units [4-6].

Hypomagnesemia can result from gastrointestinal or renal dysfunction, cellular magnesium reabsorption, malnutrition, endocrine gland disorders, or metabolic disease [7-8].

Magnesium, the fourth most abundant cation in the human body [9-10] and the second most abundant intracellular cation [11-12] plays vital roles in various biochemical and physiological processes, acting as a cofactor for around 300 cellular enzymes, particularly those involving ATP-dependant reactions [13-14]. Despite its importance, magnesium deficiency is often overlooked, earning it the moniker of ''forgotten electrolyte'' [15-16].

Most magnesium is intracellular, with only about 1% in the bloodstream, predominantly in serum [16-17]. Symptoms of hypomagnesemia may not manifest until the magnesium level drops below 0.5 mg/dL [18]. Hypomagnesemia is associated with increased morbidity and mortality in ICU patients, emphasizing the significance of its detection and management [19-24].

Various methods, including monitoring serum magnesium levels, measuring magnesium in red blood cells, and assessing urinary magnesium, are magnesium measurement is the preferred method in most hospitals [25-26]. it may not always detect hypomagnesemia accurately, leading to the adoption of alternative diagnostic approaches.

Methods

The clinical trial was designed as a cross-sectional study, and the population under investigation included patients admitted to the ICU of the BooAli Hospital of Tehran, who had spent at least 72 hours in the ICU and met the inclusion criteria while lacking the exclusion criteria. A total of 30 patients were enrolled. Inclusion criteria comprised age over 18 years, ICU stay exceeding 72 hours, non-pregnancy and non-lactation status, while exclusion criteria included renal dysfunction (serum creatinine>1.5 mg/ dl), heart rate <60 beats per minute, severe metabolic disorder, diuretic therapy, coagulopathy, myasthenia gravis, discharge or death during the study, and occurrence of hypermagnesemia symptoms during the study.

For eligible patients, we collect 2 ml of blood samples in a vacuum tube for serum magnesium level and 0.5 ml of blood samples in a vacuum tube with EDTA for RBC magnesium level [27-28]. Then we had to transfer these samples in 2 hours to the laboratory.

The serum magnesium level was measured using the endpoint colorimetric method and the Roche/Hitachi Cobas c Analyzer, which is based on the reaction of magnesium with xylidyl blue in an alkaline solution containing EDTA to bind the Ca present in the samples [29-30].

For measuring RBC magnesium level, we placed the serum samples in a centrifuge, then washed them with normal saline three times and lysed them with hypotonic NaCl and then we used the ICP-OS method for measuring RBC magnesium [19, 31].

After measuring serum and RBC magnesium levels, they received 7.5 grams of magnesium sulfate in 1000 ml of isotonic saline at a rate of 125 ml per hour over 8 hours. Urine samples were collected for 24 hours starting from the beginning of the infusion in 24-hour-plastic bottles with 15 ml of HCl 10% and transferred to the laboratory for measuring magnesium level with atomic absorption spectroscopy [32-34]. The uptake of magnesium is calculated from the following formula [32, 35]:

$$\frac{(7.5\ g\ Mg^{2+}\ infused - amount\ of\ Mg^{2+}\ excreted\ in\ urine) \times 100}{7.5\ g\ Mg^{2+}\ infused}$$

Now people are classified into three categories:

1) The amount of magnesium absorbed is more than 75%

2) The amount of magnesium absorbed is between 75 and 50%

3) The amount of added magnesium is less than 50%

Mg deficiency is considered for category 1 and 2 (36, 37) (Figure 1).

According to the serum magnesium levels of the patients before MLT (Figure 1, 2) patients have hypermagnesemia. The magnesium level information of these patients is given in (Table 1).

Baseline assessment before the study initiation evaluated factors such as gender, age, medication history, weight, height, reason for admission, serum creatinine, pulse rate, surgical and medical history, temperature, mean arterial pressure, deep tendon reflux (DTR), blood pH, respiratory rate, blood sodium and potassium, hematocrit, white blood cell count, Glasgow coma scale (GCS), fraction of inspired oxygen (FiO2) and partial pressure of oxygen (PaO2).

Then a comparison was made among the three methods of measuring serum, RBC, and urine magnesium.

Table 1- Magnesium levels in three patients.

Number of patients	Serum magnesium level (mg/dL)	RBC magnesium level (mg/dL)	Magnesium uptake (%)
1	2.7	1.3	87.72
2	3	2.3	79.88
3	3	4.2	70.66

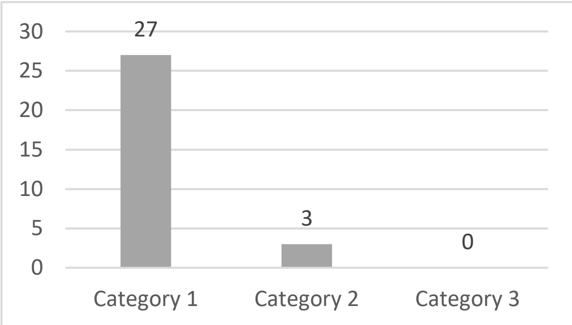

Figure 1- Patient's Magnesium Status.

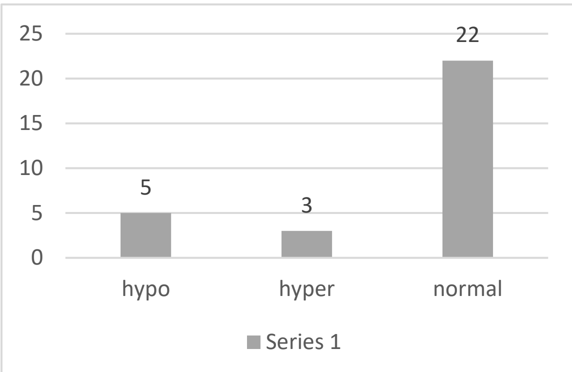

Figure 2-Serum Magnesium Status Before MLT.

Results

Mean patients age was 71 years (14 male, 16 female).

To investigate the relationship between Mg uptake and age, Pearson correlation coefficient was used. the results indicated a negligible correlation between them (correlation coefficient= 0.029), and furthermore, This correlation was not significant (P>0.05) (Figure 9).

To compare the level of Mg uptake in two groups of women and men, firstly, the normality of Mg uptake values in these two groups was examined using the Kolmogorov-Smirnov test. The Mg uptake values in men are normal (P>0.05), while in women, they are not normal (P<0.05). Thus, the non-parametric Mann-Whitney test was employed to compare the mean values of Mg infusion in these two groups. The median level of magnesium infusion in women was 94.06, and in men, it was 90.59. The results demonstrated no significant difference in the level of magnesium infusion between these two groups (U statistic = 100 and P>0.05).

To compare the mean serum Mg, urinary Mg, and RBC Mg, initially, the normality of the data values in all three groups was assessed using the Kolmogorov-Smirnov test. The results indicated that the serum Mg data are normal (P>0.05), while urinary magnesium and RBC magnesium data are not normal (P<0.05). Therefore, the non-parametric Mann-Whitney test was utilized to compare the mean values in these three groups.

To investigate the relationship between serum magnesium and magnesium uptake, Pearson correlation coefficient was employed. The results revealed a strong inverse correlation between them (correlation coefficient= -0.674), and this correlation was significant (P<0.05) (Figure 3).

Pearson correlation coefficient was used to investigate the relationship between serum magnesium and RBC magnesium. The results showed that the relationship was low (relationship strength 0.29), but this relationship was not significant (P<0.05) (Figure 4).

Pearson's correlation coefficient was used to examine the relationship between RBC magnesium and Mg uptake. The results showed that the magnitude of their relationship was inverse and strong (relationship strength -0.648) and this relationship was significant (P<0.05) (Figure 5).

The median of serum Mg was 2.0850, and for RBC Mg, it was 1.555. The results demonstrated a significant difference between the levels of serum Mg and RBC Mg (U statistic = 266 and P<0.05) (Figure 6).

The median of serum Mg was 2.0850, and for urinary Mg, it was 494.8. the results showed a significant difference between the levels of serum Mg and urinary Mg (U statistic was almost 0 and P<0.05) (Figure 7).

The median of urinary Mg was 494.8, and for RBC Mg, it was 1.555. the results indicated a significant difference between the levels of urinary Mg and RBC Mg (U statistic was almost 0 and P<0.05) (Figure 8).

To examine the relationship between magnesium infusion and APACHE II score, Pearson correlation coefficient was utilized. The results showed a negligible correlation between them (correlation coefficient = 0.144), and, this correlation was not significant (P>0.05).

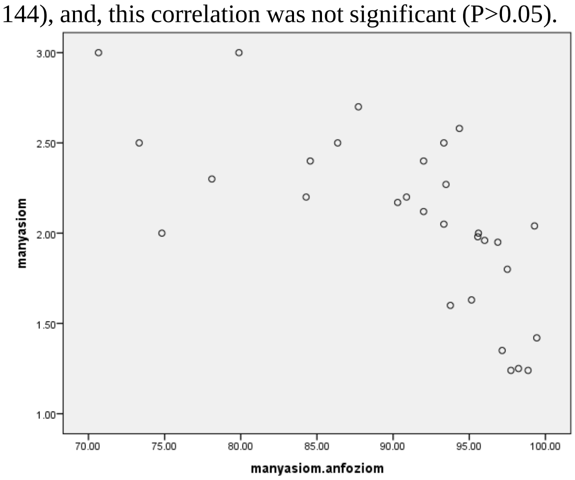

Figure 3- Correlation between Serum magnesium and magnesium uptake.

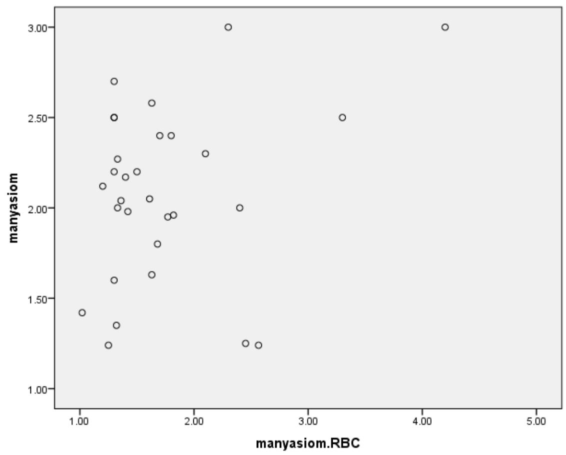

Figure 4- Correlation between serum magnesium and RBC magnesium.

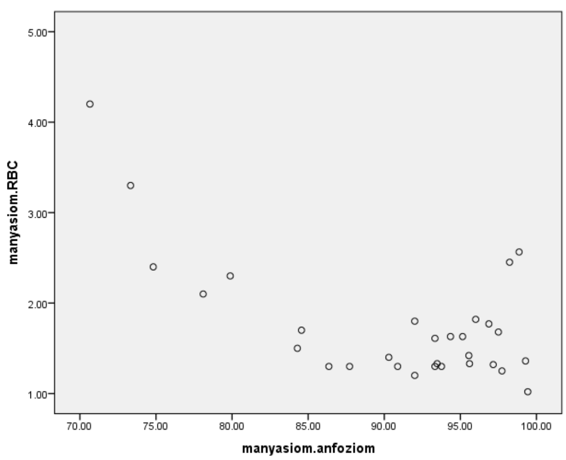

Figure 5- Correlation between RBC magnesium and magnesium uptake.

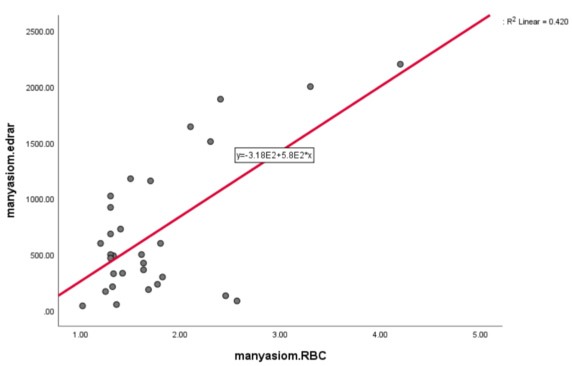

Figure 6- Correlation between urine magnesium and RBC magnesium.

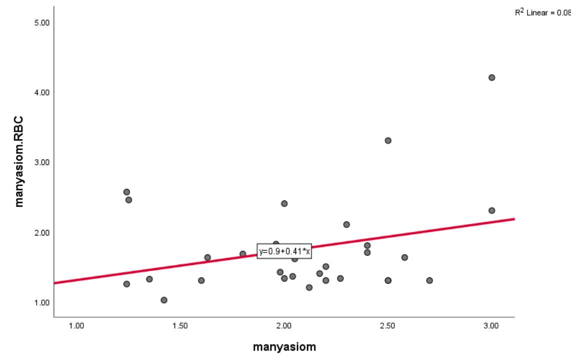

Figure 7- Correlation between RBC magnesium and RBC magnesium.

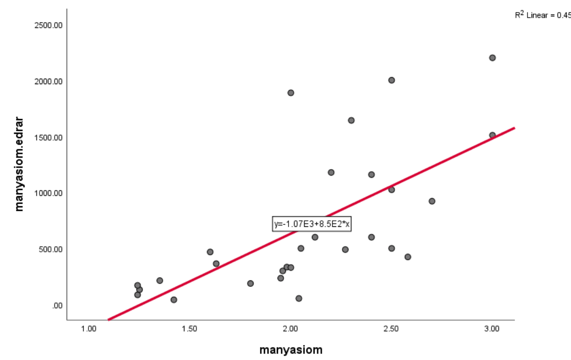

Figure 8- Correlation between urine magnesium and magnesium uptake.

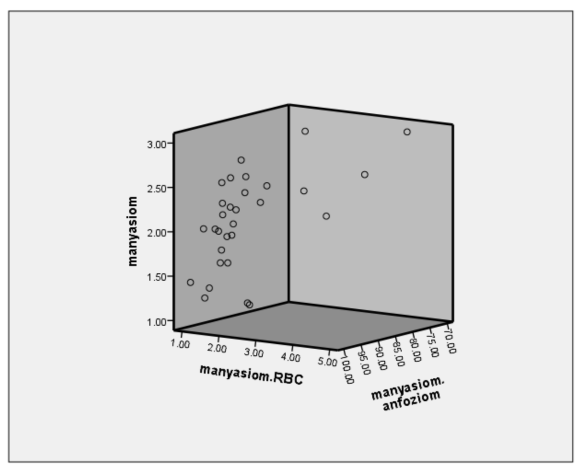

Figure 9- 3D diagram of each magnesium sample.

Discussion

Hypomagnesemia is a very common problem in patients of ICU [38-39]. Hypomagnesemia in these patients is probably due to using diuretic drugs and nephrotoxic drugs such as amphotericin B and cisplatin, or disorders in renal function or insufficient gastrointestinal absorption [40-42]. All the patients admitted in this study showed hypomagnesemia based on

RBC magnesium and MLT results. This finding agrees with previous studies showing most patients hospitalized in ICU, especially critically ill patients, had hypomagnesemia [1-3].

As the level of magnesium in the body increases, the body's reaction will be accompanied by a decrease in blood pressure, bradypnea, bradycardia, and a decrease in MAP [43]. No signs of bradycardia were observed in patients during the study. However, we observed symptoms of tachycardia in several patients (10%), which, according to previous studies, can be attributed to pain in intensive care unit patients [44]. Acute pain, from a physiological perspective, triggers a stress response that includes an increased heart rate [45]. Oral and parenteral administration of magnesium may reduce pain and postoperative anesthesia and analgesia requirements. These beneficial effects of magnesium therapy have also been reported in patients with neuropathic pain [46].

Magnesium decreases significantly the MAP therefore Delhumeau et al. declared that it helps treat hypertensive peaks that occur during cardiopulmonary bypass [47]. According to our findings, about 3% of the patients exhibited decreasing MAP. There are no symptoms of hypopnea caused by hypermagnesemia observed in any of the patients.

The detection and management of hypomagnesemia are of paramount importance due to the pivotal role magnesium plays in numerous physiological functions. Insufficient magnesium levels can manifest in a range of symptoms, including muscle weakness, tremors, cardiac arrhythmias, and neurological impairments. Furthermore, hypomagnesemia has been associated with increased morbidity and mortality in various clinical conditions, such as cardiovascular disease, diabetes, and renal disorders. Prompt diagnosis through the best method of analysis and subsequent treatment with magnesium supplementation can help alleviate symptoms, prevent complications, and improve patient outcomes [48].

Despite the normal serum magnesium level, patients may have low RBC or intracellular magnesium levels, which can cause disorders in cellular function and, to a greater extent, may cause disorders in system function.

According to Table1, it seems three patients who had hypermagnesemia based on serum magnesium, showed different results in RBC magnesium. Two of these patients had hypomagnesemia and one of them was normomagnesemic based on levels of RBC magnesium, and it can show that patients with high levels of serum magnesium may have severe hypomagnesemia, which MLT can confirm these results too. In line with our findings, Yousif et al. demonstrated that RBC magnesium level correlated with vaso-occlusive crisis, but serum magnesium levels are not associated [49]. In contrast, Vanroelen et al. assert that there is no significant difference in serum and RBC magnesium levels in type I & II diabetics [50].

It seems that there is a significant difference between the level of serum magnesium and MLT, and these two do not reflect each other. As reported by Huijgen et al., the MLT possibly is the only test that can approve magnesium deficiency in ICU patients [51]. MLT is a more reliable method of potential magnesium deficiency than the serum magnesium level, which is abatement only in severe hypomagnesemia [52]. Additionally, Spisák stated that in clinical experience, the MLT is the most convenient indicator for body magnesium reserves [53].

This study also indicated that there is no correlation between age and gender and magnesium uptake and there is also no correlation between the APACHE II score and the level of magnesium uptake.

Conclusion

In conclusion, our data demonstrated that there is no correlation between serum magnesium and the body's magnesium requirement in patients, and serum magnesium does not reflect the actual status of patients in the ICU. Moreover, measuring the RBC magnesium level is preferable to urinary magnesium and serum magnesium to investigate hypomagnesemia in the ICU.

Further studies with larger numbers of patients, and with other reasons for hospitalization, need to approve these results.

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