

Serum Mg Levels and Its Relationship with Unfavourable Effects of Critically Patients

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Abstract

Deficiency of Mg leads to activation of neuroendocrine pathways which induces systemic stress response, which in turn takes part in the pathogenesis of numerous disease and also implicated in an increased mortality rate among ICU patients. The above said effects of Mg on immune system play a crucial role in the pathogenesis of sepsis. In hypomagnesemic state, cardiac tolerance to reduced oxygen level is reduced significantly. Electromechanical activities of cardiac smooth muscles and vascular endothelial cells can get affected largely by small changes in free Mg levels.

Keywords: Serum Mg Levels, ICU Patients, Hypomagnesemia, Ventilator Support.

Introduction

In the human body Mg is known to be the fourth abundant cation and next to potassium which is known to be second most abundant cation intracellularly. And it helps in completing reaction as cofactor nearly for 300 enzymes more commonly involving transferring of phosphate group; it is the major intracellular divalent

cation. And it also helps in the formation of ATP. And maintain neuromuscular excitability and maintenance of cardiac function is also its major action. With ATP, Intracellular Mg will form key complex and acts as an important cofactor for transporters, enzymes, and nucleic acids needed for normal cellular function, energy metabolism and replication. The normal concentration of serum Mg is between the ranges of 1.8 to 2.5 mg/dl, in that 30% will be bound to the protein and 15% is loosely bound to the many other anions and phosphate. According to studies during the ICU stay 20 to 65% of critically ill patients develop hypomagnesemia. It is very important to consider Hypomagnesemia, as it is very common in patients with critical illness.

Mg is the major intracellular divalent cation. One-half of the 25 g (1000 mmol) of total body Mg is located in bone, only one-half of which is insoluble in the mineral phase. Almost all extras-skeletal Mg is present within cells, where the total concentration is 5 mm, 95% of which is bound to proteins and other macromolecules.

Because only 1% of body Mg resides in the ECF, measurements of serum Mg levels may not accurately reflect the level of total body Mg stores.

Dietary Mg content normally ranges from 6 to 15 mmol/d (140–360 mg/d), of which 30–40% is absorbed, mainly in the jejunum and ileum. Intestinal Mg absorptive efficiency is stimulated by 1,25(OH)₂D and can reach 70% during Mg deprivation.

The body contains the total Mg of around 21-28grams. 53% of total Mg is found in bone, 19% in non-muscular tissue and 1% in extracellular fluid. The majority of serum Mg is bound to chelators such as ATP, ADP, proteins and citrate. Approximately 33% of serum Mg is bound to proteins and 5-10% is not bound. In the regulation of intracellular Mg, this unbound form plays an essential role. In the regulation of serum Mg kidneys play an important role. 60% of filtered Mg is getting absorbed from the loop of Henle. So it is the major site for Mg homeostasis. Only 120 mg of Mg is excreted through urine as against 2400 mg of filtered Mg.

Mg is primarily found within the cell where it acts as a counter ion for the energy-rich ATP and nuclear acids Mg critically stabilizes enzymes, including many ATP-generating reactions. ATP is required universally for glucose utilization, synthesis of fat, proteins, nucleic acids and coenzymes, muscle contraction, methyl group transfer and many other processes, and interference with Mg metabolism also influences these functions.

Thus, one should keep in mind that ATP metabolism, muscle contraction and relaxation, normal neurological function and release of neurotransmitters are all Mg dependent. It is also important to note that Mg contributes to the regulation of vascular tone, heart rhythm, platelet-activated thrombosis and bone formation.

Mg has numerous functions in the body, for example, serving as a cofactor in enzymatic reactions. In muscle contraction, for example, Mg stimulates calcium re-uptake by the calcium-activated ATPase of the sarcoplasmic reticulum.

Mg further modulates insulin signal transduction and cell proliferation and is important for cell adhesion and transmembrane transport including transport of potassium and calcium ions. It also maintains the conformation of nucleic acids and is essential for the structural function of proteins and mitochondria.

It has long been suspected that Mg may have a role in insulin secretion owing to the altered insulin secretion and sensitivity observed in Mg-deficient animals.

Recent epidemiological studies have suggested that a relatively young gestational age is associated with Mg deficiency during pregnancy, which not only induces maternal and foetal nutritional problems but also leads to other consequences that might affect the offspring throughout life.

The incidence of hypomagnesemia varies from 20% to 65% in intensive care unit (ICU) patients. Hypomagnesemia may present as tetany, vertigo, reversible psychiatric aberrations, seizures, cardiac arrhythmias, hypertension, muscular weakness, acute cerebral ischemia and asthma. The pathology of Mg deficiencies is multifactorial including gastrointestinal disorders, renal loss, renal diseases, drug-induced loss, metabolic acidosis, and other causes. In addition, critically ill patients have several potential risks of Mg dysregulation. It was significantly associated with increased and prolonged need for mechanical ventilation, difficulty to wean, prolonged ICU stay and increased mortality in critically ill patients. Hypermagnesemia is less common and mostly due to renal failure or iatrogenic. Prevalence of hypermagnesemia was reported

to be 7.3%. It can lead to severe muscle weakness, respiratory depression, hypotension, cardiac arrhythmia and ultimately progress to cardiac arrest. Many studies found that only hypomagnesemia, but not hypermagnesemia is linked with increased mortality. However, reports of mortality due to Mg dysregulation in the critical care setting are controversial. Also, it is unknown whether comorbidities of the study population has any effect on this association. Whether hypomagnesemia directly contributes to cellular alterations leading to increased mortality, morbidity and poor patient outcome in critically ill patients or it is just a marker of critical illness, is not clear. Hence, an attempt was made to study serum Mg levels in critically ill patients on admission in ICU and its correlation with patient's need and duration for ventilator support, duration of ICU stay, incidence of cardiac arrhythmias and mortality.

Mg consumption

Humans need to consume Mg regularly to prevent Mg deficiency, but as the recommended daily allowance for Mg varies, it is difficult to define accurately what the exact optimal intake should be. Values of ≥ 300 mg are usually reported with adjusted dosages for age, sex and nutritional status. The Institute of Medicine recommends 310–360 mg and 400–420 mg for adult women and men, respectively. Other recommendations in the literature suggest a lower daily minimum intake of 350 mg for men and 280–300 mg Mg for women (355 mg during pregnancy and lactation).

While drinking water accounts for ~10% of daily Mg intake, chlorophyll (and thus green vegetables) is the major source of Mg. Nuts, seeds and unprocessed cereals are also rich in Mg.

Legumes, fruit, meat and fish have an intermediate Mg concentration. Low Mg concentrations are found in dairy

products. It is noteworthy that processed foods have a much lower Mg content than unrefined grain products.

Transcription of nucleic acids, translation of mRNA, synthesis of proteins and also regulation of mitochondrial function need adequate Mg levels. Numerous immunological functions like activation and adherence of macrophages, granulocytes oxidative burst needed for bacterial killing and proliferation of lymphocytes depends on adequate Mg levels.

When comparing to respective calcium salts, Mg salts dissolve in water easily. So the availability of Mg to organisms is easy. Mg is acting as a central ion in chlorophyll of plants. In vertebrates it is the 4th most abundant cation and after potassium, it is the second most abundant intracellular cation. Both of them are considered as a vital element for numerous physiological functions. The salts of Mg are used in the form of Mg hydroxide, Mg citrate, Mg sulphate or Mg chloride, in laxatives or antacids.

Mg consumption

To prevent Mg deficiency we consume it regularly. Since the recommended daily allowance of Mg varies, it is difficult to assess the exact intake of Mg. Dose of more than 300 mg which should be adjusted for age, sex and nutritional status. Drinking water responsible for 10% of total daily Mg intake. Green vegetables which is the richest source for chlorophyll contribute to the major source of Mg. Seeds, nuts and unprocessed cereals are also contributing to the rich source of Mg. Fish, meat, fruits and legumes have an intermediate Mg concentration. Dairy products have low Mg concentration. Processed foods have much lower serum concentration when compared to unrefined grain products.

The normal fractional urinary excretion of filtered Mg is about 5%. Mg reabsorption in the kidneys involves the

proximal tubule, the thick ascending loop of Henle (TAL), and the distal tubule.

TAL is the major site of Mg reabsorption and reabsorbs about 60–70% of filtered Mg extracellular calcium sensing receptors modulate the Mg absorption through changes in the transepithelial voltage and alterations of the permeability of the paracellular tight junctions.

The mechanisms of basolateral transport into the interstitium are not fully understood. Moreover, the proximal tubule reabsorbs 15–20% of filtered Mg, and the distal tubule only 5–10%.

whereas there is no significant reabsorption of Mg in the collecting ducts.

Mg homeostasis- The figure gives an overview of the Mg homeostasis and the distribution of Mg throughout the human body including gastrointestinal absorption and renal excretion

Renal Mg handling- The figure gives an overview of the renal handling of Mg in the proximal convoluted tubule, loop of Henle, and distal convoluted tubule

Pathophysiology: To diagnose hypomagnesemia, measurement of serum Mg levels and 24 hours of urinary Mg excretion are the most important laboratory tests.

Further step would be to perform Mg retention test. The prevalence of hypomagnesemia is ranging from 9-65% among hospitalized patients, that too in intensive care units. Numerous factors may play a role for example insufficient intake of nutritional Mg, drugs like digoxin, aminoglycosides, furosemide, cisplatin amphotericin B and cyclosporine. Hypomagnesemia also associated with chronic conditions like malignancy, CVA, cirrhosis and a number of other conditions. In conditions like acute pancreatitis, there is compartmental redistribution of Mg.

Chronic hypomagnesemia

Diagnosis of chronic hypomagnesaemia is difficult as there may be only a slightly negative Mg balance over time. There is equilibrium among certain tissue pools, and serum concentration is balanced by Mg from bone. Thus, there are individuals with a serum Mg concentration within the reference interval who have a total body deficit for Mg. Mg levels in serum and 24-h urine samples may be normal, and so parenteral administration of Mg with assessment of retention should be considered if in doubt. Chronic latent Mg deficiency has been linked to atherosclerosis, myocardial infarction, hypertension malignant tumours, kidney stones, alteration in blood lipids, premenstrual syndrome and psychiatric disorders.

Hypomagnesaemia has been linked to poor condition (malignant tumours, cirrhosis or cerebrovascular disease)

the following conditions are associated with chronic latent Mg deficiency.

1. Atherosclerosis
2. Essential hypertension
3. Acute coronary syndrome
4. Renal calculi
5. Malignant tumours
6. Dyslipidemia
7. Psychiatric disorders and
8. Premenstrual syndromes.

Deficiency of Mg leads to activation of neuroendocrine pathways which induces systemic stress response, which in turn takes part in the pathogenesis of numerous disease and also implicated in an increased mortality rate among ICU patients. The above said effects of Mg on immune system play a crucial role in the pathogenesis of sepsis. In hypomagnesemic state, cardiac tolerance to reduced oxygen level is reduced significantly.

Electromechanical activities of cardiac smooth muscles and vascular endothelial cells can get affected largely by small changes in free Mg levels.

Normal serum Mg levels in humans fall between 1.7-2.2mg/dl. Usually a serum level less than 1.7mg/dl is used as a reference for hypomagnesemia.

Clinical features of hypomagnesemia

Early signs include nausea, vomiting, anorexia, easy fatigue and weakness. Other manifestations include agitation, tremors, fasciculations, depression, hypokalemia and cardiac arrhythmias. In severe hypomagnesemia tingling, numbness, cramps, muscle contractions, seizures, sudden onset of altered behaviour caused by excess electrical activity of the brain, changes in personality, irregularities in heart beat and coronary spasm can occur. Other electrolyte imbalances such as hypokalemia and hypocalcemia may accompany severe hypomagnesemia.

Hypomagnesemia

1. In maintaining Mg homeostasis kidneys play a crucial role. So in chronic renal failure, the compensatory mechanisms become inadequate and results in hypermagnesemia.
2. Antacids and laxatives which contain Mg when used therapeutically especially in elderly patients and in combinations they are more prone to develop hypermagnesemia.
3. Iatrogenic hypomagnesemia in pregnancy- Mg infusion used for the treatment of eclampsia.
4. Excessive ingestion of Mg has been reported in people who have near drowned in dead sea.

Clinical features of hypermagnesemia

1. Nausea, vomiting, cutaneous flushing and hypotension are associated with moderate hypermagnesemia.

2. Neuromuscular dysfunction ranges from drowsiness to respiratory depression, areflexia, hypotonia or even coma can occur in a higher concentrations.
3. Cardiac manifestations include bradycardia, nonspecific ECG changes like prolonged PR interval, QRS and QT interval, 3rd degree AV block, atrial fibrillation and in advanced cases even asystole may occur.

Conclusion

Although APACHE II is the oldest scoring system, still it is most widely used among others. Because the data need for its calculation are reproducible, simple, well defined and can be collected on a routine basis. The critically ill patient is defined as, the one who is at imminent risk of death. The measures should be taken to assess the severity of illness as early as possible and appropriate measures should be taken promptly to assess, diagnose and manage the illness. The critical illness is defined as any disease process which leads to physiological instability leads to disability or death within minutes or hours.

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