

Mgr Justyna Malinowska

Assessment of the incidence of calcium-magnesium-phosphate homeostasis disturbances increasing in-hospital mortality and analysis of mechanisms of their causes in a selected population of hospitalized patients

Abstract

Calcium, magnesium, and phosphorus are minerals with an extremely important impact on the functioning of the human body. Most of them are found in the intracellular space, mainly in bones and teeth, where they serve as a building material. They also participate in the regulation of many processes necessary for maintaining homeostasis of the body, including the process of energy production, storage and release, neuromuscular conduction, and hemostasis. The homeostasis of calcium, magnesium, and phosphorus is regulated by absorption in the gastrointestinal tract, excretion by the kidneys, and storage in hard tissues, but also by the shifting of ions from the extracellular space into the intracellular space via ion channels. In addition, their homeostasis is also regulated by hormones, including vitamin D. Due to the important functions of calcium, magnesium, and phosphates, their abnormal concentrations lead to serious respiratory, circulatory, and nervous disorders. However, the results of studies assessing their prevalence are inconsistent and probably underestimated. In addition, the impact of calcium-magnesium-phosphate disorders on hospital mortality, as well as the mechanisms of their formation, has not yet been fully analyzed.

The aim of this dissertation entitled “Assessment of the incidence of calcium-magnesium-phosphate homeostasis disturbances increasing in-hospital mortality and analysis of mechanisms of their causes in a selected population of hospitalized patients” and conducted studies was to determine the incidence of calcium-magnesium-phosphate homeostasis disorders in selected groups of hospitalized patients, to assess its impact on overall hospital mortality, and to investigate the mechanism of development of these disorders.

An analysis of laboratory results of patients hospitalized at the Medical University of Warsaw Central Clinical Hospital was performed. The included groups of patients were: elderly (at least 65 years of age), infected with SARS-CoV-2, recipients of massive transfusions, and subjects from the general hospital population who had their blood serum calcium, magnesium

and phosphorus concentrations tested. In addition, intracellular levels of magnesium in packed red blood cell concentrates (RBCs) that were transfused to patients were analyzed. The studies assessed the incidence of magnesium, calcium, phosphorus and vitamin D disorders and their relationship with age and gender; the incidence of calcium-magnesium-phosphate and vitamin D disorders with age, gender, renal function, comorbidities and severity of SARS-CoV-2 infection and their impact on the risk of death in hospitalized patients due to COVID-19; and the impact of massive transfusions on magnesium concentration in serum.

The results of the studies show that calcium, magnesium and phosphorus disorders are very common in hospitalized patients – abnormal magnesium levels were found in every third patient aged 65 years or over. Magnesium and vitamin D levels were age-dependent, and calcium, magnesium and vitamin D levels were sex-dependent. In the study of patients hospitalized for COVID-19, calcium, magnesium, phosphorus and vitamin D disorders were very common, but only phosphate disorders depended on the severity of the disease. Renal failure was associated with higher magnesium and phosphate levels. Also, abnormal concentrations were more common in patients with fatal outcome. A logistic regression analysis was performed, taking into account factors potentially affecting calcium-magnesium-phosphate homeostasis, i. e. age, sex, chronic diseases, and renal function. It was found that statistically significant factors increasing the risk of death in the group of patients hospitalized for COVID-19 were hypermagnesemia (by 50%) and hyperphosphatemia (by 240%).

The effect of massive packed RBCs transfusions on the serum magnesium levels of recipients at 24 and 48 hours after transfusion was also investigated. The analysis took into account the presence of factors that could affect the studied parameter, i. e. renal failure, surgery, intravenous drug administration during hospitalization, comorbidities, and dialysis. The massive transfusion resulted in a significant increase in serum magnesium in most patients, as well as a higher incidence of hypermagnesemia in this group. In addition, hypermagnesemia occurred more frequently in patients with fatal outcome. Serum magnesium levels were positively correlated with the volume of transfused packed RBCs, but not with their intracellular magnesium concentration. The hypermagnesemia was probably due to mild hemolysis under the influence of blood warming before transfusion. This study is an example of a greater number of factors causing hypermagnesemia in the hospital population than previously reported in the scientific literature.

An analysis of calcium-magnesium-phosphate homeostasis disturbances, their incidence, association with reasons for hospitalization and outcome, comorbidities, and chronically used medications was performed using various statistical methods. Hypercalcemia

(40.4%) and hypomagnesemia (22.1%) were the most common disturbances. It was observed that especially parathyroid and liver diseases influenced the serum concentration of calcium, magnesium and phosphates. Among the drugs, spironolactone, ursodeoxycholic acid and loop diuretics had the greatest effect. Moreover, polypharmacy was associated with significantly higher calcium and phosphate concentrations and lower magnesium concentration in the serum. Linear regression analysis additionally showed correlations between the concentrations of calcium, magnesium and phosphates and unusual factors, among others liver diseases and the use of calcium and potassium supplements. An association was also observed between the occurrence of abnormal concentrations of tested parameters in serum and an increased risk of death, especially for concentrations above the upper limit of the reference range.

Based on these studies, it was concluded that calcium-magnesium-phosphate disorders are very common in hospitalized patients and increase the risk of death regardless of renal function. Particularly noteworthy is hypermagnesemia, which is not as rare as previously thought, and occurring not only in patients with advanced chronic kidney disease. Moreover, also associated with a significantly increased risk of death.