A Renewed Question in Haemodialysis Patients: Should We Correct Low Serum Magnesium Levels?

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Key Words

Magnesium · CKD-MBD

Disturbances in magnesium (Mg) metabolism are not so rare in chronic kidney disease (CKD) and dialysis patients, especially in those affected by diabetes, insulin resistance, inflammation, vascular calcification (VC), and higher mortality [1]. Furthermore, renal patients are prone to higher cardiovascular (CV) morbidity and mortality. CV disease in CKD is associated with VC and mineral bone disorders, which are regulated by hormone disturbances (FGF23/klotho-PTH-Vitamin D axis) [2]. Recently, an independent association between low Mg levels and CV disease in dialysis patients has been observed, resuscitating this ion as a renewed and active player in vascular aging.

Consistent results from both pre-clinical and clinical research showed that CV susceptibility in CKD is strongly associated with a considerable acceleration of vascular aging in the context of the *chronic kidney disease-mineral bone disorder* syndrome (CKD-MBD), in which new biomarkers are needed to improve the understanding toward further intervention strategies [3].

In the present issue of the *Blood Purification*, Matias et al. show the association between low serum Mg levels and increased CV risk factor in 206 haemodialysis (HD) pa-

tients [4]. This elegant observational analysis illustrates that patients with higher pulse pressure (PP) (≥ 65 mm Hg) ($p = 0.01$), left ventricular hypertrophy (LVMI ≥ 125 g/m²) ($p = 0.02$), and higher VC (SVCS ≥ 3) ($p = 0.008$) have significantly lower serum Mg concentrations.

In addition, Kaplan-Meier analysis shows that both all-cause and CV mortality were associated with a significant lower 48-month survival in HD patients with the level of serum Mg being lower than 1.15 mmol/l, thereby assigning Mg a role of a 'renewed' independent negative predictor of mortality.

A growing body of evidence is suggesting a potential role for Mg in different diseases such as CKD-MBD, diabetes, low insulin resistance, poor endothelial reactivity, higher oxidative stress, increased intima-media thickness, vascular calcification, progression of CKD, and mortality [5].

Nevertheless, the maintenance of adequate intracellular Mg levels appears essential for life per se, considering that Mg is a fundamental co-enzyme of vital biochemical reactions just like Krebs cycle and glycolysis and it is essential for the maintenance of RNA and DNA stability. Thus, Mg may represent a cardinal biomarker and regulator of vascular aging in humans, with special emphasis in CKD patients. Furthermore, nephrologists are called to a growing comprehension of Mg physiology as a consequence of the renewed adoption of Mg as a phosphate

binder. Data by Matias et al. [4] confirm the growing interest of the nephrology community pointing toward Mg metabolism with particular emphasis on CKD-MBD patients.

In summary, it can be argued that hypomagnesemia or, even more strikingly, lower Mg levels may be actively detrimental for CKD-MBD in HD patients, contributing to low bone turnover, poor insulin sensitivity and lower protection against inflammation and oxidative stress in arteries leading to higher VC. This study by Matias et al. [4] signals a relevant step forward in our epidemiological knowledge about the important role played by Mg in the arena of

vascular aging in CKD-MBD. However, further investigations are required to better elucidate whether Mg supplementation may improve vascular aging in HD patients and to identify the optimal serum Mg levels in this population.

Despite all that we learned, learn, and will learn about the role of Mg on CV disease in CKD patients, we have been left only with a hypothetical framework about how to treat patients with lower serum Mg levels. A putative 'final' answer should be tested with a global-multiple therapeutic approach to treat simultaneously several components of CKD-MBD, through a well-designed, new randomised controlled trial.

References

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