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Mineral Nutrient Linked Anti-aging Regulation: A Novel Mechanism Involving Magnesium

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Summary

Hyperphosphatemia in chronic kidney disease (CKD) leads to ectopic calcification and secondary hyperparathyroidism and is considered an aggravating factor in cardiovascular mortality. Currently, not only blood phosphorus levels but also the phosphorus diuretic factor Fibroblast growth factor (FGF)23 and parathyroid hormone (PTH) are thought to have adverse effects on various organs and cells. FGF23 has been reported to be involved in various organ damage and aging progression throughout the body. On the other hand, hypomagnesemia is a predictor of death in any stage of CKD, and magnesium has been reported to have an inhibitory effect on vascular calcification associated with hyperphosphatemia. Thus, the presence of magnesium is very important in a state of disrupted phosphorus metabolism. Klotho acts as a co-receptor for FGF23. α-Klotho knockout (KO) mice show hyperphosphatemia, hypervitaminosis D, growth retardation, and short life span, thus acting as an anti-aging factor via mineral regulation. We recently identified a molecule involved in this system, αKlotho-regulatory factor (KRF), and KRF KOs show elevated levels of FGF23 in blood, comparable to αKlotho KO mice. In addition, KRF and related molecules were searched for, and magnesium-related molecules were detected, suggesting that KRF may be involved in magnesium metabolism. In this study, we examined the basic analysis of magnesium in KRF KO mice to clarify the FGF23/αKlotho-KRP-magnesium metabolic system.

Although there were no significant differences in calcium, phosphate, magnesium blood levels, fecal and urinary excretion in KRF KO mice compared to wild-type mice, blood FGF23 and PTH levels were highly increased in KRF KO mice. Kidney Trpm6 mRNA expression was significantly decreased, but no organ damage such as vascular calcification or inflammation was observed in KRF KO mice.

Although we were unable to clarify the relationship between KRF and magnesium metabolism in this study, we plan to examine extrarenal organs and intracellular magnesium content using dietary modulation and CKD models in the future.