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Magnesium Attenuates Phosphate-Induced Kidney Injury by Inhibiting Rubicon and Restoring Autophagic Activity

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Summary

With the aging of the population and the increase in lifestyle-related diseases, the number of patients with chronic kidney disease (CKD) and dialysis is increasing. Thus, there is an urgent need for medical and social measures to address this problem. Hyperphosphatemia accelerates vascular calcification and its health hazards have long been a problem in CKD patients. It has been reported that a high phosphate diet increases phosphate excretion from the renal tubules, resulting in the formation of fine calcium-phosphate crystals, calciprotein particles (CPP), in the renal tubules, which can damage the tubules. Epidemiological studies have shown that magnesium intake reduces the risk of CKD and heart disease, but the underlying mechanisms are not clear.

Autophagy is the main degradation mechanism in the cell and plays a role in maintaining cellular homeostasis. We have studied the effects of lifestyle-related diseases such as aging, obesity, and diabetes, on autophagy in kidney proximal tubules and found that autophagy protects against the phosphate-induced kidney injury via mitochondrial quality control, although high phosphate impairs autophagy, which diminishes its protective effect.

Based on the background information, we hypothesized that magnesium can attenuate the high phosphate toxicity by inhibiting the CPP formation and restoring the autophagic activity. Main findings are as follows;
1) high phosphate load gradually causes fusion failure of autophagosomes and lysosomes, 2) high phosphate load increases expression of Rubicon in the kidney, 3) phosphate-induced kidney injury is ameliorated by Rubicon deficiency, and 4) a high-phosphate/low-magnesium diet markedly increases Rubicon in the kidneys and causes autophagy failure, which is ameliorated by magnesium supplementation. In conclusion, in this study, we found that magnesium attenuates phosphate-induced kidney injury by inhibiting Rubicon and restoring autophagic activity.