

Mechanistic Analyses of Circadian Variation of Blood Pressure Triggered by Renal Response to Magnesium.

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Summary

TRPM6 is strongly expressed in renal distal convoluted tubule (DCT) cells and plays an essential role in magnesium reabsorption. We have previously shown a novel role of TRPM6 in regulating the circadian variation of blood pressure. Kidney-specific TRPM6-KO mice not only showed impaired renal magnesium reabsorption but also showed attenuated circadian blood pressure variation. Furthermore, mice fed a high-magnesium diet showed decreased TRPM6 expression in DCT and suppressed circadian blood pressure variation. These results suggest an interesting possibility that blood pressure, especially its circadian variation can be controlled by magnesium administration and subsequent suppression of TRPM6 expression. However, little is known about how continuous administration of magnesium affects organisms, especially its adverse effects.

To clarify this issue, mice were fed diets containing various amounts of magnesium (0.0027%, 0.1%, 0.3%, or 0.6%) for 2-4 weeks. First, we checked the serum magnesium levels, and confirmed that it correlates with the amount of magnesium in their diets. Also, the expression level of TRPM6 was inversely correlated with the dietary magnesium content, and typically it was almost undetectable in mice fed a high-magnesium diet. In these mice, there were no significant difference on growth, kidney tissue architectures, and cell senescence, but mice fed high magnesium diet showed symptoms of diarrhea.

These results suggest that by optimizing the route of magnesium administration may avoid diarrhea and provide a safe blood pressure control method without obvious adverse effects. Nevertheless, further experiments will be required, including further long-term administration in older mice and in induced hypertension models, to evaluate the efficacy and safety of magnesium administration as novel methods to control circadian blood pressure variation.