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Elucidation of Cognitive Impairment Induced by Chronic Kidney Disease and Development of Therapeutic Methods Focusing on the Brain Mg^{2+} Contents

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Summary

Chronic kidney disease (CKD) is characterized by progressive deterioration of renal function. CKD has been recognized as a growing global health problem because of its associated risk of all-cause mortality, cardiovascular disease, and other comorbid diseases. Several clinical studies have demonstrated that CKD is associated with uremic encephalopathy and cognitive impairment. However, the pathological role of CKD in cognitive impairment or dementia is not fully understood. In the present study, the effects of Mg^{2+} intake were investigated in CKD mice.

CKD was induced in male C57BL/6 mice by left nephrectomy and 2/3 electrocoagulation of the right renal cortex. Mice were monitored daily, and body weights and food intake were measured weekly throughout the protocol. Eight weeks after the second renal surgery, the brains were rapidly removed from mice. Blood collected at time of euthanasia was used to measure serum biochemical parameters.

The orally administration of $MgCl_2$ (1%) did not significantly affect the duration of survival in the CKD mice. There were no significant differences in body weight, food intake and water intake between Mg^{2+}-treated CKD mice and vehicle-treated CKD mice. The blood Mg levels in the Mg^{2+}-treated CKD mice were significantly higher than those in the vehicle-treated CKD mice. The concentration of blood urea nitrogen (BUN) in Mg^{2+}-treated CKD mice were significantly higher than that in CKD mice with vehicle treatment. Western blotting revealed that the expression level of 4-hydroxy-2-nonenal (HNE)-protein adducts, a hallmark of oxidative stress, and glucose-regulated protein 78 (GRP78), a typical ER stress marker, were increased in the hippocampus of CKD mine. These stress levels were climbed under the influence of Mg^{2+} in CKD mice. These results suggest that high Mg^{2+} intake acts as a worsening factor for CKD-induced hippocampal impairment through exacerbated renal impairment.