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Methionine sulfoxide reductase B3 (MsrB3)-gene deletion exacerbates VitaminD3-induced kidney injury

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Objectives : Methionine sulfoxide reductase B3 (MsrB3) catalyzes the reduction of methionine-R-sulfoxide to methionine and which protects cells against oxidative stress. Vitamin D3 (cholecalciferol) supplement is commonly used to treat renal osteodystrophy in dialysis patients with chronic kidney disease. However, high dose vitamin D3 abnormally increases levels of calcium in the blood (hypercalcemia), leading to damages of organs including kidneys. Here, we investigated the role of MsrB3 in vitamin D3-induced kidney injury using MsrB3 knock-out (MsrB3 KO) mice.

Methods : To induce hypercalcemia, mice were administered subcutaneously vitaminD3 for 3 days daily. Kidneys were collected for biochemical and histological studies at 7 days after last administration.

Results : After vitamin D3 injection, calcium levels in the kidney and serum significantly increased, and these increases were greater in MsrB3 KO than in MsrB3 wild-type (MsrB3 WT) mice and kidney tubule damages were greater in MsrB3 KO than in MsrB3 WT mice. VitaminD3 injection decreased expressions of Msrs and antioxidant enzymes; manganese superoxide dismutase (MnSOD), cupper zinc SOD (CuZnSOD), and catalase, whereas it increased the expression of vitamin D receptor (VDR), and osteogenic transcription factors in kidneys. These expression changes were greater in MsrB3 KO than in MsrB3 WT mouse kidneys. Hydrogen peroxide and lipid peroxidation levels were greater in MsrB3 KO than in MsrB3 WT mouse kidneys after VitaminD3 injection.

Conclusions : MsrB3 gene-deletion exacerbates high dose of vitaminD3-induced kidney injury by increased in oxidative damage and increases of osteogenic factors, suggesting that MsrB3 protein could be considered as a potential target for the treatment of hypercalcemia-induced kidney injury.

Keywords : Hypercalcemia, VitaminD3, Oxidative stress, Methionine sulfoxide reductase, Acute kidney injury