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Regulation of hepcidin levels by vitamin D and omega-3 fatty acid in 5/6 nephrectomy rat model

Su Mi Lee, Young Ki Son, Seong Eun Kim, Won Suk An
Department of Internal Medicine-Nephrology, Dong-A University, College of Medicine, Korea, Republic of

Objectives:

Anemia is a common complication of chronic kidney disease (CKD). Vitamin D insufficiency correlates inversely with the prevalence of anemia. Hepcidin is a key regulator of iron homeostasis by its binding to ferroportin. Via hepcin-ferroportin axis, hepcidin inhibits intestinal iron absorption and iron release from macrophages and hepatocyte. In CKD patients, hepcidin levels increased and an inverse relationship between vitamin D and hepcidin levels was found. The aim of this study was to investigate the role of vitamin D and omega-3 fatty acid (FA) in iron homeostasis through regulation of hepcidin-ferroportin axis in 5/6 nephrectomized (Nx) rat model.

Methods:

Male Sprague Dawley rats were divided into five groups: sham control (0.9% saline), 5/6 Nx (0.9% saline), 5/6 Nx treated with vitamin D (cholecalciferol 3000 IU/kg/week) group, 5/6 Nx treated with omega-3 FA (300 mg/kg/day by gastric gavage) group, 5/6 Nx treated with vitamin D and omega-3 FA groups. Levels of hemoglobin (Hb), 25(OH)D, 1,25(OH)2D, ferritin, ferroportin, TIBC, and hepcidin were checked by ELISA.

Results:

Serum BUN and creatinine levels were the lowest in 5/6 Nx treated with omega-3 FA and vitamin D group among 5/6 Nx rat models. Compared with control, 5/6 Nx group significantly up-regulated hepcidin levels and down-regulated 25(OH)D and 1,25(OH)2D levels. After supplementation with omega-3 FA or vitamin D, hepcidin levels decreased and 25(OH)D and 1,25(OH)D levels increased with an improvement in anemia. These effects were greatest when vitamin D and omega-3 FA were taken together. Ferroportin and ferritin levels increased and iron and TIBC level decreased in in 5/6 Nx rats. These tended to reversed after omega-3 FA or vitamin D supplementation.

Conclusions:

These data show that vitamin D and omega-3 FA are potent regulators of the hepcidin-ferroportin axis and highlight a potential new strategy for the management of anemia in patients with low vitamin D and/or CKD.