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COMBINED TREATMENT WITH OMEGA-3 FATTY ACID AND CHOLECALCIFEROL INCREASES 1 25 DIHYDROXY VITAMIN D LEVEL BY INHIBITING 24 HYDROXYLASE OF KIDNEY AND LIVER IN 5/6 NEPHRECTOMY RAT MODEL

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Objectives : The 1 α-hydroxylase (CYP27b1) and 24-hydroxylase (CYP24) in renal proximal tubules primarily involve vitamin D metabolsim. Increased activity of CYP24 contributes vitamin D catabolism in chronic kidney disease (CKD). Recent reports showed that CYP27b1 was strongly expressed in monocytes developing into hepatic macrophages and omega-3 fatty acid (FA) elevated 1, 25-dihydroxy vitamin D level in dialysis patients with scanty renal function. In this study, we evaluated whether the effect of omega-3 FA and cholecalciferol on vitamin D metabolism are related with the activity of CYP27b1 and CYP24 in liver and kidney of 5/6 nephrectomy (Nx) rat model.

Methods : Male Sprague Dawley rats were divided into five groups and treated for 6 weeks: sham control (0.9% saline), 5/6 subtotal nephrectomy (Nx) control (0.9% saline), 5/6 Nx treated with vitamin D (cholecalciferol 3000 IU/kg/week by gastric gavage), 5/6 Nx treated with omega-3 FA (300 mg/kg/day by gastric gavage), 5/6 Nx treated with vitamin D and omega-3 FA. CYP27b1 and CYP24 in remnant kidney and liver were measured by western blot analysis. Serum 1, 25-dihydroxy vitamin D and 25-hydroxy vitamin D levels were also checked.

Results : Serum BUN and creatinine were the lowest in 5/6 Nx group treated with omega-3 FA and vitamin D among other 5/6 Nx groups. The levels of serum 1, 25-dihydroxy vitamin D and 25-hydroxy vitamin D were the highest in 5/6 Nx group treated with omega-3 FA and vitamin D among other 5/6 Nx groups. The expression of CYP24 was significantly increased in remnant kidney and liver of 5/6 Nx control compared to sham control. Increased expression of CYP24 in remnant kidney and liver of 5/6 Nx control was significantly decreased by combined treatment with omega-3 FA and cholecalciferol. The expression of CYP27b1 was significantly increased in remnant kidney and significantly decreased in liver of 5/6 Nx control compared to sham control. The increased expression of CYP27b1 in remnant kidney and decreased expression of CYP27b1 in liver of 5/6 Nx control was nearly normalized by combined treatment with omega-3 FA and vitamin D.

Conclusions : Combined treatment with omega-3 FA and cholecalciferol

definitely increases 1, 25-dihydroxy vitamin D level by inhibiting expression of 24-hydroxylase in remnant kidney and liver and activating expression of 1 α-hydroxylase in liver of 5/6 Nx rats.

Keywords : omega-3 fatty acid, cholecalciferol, 1 α-hydroxylase, 24-hydroxylase