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COMBINATION OF OMEGA-3 FATTY ACIDS AND VITAMIN D HAS SYNERGIC EFFECT ON UP-REGULATION OF NRF-2 EXPRESSION AND DOWN-REGULATION OF SREBP-1 IN 5/6 NEPHRECTOMY RATS

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Background: The Nrf-2 regulates antioxidant and anti-inflammatory process in kidney injury model. Recent study showed that SREBP-1 mediates angiotensin II-induced pro-fibrogenic responses. The present study aimed to investigate whether omega-3 FA and vitamin D which were related with anti- inflammatory process affects the Nrf-2 and SREBP-1expression and has anti-inflammatory, anti-apoptotic, and anti-fibrotic processes in 5/6 nephrectomy rats

Methods: Male Sprague Dawley rats were divided into five groups: sham control (0.9% saline), 5/6 subtotal nephrectomy (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. The expression of IK-b, transforming growth factor (TGF-β1), α-smooth muscle actin (α-SMA), E-cadherin, Smads for inflammation and fibrosis, caspase-3, caspase-7, BAX, and Bcl-2 for apoptosis, and Nrf2 and SREBP-1 were examined by western blot analysis. The expression levels of apoptosis-associated factors were examined by western blot analysis.

Results: Serum BUN and creatinine was 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 caspase 3, caspase7, IkB, a-SMA, E-cadherin, SREBP-1, TGF β and Smad2/3 expression and down-regulated Smad6 and Nrf2 expression. We found that omega-3 FA prevented these up and down regulations related with apoptosis, inflammation, and renal fibrosis. There were no significant differences on expression of these factors between 5/6 Nx with untreated group and 5/6 Nx with vitamin D group. However, increased expression of Nrf2 and decreased SREBP-1 expression was distinguished by omega-3 FA and vitamin D combination in 5/6 Nx rats.

Conclusion: Nrf-2 activation and SREBP-1 reduction are potential mechanism induced by omega-3 FA supplementation attenuating pro-inflammatory pathway, fibrotic processes and apoptosis. These mechanisms may be reinforced by additional vitamin D supplementation.

Keywords: apoptosis, fatty acid, fibrosis, omega-3, vitamin D