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Dysregulation of Hepatic Fatty Acid Metabolism in Chronic Kidney Disease: Effect of Niacin Supplementation

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Background: Chronic kidney disease (CKD) results in hypertriglyceridemia which is largely due to impaired clearance of triglyceride-rich lipoproteins occasioned by down-regulation of lipoprotein lipase and VLDL receptor in the skeletal muscle and adipose tissue and of hepatic lipase and LDL receptor-related protein (LRP) in the liver. However information on the effects of CKD and niacin administration on fatty acid metabolism in the liver is limited and was investigated here.

Methods: Expression of molecules involved in fatty acid metabolism in the liver were determined in untreated CKD (5/6 nephrectomized), niacin-treated CKD (50 mg/Kg/day in drinking water for 12 weeks) and control rats.

Results: The CKD rats exhibited hypertension, proteinuria, hypertriglyceridemia, up-regulation of hepatic tissue carbohydrate-responsive element binding protein (ChREBP), fatty acid synthase (FAS), and acyl-CoA carboxylase (ACC), and down-regulation of sterol responsive element binding protein-1 (SREBP-1), SREBP-2, HMG-CoA reductase, fatty acid binding protein (L-FABP), CPT1A, ATP synthase α, ATP synthase β, glycogen synthase, and diglyceride acyltransferase 1 (DGAT1), DGAT2. Niacin therapy attenuated hypertension, proteinuria, hypertriglyceridemia, reduced ChREBP, FAS, ACC abundance and raised SREBP-1, L-FABP, ATP synthase α, and DGAT1.

Conclusion: Advanced CKD results in carbohydrate responsive element binding protein driven upregulation of key enzymes involved in fatty acid synthesis and down-regulation of the key enzymes involved fatty acid catabolism in the liver. Niacin administration attenuates these abnormalities and improves plasma lipid profile in the CKD animals.

Key Words: Fatty acid, TG, Niacin