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APX-501 protein is a novel biomarker for diabetic nephropathy in type 2 diabetic patients

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Background: Oxidative stress plays an important pathogenic role in various pathologic conditions. ROS are important regulators of various transcription factors and gene expression. Excess production of ROS in many tissues leads to oxidative stress resulting in various tissue injuries through inflammation and fibrosis. Recently we identified that APX-501 protein was synthesized from endothelial cells, and found that APX-501 is involved in oxidative stress in the kidney. Therefore, we investigated the role of APX-501 as a new biomarker for diabetic nephropathy in type 2 diabetic patients.

Methods: 171 type 2 diabetic patients and 65 healthy control subjects were enrolled. The study subjects were divided into four groups: 1) nondiabetic healthy controls with normal ACR (n=65), 2) normo-albuminuric diabetic group (n=66), 3) microalbuminuric diabetic group (n=52) and 4) overt proteinuria group (n=53). Plasma levels of APX-501 were measured by ELISA. In addition, we examined the physiological action of APX-501 in cultured podocytes in diabetic condition.

Results: Plasma APX-501 concentrations were significantly higher in the diabetic groups than in the controls. Plasma APX-501 levels showed highest levels in overt proteinuria group. Plasma APX-501 levels were positively correlated with systolic blood pressure, postprandial glucose levels, HOMA-IR, plasma retinol binding protein 4 (RBP-4) and urinary albumin excretion (UAE), and were inversely correlated with body mass index (BMI). However, we could not detect urinary excretion of APX-501 even in the overt proteinuria group. Regression analysis showed that plasma levels of APX-501 showed significant relationship with systolic blood pressure, postprandial glucose levels, HOMA-IR, plasma retinol binding protein 4 (RBP-4) and urinary albumin excretion (UAE), and were inversely correlated with eGFR. UAE. RBP-4 and BMI were only independent determinants of plasma APX-501 concentration. In type 2 diabetic db/db mice, plasma levels and renal expression of APX-501 showed significant increase according to their age compared with those in nondiabetic db/m mice. In cultured podocytes, high glucose, angiotensin II and free fatty acids stimuli markedly increased APX-501 synthesis and secretion.

Conclusion: These findings suggest that APX-501 synthesis is activated in early stage of diabetic environment, and may be a novel new biomarker for diabetic nephropathy in type 2 diabetic patients.

Keywords: biomarker, diabetic nephropathy , type 2 diabetes