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Urinary CYP eicosanoid excretion correlates with glomerular filtration in African-Americans with chronic kidney disease

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Previous studies have indicated that cytochrome P450 (CYP) metabolites of arachidonic acid, ie, 20-hydroxyeicosatetraenoic acid (20-HETE) and epoxyeicosatrienoic acids (EETs) play an important role in the regulation of renal tubular function and vascular tone. More recent studies suggest that variants in the *CYP4A11* and *CYP4F2* genes are linked to the development of hypertension in a variety of human population studies. However, little is known about the role of 20-HETE or EETs in the pathogenesis of hypertension or diabetic induced renal disease because CYP eicosanoids have not been measured in patients with CKD. The present study profiled HETEs and the dihydroxymetabolites of EETs (DHETs) levels, from spot urines at the time of their clinic visit using LC/MS/MSin 106 African-American patients from the University of Mississippi (UMC) Chronic Kidney Disease (CKD) Clinic with various etiologies of renal disease. Informed consent was obtained for this UMMC IRB approved protocol. Significant positive correlations were found between urinary 5,6- DHETE, 8,9-DHETE, 11,12-DIHETE, 14,15-DHETE, 20-HETE and 19-, 15- and 8-HETE levels and estimated GFR (eGFR) as derived from the MDRD. The magnitude of the influence of urinary eicosanoid levels on eGFR was relatively profound since the slopes of these relationships indicated that there is a 5-10% decrement eGFR associated with each ng/ml fall in urinary eicosanoid levels. These results suggest that a decline in the renal formation of 20-HETE and/or EETs may contribute to the pathogenesis of CKD. At very least, urinary CYP eicosanoids may serve as a useful biomarker for progressive disease.

Biography

Albert W Dreisbach has completed his M.D. at the age of 25 years from UMDNJ- NJ Medical School and Clinical Pharmacology and Nephrology Fellowships at Tulane and Cornell University Weill School of Medicine. He is the Director of Nephrology Research at University of Mississippi. He has published more than 40 papers in reputed journals and has been serving as an editorial board member of repute. He is currently investigating the role of CYP 450 eicosanoids in hypertension and chronic kidney disease.

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