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ELEVATED PLASMA CYCLOPHILIN A IN HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS: A NOVEL LINK TO SYSTEMIC INFLAMMATION AND CARDIOVASCULAR DISEASE

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Background: Cyclophilin A (CyPA) has emerged as a novel mediator of oxidative stress and inflammation and a major player in cardiovascular disease, diabetes, viral infections, and neurodegenerative and thrombotic disorders. CyPA is an abundant intra-cellular protein which is released by certain cell types spontaneously or in response to inflammatory mediators, hypoxia, oxidative stress and hyperglycemia. Many of these conditions are either present or frequently occur in ESRD patients and can thus stimulate release of CyPA thereby amplifying systemic inflammation. To our knowledge, the effect of ESRD and dialysis modalities on circulating CyPA has not been previously investigated. This study tested the hypothesis that extracellular CyPA is elevated in ESRD patients maintained on hemodialysis and peritoneal dialysis.

Methods: CyPA, hsCRP, and lipid levels were measured in the fasting plasma samples from 20 hemodialysis and 20 peritoneal dialysis patients, and 20 healthy age- and gender-matched controls. Left ventricular (LV) mass, LV end-systolic and end-diastolic volumes, ejection fraction and pulse wave velocity and ankle-brachial index were determined.

Results: Plasma CyPA concentration in the hemodialysis (105.3 ± 6.2 ng/ml) and PD (106.8 ± 9.0 ng/ml) groups were significantly higher than that in the control group (29.7 ± 4.1 ng/ml). This was associated with significant elevation of hsCRP, IL-6, TNF- α , plasma atherogenic index [$\log(\text{triglyceride}/\text{HDL-cholesterol})$], systolic and diastolic blood pressure, LV mass, LV end-diastolic and end-systolic volumes, and pulse wave velocity coupled with significant reduction in LV ejection fraction and ankle-brachial index. Plasma CyPA concentration showed direct correlation with hsCRP, IL-6, TNF- α , plasma atherogenic index, pulse wave velocity, systolic and diastolic blood pressure and inverse correlation with ankle-brachial index and HDL-cholesterol concentration.

Conclusion: Plasma CyPA concentration is markedly elevated and positively correlates with the markers of systemic inflammation and cardiovascular disease in hemodialysis and peritoneal dialysis patients.

Keywords: cardiovascular disease, Cyclophilin, Dialysis Patients