

Inflammation and advanced glycation end products in uremia: simple coexistence, potentiation or causal relationship?

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The causes for the high frequency of cardiovascular disease in dialysis patients are multifactorial in origin. Disturbances in the carbohydrate and lipid metabolism, the balance between oxidants and antioxidants and the immuno-inflammatory system are thought to play a role. Chronic uremia is characterized by the accumulation of advanced glycation end products (AGEs) and advanced oxidation products (AOPP) as well as activation of the acute phase response. High serum levels of these products and acute phase reactants such as C-reactive protein (CRP), fibrinogen and serum amyloid A can be found. CRP has been shown to predict cardiovascular and overall mortality in hemodialysis patients. Whether CRP is involved causally in atherosclerosis or merely represents a marker of disease is as yet unknown. Since CRP has been detected in colocalization with modified apolipoproteins or complement components in atherosclerotic lesions, a pathophysiological role seems very likely. AGEs as well have been detected in aortas of hemodialysis patients. Incubation of endothelial cells with AGEs induced expression of adhesion molecules with consecutive attraction of monocytes to the vessel wall. Thus far, clinical studies investigating the predictive effects of AGEs on cardiovascular mortality in hemodialysis patients are lacking. There is considerable debate about what factors turn on the acute phase response in this population. Proinflammatory effects of AGEs mediated through one receptor for AGEs, RAGE, have been described. We hypothesize that there may be a link between increased hepatic CRP production and the accumulation of AGEs in uremia. AGEs may stimulate CRP production in hepatocytes either directly or indirectly via interaction with monocytes.

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