New Insight into the Role of Uric Acid in Hypertension and Renal Disease

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An elevated uric acid is commonly observed in patients with hypertension and renal disease. Most authorities have viewed the elevation as innocuous unless there is concurrent gout or nephrolithiasis. However, a number of epidemiological studies have suggested that an elevated serum uric acid may be a risk factor for the development of hypertension or for the progression of renal disease. Nevertheless, it has been difficult to ascribe a mechanism by which uric acid could mediate these events. Recent studies from our laboratory have suggested that uric acid may, in fact, be an important pathogenic mediator.

Studies initiated by Drs Yoon Goo Kim and Duk-Hee Kang have clearly found evidence that an elevated uric acid accelerates the renal injury induced in rats by cyclosporine and in the remnant kidney. An elevated uric acid will also induce renal injury in the normal rat, and this is not mediated by crystal deposition.

Further studies by M Mazzali have also found that an elevated uric acid in rats leads to hypertension, through a mechanism involving renin activation and a decrease in intrarenal nitric oxide synthases (especially NOS1). A major mechanism appears to be the induction of vascular smooth muscle cell proliferation, which can be shown to be prominent in the preglomerular arterioles and arteries. This appears to be mediated by entry of uric acid into the vascular smooth muscle cell via an organic anion transporter, the alteration in intracellular redox, the activation of mitogen activated protein kinases, and the activation of nuclear transcription factors such as NF-KappaB. There is then an increase in synthesis of platelet-derived growth factor (PDGF), cyclo-oxygenase 2 (COX-2), and monocyte chemoattractant protein-1 (MCP-1) that results in stimulating cell proliferation and an inflammatory response. These studies suggest that uric acid may have an important and previously unrecognized role in mediating hypertension, microvascular disease, renal injury and the inflammatory response, and emphasizes the need to perform clinical studies to determine if lowering uric acid can prevent or treat hypertension and renal disease in man.