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Anti-fibrotic actions of suramin: Novel uses of an old drug

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Chronic kidney disease (CKD) is the result of various insults to the kidney, affecting approximately 10% of the normal population. Current drug discovery efforts for fighting renal fibrosis are largely focused on compounds that are specific for a particular receptor or protein kinase. Given that renal fibrogenesis is associated with increased production of multiple cytokines/growth factors and subsequent activation of their receptors and signalings pathways, it is expected that inhibitors with broad specificity might offer improved therepautic benefit in fibrotic diseases of the kidney. On this basis, we assessed the effect of suramin, an FDA approved drug for treating selected malignancies through its inhibitory effect on activation of multiple growth factor/cytokine receptors, on the activation of renal interstitial fibroblasts and the development/progression of renal fibrosis in animal models of chronic kidney injury. In a model of obstructive nephropathy induced by unilateral ureteral obstruction (UUO), administration of suramin immediately after injury prevented the onset of renal fibrosis as evidenced by suppression of α-smooth muscle actin (α-SMA) and type 1 collagen expression and reduction of extracellular matrix protein deposition. Delayed administration of suramin at day 3 of ureteral obstruction also inhibited the progression of tubulointerstial fibrosis. In a rat model of remnant kidney disease, suramin prevented progressive renal injury as demonstrated by inhibiting the rise of 24 hour-proteinuria and serum creatinine, preserving renal tissue architecture and preventing glomerular and tubulointerstitial damage. UUO injury or renal ablation induced phosphorylation of epidermal growth factor receptor, platelet derived growth factor receptor, and several signaling pathways associated renal fibrogenesis. Treatment with suramin blocked phosphorylation of all these molecules in the injured kidney. Moreover, suramin repressed expression of multiple cytokines including TGF-beta1 and decreased leukocyte infiltration to the interstitium. These findings indicate that suramin is a potent anti-fibrotic agent and may have therapeutic potential in treating patients with CKD.

Biography

Shougang Zhuang, MD, PhD, is an Associate Professor of Medicine at Brown University School of Medicine, Director of Kidney Research at Rhode Island Hospital, Chief of Nephrology at Shanghai East Hospital, Tongji University School of Medicine. His research is focused on the pathophysiology and drug discovery in acute kidney injury and chronic kidney disease. He has published 55 articles in peer-reviewed journals and serving on the Open Pathology Journal editorial broard.