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Pancreatic kininogenase protects against renal fibrosis in rat model of unilateral ureteral obstruction

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Objectives: Tissue kallikrein has protective effects against various types of injury. This study aimed to assess the beneficial effects of pancreatic kininogenase (PK) on renal fibrosis in a rat model of unilateral ureteral obstruction (UUO) and *in vitro*.

Methods: Sprague Dawley rats underwent UUO surgery and were treated daily with PK for 7 or 14 days. HK-2 cells treated with H_2O_2 and PK were also studied.

Results: PK treatment significantly attenuated interstitial inflammation and fibrosis and downregulated proinflammatory and profibrotic cytokine expression. Augmented oxidative stress induced by UUO was closely associated with excessive apoptotic cell death and autophagy via PI3k/AKT/FoXo1a signaling, which were abolished by administration of PK. Moreover, PK activated expression of bradykinin receptors 1 and 2 (B1R and B2R) mRNA and increased bioactive nitric oxide (NO) and adenosine 3¢5¢cyclic monophosphate (cAMP) concentrations. Blockade of either B1R or B2R abrogated the renoprotective effects of PK and reduced levels of NO and cAMP. In H_2O_2-treated HK-2 cells, PK decreased reactive oxygen species (ROS) production and regulated expression of oxidant and antioxidant enzymes, suppressed expression of transforming growth factor (TGF-b1) and monocyte chemoattractant protein-1 (MCP-1), and inhibited programmed cell death.

Conclusions: Our data suggest that PK treatment protects against the progression of renal fibrosis in obstructed kidneys.