Evaluation of a Novel Strategy to Extend Warm Ischemia Time in Complex Partial Nephrectomies

Introduction and Objective: Extended warm ischemia time during partial nephrectomy leads to considerable renal injury. Using a rat model of renal ischemia, we examined the ability of a unique renoprotective cocktail to ameliorate warm ischemia-reperfusion injury and extend warm ischemia time.
Materials and Methods: A warm renal ischemia model was developed using Sprague–Dawley rats, clamping the left renal artery for 40, 50, 60 and 70 minutes, followed by 48 hours of reperfusion. An improved renoprotective cocktail referred to as I-GPM (a mixture of specific growth factors and mitochondria protecting biochemicals) was administered -24 hours, 0 hours and +24 hours after surgery. At 48 hours, both kidneys were harvested and examined with hematoxylin-eosin and periodic acid-Schiff (PAS) stains for the analysis of renal tubular necrosis. Creatinine, protein, and gene expression levels were also analyzed to evaluate several ischemia-specific and anti-oxidant response markers.
Results: I-GPM treated kidneys showed significant reversal of morphological changes and a significant reduction in specific ischemic markers lipocalin-2, galectin-3, GRP-78 and HMGB1 as compared to ischemic controls. These experiments also showed an upregulation of the stress response protein HSP-70 as well as the phosphorylated active form of the transcription factor HSF-1. Additionally, quantitative RT-PCR analyses revealed a robust upregulation of several antioxidant pathway response genes in I-GPM treated animals.
Conclusions: By histopathologic and several molecular measures, our unique renoprotective cocktail mitigated ischemia-reperfusion injury. Our cocktail minimized oxidative stress in an ischemic kidney rat model while at the same time protecting the global parenchymal function during extended periods of ischemia.