BASIC SCIENCE RESEARCH

**Protective Role of Acute Testosterone Infusion during Acute Kidney Injury (AKI)**

Arnaldo Lopez-Ruiz, Andrea Soljancic, Kiran Chandrashekar and Luis A. Juncos

Department of Medicine-Division of Nephrology – University of Mississippi Medical Center

**Introduction**: Ischemia-reperfusion (I/R) injury commonly causes AKI during cardiac or aortic surgery and is associated with 60% mortality. The incidence and severity of I/R-induced AKI is higher in male surgical patients compared to females. Acute conditions like myocardial infarction or sepsis are associated with low testosterone levels. It is known that testosterone exerts cytoprotective actions through vasodilatation and modulating inflammation. Since I/R-induced AKI in males is associated with low testosterone levels, we believe that reduced testosterone levels during acute conditions like AKI contribute to increased renal damage due to greater intrarenal inflammation and vasoconstriction.

**Hypothesis**: “Infusing a bolus dose of testosterone during AKI reduces the pro-inflammatory response and improves the renal hemodynamics abnormalities leading to a lower renal dysfunction”

**Methods**: 4 groups of male SD rats; Sham, Sham + Testosterone, I/R-AKI and I/R-AKI + Testosterone. AKI was induced by placing intra-abdominal clamps in both renal pedicles for 40 min (ischemic period); clamps were then released and the rats followed for 48hs (reperfusion period). Testosterone propionate (20 µg/kg/min iv) was given at 3 hours post ischemia. During reperfusion, urine and blood were collected to evaluate renal function (plasma creatinine) and tubular injury (urine KIM-1). After 48hs, the renal medullary blood flow (RMBF) was measured in vivo and then the kidneys were harvested to measure intra-renal TNFα (Tumor necrosis factor-alpha) and VEGF (vascular endothelial growth factor) using Elisa Kits.

**Results**: Plasma creatinine (0.5 mg/dl vs 2.2mg/dl) and urine KIM-1 (380 pg/24h vs. 2200 pg/24h) were higher in AKI rats vs. controls (Sham). Also, RMBF was lower in rats with AKI (9 tpu vs 19 tpu) vs. controls. Intra-renal TNFα was elevated in AKI rats vs. controls (1.2 pg/mg vs 5.9 pg/mg). However, intra-renal VEGF was markedly reduced post-AKI (35 pg/mg vs 12 pg/mg). Rats receiving testosterone had lower creatinine (1.4 mg/dl vs 2.2 mg/dl) and less tubular injury (1300 pg/24h vs 2200 pg/24h) than rats with AKI. Furthermore, testosterone improved RMBF (15 tpu vs 9 tpu), reduced intra-renal TNFα (3.1 pg/mg vs 5.9 pg/mg) and increased intra-renal VEGF (21 pg/mg vs 12 pg/mg).

**Conclusion**: A bolus dose of testosterone given after the ischemic period improved renal function (creatinine) and attenuated tubular injury (KIM-1). Also, testosterone improved the RMBF, reduced intra-renal TNFα (pro-inflammatory cytokine) and increased intra-renal VEGF (cytoprotective factor), suggesting that a bolus dose of testosterone following cardiac or aortic surgeries may improve renal function in patients who have developed AKI.