Intra-Abdominal Pressure-Induced Renal Failure in CHF: Nephroprotective Effects of PDE-5 Inhibition

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Background: The deleterious effects of elevated intra-abdominal pressure (IAP) on the kidneys are widely recognized in abdominal compartment syndrome, visceral edema and laparoscopic surgery. Previously, we demonstrated that rats with congestive heart failure (CHF) exhibited exaggerated sensitivity to the adverse renal effects of elevated IAP compared with sham controls. In the present study we tested whether IAP induces acute kidney injury (AKI), and whether phosphodiesterase-5 (PDE5) inhibition ameliorates the adverse renal effects of elevated IAP in rats with CHF.
Methods: Following a baseline period, rats with high- and low-output CHF induced by the placement of aorto-caval fistula or LAD ligation, respectively, and sham-controls were subjected to consecutive IAPs of 7, 10, or 14 mmHg for 45 min each by CO2 insufflation. Urine flow (V), Na+ excretion (UNaV), glomerular filtration rate (GFR), renal plasma flow (RPF) and NGAL excretion were determined. The effects of pretreatment with Tadalafil (10 mg/day, PO) on the adverse renal effects of elevated IAP were examined in these rats.
Results: While IAP of 7 mmHg in sham-controls did not affect V, UNaV, GFR and RPF, IAPs of 10 and 14 mmHg produced dose-dependent reductions in these parameters. Basal kidney function and renal hemodynamics were lower in both low- and high-output CHF rats. When subjected to 10 and 14 mmHg, CHF rats exhibited exaggerated declines in V, UNaV, GFR, RPF and increased NGAL excretion compared to sham controls. Pretreatment with Tadalafil ameliorated the deleterious renal effects of high IAP in both CHF models.
Conclusions: Rats with CHF are vulnerable to the adverse renal effects of pneumoperitoneum. Tadalafil abolishes renal dysfunction and AKI induced by high IAP, supporting a therapeutic role for PDE5 inhibition in laparoscopic surgery in CHF states.