Effects of 7, 10, and 14 mmHg insufflation with CO2 on:

1Department of Physiology and Biophysics, Rappaport Faculty of Medicine, Technion, 2Departments of General Medicine, and improvement in renal function after medical therapy is required to protect the kidneys and improve clinical outcomes.

Studies were conducted on male Sprague Dawley rats, weighing ~300 g. The animals were housed in metabolic cages for daily monitoring of urine output and sodium excretion. A matched group of sham-operated rats served as controls.

Two experimental models of heart failure were applied: High and low cardiac output CHF. High cardiac output CHF was induced by surgical creation of a aorto-caval fistula (ACF), and skin layer of the abdominal wall were closed separately by silk sutures. The abdominal aorta and inferior vena cava were exposed through a mid-line incision between the xiphoid and pubis, through which a regular Veress needle was inserted into the abdominal cavity. Sequential IAPs of 7, 10, 14 mmHg were administered after creation of aorto-caval fistula. The experimental model of pneumoperitoneum: A small incision in the lower abdomen was made, through which a regular Veress needle was inserted into the abdominal cavity. Sequential IAPs of 7, 10, 14 mmHg were administered after creation of a pneumoperitoneum.

Results

Introduction and Aims: Studies were conducted on male Sprague Dawley rats, weighing ~300 g. The animals were housed in metabolic cages for daily monitoring of urine output and sodium excretion. A matched group of sham-operated rats served as controls.

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Conclusion: Decompensated CHF rats are vulnerable to the adverse renal effects of intra-abdominal pressure (IAP) that promote renal dysfunction in decompensated CHF.

Clinical heart failure (CHF) entails a complex interaction between the heart and the kidneys that represents the pathophysiological basis for a clinical entity called the cardio-renal syndrome.

1. Worsening of renal function is frequently observed in patients hospitalized for acute decompensated heart failure (ADHF) at the time of admission.

2. Understanding the mechanisms involved in the deterioration of renal function and the setting of abdominal compartment syndrome or other surgical conditions involving visceral edema, as well as during laparoscopic surgery.

4. The deleterious effects of elevated intra-abdominal pressure (IAP) on the kidney function and renal hemodynamics were lower in CHF rats in correlation with the severity of the disease. Decompensated CHF rats induced by either ACF or IAP elevation exhibited exaggerated declines in UNaV, GFR, and RPF as compared to sham controls or compensated CHF that were exposed to identical IAP conditions. Pretreatment of decompensated CHF rats with Tadalafil imitated the detrimental renal effects of high IAP.

5. Recent studies demonstrate that patients with ADHF have a high prevalence of elevated IAP in the absence of overt abdominal compartment syndrome. Furthermore, elevated IAP in these patients is associated with impaired renal function, which is not improved in renal function after medical therapy is associated with a reduction of IAP (J Urol 2011).

6. These initial studies also demonstrated that rats with decompensated CHF displayed lower urinary excretion of NOx+NO3+GMP in association with reduced UNaV and urine flow when exposed to elevated IAP, compared with normal controls or compensated CHF animals.

This study tested whether phosphodiesterase 5 (PDE5) inhibition via Tadalafil protects against the adverse renal effects of intra-abdominal pressure (IAP, pneumoperitoneum) in rats with CHF.

Materials and Methods

Studies were conducted on male Sprague Dawley rats, weighing ~300 g. The animals were fed standard rat chow containing 5.5% NaCl and tap water ad lib. All experiments were performed in accordance with the guidelines of the Committee for the Supervision of Animal Experiments, Technion, Haifa.

The experimental model of pneumoperitoneum: A small incision in the lower third between the xiphoid and pubis was made, through which a regular Veress needle was inserted into the abdominal cavity. Sequential IAPs of 7, 10, 14 mmHg were established and maintained with CO2 gas supply using a special insufflator (Karl Storz, Tuttlingen, Germany). Connected to the Veress needle is a peritoneal balloon layer and skin layer of the abdominal wall were closed separately by silk sutures using interrupted sutures.

The experimental models of CHF Two experimental models of heart failure were applied: High and low cardiac output.

1) High cardiac output CHF was induced by surgical creation of aorto-caval fistula (ACF) between the abdominal aorta and the inferior vena cava. To show the abdominal aorta and inferior vena cava were exposed through a mid-line incision under general anesthesia (80 mg/kg), an anterior venous shunt was surgically created between the two vessels (side to side, 1.2-mm o.d.) using running 5-0 silk. The animals were housed in metabolic cages for daily monitoring of urine output and sodium excretion. A matched group of sham-operated rats served as controls.

2) Low cardiac output CHF due to myocardial infarction (MI) was induced by left interior descending (LAD) artery occlusion. Rats were anaesthetized with a combination of 87 mg/kg ketamine and 13 mg/kg xylazine, intubated, and ventilated. The animals were housed in metabolic cages for daily monitoring of urine output and sodium excretion. A matched group of sham-operated rats served as controls.

Figure 6: Effects of 7, 10, and 14 mmHg insufflation with CO2 on A) Glomerular filtration rate (GFR), B) Percentage change in GFR from baseline, C) Renal plasma flow (RPF) and D) Percentage change in RPF from baseline in rats with decompensated CHF pretreated with Tadalafil. (*) P<0.05 vs. Baseline, (##) P<0.05 vs. sham controls. (Recovery) P<0.05 vs. decompensated CHF with Tadalafil pretreatment with Tadalafil.