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Title: Canine IT-HCL Induced Acute Lung Injury Does Not Alter Renal Function Early in the Course of Injury

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Introduction: ALI and mechanical ventilation are associated with acute kidney injury in patients and small animal disease models. We attempted to replicate kidney dysfunction seen in small animal studies with intratracheal (IT)-HCL ALI in canines with careful hemodynamic control.

Methods: Anesthetized, mechanically ventilated (Vt 25 ml/kg, 5 PEEP) canines were randomized to IT-HCL (0.5N, 1.5ml/kg; n=6) or sham (n=4) and followed for 300 min after ALI. Hemodynamics (CO, MAP, PAP, P_{aop}, RBF), pulmonary measurements (PF ratio, P_{plateau}, Qs/Qt), ABG and hematocrit were measured. Renal outcomes included plasma

(P_{Cr}) and urine (U_{Cr}) creatinine, urine albumin/creatinine ratio (ACR), GFR, and histology. Serum IL-6, IL-10, TNF- α , and INF-g were also measured.

Results: IT-HCL resulted in ALI (PaO_2/FiO_2 84 ± 20 vs 410 ± 143 , Q_s/Q_t (%) 49.4 ± 15.7 vs 10.1 ± 8.1 , $P_{plateau}$ (cmH₂O) 28 ± 5 vs 12 ± 2 , $p < 0.01$). MAP was not different between groups throughout. Mean CO was 33% lower in the IT-HCL group (1.7 ± 0.8 vs 2.5 ± 0.5 l/min, $p < 0.05$) mid-protocol, but returned to comparable values at 300min. RBF was stable throughout the time course and not different between sham and IT-HCL animals. Renal outcomes including urine flow, P_{Cr} , U_{osm} , U_{Na} , ACR, and renal histology scores were not different between groups. ACR increased an average of 3.8 fold over the duration of the experiments, possibly related to mechanical ventilation. All cytokines were comparable between groups.

Discussion: Although small animal models of ALI have shown changes in kidney function including alterations in water channel expression, cytokines, and degree of apoptosis, we did not see changes in renal function over the period studied in this canine IT-HCL model of ALI. Control of hemodynamics, acid/base status, and oxygen delivery may abrogate renal changes seen in small animal models of aspiration-induced ALI. Confounding factors may include the duration of study and more robust animal models.

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I hereby confirm the Disclosure information above is accurate at the time of this submission. I acknowledge that keying in my name and date of completion below indicates assent to this agreement and is equivalent to my signature.

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