YOUNG INVESTIGATOR PRESENTATION

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Title: Therapeutic Hypercapnia Attenuates Acute Lung Injury following Splanchnic Ischemia Reperfusion in the *in vivo* Rat.

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Introduction: Acute Lung Injury [ALI] is a major cause of morbidity and mortality in critical care. Although the pathobiology of multi-organ dysfunction is complex, ischemia-reperfusion [IR] injury, particularly in the splanchnic vasculature, is considered to play a pivotal role[1]. We have previously demonstrated that CO_2, can modify lung injury independent of alterations in lung stretch [2,3,4], and have hypothesized that deliberate elevation of $FiCO_2$ [Therapeutic Hypercapnia, TH] may protect in a broad spectrum of critical illnesses.[5] In this study, we hypothesized that TH would protect against splanchnic IR injury.

Methods: We utilized an *in vivo* anesthetized, mechanically ventilated, rat model of Superior Mesenteric Artery (SMA) IR induced ALI. In the first series animals were randomized to: [1] TH-IR, ($FiCO_2$ 0.05), [2] CON-IR, and [3] TH-SHAM, [4] CON-SHAM, where no IR was applied. All animals received standard FiO_2 (0.21), fluid management and ventilation parameters. After laparotomy, the SMA was occluded for 40 minutes, then reperfused for 60 minutes in TH-IR and CON-IR. In the second series randomized animals received TH either: [1] 15 mins pre- or, [2] 15 mins post-reperfusion *vs* [3] CON.

Results: Following IR injury, TH was associated with better preservation of lung capillary permeability, lung mechanics, systemic oxygenation, A-a gradient (222±23 *vs* 303±22mmHg, $P<0.05$) *vs* control. Furthermore, TH was associated with an improved acid-base (Base excess 1.9±0.8 *vs* 6.8±0.8, $P<0.05$) and lactate profile. In the second series, the degree of ALI was as follows: TH pre-reperfusion < TH post reperfusion < Control.

Conclusions: We conclude that in the current model: [1] TH is protective *vs* splanchnic IR induced ALI; [2] TH may confer protection *vs* extrapulmonary injury. [3] Application of TH post reperfusion is protective, thought to a lesser degree than TH pre-reperfusion. If these findings are confirmed in additional models, TH may become a candidate for clinical testing in critical care.

References:

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