Hypercapnic Acidosis Inhibits NF-κB Mediated Inflammation in a Rodent Model of Ventilator Induced Lung Injury
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Introduction
Lung protective mechanical ventilation strategies are often associated with elevated PaCO2, termed “permissive hypercapnia”. Hypercapnic acidosis (HCA) protects against lung injury in several contexts, including ischaemia-reperfusion1, sepsis2 and ventilator induced lung injury (VILI)3. The anti-inflammatory effect of CO2 may be mediated through the inhibition of one of the ubiquitously expressed transcription factors, nuclear factor kappa B (NF-κB)4. Early activation of the NF-κB pathway in organ injury results in gene expression central to inflammatory response5. We wished to determine the role of NF-κB pathway mediating the effect of HCA in in vivo rat VILI models.

Materials and Methods
Following induction of anaesthesia and tracheostomy placement adult male Sprague-Dawley rats were randomised in each series to receive either normocapnia (FiCO2 0.0) or HCA (FiCO2 0.05) for 4 hours. In the severe VILI series (n = 7), animals underwent ventilation with peak inspiratory pressure (PIP): 30 cmH2O, PEEP: 0 cmH2O, and respiratory rate (RR): 18 breaths/min for 4 hours. In the moderate VILI series (n = 6), animals underwent ventilation with PIP: 30 cmH2O, PEEP: 0 cmH2O at a RR: 15 breaths/min. Survival, haemodynamic profile, severity of lung injury and indices of activation of the NF-κB pathway were assessed.

Results
HCA reduced the severity of both moderate and more severe ventilation induced lung injury. In severe VILI, HCA significantly improved survival compared to normocapnia, reduced the decrement in systemic oxygenation and decreased lung permeability. HCA decreased bronchoalveolar lavage (BAL) neutrophil count (p<0.05) and reduced BAL CINC-1 and IL-6 levels. In moderate VILI, HCA reduced lung injury and decreased the degradation of the cytoplasmic NF-κB inhibitor, IκBα.

Discussion and Conclusions
These findings demonstrate that hypercapnic acidosis reduces ventilator induced inflammation and lung injury in an in vivo rat model of VILI via inhibition of the NF-κB dependent signalling pathway. Furthermore, the severity of injury seems to determine the detectability of early and late inflammatory signals in response to HCA in VILI.

References:

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