



## Evidence-Based Medicine Journal Club

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### Journal club critique

## Hypercapnic acidosis in ARDS: A tolerated side effect or an important therapeutic modality?

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### Expanded Abstract

#### Citation

Kregenow DA, Rubenfeld GD, Hudson LD, Swenson ER. Hypercapnic acidosis and mortality in acute lung injury. Crit Care Med 2006;34:1-7 [1].

#### Background

Evidence suggests that hypercapnic acidosis may be beneficial in patients with acute lung injury, though studies have not separated the effects of HA from the effects of changes in mechanical ventilation.

#### Methods

**Objective:** We tested the hypothesis that hypercapnic acidosis is associated with reduced mortality rate in patients with acute lung injury independent of changes in mechanical ventilation.

**Design:** Secondary analysis of randomized clinical trial data using hypothesis-driven multivariate logistic regression.

**Setting:** Randomized, multiple-center trial comparing 12 mL/kg to 6 mL/kg predicted body weight (PBW) tidal volumes previously published by the National Institutes of Health Acute Respiratory Distress Syndrome (ARDS) Network.

**Subjects:** 861 acute lung injury patients enrolled in a randomized, multiple-center trial.

**Intervention:** None.

**Measurements and main results:** The adjusted odds ratio and 95% confidence intervals (CI) for 28-day mortality rate associated with hypercapnic acidosis defined as day 1 pH <7.35 and PaCO<sub>2</sub> >45 mm Hg were 0.14 (95% CI 0.03-0.70, p = .016) in the 12 mL/kg PBW tidal volume group and 1.18

(95% CI 0.59-2.35, p = .639) in the 6 mL/kg PBW tidal volume group. Other definitions of hypercapnic acidosis spanning a range of magnitudes suggest a dose-response association between hypercapnic acidosis and 28-day mortality in the 12 mL/kg PBW tidal volume group. None of our definitions of hypercapnic acidosis were associated with reduction in 28-day mortality in the 6 mL/kg PBW tidal volume group.

#### Conclusion

Hypercapnic acidosis was associated with reduced 28-day mortality in the 12 mL/kg PBW tidal volume group after controlling for co-morbidities and severity of lung injury. These results are consistent with a protective effect of hypercapnic acidosis against ventilator-associated lung injury that was not found when the further ongoing injury was reduced by 6 mL/kg PBW tidal volumes.

#### Commentary

Hypercapnic acidosis (HA) is often thought of as a tolerated side effect of lung protective ventilation strategies. There is a growing body of experimental evidence, however, suggesting that HA may be intrinsically protective in ventilator-induced lung injury and acute lung injury (ALI) [2-4] and that buffering HA may be detrimental [5]. Certain patient populations, such as those with cardiovascular disease or central nervous system injuries, have the potential to be harmed by HA. To date, no clinical trial has examined the independent effects of HA in patients with acute respiratory distress syndrome (ARDS) or ALI.

In the current study [1], Kregenow and coworkers explored the association of HA and mortality in a retrospective secondary analysis of 861 subjects with ALI/ARDS enrolled in the ARDS Network low vs. high tidal volume trial [6]. HA was defined as day 1 pH <7.35 and PaCO<sub>2</sub> >45 mm Hg.

The authors found that HA was associated with reduced 28-day mortality in the high tidal volume (12 mL/kg PBW), but not low tidal volume (6 mL/kg PBW), group after controlling for comorbidities and severity of lung injury. In the high tidal volume group, there was an apparent dose-response relationship between HA and mortality. The authors speculate HA may have mitigated high tidal volume-induced lung injury, an effect that was no longer significant when lung protective ventilation was utilized.

As with all observational studies, this study was intended to be hypothesis generating and does not prove cause and effect. The definition of HA was based on a single day 1 measurement, rather than by sustained HA over time. As noted by the authors, there were too few patients with sustained HA to evaluate its effects. Nevertheless, animal studies suggest a protective effect of even short duration HA. The lack of observed benefit in low tidal volume patients may be because there was no effect in this group or HA was not extreme enough to exert a physiologic benefit [3]. Because the authors did not have data on sodium bicarbonate use, dead space ventilation, or accurate estimates of CO<sub>2</sub> production, this study cannot address whether the mechanism of HA is important.

## Recommendation

A randomized clinical trial of HA in patients with ALI/ARDS undergoing lung protective ventilation seems warranted. However, greater extremes of HA than seen in the ARDS Network low vs. high tidal volume trial will likely be needed in order to see a benefit. Until the results of such a trial are available, we cannot recommend HA as a specific therapeutic goal. For now, HA remains a tolerated side effect of lung protective ventilation.

## Competing interests

The authors declare no competing interests.

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