CROSSTALK

Last Word on the CrossTalk proposal and opposing view: There is/there is not added benefit to providing permissive hypercapnia in the treatment of ARDS

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Uncertainty remains regarding potential benefit or harm of hypercapnia in ARDS. Diverse and sometimes competing molecular and physiological effects of hypercapnia require additional investigation to understand clinical translation.

We agree fully with the comments of our colleagues (CrossTalk Comments: Swenson & Lang; Cummins; Akca & Bautista). Carefully planned dose-finding human studies evaluating safety and biological mechanisms in patients are needed to move the debate forward. The numerous effects of CO₂, diversity of critical illnesses, and heterogeneity of disease processes classified as ARDS (which, as currently defined, has highly variable pathogenic mechanisms) virtually guarantee effect heterogeneity among patients.

Therefore, we advocate for individualized therapy trials as the next step. Study design must account for likely differences of effect across clinical scenarios (e.g. immunomodulation in infectious versus non-infectious ARDS) and physiological characteristics (e.g. presence of pulmonary vascular dysfunction, which may exacerbate consequences of CO₂-induced pulmonary vasoconstriction).

An ideal strategy may be to titrate CO₂ levels to pre-defined physiological and molecular biomarkers of potential benefit and harm. With this approach, the ‘CO₂ target’ may be reduced in patients with pulmonary hypertension and right ventricular failure, while in others it may be increased to affect immunomodulation or oxygen delivery. That is, a given level of CO₂ may create toxicity via tachycardia, pulmonary vasoconstriction and mitochondrial dysfunction in one patient but may be beneficial via reduced hyperinflammation and enhanced oxygen delivery in another. Without such individualized approaches (Talmor et al. 2008), finding a signal for therapeutic benefit or harm from hypercapnia will prove elusive.

Reference


Competing interests

J. R. Beitler and R. D. Hubmayr have no conflicts of interest to declare. A. Malhotra previously received consulting and/or research income from Philips, SGS, SHC, Apnex, Apnicure and Pfizer, but has relinquished all outside personal income since May 2012.

Published September 16, 2013