Reply: Carbon Dioxide Narcosis or Sleep Deprivation?

From the Authors:

We thank Drs. Aberegg and Carr for their interesting perspective on our patient (1). What they refer to as "assumptions," we prefer to think of as clinical hypotheses, which are formed on the basis of the information at hand. In clinical decision making, the hypothesis that is ultimately acted upon must not only be the one that is most supported by clinical evidence, but also the one that puts the patient at minimal risk if we are wrong. When we "assumed" that our patient's Pa_{CO_2} was rapidly climbing and that his altered level of consciousness was at least partially related to severe acidemia (pH 7.11) and hypercapnia (Pa_{CO_2} > 99 mm Hg), we were compelled to take appropriately proactive measures, including intubation and mechanical ventilation, to ensure his safety. Although Aberegg and Carr's alternative narrative of chronic sleep deprivation may be correct in a handful of patients, universally relying on that hypothesis to manage unstable patients with obesity hypoventilation syndrome (OHS) could lead to undertreatment of an inherently tenuous population that is at risk for rapid and catastrophic decompensation.

First, let us address the authors' assertion that Pa_{CO_2} is not affected by increasing Pa_{O_2}. In our study, we summarize the physiologic mechanisms that explain this relationship. Because peripheral chemoreceptors effect an increased ventilatory drive in states of hypoxia (Pa_{O_2} < ~55 mm Hg), the reversal of hypoxemia leads to relatively decreased drive. This can be devastating in patients with OHS, who are already, by definition, hypoventilating. The study the authors cited by Hollier and colleagues noted only a modest increase in Pa_{CO_2} after application of 28% oxygen (2). However, that study was not designed to address the point that we make in our study. Those patients did not suffer from chronic hypoxia, and therefore 28% oxygen was neither excessive nor clinically consequential for them. In our hypoxemic patient, application of 28% oxygen resulted in Pa_{O_2} > 150 mm Hg, which was excessive for him at the time. In studies that addressed excessive oxygen administration to patients with OHS, FI_{O_2} values of 0.5 (2) and 1.0 (3) both led to significant increases in Pa_{CO_2}.

Next, let us address our patient's acute change in mental status. Regardless of the etiology, noninvasive ventilation (NIV) for a somnolent, morbidly obese patient with a pH of 7.11 who appears to be in the midst of clinical decompensation is fraught with risk. Although NIV may be as effective as invasive mechanical ventilation for augmenting minute ventilation and improving CO_2 elimination, it does nothing to address the issue of airway protection in a patient with an inherently difficult airway (recall our patient's body mass index of 81 kg/m^2). Choosing NIV for a patient who will ultimately decompensate and require endotracheal intubation is associated with an increased risk of intubation-related complication and death (4).

Finally, let us address acetazolamide administration in patients with compensated respiratory acidosis. It is important to note that the bicarbonate elevation in our patient was not purely compensatory and was partially the result of diuresis. We agree that hypercapnia alone, if well tolerated physiologically, is not reason enough to delay extubation in an otherwise stable patient. We are careful to point out that correction of iatrogenic metabolic alkalosis was performed in tandem with the "correction of other patient factors contributing to difficult weaning." Progressive metabolic alkalosis in patients with OHS likely contributes to a cycle of impaired CO_2 elimination that facilitates the transition from acute to chronic hypercapnia (5). As minute ventilation and Pa_{CO_2} are inversely related, when Pa_{CO_2} approaches extremely high values, a miniscule decrease in minute ventilation (as might occur in sleep, for example), will cause a disproportionately large increase in Pa_{CO_2} with potentially catastrophic effects. This is the result of the inverse hyperbolic nature of their relationship, with Pa_{CO_2} asymptotically approaching infinity as minute ventilation approaches zero. This phenomenon may be counteracted through the administration of acetazolamide (6), although outcome data from critically ill patients are lacking. Returning a patient to nearer his or her baseline acid–base equilibrium is a good rule of thumb, particularly if the disturbance is both iatrogenic and unintended.

In summary, although all of Aberegg and Carr's points are well made, I fear that they might serve to minimize the condition of a very ill individual who required a rapid change in management once the physiologic principles underlying his decompensation were understood. It is fascinating that the physiologic principles that drive patient care remain controversial, underlining the importance of the clinical physiologist.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References

1 Lanks CW, Sue DY, Rossiter HB. A Pickwickian problem: how is breathing controlled? *Ann Am Thorac Soc* 2019;16:138–143.
2 Hollier CA, Harmer AR, Maxwell LJ, Menadue C, Willson GN, Unger G, *et al*. Moderate concentrations of supplemental oxygen worsen hypercapnia in obesity hypoventilation syndrome: a randomised crossover study. *Thorax* 2014;69:346–353.
3 Wijesinghe M, Williams M, Perrin K, Weatherall M, Beasley R. The effect of supplemental oxygen on hypercapnia in subjects with obesity-associated hypoventilation: a randomized, crossover, clinical study. *Chest* 2011;139:1018–1024.
4 Mosier JM, Sakles JC, Whitmore SP, Hypes CD, Hallett DK, Hawbaker KE, *et al*. Failed noninvasive positive-pressure ventilation is associated with an increased risk of intubation-related complications. *Ann Intensive Care* 2015;5:4.
5 Norman RG, Goldring RM, Clain JM, Oppenheimer BW, Charney AN, Rapoport DM, *et al*. Transition from acute to chronic hypercapnia in patients with periodic breathing: predictions from a computer model. *J Appl Physiol (1985)* 2006;100:1733–1741.
6 Raurich JM, Rialp G, Ibáñez J, Llompart-Pou JA, Ayestarán I. Hypercapnic respiratory failure in obesity-hypoventilation syndrome: CO_2 response and acetazolamide treatment effects. *Respir Care* 2010;55:1442–1448.