Determinants of Daytime Hypercapnia in Obstructive Sleep Apnea

Is Obesity the Only One To Blame?

In contrast with COPD patients, patients with obstructive sleep apnea (OSA) have a priori normal respiratory mechanics and normal gas exchange during wakefulness. Increased upper airway resistance on sleep onset in OSA patients leads to intermittent or sustained alveolar hypoventilation during the night, but this process usually reverses within a short time after the patients wake up. However, about 30 to 40% of patients with OSA will continue to exhibit elevated PCO2 levels throughout the waking period, despite the absence of severe lung disease. In other words, OSA patients are at high risk for hypoventilation syndrome. Therefore, our primary gut feeling would be to attribute the daytime alveolar hypoventilation in patients with OSA to obesity, since it has been clearly implicated in the pathophysiology of OSA patients. Furthermore, we have now all become familiar with obesity hypoventilation syndrome (OHS), a complex condition that associates morbid obesity with severe daytime gas exchange abnormalities, such that we may have intuitively associated the daytime hypercapnia of OSA patients with obesity.

In this issue of CHEST, we are reminded that, as is usual in medicine, things are not so simple. Indeed, Akashiba and colleagues (see page 415) report on their analysis of potential correlates of daytime hypercapnia in 143 male patients with OSA. Using a stepwise logistic regression approach, these investigators found that 43% of the variance in daytime PaCO2 levels could be attributed to the mean oxyhemoglobin saturation during sleep and to the degree of vital capacity dysfunction, while the body mass index and the apnea index did not emerge from this analysis as exerting any additional effect on the predictive value of the model. Taken together, these findings would suggest that respiratory mechanics and nighttime hypoxemia may interact during sleep and during wakefulness in patients with OSA.

How do we reconcile these findings with those from patients with OHS? A unifying concept for the pathogenesis of OHS has been formulated in a recent editorial in CHEST by Teichtahl. Respiratory muscle fatigue and diminished ventilatory response to a respiratory load, adverse respiratory mechanics and decreased leptin levels or leptin receptor density, which may attenuate hypercapnic ventilatory responsiveness, may all interact to promote the development of OHS. However, while the possibility of respiratory muscle fatigue in patients with OSA has not been explored systematically, leptin levels are not low but, rather, have been found to be elevated in these patients. Indeed, the mean (± SD) leptin levels were 13.7 ± 1.3 ng/mL in 32 male patients with OSA whose conditions were newly diagnosed and had never been treated, and 9.2 ± 1.2 ng/mL in 32 similarly obese, closely matched subjects (p = 0.02). Thus, if leptin is indeed a modulator of central chemosensitivity, then OSA patients would be expected to display enhanced rather than attenuated CO2 ventilatory responses.

An alternative explanation to the daytime hypercapnia of OSA patients could involve the characteristics of the events occurring during sleep. This explanation, which is based on the observation that eucapnic and hypercapnic OSA patients do not exhibit major differences in the number and duration of apneic episodes that they experience during the night, proposes that the ventilatory output during sleep will play a major deterministic role in the daytime ventilation characteristics of OSA patients. Rapoport and colleagues identified the following two major components affecting daytime gas exchange in OSA: (1) the occurrence of sustained hypoventilation independent of apnea and therefore not reversed by continuous positive airway pressure therapy, which would primarily reflect a low level of ventilatory drive in the awake state; and (2) a critical interdependency between the overall ventilation during the time spent awake and asleep, and the degree of CO2 loading induced by the apneic episodes that is not compensated for during the post-apnea period. This second component was reversible with treatment of the apnea, such that conceptually, the balance between the kinetics of CO2 accumulation and elimination during the apnea and interapnea periods would impose the resultant PaCO2 level during the daytime. Thus, we could interpret the findings of Akashiba and colleagues as being indicative of close interactions between a ventilatory debt incurred during OSA-disturbed sleep (which can be modified by effective therapy) and intrinsic individual factors associated with respiratory drive and gas exchange. In this context, breath-by-breath measurements of CO2 and O2 levels during sleep and wakefulness may provide important insights into the potential imbalances in CO2 homeostasis that are generated during sleep in patients with eucapnia and hypercapnia during the
daytime and into the potential role of ventilation-perfusion mismatch, even during respiratory oscillatory conditions that are not associated with diminished ventilatory output (as exemplified by the studies of Rapoport et al15 and Berger et al16).

In summary, the study by Akashiba and colleagues allows us to further reinforce the concept that nighttime desaturation and vital lung capacity may contribute to the maintenance of CO₂ homeostasis and daytime PaCO₂ levels in OSA patients. However, we need to keep in mind that daytime eucapnia is the end result of a complex conglomerate of factors, for which no single factor can reliably account for the daytime PaCO₂ level in any given patient. Changes in cardiac output, ventilation-perfusion matching, metabolic rate and fuel type utilization, sleep stage, circadian regulation, obesity, intrinsic ventilatory drive, endocrine modulation, respiratory muscle strength and endurance, and pulmonary mechanics all seem to be active players in this complex equation, which allows for as many permutations as the number of individuals experiencing OSA.

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REFERENCES

Noninvasive Mechanical Ventilation at Home

Building Upon the Tradition

The modern era of mechanical ventilation began during the poliomyelitis epidemics of the mid-20th century. According to personal accounts from the late historian Gini Laurie and innovative engineer Jack Emerson, deaths from bulbar poliomyelitis inspired a dramatic global response similar to an allied army fighting a war against a merciless enemy.1,2 Noninvasive negative-pressure ventilation by the iron lung and other means had been the only weapons available.3 Mounting deaths from bulbar poliomyelitis demanded another maneuver: the modern positive-pressure ventilator (Engström4) and the use of positive-pressure ventilation by tracheostomy.5 These advances led to a reduction in mortality from bulbar polio from 90 to 20%, and the era of long-term invasive positive pressure ventilation was begun.6 Victory came because of the dedication of voluntary organizations and public awareness and support.4 In the United States, the work of the National Foundation-March of Dimes and the public made possible what would never have occurred otherwise.1,6 The definitive defeat of polio came from teamwork: the public responding to a crisis, clinicians and engineers developing innovative technologies, and interdisciplinary clinical teams—including patients—applying new techniques in dedicated respiratory-care centers building upon a foundation of combined extensive experience.1,2

One unexpected by-product of success was develop-