NEW RESEARCH

COMMENTARY

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The Complexities of Complex Sleep Apnea

Commentary on Montesi et al. Air leak during CPAP titration as a risk factor for central apnea. J Clin Sleep Med 2013;9:1187-1191.

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The discussion regarding the pathophysiology of complex sleep apnea (CompSAS, CPAP-emergent sleep apnea) has been taking place for about a decade, since the original description of this syndrome by Gilmartin et al.[1] Several mechanisms, including elevated chemoreceptor sensitivity, decreased arousal threshold, prolonged circulation time, and use of opioid medications have been suggested to induce central apneas in patients with obstructive sleep apnea (OSA) treated with continuous positive airway pressure (CPAP) and other methods. These diverse processes likely all have some merit as contributors to the pathophysiology of CompSAS, leading to the striking heterogeneity of phenotypes in this disorder.[2]

The work of Montesi et al.[3] introduces another piece to this puzzle. In a subset of patients with OSA and without significant cardiac disease, the authors observed an association between the appearance of central apneas at CPAP pressure controlling the airway obstruction and the mask leak at that pressure. Having divided their group of patients with OSA into patients displaying central apneas with central apnea index (CAI) of more than 5 (consistent with CompSAS) and less than 5, they reported significantly higher mask leaks in patients with higher CAIs. The authors speculate that improving mask leakage over time might be the factor responsible for known decline in central apneas with continued CPAP therapy in some patients.

Unfortunately, as the authors themselves admit, the design of the study does not allow making any conclusions as to the causal relationships between mask leak and central apneas, nor does it allow answering what about the leaking mask might make the central apneas appear. They propose that the higher CAIs observed in patients with leaking masks were due to an increased washout of the CO_2 in the upper airway dead space leading to a drop in pCO_2 closer to the apneic threshold, thus making the central apneas appear. While this is possible, the paucity of presented data (lack of polysomnographic variables such as arousal indices during the PAP titration, noninvasive measurements of pCO_2 at night, or blood gas pCO_2 following the treatment) does not support making any such firm conclusions. Taking another perspective, one might equally plausibly explain the association between leaks and CAI by increased arousals in patients with CompSAS; such arousals might then lead to frequent oscillations between sleep and wakefulness, with a known "sleep-onset central apnea" phenomenon. In this regard, lower sleep efficiency in patients with high CAI that Montesi et al. reported would also be consistent with findings of prior studies on CompSAS. Additionally, mask leakage could potentially be a phenomenon secondary to more fragmented sleep in patients developing central apneas for another reason.

Recognizing these methodological shortcomings of the study by Montesi et al., there remains an interesting point that warrants further exploration. The issue of decreasing of pCO_2 by PAP, either though breath holding and thus lowering physiological dead space (through the mechanism proposed by Fowler, a precious reference that the authors cite),[4] or via mask leakage causing dead space washout is still crucial in developing central apneas, and has practical applications. There is a growing body of evidence that increasing pCO_2 either by increasing dead space or timed supplementation with external CO_2 helps resolve central apneas in heart failure.[5] Going forward, analyzing the whole population of patients with CompSAS, (including those with heart failure excluded from the current study), measuring this drop in pCO_2, timing of central apneas to the arousals and periods of maximal mask leak, and longitudinal studies on mask leak and central apneas might give us more insight into the pathophysiology of CompSAS. Another area of untapped knowledge in this regard is the data contained in the CPAP compliance data, which typically report such leaks.

In the background of this research, there is another, more practical issue. There is an ongoing discussion about the most appropriate treatment for patients with CompSAS. While adaptive servoventilation offers better and faster control of obstructive and central apneas, it is also more costly than CPAP. Proponents of CPAP argue that, due to dynamic factors in a new CPAP user stabilizing sleep, such as decreasing chemoresponsiveness (and as Montesi et al. propose, improving mask leak), starting CPAP and "waiting and seeing" might be the best therapeutic option in patients with CompSAS. I do not think the data they present can just support this approach, both due to methodological shortcomings of the study and because many "real life" patients with CompSAS have comorbidities that would have excluded them from their study. Therefore, from the practical standpoint, the take home message to me is that one needs to pay close attention to the mask interface and its leakage during the PAP titration study, when trying to resolve the complexities of complex sleep apnea.

CITATION

Kuźniar TJ. The complexities of complex sleep apnea. *J Clin Sleep Med* 2013;9(11):1193-1194.

REFERENCES

1. Gilmartin GS, Daly RW, Thomas RJ. Recognition and management of complex sleep-disordered breathing. *Curr Opin Pulm Med* 2005;11:485-93.
2. Kuźniar TJ, Kasibowska-Kuzniar K, Ray DW, Freedom T. Clinical heterogeneity of patients with complex sleep apnea syndrome. *Sleep Breath* 2013;17:1209-14.
3. Montesi SB, Bakker JP, Macdonald M, et al. Air leak during CPAP titration as a risk factor for central apnea. *J Clin Sleep Med* 2013;9:1187-91.
4. Fowler WS. Lung function studies; the respiratory dead space. *Am J Physiol* 1948;154:405-16.
5. Wan ZH, Wen FJ, Hu K. Dynamic CO_2 inhalation: a novel treatment for CSR-CSA associated with CHF. *Sleep Breath* 2013;17:487-93.

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