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SLEEP MEDICINE PEARLS

Blowing past the apneic threshold

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An 81-year-old man with severe obstructive sleep apnea, hypertension, and obesity (body mass index 32 kg/m^2) presented to the sleep clinic for an initial evaluation. He has been on auto-titrating bilevel positive airway pressure (BPAP) with 2 L/min nocturnal oxygen for more than 10 years and has been adherent to therapy. He has no known cardiopulmonary disorder and was not on opiates, benzodiazepines, or other respiratory depressants. He denied tobacco, drug, or alcohol use. His initial sleep study, the indication for nocturnal oxygen supplementation, and serum bicarbonate level were not available for review. On a setting of inspiratory positive airway pressure $(IPAP)_{max}$ 24, expiratory positive airway pressure $(EPAP)_{min}$ 12, pressure support $(PS)_{max}$ 8, PS_{min} 4 (90th percentile IPAP/EPAP of 17/12 cmH_2O), his device download information showed a residual apnea-hypopnea index (AHI) of 5.9 events/h with a clear airway index of 4.3 events/h (**Table 1** and **Figure 1**). He was unsure why he was on 2 L/min nocturnal oxygen and wanted to discontinue it. He declined a PAP titration study, so the auto-titrating BPAP settings were changed to a fixed BPAP of 21/13 cmH_2O with plan for a follow-up machine download and overnight oximetry. Two months later, the download showed a markedly elevated AHI of 51.3 events/h and clear airway index 50.3 events/h (**Table 1**). Leaks were not a factor. He denied worsening symptoms or new medications. Nocturnal oximetry on room air with BPAP 21/13 cmH_2O showed an oxygen desaturation index of 13.4 events/h, mean oxygen saturation of 93.9%, O_2 nadir of 83%, and 13.7 minutes with SpO_2 < 88% (**Figure 2**).

QUESTION: What mechanism is responsible for the worsening central apneas observed with the fixed BPAP settings?

ANSWER: Hyperventilation caused the $PaCO_2$ to drop below the apneic threshold, eventually resulting in worsening central sleep apnea.

DISCUSSION

Arterial PCO_2 is a major stimulus for ventilation and is tightly regulated by the interrelation of chemoreceptors and the brainstem.[1,2] With sleep onset, tidal volume decreases and there is a small rise in $PaCO_2$.[2,3] Ventilation becomes very sensitive to small changes in $PaCO_2$ and maintaining $PaCO_2$ above the apneic $PaCO_2$ is crucial for rhythmic breathing.[2–4] For example, after an arousal-related hyperventilation, $PaCO_2$ can fall below the apneic threshold, leading to a central apnea, and breathing resumes once $PaCO_2$ is above the apneic threshold.[2,4] This arousal-related ventilatory overshoot can also be seen in Cheyne-Stokes respiration where arousals are associated with increased posthyperpnea apnea duration which contributes to ventilator instability.[5] A study in patients with tracheostomy showed that tracheostomy occlusion (experimental obstructive apnea) led to hyperventilation, hypocapnia, hypopnea, and cessation of inspiratory effort (central apnea) at the termination of the apnea, which suggests that obstructive apneas can increase risk of central apneas.[6]

With BPAP, the EPAP helps splint the airway while the IPAP–EPAP difference (pressure support) sustains ventilation by augmenting the tidal volume. One retrospective analysis study has shown that BPAP is more likely to worsen central apneas than continuous PAP.[7] Our patient had worsening central apneas because of hyperventilation. The increased pressure support led to a dramatic increase in tidal volume and decrease in respiratory rate (**Table 1** and **Figure 1**). This resulted in a higher minute ventilation which likely lowered his $PaCO_2$ below the apneic threshold, eventually causing central apneas. These respiratory changes occurred the same night that the machine settings were modified, which is evidence for the delicate balance of ventilation, $PaCO_2$, and apneic threshold.

Our patient's overnight oximetry showed significant desaturations which were likely due to the worsening apneic events on the fixed BPAP setting. This was supported by data from his machine download on the night of the overnight oximetry which showed an AHI of 42.8 events/h and clear airway index 41.9 events/h. His nocturnal oxygen supplementation was discontinued and the device settings were changed back to auto-titrating BPAP with $IPAP_{max}$ 20, $EPAP_{min}$ 12, PS 4. After 1 month of usage without oxygen, his 90th percentile pressures were 16.5/12.5 cmH_2O and his AHI improved to 5.8 events/h and clear airway index to 4.6 events/h (**Table 1** and **Figure 1**).

Since the patient declined a PAP titration study on his initial visit, an overnight oximetry on room air with the initial BPAP pressures would have been the better and more efficient approach to evaluate his nocturnal oxygen needs. Adjusting his BPAP settings by using the 90th percentile pressure from the device download would have been a safer method to decrease his AHI and avoid hyperventilation.

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1. With BPAP mode, EPAP opens the airway while the IPAP–EPAP difference (pressure support) augments the tidal volume.
2. PAP therapy can lead to a reduction in $PaCO_2$ below the apneic threshold, resulting in central apneas.
3. When there is a drastic increase in AHI or clear airway index with PAP, hyperventilation should be considered and a reduction in pressure should be undertaken.
4. Overnight oximetry is a cost-effective approach for evaluating the need for nocturnal oxygen

Table 1—Summary of auto-titrating BPAP settings and device download data.

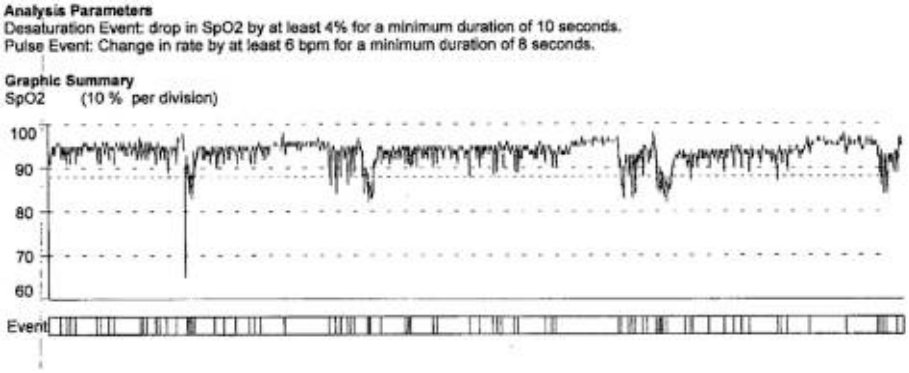
Date	Device Settings (cmH_2O)	90th percentile (IPAP/EPAP cmH_2O)	Average Tidal Volume, mL	Average Respiratory Rate (breaths/min)	AHI (events/h)	Clear Airway Index (events/h)
4/28/21 to 5/27/21	Auto-titrating BPAP Max IPAP: 24 Min EPAP: 12 Max PS: 8 Min PS: 4	17/12	423.8	22	5.9	4.3
5/28/21 to 8/9/21	IPAP: 21 EPAP: 13 PS: 8	21/13	881.1	12.4	51.3	50.3
8/10/21 to 9/8/21	Autotitrating BPAP Max IPAP: 20 Min EPAP: 12 Max PS: 4 Min PS: 4	16.5/12.5	516.8	16.7	5.8	4.6

A marked increase and then decrease in tidal volume, AHI and clear airway index occurred when BPAP settings were changed. AHI = apnea-hypopnea index, BPAP = bilevel positive airway pressure, EPAP = expiratory positive airway pressure, IPAP = inspiratory positive airway pressure, PS = pressure support.

Figure 1—Device download from April 28–September 8, 2021.

A graphic overview of the changes in clear airway index, tidal volume, and respiratory rate resulting from changes in inspiratory positive airway pressure and expiratory positive airway pressure.

Figure 2—Overnight oximetry on room air with bilevel positive airway pressure (BPAP) on July 23, 2021.



Oximetry on room air with BPAP 21/13 cmH_2O. Oxygen desaturation index (ODI) 13.4 events/h. Mean oxygen saturation of 93.9%. O_2 nadir: 83%. Total duration SpO_2 < 88%: 13.7 minutes.

supplementation, particularly when a PAP titration cannot be performed. The oxygen desaturation index and the overall pattern of desaturation can help identify the potential cause of the hypoxemia.

5. The 90th percentile pressures on device downloads can serve as an important guide for avoiding hyperventilation.

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All authors have seen and approved the manuscript. Work for this study was performed at the Roudebush VA Medical Center and Indiana University School of Medicine, Indianapolis. The authors report no conflicts of interest.