NEW RESEARCH

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COMMENTARY

Which OSA Patients Might Respond to Nasal Valves?

Commentary on Patel AV, et al. Predictors of response to a nasal expiratory resistor device and its potential mechanisms of action for treatment of obstructive sleep apnea. *J Clin Sleep Med* 2011;7(1):13-22.

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In this issue of *JCSM*, Patel and colleagues[1] address a second vital question regarding expiratory resistance devices: Which patients might benefit? The first vital question—Can expiratory resistance be used to treat OSA?—has already been addressed and the answer is possibly. Prior smaller studies and a recently reported large study by Berry et al.[2] have shown some improvement using an expiratory resistance device across a range of OSA severity. Specifically, the use of the expiratory resistance device lowered AHI by roughly 40% after 3 months of use. Approximately 50% of patients were labeled as complete responders (i.e., > 50% reduction OR residual AHI < 10/h), although the clinical benefit of a 50% reduction could be debated if substantial residual apnea persists. In addition, a considerable number of dropouts and the use of nasal pressure to define respiratory events (which may be insensitive during device-induced mouth breathing) complicate interpretation of these data. Subjective sleepiness was also improved compared to a sham device, albeit an incompletely blinded assessment. Assuming these results are reproducible and/or generalizable in clinical practice, and that expiratory resistance devices yield improvements in harder outcomes, these devices maybe a useful therapeutic option for selected OSA patients. Our limited clinical experience has been less favorable than the published data, emphasizing the importance of the Patel investigations.[1]

In Patel's relatively small sample, roughly 50% had improvement with the use of the device. However, among the patient characteristics tested, which included demographic, lung volume during wakefulness and polysomnographic measures, none was predictive of therapeutic benefit. This result is disappointing, and reminds us how little we know about OSA pathogenesis, or how these devices might work. So what characteristics or traits are important? Some have considered OSA as a multifactorial disease, with airway anatomy (defined by critical closing pressure, Pcrit), arousal threshold, control of breathing (loop gain), muscle recruitment, and lung volume during sleep all contributing to OSA to variable extents in different patients.[3] Although these contributing factors are not definitively related to the characteristics measured, the current study does shed light on the possible mechanisms underlying expiratory resistance devices.

As noted, those who had improvement with the device were able to "*generate* and *maintain* elevated end expiratory pressure," and that arousal was an important reason for treatment failure. This finding suggests that those who are least arousable (i.e., highest arousal threshold) are best able to respond favorably to expiratory resistance devices. Most of the available evidence suggests that pleural pressure generated by respiratory effort is the key trigger for inducing arousal from NREM sleep.[4] In the responders, the expiratory resistor created intrinsic positive end-expiratory airway pressure (PEEP) that could persist into the start of inspiration (see Figure 1 in original article). Non-responders may wake up prior to generating the more negative pleural pressures required to overcome PEEP to start inspiratory flow. Although the authors identify mouth opening as another cause of treatment failure (Figure 6 in original article), the proximate cause of mouth opening may be respiratory arousal.

If increased inspiratory effort is a disadvantage of intrinsic PEEP (i.e., requires a high arousal threshold to tolerate) what are the advantages to PEEP? Presumably PEEP provides a dilating force that opposes airway collapse and improves pharyngeal diameter by raising transmural pressure. Additionally, the authors observed that some patients are able to "pump up" nasal pressure with successive breaths, which should also literally pump up end-expiratory lung volume (EELV)—this assumption is supported, but not definitively confirmed, by lung volume data recorded during wakefulness. Based on a total respiratory system compliance in sleeping, obese OSA subjects of ~70 mL/cm H_2O, an EPAP of 10 cm H_2O should increase EELV ~700 cc; such an increase would be expected to improve Pcrit substantially (by 2-7 cm H_2O).[5,6] However, such conjecture must be balanced by the report from Heinzer, in which extrinsic expiratory positive airway pressure applied to sleeping OSA patients had no effect on EELV or AHI.[7] Instead, expiratory time increased to compensate for decreased expiratory flow, i.e., reduced duty cycle. Regardless, even if lung volume does increase, it may not be enough to overcome a very floppy airway, or lung hyperinflation may trigger arousal in some patients.[8,9] One other important consideration is the timing of airway collapse. Some patients occlude the airway during expiration due to passive collapse from a positive surrounding pressure; they should improve with a device that dilates the airway during expiration. Others (presumably with poor upper airway muscle responsiveness) have an open airway during expiration

and then suck the pharynx closed, or near closed, during inspiration.[10] These patients probably require inspiratory, not expiratory, positive pressure and would not be expected to improve greatly with expiratory resistance.

So who should benefit from an expiratory resistance device? We hypothesize that patients with a high arousal threshold, relatively poor upper airway anatomy, and collapse on expiration should benefit. We expect little improvement in those patients in which other factors such as ventilatory control instability, low arousal threshold, and poor pharyngeal muscle responsiveness are prominent pathogenic features. Patel's study highlights the need for comprehensive characterization of OSA pathophysiology in the research laboratory to elucidate mechanisms through which expiratory resistance might work. In the meantime, how could/should expiratory resistance be used clinically? Continuous positive airway pressure (CPAP) remains the treatment of choice for OSA. If CPAP will not/cannot be tolerated, expiratory resistance devices could be offered as an alternative therapeutic option. If tolerated, we would advocate for reassessment on therapy for residual disease (using hypoxemia and arousal criteria rather than nasal pressure-defined events). In areas of the world where CPAP is not readily available, expiratory resistance devices may also have a role, although cost-effectiveness analyses will be required to justify the ongoing expense of the disposable resistance devices.

Unfortunately, it remains unclear *a priori* which patients will benefit from such devices, although there appears to be little downside to a cautious therapeutic trial. Overall, we applaud the work by Patel et al. for reminding us that OSA is a complex, heterogeneous disease.

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