EDITORIAL

Stimulating Progress in the Upper Airway

Commentary on Dedhia et al. Upper airway stimulation for obstructive sleep apnea: past, present, and future. *SLEEP* 2015;38:899–906.

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Pathogenesis of obstructive sleep apnea (OSA) is multifactorial and largely due to anatomic predisposition, ventilatory control abnormalities, and ineffective pharyngeal dilator muscles.¹ Gold standard treatment for OSA is continuous positive airway pressure (CPAP), which provides a pneumatic splint of the upper airway. While impressively efficacious, CPAP use in the real world suffers from the same 50% compliance ceiling that plagues treatments of many other chronic diseases.² There has been a call within the sleep field to develop alternate treatment options not only to improve compliance, but also to personalize the approach to therapy. An intervention targeting specific pathogenic mechanisms of OSA, such as ineffective upper airway dilator muscles, offers the appeal of tailored therapy rather than a one-size-fits-all approach.

In this month's issue of *SLEEP*, Dedhia and colleagues³ review 25 years of progress in upper airway stimulation (UAS), including the multitude of proof-of-concept animal and human studies, which contributed to the recent FDA approval of this therapy. The authors are commended on their excellent review of the historical proof-of-concept studies leading to the recent randomized clinical trials of UAS therapy. Understanding the basis for this new therapeutic is critical in promoting acceptance and understanding of its role in the sleep physician's armamentarium. Their review by Dedhia et al.³ addresses commonly asked questions, including why unilateral lead placement suffices; whether this single lead results in concentric contraction of airway dilator muscles; whether multi-level activation of pharyngeal dilator muscles occurs; and what the role is of inspiratory gating for this device. One of the most interesting facets of this review is the discussion of the effectiveness of this device to address airway collapsibility at multiple levels, a novel departure from most other surgical interventions for OSA. Moreover, the steps involved in implantation of these stimulators are thoroughly described in the review.³ Given the fact that the device is not yet widely available, most readers of this review will benefit from these historical and current perspectives.

The approach to treating patients with OSA is complex and involves consideration of several available treatment modalities in concert with preferences of the patient. Compliance

with therapy is higher when patients are engaged in the decision-making process, thus patient education about sleep apnea is as important as the treatment being considered.⁴ Nonetheless, presenting treatment recommendations requires both knowledge of the relative efficacy of these therapies and an understanding of the likelihood of compliance with each option. CPAP, when tolerated, is still the most efficacious form of treatment, however compliance remains an issue. Similarly, mandibular repositioning devices may benefit patients whose airway obstruction is caused primarily by retrognathia or excessive posterior displacement of the mandible during sleep, but suboptimal insurance coverage and tolerance limit their utilization. Counseling of patients to lose weight is indicated, especially when a history of weight gain is clearly associated with the onset of OSA-related symptoms.

Determination of benefit from UAS is challenging for several reasons: (1) Assessment of candidacy has relied on drug-induced sedation endoscopy (DISE), requiring expertise which may not be locally available; (2) Costs associated with performing DISE might be prohibitive when placed in context of screening the substantial number patients intolerant of CPAP; (3) Even with selection as currently recommended, one third of patients do not completely respond to therapy.⁵ However, Dedhia and colleagues convincingly argue the cost-effectiveness of stimulation therapy versus no treatment may be worthwhile given risk of 10-year cardiovascular outcomes and daily dangers of drowsy driving. We agree for patients who cannot tolerate PAP therapy, and who meet the specific criteria for implantation in the STAR trial protocol, UAS should be considered.⁶

As with every new therapy, opportunities for future research are plentiful. The authors highlight several areas meriting further investigation, including the need for cost-effective and non-invasive assessments for UAS candidacy, and long-term outcome evaluations comparing the cost-effectiveness of different treatment options. With limited access to centers of excellence designated to perform this procedure, preliminary candidacy evaluations including DISE would ideally occur at the referring institution, particularly if long-distance travel is required for initial screening. In addition, more otolaryngologists should be trained to implant and oversee stimulation therapy in the context of chronic disease management. Increasing the number of providers capable of performing DISE, including otolaryngologists, pulmonologists, anesthesiologists, and other specialists trained in evaluation of the upper airway is needed for widespread implementation. Methods predicting candidacy other than DISE, including examination of specific

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flow patterns on sleep testing (e.g., negative effort dependence), advanced imaging, or other physiological investigations, may also facilitate wider consideration of this treatment option.

Additional questions remain regarding titration of the UAS device. Considerable night-to-night variability in AHI may not be adequately addressed by fixed stimulation patterns. Similarly, it is unclear how adjustments to the stimulator should be made, and by whom. Certainly, as the authors suggest, the development of “auto-titrating” stimulators would facilitate follow up and long-term management of the device. Lastly, it is important to note only 1 in 7 subjects enrolled in the STAR trial were deemed eligible for implantation, with most ruled out ($n = 347$) by having an apnea-hypopnea index $< 20/h$. With CPAP compliance poor and long term outcomes of uncertain significance at this lower level of apnea severity, the role of UAS is also questionable but worth further investigation.

In summary, the Dedhia et al.³ authors present convincing evidence that the science behind upper airway nerve stimulation has progressed substantially, and now presents a viable option for the treatment of OSA. While use should be currently confined to those patients intolerant of CPAP, further refinement and understanding of OSA may move UAS beyond its use as “salvage” therapy. Unlike initiation of CPAP, which is often a decision made between the patient and sleep practitioner, UAS implantation should involve a multidisciplinary

team approach, consisting of providers who will remain engaged in the long-term management of this chronic disease.

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DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.

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