Title

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Journal

Journal of Clinical Sleep Medicine, 16(4)

ISSN

1550-9389

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Publication Date

2020-04-15

DOI

10.5664/jcsm.8310

Peer reviewed

https://doi.org/10.5664/jcsm.8310

JCSM | Journal of Clinical Sleep Medicine

LETTERS TO THE EDITOR

Why do we sometimes ignore the chief complaint in patients evaluated for obstructive sleep apnea?

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> The good physician treats the disease; the great physician treats the patient who has the disease.
>
> —William Osler

During a recent call with the Food and Drug Administration, a respected colleague questioned the need for treatment of mild obstructive sleep apnea (OSA) based on society guidelines, which suggested that treatment may not be required.[1] At first glance, this skepticism of the need for treatment of mild OSA seems well founded based on randomized trials of continuous positive airway pressure (CPAP)[2,3]; however, we question the wisdom of this proscriptive approach for several reasons:

1. Patients often present to clinic because of snoring, which, in some cases, leads to marital discord and social embarrassment (and theoretical effects on carotid arteries, etc).[4–7] The response of many sleep clinicians is to rule out OSA—clearly a major priority—but a negative sleep test can often be the end of the evaluation/management. A study with an apnea-hypopnea index (AHI) < 5 events/h should clearly not be a time to declare victory until the patient's voice has been heard. Loud snoring is an important chief complaint, yet treatment in the absence of OSA will likely vary greatly by provider type: for example, while some sleep medicine internists provide reassurance, primary care physicians give nasal decongestants, otolaryngologists offer surgery, and dentists will often provide oral appliances. Some of this inconsistency may reflect patients "voting with their feet," but there is generally a lack of rigor in management of snoring per se.
2. Mild OSA is typically defined based on AHI, but there is no consistent AHI cutoff. The type of equipment used (nasal pressure, characteristics of the oximeter, etc) to measure AHI can be highly variable.[8] Moreover, home sleep testing versus in-lab polysomnography frequently relies on different denominators since the former commonly relies on recording time typically, whereas the latter uses total sleep time.[9] Even with standard equipment, night-to-night variability can add further variance (eg, based on positionality, sleep architecture, varying alcohol intake, etc). The definitions of hypopnea also vary widely, sometimes predicated on desaturation (of varying thresholds) and sometimes including arousal from sleep in the definition.[10–12] Rarely are these factors taken into consideration by the treating clinician or payor when trying to define an AHI threshold or cutoff.
3. Based on the foregoing, it may not be surprising that, although the AHI remains the standard predictor of OSA severity, it correlates only loosely with symptoms[13] or hard outcomes.[14,15] For example, even those with "mild" disease by AHI may experience a drop in blood pressure with positive airway pressure (PAP) therapy.[16] Of note, the optimal hypopnea definition likely depends on the outcome of interest since different levels of hypoxia predict insulin resistance versus hypertension, arousal frequency predicts memory consolidation, duration of desaturation predicts platelet aggregation, nothing reliably predicts motor vehicle accidents, etc.[17–22] This uncertainty in optimal hypopnea definition makes an optimal metric of OSA severity challenging to define since the ideal metric will likely depend on the outcome of interest.
4. The normal value for AHI is unclear.[23,24] Although thresholds of 5 or 15 events/h are commonly used, these values are relatively arbitrary with no evidence to our knowledge suggesting important biological differences between AHI = 4.8 events/h versus AHI = 5.2 event /h, for example. We have recently estimated up to 1 billion people affected by OSA globally, although this prevalence estimate also is highly subject to the definitions used.[25] Some have suggested that rather than an arbitrary threshold for AHI, perhaps, akin to cholesterol, a dose–response relationship may be a useful concept. That is, worsening AHI may predict worsening complications with no "safe" amount of hypoxia or asphyxia but rather "less is better."
5. The degree of change in AHI required to produce clinical improvements is unclear. Some have suggested that the elimination of apnea is a desirable goal and can be realistically achieved with nasal CPAP. However, in reality, some residual apnea is commonly present on PAP therapy and 100% adherence with PAP is only theoretically achievable. Thus, improvement but not

elimination of OSA is more realistically achievable even with "optimal" CPAP.[26,27] On the other hand, some have suggested that lowering of AHI (eg, a 50% reduction) may be a desirable goal, even though, to our knowledge, no compelling data have shown concomitant improvement in important health outcomes, for example, if AHI falls from 80 events/h to 40 events/h. As a result, many authors have used a composite endpoint including a relative and an absolute fall in AHI (eg, 50% reduction in AHI and a residual AHI <10 events/h); however, these criteria are again arbitrary. In some studies, improvement in vascular function has been observed with oral appliance therapy for OSA even when only modest AHI changes were observed, again speaking to the complexity in interpreting the AHI change.[28] Of note, treatment recommendations are logically based on risk/benefit assessments, such that the risk of surgery and the burden of CPAP may be important considerations. In contrast, for interventions that are safe and generally advisable, such as diet and exercise, we see no logical reason to restrict such recommendations to a certain arbitrary AHI level.[29] Thus, novel therapies (if safe, accessible, and cost-effective) may well change our approach to mild OSA management.

We are highly supportive of ongoing efforts to define new metrics of OSA severity, to develop new biomarkers, and to facilitate panels of biomarkers to predict important health outcomes.[30,31] Clearly, variability has been shown in mechanisms underlying OSA (endotypes) and in clinical expression of disease (phenotypes).[32–35] Thus, the optimal OSA metric will likely need to capture these sources of variability in order to predict accurately clinical complications and to guide optimal interventions.[36] Until such approaches are refined, we emphasize the importance of the patient's symptoms in making therapeutic decisions for a number of reasons. First, the phenotypic cluster including OSA patients with sleepiness appears to be at greatest cardiovascular risk, making targeted intervention of this group appealing to consider in well-designed clinical trials.[37] Second, studies of treating asymptomatic patients have been largely disappointing, showing no major benefits to therapy.[3] Similarly, studies to prevent major cardiovascular events by treating OSA have been negative to date.[38] Thus, focusing on treating symptoms would seem prudent until prevention of hard outcomes can be demonstrated persuasively. Third, we know of no other entity in clinical medicine where the chief complaint is routinely overlooked or ignored. In our view, the optimal treatment of medical conditions in general and sleep issues in particular should be individualized based on available data including patient-reported outcomes.[39]

CITATION

Malhotra A, Nokes B, DeYoung P, Owens R. Why do we sometimes ignore the chief complaint in patients evaluated for obstructive sleep apnea? *J Clin Sleep Med*. 2020;16(4):657–659.

ABBREVIATIONS

AHI, apnea-hypopnea index
CPAP, continuous positive airway pressure
OSA, obstructive sleep apnea
PAP, positive airway pressure

REFERENCES

1. Chowdhuri S, Quan SF, Almeida F, et al. An official American Thoracic Society research statement: impact of mild obstructive sleep apnea in adults. *Am J Respir Crit Care Med*. 2016;193(9):e37–e54.
2. Quan SF, Budhiraja R, Batool-Anwar S, et al. Lack of impact of mild obstructive sleep apnea on sleepiness, mood and quality of life. *Southwest J Pulm Crit Care*. 2014;9(1):44–56.
3. Barbé F, Mayoralas LR, Duran J, et al. Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness: a randomized, controlled trial. *Ann Intern Med*. 2001;134(11):1015–1023.
4. Hoffstein V, Mateika S, Hanly P. Snoring and arousals: a retrospective analysis. *Sleep*. 1995;18(10):866–872.
5. Hoffstein V. Snoring and hypertension. *Prog Clin Biol Res*. 1990;345:371–375; discussion 375-376.
6. Hicks RA, Bautista J. Snoring and nightmares. *Percept Mot Skills*. 1993;77(2):433–434.
7. Hu FB, Willett W, Manson JE, et al. Snoring and risk of cardiovascular disease in women. *J Am Coll Cardiol*. 2000;35(2):308–313.
8. Ng Y, Joosten SA, Edwards BA, et al. Oxygen desaturation index differs significantly between types of sleep software. *J Clin Sleep Med*. 2017;13(4):599–605.
9. Hedner J, White DP, Malhotra A, et al. Sleep staging based on autonomic signals: a multi-center validation study. *J Clin Sleep Med*. 2011;7(3):301–306.
10. American Academy of Sleep Medicine. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in adults. *Sleep*. 1999;22(5):667–689.
11. American Academy of Sleep Medicine. *International Classification of Sleep Disorders: Diagnostic and Coding Manual*. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
12. Ruehland WR, Rochford PD, O'Donoghue FJ, Pierce RJ, Singh P, Thornton AT. The new AASM criteria for scoring hypopneas: impact on the apnea hypopnea index. *Sleep*. 2009;32(2):150–157.
13. Gottlieb DJ, Whitney CW, Bonekat WH, et al. Relation of sleepiness to respiratory disturbance index: the Sleep Heart Health Study. *Am J Respir Crit Care Med*. 1999;159(2):502–507.
14. Redline S, Yenokyan G, Gottlieb DJ, et al. Obstructive sleep apnea-hypopnea and incident stroke: the Sleep Heart Health Study. *Am J Respir Crit Care Med*. 2010;182(2):269–277.
15. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med*. 2001;163(1):19–25.
16. Bakker JP, Edwards BA, Gautam SP, et al. Blood pressure improvement with continuous positive airway pressure is independent of obstructive sleep apnea severity. *J Clin Sleep Med*. 2014;10(4):365–369.
17. Terán-Santos J, Jimenez-Gomez A, Cordero-Guevara J; Cooperative Group Burgos-Santander. The association between sleep apnea and the risk of traffic accidents. *N Engl J Med*. 1999;340(11):847–851.
18. Punjabi N, Sorkin J, Katzel L, Goldberg A, Schwartz A, Smith P. Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. *Am J Respir Crit Care Med*. 2002;165(5):677–682.
19. Punjabi NM, Ahmed MM, Polotsky VY, Beamer BA, O'Donnell CP. Sleep-disordered breathing, glucose intolerance, and insulin resistance. *Respir Physiol Neurobiol*. 2003;136(2-3):167–178.

20. Punjabi NM, Newman AB, Young TB, Resnick HE, Sanders MH. Sleep-disordered breathing and cardiovascular disease: an outcome-based definition of hypopneas. *Am J Respir Crit Care Med*. 2008;177(10):1150–1155.
21. Djonlagic I, Saboisky J, Carusona A, Stickgold R, Malhotra A. Increased sleep fragmentation leads to impaired off-line consolidation of motor memories in humans. *PLoS One*. 2012;7(3):e34106.
22. Rahangdale S, Yeh SY, Novack V, et al. The influence of intermittent hypoxemia on platelet activation in obese patients with obstructive sleep apnea. *J Clin Sleep Med*. 2011;7(2):172–178.
23. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol*. 2013;177(9):1006–1014.
24. Heinzer R, Vat S, Marques-Vidal P, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. *Lancet Respir Med*. 2015;3(4):310–318.
25. Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med*. 2019;7(8):687–698.
26. Malhotra A, Crocker ME, Willes L, Kelly C, Lynch S, Benjafield AV. Patient engagement using new technology to improve adherence to positive airway pressure therapy: a retrospective analysis. *Chest*. 2018;153(4):843–850.
27. Weaver TE, et al. Night-to-night variability in CPAP use over the first three months of treatment. *Sleep*. 1997;20(4):278–283.
28. Itzhaki S, Dorchin H, Clark G, Lavie L, Lavie P, Pillar G. The effects of 1-year treatment with a herbst mandibular advancement splint on obstructive sleep apnea, oxidative stress, and endothelial function. *Chest*. 2007;131(3):740–749.
29. Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. *Arch Intern Med*. 2009;169(17):1619–1626.
30. Montesi SB, Bajwa EK, Malhotra A. Biomarkers of sleep apnea. *Chest*. 2012;142(1):239–245.
31. Bhattacharjee R, Khalyfa A, Khalyfa AA, et al. Exosomal cargo properties, endothelial function and treatment of obesity hypoventilation syndrome: a proof of concept study. *J Clin Sleep Med*. 2018;14(5):797–807.
32. Ye L, Pien GW, Ratcliffe SJ, et al. The different clinical faces of obstructive sleep apnoea: a cluster analysis. *Eur Respir J*. 2014;44(6):1600–1607.
33. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. *Lancet*. 2014;383(9918):736–747.
34. Sands SA, Mebrate Y, Edwards BA, et al. Resonance as the mechanism of daytime periodic breathing in patients with heart failure. *Am J Respir Crit Care Med*. 2017;195(2):237–246.
35. Loewen A, Ostrowski M, Laprairie J, et al. Determinants of ventilatory instability in obstructive sleep apnea: inherent or acquired? *Sleep*. 2009;32(10):1355–1365.
36. Schmickl CN, Owens RL, Edwards BA, Malhotra A. OSA endotypes: what are they and what are their potential clinical implications? *Curr Sleep Med Rep*. 2018;4:231–242.
37. Mazzotti DR, Keenan BT, Lim DC, Gottlieb DJ, Kim J, Pack AI. Symptom subtypes of obstructive sleep apnea predict incidence of cardiovascular outcomes. *Am J Respir Crit Care Med*. 2019;200(4):493–506.
38. McEvoy RD, Antic NA, Heeley E, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med*. 2016;375(10):919–931.
39. Weaver TE, Mancini C, Maislin G, et al. Continuous positive airway pressure treatment of sleepy patients with milder OSA: results of the CATNAP randomized clinical trial. *Am J Respir Crit Care Med*. 2012;186(7):677–683.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication January 1, 2020
Submitted in final revised form January 10, 2020
Accepted for publication January 10, 2020
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DISCLOSURE STATEMENT

A.M. and R.O. are funded by the National Institutes of Health. Resmed provided a philanthropic donation to UC-San Diego. A.M. received income from Merck for medical education related to drug discovery. R.O. is a Principal Investigator on a grant from Signifier Medical but receives no personal income from the company. The other authors report no conflicts of interest.