doi.org/10.58931/cait.2024.4163

Adult Obstructive Sleep Apnea: A Practical Guide for the Allergist

Jalal Moolji, MD
Adil Adatia, MD

Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder, affecting 15-30% of males and 10-15% of females in North America.[1,2] OSA is characterized by the recurrent obstruction of the upper airway during sleep resulting in apneas and hypopneas. OSA can be diagnosed using a home sleep apnea test (i.e., a level 3 sleep study) or a polysomnogram (PSG) (i.e., a level 1 study or PSG) in a supervised sleep laboratory which quantifies the number of apneas and hypopneas per hour using the apnea-hypopnea index (AHI). In broad terms, the diagnosis is made when an individual with symptoms or cardiac risk factors has an AHI of ≥5, or an asymptomatic individual has an AHI of ≥15.[3] Continuous Positive Airway Pressure (CPAP) is considered the first-line treatment of OSA. Other treatment options include an oral appliance called a mandibular advancement device, or multilevel surgery of the upper airway, especially uvulopalatopharyngoplasty (UPPP).[4] Herein we review OSA in the context of conditions commonly observed in the allergy clinic, namely asthma, chronic rhinosinusitis, rhinitis, and contact dermatitis.

OSA in Asthma

Asthma is a highly prevalent respiratory disease affecting ~8% of Canadian adults.[5] Roughly 5–10% of asthmatics have severe asthma, which is defined by inadequate control, despite intensive treatment with high-dose inhaled corticosteroids (ICS), long-acting beta agonists, or oral corticosteroids (OCS). A broader category, difficult-to-treat asthma, encompasses those whose condition remains unmanaged owing to factors such as treatment non-compliance or the presence of other medical conditions.[6] Among these, OSA is emerging as a significant comorbidity.

Given that the adult prevalence of moderate-to-severe OSA (AHI ≥15) ranges from 6% to 17%,[7] a considerable overlap between asthma and OSA in patients is anticipated. However, emerging evidence underscores a potential bidirectional link between asthma and OSA beyond simple coincidence. A meta-analysis conducted in 2017 found that approximately 50% of asthma patients have OSA and the odds ratio for prevalent OSA in asthmatics was 2.64.[8] Incident OSA is also increased in asthma. The prospective Wisconsin Sleep Cohort study found that the relative risk of developing OSA and OSA with habitual sleepiness in asthmatics was 1.39 and 2.72, respectively, after adjusting for relevant confounders such as body mass index (BMI).[9] A key reason for the increased risk of incident OSA in asthmatics may be the cumulative effects of intermittent bursts of OCS used to treat exacerbations. A recent study from the United Kingdom using primary care databases studied >450,000 asthmatics receiving intermittent OCS and found a strong, dose-dependent relationship between OCS use and OSA, which exceeded the risk between OCS use and commonly cited adverse outcomes such as diabetes and osteoporosis.[10] Conversely, OSA has also been identified as a factor contributing to frequent exacerbations in patients with difficult-to-treat asthma,[11] highlighting the intricate interplay between these conditions.

Despite the clear epidemiologic relationship between OSA and asthma in adults, the mechanisms underlying this association are poorly understood. There does however appear to be an effect of OSA on the inflammatory endotype in severe asthma. A study of more than 300 patients in the Severe Asthma Research Program found that probable OSA (based on questionnaire data) was associated with sputum neutrophilia, but not eosinophilia.[12] Similarly, a prospective cohort of 55 severe asthmatics with OSA, confirmed using home

sleep apnea tests, found that those with OSA had a greater proportion of neutrophils and greater concentrations of the non-type 2 inflammatory cytokine interleukin-18 (IL-18), in induced sputum.[13] Interestingly, in a recent placebo-controlled crossover study of severe asthmatics treated with the biologic treatment benralizumab, patients with a persistently high symptom burden despite benralizumab treatment also had elevated levels of IL-18 in their sputum.[14] Together these data raise the question of whether ongoing respiratory symptoms refractory to biologic treatments could be due to unrecognized OSA.

There is limited evidence available regarding the effects of OSA treatment on asthma. In the only randomized placebo-controlled trial to date (n=37), CPAP therapy for three months did not improve asthma control (as measured by the Asthma Control Test score) but did improve daytime sleepiness and asthma-related quality of life.[15] CPAP also does not impact bronchial responsiveness to methacholine or lung function.[16]

Patients with asthma and OSA frequently also have gastroesophageal reflux disease and obesity and these collinear comorbidities must be considered together.[17] Patients with asthma and fixed airflow obstruction may have sleep-disordered breathing which resembles OSA-Chronic Obstructive Pulmonary Disease (COPD) overlap syndrome, and have significant hypoxemia associated with nocturnal hypoventilation. These patients are probably best referred to a respirologist with experience in sleep-disordered breathing.

In summary, allergists are advised to routinely assess patients with asthma for OSA, especially in cases of long-standing asthma, poorly managed symptoms, frequent bursts of OCS, and high-dose ICS therapy. Home sleep apnea tests are usually sufficient provided the lung function is normal or only mildly impaired. CPAP therapy should be considered, and adherence to this treatment stressed, given its capacity to diminish asthma-related morbidity and enhance life quality.

CPAP Rhinitis

CPAP rhinitis occurs primarily due to irritation of the nasal mucosa from the cold, dry air delivered by the CPAP machine. Symptoms typically include nasal congestion, dryness, and irritation, and the nasal mucosa appears dry and erythematous on anterior rhinoscopy. This probably results from damage to the nasal mucosa by cold, dry air under pressure. Nasal symptoms due to CPAP therapy are commonly cited as the reason for treatment non-adherence,[18] and allergists can thus play an important role in symptom control to improve compliance.

Reducing nasal mucosa dryness is the cornerstone of CPAP rhinitis management. Lubricating nasal gel or saline irrigation can relieve nasal discomfort, although petroleum jelly should be avoided due to the theoretical risk of lipoid pneumonia.[19] Adjusting the CPAP humidity settings can alleviate nasal symptoms; however, this does not necessarily improve device compliance. Ensuring a proper mask fit can prevent air leaks, maintain device efficacy, and improve comfort. A common problem is that the water chamber dries out before the end of the night resulting in nasal dryness, and this is usually due to excessive mask leak. Regular mask and filter replacements are recommended in accordance with manufacturers recommendations.[18]

Distinguishing CPAP rhinitis from other forms of rhinitis is vital for proper treatment. Symptoms such as conjunctivitis, frequent sneezing, seasonality, and aeroallergen sensitivity, point toward allergic rhinitis, which may occur alongside CPAP-induced rhinitis. For those with baseline allergic rhinitis, CPAP can exacerbate nasal congestion. Although intranasal corticosteroids usually do not treat CPAP rhinitis,[20] they could help with underlying allergic or vasomotor rhinitis. Patients should be advised to avoid the chronic use of nasal decongestants to prevent rhinitis medicamentosa.

In patients with CPAP rhinitis refractory to medical management, surgical interventions such as nasal septoplasty or turbinoplasty might enhance CPAP adherence. Alternatives to CPAP could also be considered. Oral appliance therapy, using custom-fitted devices, works well for mild-to-moderate OSA.[21] UPPP, suitable for various severities of OSA, involves the surgical modification of the airway to improve airway patency, but is less effective for individuals with a BMI greater than 40 kg/m.[4]

OSA in Chronic Rhinosinusitis

Chronic rhinosinusitis (CRS) is associated with poor sleep quality, snoring, increased AHI,

and CPAP intolerance.[22] Medical management of CRS with intranasal steroids may improve OSA symptoms and CPAP tolerance by ensuring the comfortable delivery of pressure through the nose. A small case series demonstrated that dupilumab improves OSA symptoms in patients with CRS with polyposis,[23] and further research in this area is warranted given the increasing use of biologic therapies to treat this condition. Flares of CRS due to bacterial infection do not appear to be caused by bacterial colonization of the CPAP reservoir.[24]

When considering referral to otolaryngology for surgical management of CRS, patients should be asked about OSA symptoms, and a home sleep apnea test should be obtained in suspected cases. The presence of significant OSA may tip the balance in favour of surgical intervention for CRS in patients who otherwise would not receive surgery. However, though OSA symptoms may improve with sinus surgery, it is generally not considered curative. In some cases, sinonasal surgery, specifically, nasal septoplasty, turbinoplasty, and polypectomy, may be specifically indicated for OSA treatment.[22]

CPAP mask contact dermatitis

Cases of allergic contact dermatitis caused by CPAP masks have been reported, although it appears to be rare. For example, cases have been reported involving masks containing silicone,[25] neoprene,[26] or dialkyl thioureas,[27] and masks that have been cleaned with benzisothiazolinone.[28] Sensitivity can be confirmed with patch testing. The major commercial manufacturers of CPAP interfaces do not use latex. The presence of an alternative diagnosis should be strongly considered (e.g., periorificial dermatitis in patients receiving ICS). Often, examining the cleanliness and state of repair of the equipment will immediately reveal the cause of the patient's facial irritation.

Conclusion

Atopic diseases are associated with OSA, and allergists may see many patients with symptomatic OSA that interferes with the control of their allergic diseases. Conversely, the allergic conditions themselves, such as asthma, may predispose the patient to OSA. The treatment of OSA may be an important component of the management of asthma, and the presence of OSA may alter the management of CRS. CPAP rhinitis should be considered in patients with rhinitis unresponsive to intranasal steroids. Allergists should be familiar with how patients at risk of OSA are evaluated in their community and initiate appropriate testing or referrals.

Correspondence

Adil Adatia, MD
Email: adatia@ualberta.ca

Financial Disclosures

AA: Consulting fees, travel support and/or honoraria: BioCryst, Covis Pharma, CSL-Behring, GSK, and Takeda and clinical trial support from AstraZeneca Canada, Astria, BioCryst, Ionis Pharmaceuticals, Kalvista, Octapharma, Pharvaris, and Takeda, outside of the submitted work.
JM: None declared.

References

1. Young T, Palta M, Dempsey J, Peppard PE, Nieto FJ, Hla KM. Burden of sleep apnea: rationale, design, and major findings of the Wisconsin Sleep Cohort study. WMJ. 2009;108(5):246-249.
2. 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. doi:10.1093/aje/kws342
3. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd ed, text revision. 2023.
4. Kent D, Stanley J, Aurora RN, Levine C, Gottlieb DJ, Spann MD, et al. Referral of adults with obstructive sleep apnea for surgical consultation: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2021;17(12):2499-2505. doi:10.5664/jcsm.9592
5. Statistics Canada (2023). Table 13-10-0096-08 Asthma, by age group. [Data table]. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009608
6. Global Initiative for Asthma. Fontana, WI, USA: 2023 GINA MainReport. Global Strategy for Asthma Management and Prevention; 2023 [Updated: 2024, Cited: 2024 April 02] Available from: https://ginasthma.org/2023-gina-main-report/.
7. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev. 2017;34:70-81. doi:10.1016/j.smrv.2016.07.002
8. Kong DL, Qin Z, Shen H, Jin HY, Wang W, Wang ZF. Association of obstructive sleep apnea with asthma: a meta-analysis. Sci Rep. 2017;7(1):4088. doi:10.1038/s41598-017-04446-6
9. Teodorescu M, Barnet JH, Hagen EW, Palta M, Young TB, Peppard PE. Association between asthma and

risk of developing obstructive sleep apnea. JAMA. 2015;313(2):156-164. doi:10.1001/jama.2014.17822
10. Heatley H, Tran TN, Bourdin A, Menzies-Gow A, Jackson DJ, Maslova E, et al. Observational UK cohort study to describe intermittent oral corticosteroid prescribing patterns and their association with adverse outcomes in asthma. Thorax. 2023;78(9):860-867. doi:10.1136/thorax-2022-219642
11. ten Brinke A, Sterk PJ, Masclee AA, Spinhoven P, Schmidt JT, Zwinderman AH, et al. Risk factors of frequent exacerbations in difficult-to-treat asthma. Eur Respir J. 2005;26(5):812-818. doi:10.1183/09031936.05.00037905
12. Teodorescu M, Broytman O, Curran-Everett D, Sorkness RL, Crisafi G, Bleecker ER, et al. Obstructive sleep apnea risk, asthma burden, and lower airway inflammation in adults in the Severe Asthma Research Program (SARP) II. J Allergy Clin Immunol Pract. 2015;3(4):566-575 e561. doi:10.1016/j.jaip.2015.04.002
13. Taille C, Rouvel-Tallec A, Stoica M, Danel C, Dehoux M, Marin-Esteban V, et al. Obstructive sleep apnoea modulates airway inflammation and remodelling in severe asthma. PLoS One. 2016;11(3):e0150042. doi:10.1371/journal.pone.0150042
14. Mukherjee M, Huang C, Venegas-Garrido C, Zhang K, Bhalla A, Ju X, et al. Benralizumab normalizes sputum eosinophilia in severe asthma uncontrolled by anti-IL-5 antibodies: a single-blind, placebo-controlled clinical trial. Am J Respir Crit Care Med. 2023;208(12):1330-1335. doi:10.1164/rccm.202308-1413LE
15. Ng SSS, Chan TO, To KW, Chan KKP, Ngai J, Yip WH, et al. Continuous positive airway pressure for obstructive sleep apnoea does not improve asthma control. Respirology. 2018;23(11):1055-1062. doi:10.1111/resp.13363
16. Lafond C, Series F, Lemiere C. Impact of CPAP on asthmatic patients with obstructive sleep apnoea. Eur Respir J. 2007;29(2):307-311. doi:10.1183/09031936.00059706
17. Althoff MD, Ghincea A, Wood LG, Holguin F, Sharma S. Asthma and three colinear comorbidities: Obesity, OSA, and GERD. J Allergy Clin Immunol Pract. 2021;9(11):3877-3884. doi:10.1016/j.jaip.2021.09.003
18. Moolji J, Adatia A. Managing CPAP rhinitis. J Allergy Clin Immunol Pract. 2024;12(3):796. doi:10.1016/j.jaip.2023.12.040
19. Kilaru H, Prasad S, Radha S, Nallagonda R, Kilaru SC, Nandury EC. Nasal application of petrolatum ointment - a silent cause of exogenous lipoid pneumonia: Successfully treated with prednisolone. Respir Med Case Rep. 2017;22:98-100. doi:10.1016/j.rmcr.2017.07.003
20. Strobel W, Schlageter M, Andersson M, Miedinger D, Chhajed PN, Tamm M, et al. Topical nasal steroid treatment does not improve CPAP compliance in unselected patients with OSAS. Respir Med. 2011;105(2):310-315. doi:10.1016/j.rmed.2010.10.003
21. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, et al. Clinical Practice Guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an update for 2015. J Clin Sleep Med. 2015;11(7):773-827. doi:10.5664/jcsm.4858
22. Ali MM, Ellison M, Iweala OI, Spector AR. A sleep clinician's guide to runny noses: evaluation and management of chronic rhinosinusitis to improve sleep apnea care in adults. J Clin Sleep Med. 2023;19(8):1545-1552. doi:10.5664/jcsm.10608
23. Bergmann K-C, Zuberbier T. Obstructive sleep apnoe improves on dupilumab in patients treated for polyposis and severe asthma. European Respiratory Journal. 2021;58(suppl 65):PA752. doi:10.1183/13993003.congress-2021.PA752
24. Chin CJ, George C, Lannigan R, Rotenberg BW. Association of CPAP bacterial colonization with chronic rhinosinusitis. J Clin Sleep Med. 2013;9(8):747-750. doi:10.5664/jcsm.2910
25. Prasad A, Reeder MJ. Allergic contact dermatitis to silicone in a continuous positive airway pressure mask. Contact Dermatitis. 2021;84(6):460-462. doi:10.1111/cod.13759
26. Patel F, Ghosh S, Chitkara A, Patel Z, Bhakta P, Mehdizadeh C, et al. CPAP machine noncompliance secondary to the facial rash caused by 30 years of neoprene sensitization. CHEST. 2023;164(4):A104-A105. doi:10.1016/j.chest.2023.07.121
27. Scalf LA, Fowler JF, Jr. Allergic contact dermatitis caused by dialkyl thioureas in a patient with sleep apnea. Am J Contact Dermat. 1999;10(3):169-171. doi:10.1016/s1046-199x(99)90061-1
28. Felmingham C, Nixon R, Palmer A, Lee A. Allergic contact dermatitis caused by benzisothiazolinone in a continuous positive airway pressure mask liquid soap. Contact Dermatitis. 2019;81(2):152-153. doi:10.1111/cod.13273