



EDITORIAL

All that wheezes at night is not asthma

Key words: asthma, nocturnal, obstructive sleep apnoea.

Nocturnal worsening of asthma has been recognized and described for centuries. Sir John Floyer, an English physician who himself had asthma, and was the first to ascribe bronchial constriction as its cause, wrote in 1698, 'I have observed the fit [asthma] always to happen after sleep in the night...'.¹ Henry Hyde Salter, another English physician and asthma sufferer (who died of asthma at age 48), wrote: 'In 19 cases out of 20... the dyspnea first declares itself on the patient's waking in the morning, or rather wakes him from his sleep when he has had but half a night's rest'. He concluded: 'The fact is, sleep favours asthma'.² Even in the modern era, nocturnal worsening of asthma remains common and is associated with worse outcomes, but interestingly, patients often fail to report symptoms.^{3,4} Thus, nocturnal symptoms are specifically elicited and included in commonly used metrics of asthma control, such as the Asthma Control Test. Despite its importance, the underlying pathophysiology of this nocturnal worsening is not fully understood and may relate to circadian changes in endogenous cortisol or other hormones, the sleep state and/or changes in lung mechanics, among others.

More recently, with increased rates of obesity and ageing, obstructive sleep apnoea (OSA) has likely displaced asthma as the most common respiratory disorder in adults worldwide and certainly in most developed countries. Thus, it is increasingly important to understand how these two very prevalent respiratory disorders interact. Epidemiological studies suggest that asthma is a risk factor for incident OSA and that sleep apnoea is very common in those with severe or difficult-to-control asthma—more so than would be expected based on age and body mass index alone.^{5,6} Treatment of moderate to severe OSA in those with asthma has generally shown subjective improvements in asthma control and quality of life without consistent change in objective measurements such as spirometry.^{7,8} Therefore, it seems likely that a complex interplay exists between asthma and OSA, complicated by possible shared risk factors, including obesity, gastroesophageal reflux and rhinosinusitis.

Relevant to the better understanding of this relationship between asthma and OSA is how these two diseases present clinically in the same person. The study by Senaratna *et al.* in *Respirology* explores this important question.⁹ The authors performed a cohort study of the larger Tasmanian Longitudinal Health Study (originally named and designed as the Tasmanian Asthma Survey in 1968), which consists of individuals likely to have asthma, and the participants are now middle aged (43–53 years). Close to 800 subjects

underwent questionnaires about asthma, nocturnal asthma symptoms and OSA risk using the STOP-BANG questionnaire, spirometry and a methacholine challenge test (We note that about half of the subjects ultimately did undergo portable sleep testing and that STOP-BANG was, as in other cohorts, sensitive but not specific for OSA¹⁰). They found that about one-third of the entire cohort were at high risk of OSA, a finding that was consistent among those with current asthma. In fact, in those with (generally mild) asthma reporting nocturnal asthma symptoms, half of these patients were found to be high risk for OSA. As the authors mention, these data suggest that those with nocturnal symptoms should undergo evaluation for sleep-disordered breathing and that it will be found much of the time. However, based on the test characteristics for STOP-BANG, which is sensitive but not specific, and the prevalence of OSA, while most patients with OSA will be identified (true positives), there will be slightly more who undergo testing who ultimately do not have OSA (false positives). Thus, the optimal screening test and/or cut-off value is yet to be determined, especially as most of the data regarding benefits of OSA treatment in asthma come from those with moderate to severe sleep-disordered breathing.

Detection and treatment of OSA are worthy goals in and of themselves. However, detection of OSA might also prevent use of unnecessary medications with potential side effects. The 2019 Global Initiative for Asthma guidelines suggest that a person with asthma with 'any night waking due to asthma' is considered 'partly controlled' (www.ginasthma.org). Inhaled corticosteroid-containing treatment is now recommended for all adults with asthma, highlighting the importance of discriminating poorly controlled asthma from OSA. Inhaled corticosteroids have side effects, including possibly compromising upper airway patency such that the inadvertent use of corticosteroids for nocturnal symptoms due to OSA has the potential to worsen OSA and nocturnal symptoms.¹¹

The crux of the problem is that the patient with asthma and/or OSA who 'wheezes' at night (or is short of breath, coughing, choking, etc.) will undergo a different evaluation and management depending on the training and experience of the provider. While Senaratna *et al.* believe that their 'findings raise the possibility that OSA and nocturnal asthma symptoms may be confused in the general-practice setting', we would suggest that this confusion can occur in many settings. Certainly, much work needs to be carried out, given the cross-sectional nature of this study, to further clarify the strength and direction of the relationship between asthma and OSA across disease severity and phenotypes of both diseases. In the meantime, a report of night-time awakenings in a person with asthma

should at least prompt the healthcare provider to consider an alternate, perhaps equally likely, diagnosis of clinically relevant OSA.

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