Residual Daytime Sleepiness in Obstructive Sleep Apnea After Continuous Positive Airway Pressure Optimization

Causes and Management

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KEYWORDS

• Excessive daytime sleepiness • Sleep disorders • Comorbid conditions • CPAP
• Wakefulness promoters • Modafinil • Armodafinil

KEY POINTS

- Excessive daytime sleepiness (EDS) is common in obstructive sleep apnea (OSA) but is also common in the general population.
- The causes of EDS in OSA may not all be related to the OSA, and EDS may remain even with high use of continuous positive airway pressure (CPAP) therapy.
- For these patients, finding and directly treating potential alternative causes of EDS should be considered.
- Modafinil or armodafinil are the only pharmacologic agents indicated for residual sleepiness despite CPAP use in OSA.
- Further research into identifying which patients are vulnerable to the daytime effects of OSA and who is likely to respond best to each treatment is required.

PREVALENCE AND PREDICTORS OF RESIDUAL SLEEPINESS IN OBSTRUCTIVE SLEEP APNEA

A long-standing clinical conundrum in sleep medicine has been patients with obstructive sleep apnea (OSA) who remain excessively sleepy despite effective use of well-fitted continuous positive airway pressure (CPAP) therapy. Residual sleepiness has been estimated to occur in 5% to 55% of CPAP users.[1,2] In a clinical sample that excluded poor CPAP users, the estimated rate of

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residual daytime sleepiness was 12%, and when other sleep disorders and major depression were excluded as confounders the remaining prevalence was 6%.[3] However, it is difficult to predict the individuals who will have this residual sleepiness because studies have been small and conflicted.[1,2]

When determining the cause of residual sleepiness in CPAP-treated OSA, it should be remembered that, even in community-based samples, only a very weak association exists between daytime sleepiness and OSA severity.[4] Individuals with mild OSA can have high levels of EDS and individuals with severe OSA may have no symptoms of hypersomnolence.[4] Factors that may contribute to excessive daytime sleepiness (EDS) are shown in **Fig. 1** and outlined in more detail later.

The accepted prevalence of OSA (defined as an apnea hypopnea index [AHI] >5) in middle-aged men is 25% and 15% for women.[5,6] More recent prevalence estimates are as high as 80% for men and 60% for women.[7] At the same time, population-based prevalence estimates of EDS as measured by the Epworth Sleepiness Scale (ESS) are around 15%.[4,8,9] Even if these conditions (OSA and EDS) were completely unrelated, simply multiplying the prevalence of these two conditions together gives an expected coprevalence of around 4% to 20%. The accepted prevalence of sleep apnea syndrome, the combination of OSA and EDS, is between 4% and 12%[5,6,10] EDS is also associated with obesity independent of the effects of OSA.[11] It might therefore be that in individual patients only a portion of their daytime sleepiness symptoms are attributable to sleep apnea. The clinical trial data testing CPAP support this, with mild reductions in daytime sleepiness after controlling for placebo effects.[12,13] EDS may also persist in these patients because of long-term intermittent hypoxia before treatment of OSA, which may lead to irreversible changes in the brain, as has been suggested in mouse models.[14] Studies examining this patient group have found that they tend to have more reduced daytime functioning, fatigue, and poorer general health than those without residual sleepiness.[1,15,16]

This article discusses the prevalence and causes of residual sleepiness in CPAP-treated OSA, provides a diagnostic work-up for clinicians encountering this population, and discusses the treatment of these individuals.

Fatigue or Sleepiness?

Although daytime fatigue and daytime sleepiness are distinct symptoms, they have overlapping

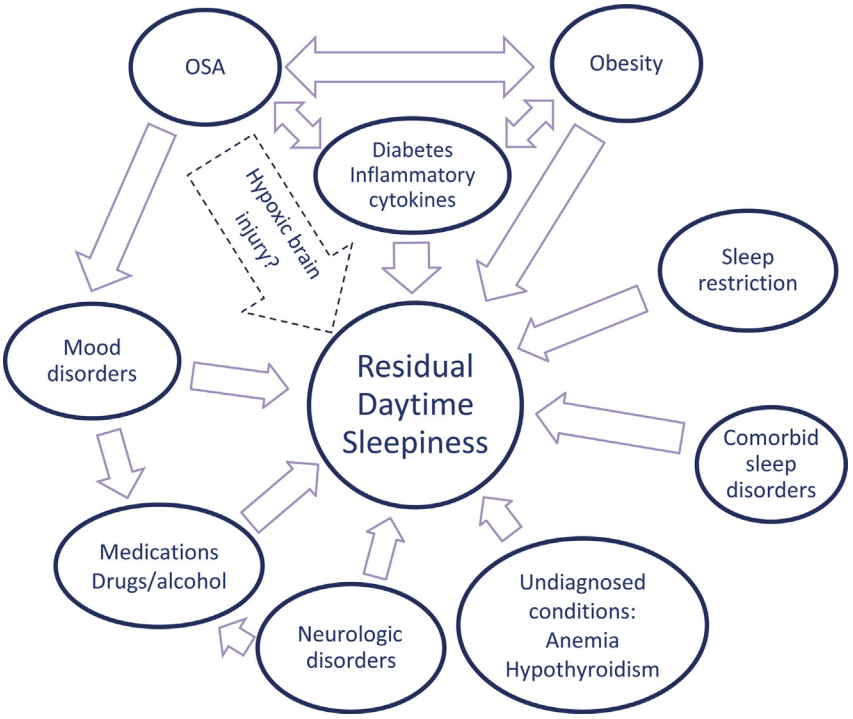

Fig. 1. Factors in ovals are potential contributing factors to the cause of residual daytime sleepiness in OSA. Arrows represent the direction of effects.