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EDITORIALS

Obstructive sleep apnea in women: scientific evidence is urgently needed

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No one doubts that obstructive sleep apnea (OSA) is a significant public health problem, because of its high prevalence and negative consequences for the general population.[1] Therefore, the treatments of choice are diet and sleep-hygiene measures and continuous positive airway pressure (CPAP) for symptomatic forms.

One of the peculiarities of OSA is its significant heterogeneity, in both its clinical presentation and its evolution, especially regarding age and sex.[2,3] The classic clinical presentation of OSA referred to and followed up in sleep units is that of a man who is middle-aged, obese, and hypertensive with daytime hypersomnia. Based on this type of patient, most observational studies and clinical trials have indicated the effectiveness of CPAP treatment and the relationship of OSA with various cardiovascular and neurocognitive diseases.

A large number of studies have shown that the quality and structure of sleep and the polysomnographic findings of sleep-disordered breathing are different in men and women. Other clinical differences are related to the anatomic structure of the pharynx, the clinical presentation and impact of OSA, and the effects of CPAP use. These differences probably result, at least in part, from women's specific hormonal status and more frequent comorbidities related to anxiety and depression and their treatments (**Table 1**).[4] Moreover, the most widely used instruments for self-reported measurement of hypersomnia, such as the Epworth Sleepiness Scale, are not validated in women in any age range, and the presence of hypersomnia (the key symptom that usually guides the indication of CPAP treatment) and felt different by women than by men with OSA.[5] Nevertheless, following the indications of most international guidelines, the diagnosis and treatment of women in OSA in sleep units are also performed on the basis of extrapolating the results of studies in middle-aged men.

According to the results of the HypnoLaus population-based study,[1] the prevalence of OSA in women ages 35–75 years is very high (60.8% among those with an apnea-hypopnea index ≥ 5 events/h and 23.4% among those with an apnea-hypopnea index ≥ 15 events/h); therefore, the lack of available knowledge on almost all aspects of OSA in women, including the effect of CPAP and its prognosis, is very striking.

Most of the evidence on the prevalence and impact of OSA in women is based on pregnancy and on patients with polycystic ovaries. However, these are not the profiles most frequently

Table 1—Main differences in sleep and sleep-disordered breathing between women and men.

Anatomic and physiological differences
• Differences in ventilator response to chemical stimuli, with men more susceptible.
• Hormonal status (menstrual cycle and menopause). Peaks of estradiol and progesterone are associated with an increased number of awakenings and more time spent awake.
• Pregnancy.
• Sex differences in upper airway anatomy and function (women have a more stable upper airway and are less susceptible to CPAP).
• Differences in neck circumference, waist-to-hip ratio, and abdominal obesity.
Polysomnographic findings
• Women present longer total sleep time, longer sleep latency, less slow-wave sleep, better objective sleep quality, shorter sleep onset latency, and better sleep efficiency.
• Fewer AHI events/h, more partial obstruction, and shorter events in women.
• Less severe OSA during the REM sleep phase in women.
• More supine OSA in men.
• More RERA in women.
Comorbidities
• More anxiety and depression, and more insomnia impacting sleep in women.
• Ovarian and hormonal disorders.
• More use of antipsychotics, antidepressants, and anxiolytics in women.
Symptoms related to OSA
• At the same level of OSA severity as men, women present a lower QoL.
• Women have fewer witnessed apneas because they more often come alone to clinical appointments and live alone.
• Less OSA classic symptomatology (more frequent insomnia, difficulties falling asleep, more awakenings and leg cramps) in women.
• Women have more pronounced sleepiness, albeit less specific as a consequence of their increased prevalence of disorders and treatment associated with hypersomnia.
Prevalence and health care
• More prevalence in men, even in older adult patients.
• Women less likely to seek help for OSA symptoms.
• Women's higher health care consumption (eg, comorbidities, depression, anxiety).

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Table 1—Main differences in sleep and sleep-disordered breathing between women and men. (*Continued*)

CPAP factors
• Women achieve less pressure with the same OSA severity (lower pharyngeal critical closing pressure in women).
• Reverse elevated systemic inflammation faster in men.
• Conflicting results with respect to adherence.

AHI = apnea-hypopnea index, CPAP = continuous positive airway pressure, OSA = obstructive sleep apnea, QoL = quality of life, REM = rapid eye movement, RERA = respiratory effort–related arousal.

observed in sleep laboratories.[6] Regarding the effect of CPAP treatment on women, so far there have been, surprisingly, only 1 relatively small clinical trial (307 women with an apnea-hypopnea index ≥ 15 events/h randomized to CPAP or placed under conservative treatment for 3 months)[7] and 1 large observational study (1,116 women followed up for a median of 72 months).[8] These two clinical-based studies suggested a positive effect of CPAP on sleep symptoms, mood state, and neurocognitive and cardiovascular outcomes in women with moderate-to-severe OSA. On the basis of these data, a large number of questions arise: Are simplified diagnostic methods valid in women? How does age influence OSA in women? Should we adopt the same CPAP treatment parameters and algorithms as in men? Is the impact of OSA on the neurocognitive and cardiovascular spheres comparable in men and women? Are clinical tests such as the Epworth Sleepiness Scale valid for selecting which patients are symptomatic or for making therapeutic recommendations?

Our editorial aims to draw the urgent attention of the sleep scientific community to this issue so that more extensive clinical trials and well-designed observational studies can be conducted to obtain some robust answers. In the meantime, the diagnosis and treatment of OSA in women of all ages will continue to be carried out by extrapolating the procedures usually performed in middle-aged men, which does not seem to be the most appropriate practice. It is the only one we have, however, until new scientific evidence arrives.

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