REVIEW ARTICLE

Sleep Disorders in Women

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Abstract

Women are more likely to have sleep-related illnesses than men. However, the diagnosis is frequently missed since the symptoms are often atypical in women. Hormonal cycles and changes during life impact the symptomatology and severity. Women are more likely to have an atypical presentation of obstructive sleep apnea (OSA) and a higher prevalence of insomnia and restless leg syndrome (RLS). We present the gender-based differences in pathophysiology and presentation of sleep illnesses. We also present the treatment differences to keep in mind while managing sleep illnesses in women. Awareness of these differences can help improve sleep health and overall quality of life in women.

Keywords: Insomnia, Pathophysiology, Symptomatology.

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Introduction

Sleep is essential for normal physiological function. Sleep disruption or chronic deprivation can cause neurocognitive impairment, depression, anxiety, metabolic diseases, and cardiovascular events.[1,2] There are key gender-based differences in sleep architecture in the adult human. diseases. These are caused by biological, environmental, social, and cultural influences.[3] The result is that disease presentation varies considerably between men and women.[3,4] The prevalence of sleep disorders in women varies with stages of life: 16–42% in premenopausal, 39–47% in perimenopausal, and 35–60% in postmenopausal.

Sex hormones have a profound impact on the sleep physiology in women. Since, these hormones vary considerably at different ages and stages of life, so does the sleep physiology. Puberty, menstruation, pregnancy, and menopause lead to gender specific clinical disorders.[5] Sleep and rapid eye movement latencies are longer in women than men. Women spend more time in stage 3 of non rapid eye movement (NREM) sleep.[6] There is more slow wave sleep in women than men (13 vs 9%).[7]

The blood levels of estrogen and progesterone fall after menopause. This is associated with vasomotor symptoms like hot flashes. Vasomotor symptoms lead to disturbed sleep.[8] Estrogen also decreases sleep latency and has an effect equivalent to a natural antidepressant.[9,10]

The suprachiasmatic nucleus has been shown to contain estrogen and progesterone receptors, which result in a more difficult adaptation to shift work for women.[11] Women shift workers experience menstrual cycle irregularities. Sleep pattern also changes with hormonal variations of puberty, menstrual cycle, pregnancy, and menopause.

Obstructive Sleep Apnea (OSA)

The prevalence of OSA is 27.3% in men and 22.5% in women.[12] Obstructive sleep apnea is marked by more hypopneas than apneas in women, however the severity of the disease is similar men.[13] Women are also more likely to have the upper airway resistance syndrome but less likely to have positional OSA.[14]

Women are more likely to have atypical presentation: insomnia, depression, restless legs, nightmares, and hallucinations.[15,16] This leads to a missed or late diagnosis of OSA.[17,18] Further, sleep questionnaires tend to perform differently in men and women. The Epworth sleepiness scale (ESS) is a more sensitive measure of sleepiness in men than in women.[19,20]

The upper airway anatomy also has gender-based differences. Women have a smaller tongue and pharyngeal muscle volume, smaller soft palate, and shorter pharynx.[21] The pharyngeal dilator tone is greater in women due to progesterone. Further, estrogen may also be protective. Women with OSA have lower levels of 17-hydroxyprogesterone, progesterone, and estradiol than those without.[22] Testosterone contributes to OSA through mechanisms independent of anatomic changes in the upper airway.[23,24] After menopause, the prevalence and severity of OSA in women increase dramatically.[21]

Despite all these differences, the treatment for OSA is largely similar in men and women. In addition to the standard treatment, hormone replacement therapy (HRT) may help in sleep restoration in sleep-affected postmenopausal women. However, the significant risk of thromboembolic disease precludes HRT for OSA alone since the risk-benefit ratio may be deemed to be low. The use of melatonin or pitolisant for excessive daytime sleepiness should be avoided during pregnancy or nursing since the safety profile in these settings has not been studied.

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Obesity Hypoventilation Syndrome (OHS)

The prevalence of OHS is higher in women (15.6%) than men (4.5%).[25] The difference is even greater for postmenopausal women. Progesterone plays an important role in protecting against hypoventilation by stimulating the respiratory center. In addition, it also increases pharyngeal dilator action.[26] Another contributory factor may be the greater blood levels of leptin in women.[27] The greater prevalence of hypothyroidism in women may also lead to a greater prevalence.[28] Even the consequences of obesity are more severe in women. Pulmonary hypertension in OHS is more commonly seen in women than men (71 vs 62%).[29] The management is similar in women and men and involves the use of BiPAP device, weight normalization, and addressing comorbidities like hypothyroidism.

Insomnia

Unlike OSA, insomnia is more common in women than in men, with a 40% greater risk.[30,31] Further, age specific risk of insomnia is 73% greater in elderly women compared to elderly men. This is likely due to hormonal differences between the genders. Insomnia is often comorbid with conditions like depression, chronic fatigue syndrome, and psychiatric disorders, which are also more common in women with insomnia.[32,33] Treatment utilizes cognitive behavioural therapy often supplemented by pharmacotherapy. Medications include orexin-receptor antagonists, melatonin supplementation, ramelteon, benzodiazepines, and Z-drugs.[34] However, caution should be practiced while prescribing these. The Food and Drug Administration (US-FDA) has recommended a half-dose reduction for zolpidem since the metabolism of zolpidem is slower in women.[35] Further, safety data on these drugs during pregnancy or lactation is scarce. It is therefore rational to use these drugs sparingly and for short duration during pregnancy or nursing. Breastfeeding mothers should avoid feeding or expressing during the first 8–10 hours of taking these medications when the blood levels are high.

Restless Leg Syndrome (RLS)

The prevalence of RLS is 10.6% with women twice as likely to have the syndrome.[30,31] Pregnancy is associated with a greater risk of symptoms.[36] The cause is likely a lower blood level of haemoglobin and/or folic acid.[36] In the years after pregnancy, the risk of RLS varies with the number of children. A woman with one child has twice the risk of RLS as a nulliparous woman, and the risk increases with additional gravida.[37] The management of RLS is similar in women and men, with correction of deficiency of iron and/or folic acid. However, benzodiazepines and dopaminergic drugs should be used with caution in pregnancy or lactation, and opioids should be completely avoided.

Narcolepsy

The general prevalence of narcolepsy is 0.05%.[38] There are no gender-specific differences in severity but women develop cataplexy at a younger age.[21] The pathogenesis involves lower levels of orexin. The weight gain that is often noted in patients with narcolepsy is more frequent among women.[39] The likely reason is differences in sex hormones and their action.

Treatment of narcolepsy involves pharmacotherapy, short daytime naps, and practicing sleep hygiene at night. Dauvilliers and colleagues found the optimal dose of modafinil to be 100 mg lower for women than men. Catechol-O-methyltransferase (COMT) gene shows dimorphism between women and men, which affects the response to modafinil and probably to other dopaminergic stimulants too.[40] Stimulants like methylphenidate or dextroamphetamines improve alertness. Cataplexy is addressed by using sodium oxybate and serotonin reuptake inhibitors. Pitolisant is a histamine autoreceptor antagonist that increases histamine levels in the crucial hypothalamic centers for sleep. All of these drugs should be used with caution or avoided during pregnancy or lactation since safety data is lacking.[41]

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