Unique Aspects of Sleep in Women

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While many aspects of sleep are similar in men and women, there are a number of important differences that need to be identified and confirmed by the health care provider. This article reviews the unique aspects of sleep in women.

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Abstract

Sleep in women differs in many respects from that of men. In general, women appear to report a greater need for sleep and more subjective complaints of non-refreshing sleep than men. Sleep in women is affected at least partially by hormonal factors, with women typically suffering from sleep disturbance in connection with the menstrual cycle, pregnancy, and menopause. Menstrual cycles are associated with prominent changes in reproductive hormones that may influence sleep. Sleep apnea and restless legs syndrome may be aggravated by pregnancy. Women may also develop insomnia during pregnancy, childbirth and menopause.

Introduction

Different phases of the life cycle in female population are associated with unique features of sleep disruption. Changes in sleep patterns are often linked to hormonal factors leading to disturbed sleep in connection with the menstrual cycle, pregnancy and menopause (See Figure 1). It has also been shown there may be a long interval between the onset of symptoms and the correct diagnosis of some sleep disorders.[1, 2]

In general, women tend to have slightly more slow wave sleep than men (13% vs 9%) and less stage 1 sleep (8% vs 11%).[3] Women also report having a greater sleep need and report poor or insufficient sleep than men.[4] Since most studies on sleep and sleep loss have been conducted in males, it is still unclear what factors contribute most to the sleep disturbances in women. It is also clear more research is required to fully elucidate the impact of life cycle on sleep parameters in women. This article will summarize what is presently known about different aspects of sleep and sleep disorders in women in relation to various lifespan stages.

Sleep during Adolescence

The transition to puberty brings with it a myriad of changes both physical and mental. These changes are influenced by age, developmental status, as well as changes in sleep schedule. In studies using actigraphy, adolescent boys were noted to sleep less, have less sleep efficiency, and awaken earlier than girls in the same age group.[5] The onset of menses may also be linked to an increased risk of insomnia. This increased risk of insomnia corresponds with an increased risk of depression, which in turn is a risk factor for insomnia.[6]

In adolescence, a striking feature in the polysomnographic data is the steep decline in the slow wave (delta) activity of non-REM sleep, by almost 50% between the ages of 10 and 20 years.[7,8] This decline in delta activity may be a component of widespread brain reorganization, of which other manifestations include

reduction in brain metabolic rate, decreased plasticity, and the emergence of adult cognitive capacity.[9] Studies have also indicated that adolescent girls undergo the steep drop in the slow wave activity earlier than boys in the corresponding age.[10]

Sleep During the Menstrual Cycle

Female reproductive hormones, specifically estrogen and progesterone, not only regulate reproductive tissue function during menstrual cycle, but also influence other physiologic principles, including sleep and circadian rhythms. Conventionally, in a normal menstrual cycle of 28 days, day 1 is identified as the first day of bleeding (menses). Ovulation usually occurs during day 14, dividing the cycle into two phases: a preovulatory follicular phase and a postovulatory luteal phase. The follicular phase is when estrogen is the predominant hormone. After ovulation, the luteal phase lasts 14-16 days and is when concentrations of estrogen and progesterone are high, and body temperature is elevated by about 0.4 degree Celsius when compared to the follicular phase. This rise in temperature is attributed to the rise in progesterone levels. Many women of reproductive age have recurrent emotional and physical symptoms in association with the menstrual cycle, particularly during the late luteal (premenstrual) and menstrual phases. These symptoms may interfere with social and occupational functioning, as well as with sleep; women who have menstrual-related problems are between two and three times more likely than other women to report insomnia and excessive sleepiness.[11]

Approximately 60% of women experience mild symptoms of premenstrual syndrome (PMS), and an estimated 20% have moderate PMS that they feel requires treatment. For 3-8% of women, the cyclical pattern of symptoms is severe and labelled as premenstrual dysmorphic disorder (PMDD). [12] Most common complaints include irritability, mood swings, depression, fatigue, headaches, bloating and cramping. Sharkey and colleagues studied twenty-seven healthy women to determine the relationship between sleep fragmentation and different points in the menstrual cycle.[13] Hormone levels were measured at two time points during a single menstrual cycle: the follicular phase and the peri-ovulatory to mid-luteal phase. A single night of home polysomnography (PSG) was recorded on the day of the peri-ovulatory/mid-luteal-phase blood draw. The study determined that the rise in progesterone level in the peri-ovulatory through mid-luteal phase resulted in an increase in the wake after sleep onset resulting in an increase in sleep fragmentation.

Figure 1
Changes in women's sleep patterns are often linked to hormonal factors leading to disturbed sleep in connection with the menstrual cycle, pregnancy and menopause.

It is surprising to note that limited research has been done on the effects of oral contraceptives (OCs) on sleep since OCs are so frequently used by women. Ho compared the sleep of three women (ages 24-34) with regular ovulatory menstrual cycles to three females taking fixed dose OCs. There was an increase in slow wave sleep (SWS) in the premenstrual phase in the cycling group, compared to the OC group in which SWS declined.[14] Another study described the sleep of three women at the follicular and luteal phases who were taking OCs. REM sleep latency was shorter in women taking OCs compared to 13 women with ovulatory cycles.[15] It is obvious that no clear link can be made about the effects of OCs on sleep, and additional research is therefore required.

Women also have more difficulty adapting to shift work than men.[16] Shift work, particularly at night, is problematic for the worker. It represents a serious risk factor for sleep disorders, such as insomnia and daytime sleepiness.[17] The frequency of sleep complaints in this population is twofold higher than in the general population. These problems are mainly due to a disruption of the normal sleep/wake pattern

but also involve other factors such as age, gender, stress at work, health problems and social and family factors.

The finding that neurons in the suprachiasmatic nucleus (the circadian clock) contain receptors for estrogen and progesterone indicates a functional interaction between the circadian system and the menstrual cycle.[18] Female shift workers experience several menstrual cycle irregularities.[19] Compared with all other fixed schedules (including nights only), rotating nurses reported lengthened menstrual cycles, visited the clinic more often with menstrual associated complaints, and experienced more "tension, nervousness, weakness, and sickness at menstruation." Shift work may also increase the risk of some forms of cancer in women. One proposed explanation is the exposure to light at night suppresses melatonin production which has potential oncostatic action. The risk of breast cancer is higher among women who frequently do not sleep at night, with an increased risk among subjects working in the bright places.[20] Another study indicated that working a rotating night shift at least three nights per month for 15 or more years increased the risk of colorectal cancer in women.[21]

Sleep During Pregnancy

Pregnancy is not free from its share of sleep-related issues. Many factors contribute to sleep disruption during pregnancy, including increased progesterone and prolactin levels, diaphragmatic elevation, fetal movement, bladder distension, temperature fluctuation and gastrointestinal discomfort. Anatomical changes during pregnancy, such as weight gain, decreased respiratory functional reserve capacity and nasopharyngeal edema (due to estrogen), and hyperventilation with increased sensitivity to carbon dioxide may predispose women to developing sleep disordered breathing (snoring, obstructive and central sleep apnea).[22,23,24,25] Despite the physiological changes conducive to the development of sleep apnea during pregnancy, a number of other physiologic adaptations may provide protection against sleep apnea. [26] For example, elevated progesterone levels during pregnancy increase the pharyngeal muscle tone. Reduction in REM sleep duration during pregnancy may also protect against sleep apnea. During late pregnancy, there is also a greater tendency for women to sleep on sides as opposed to laying supine, thereby reducing the tendency to manifest severe sleep apnea. Hedman and colleagues surveyed 325 pregnant women with a series of five questionnaires to assess the effects of pregnancy on sleep.[27] The questionnaires were asked before becoming pregnant, once during each trimester, and a final questionnaire three months post-partum. The total hours of sleep increased during the first trimester, lessened during the second trimester, and further decreased during the third trimester.

Emerging evidence suggests an increased incidence of sleep disordered breathing (SDB) during pregnancy and exacerbation of pre-existing SDB, particularly during the later stages of pregnancy. A longitudinal questionnaire study of symptoms of SDB found cumulative increase in apnea symptom scores from 14 weeks until delivery. Although 1.3% of participants in the study reported witnessed apneas on at least three nights per weeks at 14 weeks gestation, by 28 to 29 week's gestation, the figure had increased to 15% of the cohort.[28] The prevalence of obstructive sleep apnea (OSA) is approximately 5% in nonpregnant women of reproductive age.[29] The risk for OSA in women who are obese pre-pregnancy was shown to be significantly higher than in those who are non-obese. Maasilta and colleagues found that patients who were obese pre-pregnant had 1.7 events per hour versus 0.2 events per hour in the nonobese group ($P < 0.05$), and 5.3 events per hour of 4% oxygen desaturation versus 0.2 events per hour ($P < 0.005$). [30] The obese women snored 32% of the time, whereas the non-obese group snored only 1% of the time. OSA may also contribute to a higher risk of hypertension during pregnancy.[31] Women with pre-eclampsia have upper airway narrowing in both upright and supine postures.[32] These changes could contribute to the upper airway resistance episodes during sleep in patients with pre-eclampsia, which may further increase their blood pressure. Pregnant women with apnea symptoms have a higher likelihood of gestational hypertensive disorders, gestational diabetes, and unplanned Caesarian sections.[33] Treatment for OSA in pregnant patients remains to be continuous positive airway pressure (CPAP), which has been shown to be safe during pregnancy.[34] Mild OSA may respond to the use of an oral appliance or conservative measures such as sleeping on one's side.

Restless leg syndrome (Willis-Ekbom disease) is a common complaint among pregnant women. Restless leg syndrome (RLS) is defined as an irresistible desire to move the legs in response to uncomfortable sensations in the legs and is relieved by movement. RLS is two to three times more prevalent during pregnancy than in the general population, affecting 15 to 25% of pregnant women in western countries.[35,36,37] The previous three studies also noted a peak in the number of women affected by RLS in the third trimester and resolution of symptoms for many by one month after delivery. Preexisting RLS also predicts greater severity during pregnancy.[38] The exact pathophysiology is not completely understood. A study determining the relationship between estradiol and RLS

Figure 2
Women whose insomnia is apparently related to mood symptoms benefit from hormone therapy as do some women with insomnia but without vasomotor symptoms.

found that pregnant women who reported RLS had higher levels of this hormone.[39] Iron and folate deficiencies are well-recognized factors associated with RLS in pregnancy. Levels of hemoglobin, ferritin, and Vitamin B12 start to fall in the second half of pregnancy, regardless of taking iron and vitamin supplementation, due to fetal growth and hemodilution.[40,41]

The management of RLS includes behavior modification in addition to medical management. Any underlying condition should be excluded. Pregnant women suffer from leg cramps, particularly in the second part of the pregnancy. Sleep related leg cramps is reported as a primary reason for sleep disruption during pregnancy.[42] These symptoms should be carefully assessed and differentiated from RLS. Avoiding anything that can worsen RLS is beneficial. This includes smoking, certain antidepressants, and caffeine. If medication is needed for RLS, pharmacological treatment (Ropinirole, Pramipaxole, Carbidopa) should be used only during the third trimester and at the lowest effective dose owing to their possible teratogenic effects.[43] Iron supplementation is an option for pregnant women with iron deficiency. Additionally, Folate supplementation should be considered.

Postpartum blues, or baby blues, is a transient form of moodiness experienced by up to 85% of new mothers three to four days after delivery, which usually dissipates within a week.[44] A smaller but notable percentage of mothers experience a major perinatal depressive disorder during pregnancy (up to 20%) or the postpartum period (about 12%-16%).[45] Several psychosocial factors have been shown to increase the risk for perinatal mood disturbances, including antenatal anxiety and depressive symptoms, the presence of psychiatric history, stressful life events, marital conflict and lack of social support.[46] Although postpartum blues is generally considered a normal event that does not impair functioning, perinatal depression is a psychiatric condition that requires clinical attention. Breast feeding, compared with bottle feeding, has been found to influence sleep, with marked increase in slow wave sleep that may be attributed to increased levels of circulating prolactin levels.[47]

Sleep During Menopause and Post-Menopause

Menopause is defined as permanent amenorrhea for a period of twelve months. The age range for natural menopause is from 45 to 55 years with a mean age of 51 to 52 years.[48] During the climacterium, or menopausal transition, women are at increased susceptibility for several symptoms that significantly reduce their quality of life. The hallmark symptoms during the climacterium comprise hot flashes and sweating (Vasomotor symptoms).[49] Hot flashes are described as a sudden onset of redness and intense feeling of warmth or hot resulting in perspiration. Hot flashes may be the result of decrease in the levels of estrogen.

Approximately, 75% of postmenopausal women and 40% of perimenopausal women suffer from vasomotor symptoms.[50,51] The vasomotor symptoms usually last for 1 to 2 years, but about 25% of women report them for 5 years and 9% may have it all their lifetime after menopause.[52,53] When present during the night, these symptoms often disturb sleep and may result in somatic, mental, and cognitive problems.[54,55] Insomnia was reported by 25% of the women and severe insomnia by 15% of the women between 50 and 64 years of age.[56] The clinical picture of menopausal insomnia is no different from common insomnia, which manifests itself as difficulty in falling asleep, frequent awakenings or awakening too early in the morning.[57] Although vasomotor symptoms correlate strongly with sleep complaints, insomnia may occur in the absence of

vasomotor symptoms and can be the exclusive climacteric symptom.[58] During the climacterium, other symptoms including palpitations, headaches, dizziness, numbness, dry eyes and mouth, and reduced skin elasticity are commonly noted. Vaginal dryness, nocturia, and other urinary tract symptoms also get worse after menopause.[59] Mental symptoms, including anxiety, depression, a decline in libido, loss of concentration, and memory impairment commonly occur, and may in fact surpass the severity of vasomotor symptoms.

Sleep disruption associated with hot flashes can impact the quality of life and therefore may require treatment. Hormone replacement therapy (HRT) has historically been the standard treatment. Hormone therapy is as an effective therapy for reducing climacteric vasomotor symptoms and related secondary insomnia.[60,61] Women whose insomnia is apparently related to mood symptoms benefit from hormone therapy as do some women with insomnia but without vasomotor symptoms.[62] (See Figure 2.) The results of the Women's Health Initiative results showing increased risk of breast cancer, stroke, heart disease, and vascular dementia in individuals who were on HRT regimen for one to seven years suddenly changed this common practice.[63] Women are counseled to use HRT for only a short period of time to alleviate extreme form of hot flashes and other vasomotor symptoms. Those with history of breast cancer or stroke should be excluded. In women who seek treatment but prefer to avoid hormonal therapy, or for whom hormone therapy is contraindicated, other options exist. A large body of literature suggests that noradrenaline and serotonin have a central role in the pathophysiology of hot flashes.[64] Thus Clonidine (an α_2 adrenergic agonist) or serotonin-reuptake inhibitors have been found to alleviate climacterial symptoms, and accordingly, related sleep problems. Gabapentin has also shown to be beneficial although the adverse events such as dizziness, rash, or weight again, often result in discontinuation of the treatment. Good sleep hygiene can also be useful to promote good quality sleep. If a woman has vasomotor symptoms, low ambient temperature is often helpful; and lightweight bed clothes may be more comfortable. Caffeinated beverages, smoking and alcohol intake close to the bedtime can also cause sleep disruption.

Sleep disordered breathing may also contribute to sleep disturbance during menopause. The Wisconsin Sleep Cohort Data suggest that apnea hypopnea scores of 5 or higher were more prevalent among women who were 50 to 60 years old than among younger women.[65] Another study found that 3.9% of post-menopausal women had OSA defined as apnea-hypopnea index of at least 15 per hour of sleep.[66] This number was statistically greater than that found in pre-menopausal women (0.6%). However, in post-menopausal women taking hormonal replacement therapy, the prevalence of sleep apnea was not statistically different from the pre-menopausal group, although this group may have included some peri-menopausal subjects. Proposed mechanisms for this apparent rise in sleep breathing disorders have included a change in the distribution of body fat and a decrease in progesterone.[67,68] With menopause, body fat composition changes, leading in particular to increases in the waist-hip ratio and neck circumference. The decrease in female sex hormones, particularly progesterone, may partly be responsible for sleep breathing disorders. Progesterone has respiratory stimulant properties and affects genioglossus muscle tone.[69] The most effective therapy for obstructive sleep apnea is continuous positive airway pressure. Other options include positional therapy, surgery and oral appliances. The therapeutic role of hormonal therapy for sleep apnea in menopausal patients has been considered, with conflicting outcomes. Improvement of nocturnal breathing, especially reduced AHI, with hormone therapy has been found in some but not all studies.[70,71,72] Progestin has been shown to decrease the duration of apneas as well as improvement in ventilation.[73] However, because the data is limited and conflicting, no definite recommendation of hormone therapy as an option for sleep-disordered breathing can be made.

Conclusion

While many aspects of sleep are similar in men and women, there are a number of important differences that need to be identified and confirmed by the health care provider.

It is also important to recognize there are clinically unique differences in the sleep of women at different stages of life. The risk of developing sleep disruption and disorders, including insomnia, sleep disordered breathing and restless legs syndrome is also higher during key phases, including menstrual cycle, pregnancy, postpartum period and menopause. As most basic and clinical studies have been performed in male subjects, more research is needed to clarify the influence of the life cycle on sleep framework in women.

References

References exceeded space. For listing, email bhata@umkc.edu.

Disclosure

None reported. **MM**