REVIEW ARTICLE

Metabolic Women's Sleep: From the Cradle to the Hot Flash

Radhika Jindal, Mohammad Asim Siddiqui and Subhash Kumar Wangnoo

Apollo Centre for Obesity, Diabetes & Endocrinology (ACODE), Indraprastha Apollo Hospital, Sarita Vihar, New Delhi, India

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Abstract

Sleep of women differs in many respects from that of men. Women go through various phases in their life, each of these is associated with a unique hormonal milieu, which can affect the sleep significantly. Differences in the sleep of females and males have been documented across multiple studies. Various hormonal and physiological factors, as well as psychological and sociological factors, are thought to affect women's sleep.

Keywords: Sleep in women, Menopause and sleep, Sleep and metabolism

Introduction

Sleep is an important component of daily life. Sleep of women differs in many respects from that of men. Women go through various phases in their life, each of these is associated with a unique hormonal milieu, which can affect the sleep significantly. Generalizations are difficult to make due to the complexity of factors affecting women's life cycles. Differences in the sleep of females and males have been documented across multiple studies. Studies of sleep across the life cycle in women have utilized both survey and polysomnographic techniques, but have tended to be of small sample size with a diverse methodology. Various hormonal and physiological factors, as well as psychological and sociological factors, are thought to affect women's sleep. Hence, definitive conclusions about the impact of the various hormonal and physiological factors at different stages of women's life, on their sleep parameters cannot be made yet.

Address for correspondence:

Dr Subhash Kumar Wangnoo
Room 4168, Gate No 10, First Floor,
Apollo Centre for Obesity, Diabetes & Endocrinology (ACODE)
Indraprastha Apollo Hospital,
Sarita Vihar, New Delhi, India
Phone: +91-11-29874168
Email: subhashwang@hotmail.com

Sleep During Infancy, Childhood, and Adolescence

Humans begin to form various stages of sleep around the fourth month of life. Sleep differences between males and females have been seen to begin at around 9–10 months of age, with female babies sleeping longer. Around the age of 3 years, males show greater time in bed (TIB), total sleep time (TST), longer rapid eye movement (REM) cycle length and a higher percentage of stage-2 sleep. Females demonstrate increased slow-wave sleep (SWS), which continues throughout most of their lives[1]. Sleep architecture continues to evolve throughout childhood and adolescence, and subtle differences in architecture between sexes may exist at times during this period[2]. During adolescence, there is a delay in sleep timing and reduction in slow wave sleep. Teenage females tend to show less time in bed and sleep less than males. Sleep then reaches a fairly stable period

until midlife when gender differences begin to be more noticeable and suggest a female advantage[2].

Sleep During Adulthood

During adulthood, a decline of slow-wave sleep occurs with age and it begins earlier in males. Males begin to show increased levels of arousals and decreased SWS toward the end of the second decade. The decline of SWS in males continues throughout their life but this decline in SWS does not begin in females until the fourth or fifth decade (1). Females have longer sleep latency (time to fall asleep) as compared to males. However, females show "better" sleep (vs. Males) in terms of longer total sleep time, lower arousal rates, more slow-wave sleep, and less stage-1 and stage-2 sleep[3,4]. This continues till the peri-menopausal years when the sleep becomes fragmented with increased arousals. With aging, although both males and females wake up earlier, there is a significant difference in rising time between middle-aged subjects, with females rising later than males[5]. Young males slept longer than both their middle-aged and older counterparts and middle-aged females slept longer than middle-aged males. Many of these awakenings have been noted to be environmental (due to family and children's needs). This suggests that women's sleep is also dependent on social issues[5].

Sleep and the Menstrual Cycle

The reproductive years in the life of a female undergo cyclic changes during the menstrual cycle. The menstrual cycle is characterized by cyclic alterations in the production of the gonadal steroids (estradiol and progesterone), pituitary hormones (gonadotropins, prolactin, growth hormone), melatonin and cortisol, and in temperature rhythms. Various studies have evaluated the pattern of sleep during different phases of the menstrual cycle. It has been found that the sleep duration is shortest at ovulation. As compared to the follicular phase, in the luteal phase, the sleep is more disrupted with a longer sleep latency. Also, females have a lower sleep efficiency and lower subjective sleep quality in the luteal phase[6]. This is likely due to an effect of progesterone and/ or its neuroactive metabolites acting on sleep regulatory systems. Additionally, SWS was increased in the follicular phase, as was TIB and TST, suggesting that the menstrual cycle did affect melatonin and sleep/ wake rhythm[7].

In the premenstrual phase, the sleep tends to be more disrupted, with more wake-time after sleep onset. There is a significant decrease in SWS premenstrually, decreased sleep efficiency, decreased sleep quality and an increase in the time it takes to fall asleep. Because of the blunting in melatonin rhythm, some women tend to advance their circadian phase, getting sleepier early in the evening and awakening early in the morning[8].

Premenstrual Syndrome (PMS) is a common problem in women with ovulatory menstrual cycles and is characterized by mood and/or physical symptoms that appear regularly in the luteal phase and remit on menses or shortly after menses. When a woman's symptoms are severe, predominantly effective and cause a marked negative impact on her ability to function at home, workplace or in her relationships with others, she may receive a second diagnosis for Premenstrual Dysphoric Disorder (PMDD)[9]. Women who experience premenstrual syndrome (PMS) may experience more daytime sleepiness and increased sleep disturbances[8]. It has been observed that there is a delay and decrease in the secretion of melatonin during the luteal menstrual phase as compared to that during the follicular phase in females with PMDD. The authors suggested that the circadian pacemaker of females with PMDD is more responsive to the hormonal changes of the menstrual cycle[10]. Further, they postulate that this sensitivity may render these females more subject to mood, cognitive, and sleep disturbances as a result of endogenous and exogenous stimuli[11].

Both acute and chronic pain can disturb sleep. Dysmenorrhea refers to pain associated with menstruation. It can also include painful cramping before the onset of menstrual flow. Many women experience dysmenorrhea just before or at the onset of menstruation. The dysmenorrhea can decrease sleep quality and alter sleep patterns. It has been observed that menstrual pain significantly reduced REM sleep in a study of primary dysmenorrheic young women[12].

Polycystic Ovarian Syndrome and Sleep

Polycystic ovarian syndrome (PCOS) is a common disorder of the reproductive age group characterized by chronic oligo-anovulation and hyperandrogenism. Insulin resistance plays a pivotal role in the pathogenesis of PCOS. It has also been linked to an increased prevalence

of sleep disordered breathing. Sleep apnea has been increasingly prevalent in women with PCOS, with insulin resistance as the common factor between the two[13].

Sleep in Pregnancy

Pregnancy, childbirth, and the postpartum period can be associated with significant sleep disruptions. The marked rise in gonadal steroid hormones during the first trimester, the added physical discomfort associated with the growing fetus during the second and third trimesters, the precipitous drop in hormones after delivery, plus infant's irregular feeding and sleep schedule are all obvious reasons for sleep disturbances[14].

Various objective and subjective studies of sleep during pregnancy have shown that sleep may become disrupted particularly in the later stages of pregnancy. There is a decrease in sleep efficiency and REM sleep during this stage[8].

The rising hormone levels during the first trimester may partially account for the increased daytime sleepiness, as well as the total sleep time, which are commonly seen during this time.[15, 16, 17] Progesterone is known to exert soporific effects, and administration of exogenous progesterone has been shown to reduce time to sleep onset and modify sleep architecture, such that more time is spent in non-rapid eye movement sleep.[18,19] Other changes, such as organogenesis, place an additional burden on maternal energy stores and the increase in sleep time may reflect in potential mechanism to conserve energy. The first trimester is commonly associated with nausea and vomiting, which may further disrupt sleep increasing the likelihood of daytime somnolence.[20]

During the second trimester, the progressively increasing uterine size causes compression of the bladder, leading to more frequent urination. Nocturia accounts for the majority of nighttime awakenings during the second trimester.[21] Other factors such as heartburn and increasing fetal movements may further fragment sleep. In the second trimester, the sleep architecture is modified such that less time is spent in stage-3 and stage-4 non-rapid eye movement sleep and there is a concomitant decrease in rapid eye movement sleep.[15]

During the third trimester, further physical changes that occur causing significant discomfort and can impair the ability to fall asleep, as well as maintain sleep. A backache and itching are common complaints during advanced gestation. The shortest sleep durations and sleep disruptions, in particular, are commonly reported during the final trimester, despite more time spent in bed.[22]

In addition, obstructive sleep apnea (OSA) may also develop during pregnancy. OSA is characterized by repetitive episodes of upper pharyngeal obstruction resulting in decreased airflow and hypoxia. These obstructions commonly result in sleep fragmentation and nighttime awakenings. The short sleep duration and the disrupted sleep during pregnancy can compromise the glycemic control in women with gestational diabetes.[23]

The postpartum period can also be associated with severe sleep disruption. Most awakenings during the postpartum period are due to feeding and taking care of the infant. However, variables such as feeding method, co-sleeping, infant's sleep/wake rhythm, parity and psychiatric history may further add to the inherent sleep deprivation produced by caring for the infant during this period.[6]

Sleep patterns generally do not return to baseline until about 3 months postpartum, when melatonin and the sleep/wake cycle establish diurnal patterns.[8]

Sleep during Perimenopause and menopause

Menopause is an important phase during a woman's lifetime. It is characterized by various hormonal, physiological, and psychological changes. Insomnia becomes increasingly common during this time. Although menopause is defined as one year following cessation of menstrual periods, the hormonal changes begin several years prior to the final menses. The significant hormonal changes during this time include a fall in estradiol and inhibin with a rise in follicle stimulating hormone (FSH) and a lesser rise in luteinizing hormone (LH). Circulating estrogens shift from estradiol to estrone, predominantly produced by the extra-glandular conversion of androstenedione, and there is only a minimal fall in testosterone production.[24] Sleep complaints are one of the most common symptoms related to the menopausal transition, affecting 40–60% of women. During the perimenopausal transition, there is a drop in sleep quality, and the sleep becomes fragmented with increased arousals. With few exceptions, large survey studies show peri-and postmenopausal women subjectively reporting more sleeping difficulties than their premenopausal counterparts.[25]

During Menopause, the disturbed sleep mainly includes trouble falling asleep, fragmented sleep, nighttime wakefulness, and inability to resume sleep. The three defined causes of sleep disruption during the perimenopausal and postmenopausal states are hot flashes, mood disorders, and sleep-disordered breathing.[6] Estrogen treatment tends to improve sleep quality in part, by decreasing hot flashes and may differentially affect biological rhythms in depressed patients. However, there is a data conflict on the effectiveness of hormonal therapy in treating these disorders.[6]

Short Sleep Duration: Endocrine and Metabolic Effects

Short sleep duration coupled with disrupted sleep lead to various hormonal changes and metabolic effects. There occur acute changes in appetite leading to increased hunger. This results in increased caloric intake, which further predisposes to metabolic disturbances. There occurs an alteration in the levels of hormones which contribute to appetite regulation, like a decrease in leptin and an increase in ghrelin levels, and thus result in increased hunger. Disrupted sleep also results in a sustained elevation in afternoon cortisol levels. It is well known that the altered cortisol levels are linked to serious metabolic consequences. All these changes result in an increased risk for metabolic disorders such as obesity, the metabolic syndrome, and type-2 diabetes mellitus. There are various other mechanisms also through which sleep loss and sleep apnea lead to glucose dysregulation. Sleep apnea results in episodes of hypoxia and arousals. This further stimulates the sympathetic drive, resulting in an increase in secretion of catecholamines. The hypoxia also causes an increase in the inflammatory markers and activates the hypothalamic-pituitary-adrenal axis leading to an elevated cortisol production. All these factors combined together lead to the glucose dysregulation. The loss of sleep causes fatigue and reduced activity. In addition, it results in an increased opportunity to eat and there is an increase in non-homeostatic food intake. Sleep loss also stimulates the sympathetic drive and enhances cortisol production. All these combined together lead to insulin resistance, and thus predispose to metabolic disorders including glucose dysregulation and diabetes.[26, 27] It has been observed that difficulty in initiating sleep increases the diabetes risk by about 55%, and difficulty in maintaining sleep increases the diabetes risk by about 74%.[28]

The sleep disorders are also associated with the impaired cardiovascular autonomic control.[29] As stated above, obstructive sleep apnoea is associated with sympathetic overactivity. This sympathetic overactivity, associated with reduced baroreflex sensitivity have been demonstrated and play a prominent role in the development of cardiovascular diseases. In addition, an excessive daytime sleepiness may have an impact on the diagnosis or prevention of cardiovascular complications. The cardiovascular disorders have also been linked to other sleep disorders like primary insomnia, restless leg syndrome, etc. Poor sleep may also contribute to the development of hypertension. The mechanisms are likely to involve the absence of the beneficial fall of blood pressure and heart rate at night. Hence, the sleep disorders predispose to cardiovascular diseases.[29]

Summary

Thus, women go through various stages in their life, each of these is associated with a unique hormonal milieu, which affects their sleep, both in terms of quality and continuity. The disturbed sleep is in turn linked to various metabolic and cardiovascular diseases.

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