Sleep and Sleep Disturbances in Climacteric Women

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17.1 The Importance of Sleep

Good and sufficient sleep is necessary for good quality of life [1, 2] and health. Chronic sleep disturbances are associated with both physical and mental negative health consequences, like with cardiovascular diseases [3–6], diabetes [7, 8], depression [9], and cognitive impairment [10, 11]. In addition, sleep disturbances are related to increased work absenteeism [12–15], poor work performance [16, 17], accidents, and increased healthcare costs [18, 19]. Sleep disturbances increase in prevalence during climacteric [20, 21], thus influencing in health-related quality of life, work productivity, and healthcare utilization [22].

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17.2 The Sleep Regulation and Measuring the Sleep Quality

The sleep-wake cycle is regulated by two biological processes, which interact and balance each other, the circadian process C and homeostatic process S [23]. Circadian rhythm (circa *dia*) is an approximately 24-h regulation cycle of the body's internal processes and alertness levels [24]. Sleep-wake homeostasis, process S, is an internal mechanism that produces a pressure to sleep and regulates sleep intensity; i.e., the longer awake, the stronger the need to sleep, and vice versa. Several brain areas are involved in regulation of sleep, most importantly the medulla oblongata, pons, formation reticularis, midbrain, thalamus, hypothalamus, preoptic area, basal forebrain, hippocampus, and cerebral cortex. Of neurotransmitters, adenosine and nitric oxide [25] and gamma-aminobutyric acid (GABA), hypocretin, and histamine [26] are critical for sleep regulation. Also various hormones, such as growth hormone, cortisol, melatonin, prolactin, and ovarian hormones, are involved [27–34].

Sleep quality is divided to subjectively reported sleep quality (*subjective sleep quality*) and objectively measured sleep quality (*sleep architecture*). Subjective sleep quality and daytime consequences (fatigue, tiredness, reduced attention, cognition or memory impairment, mood disturbance, or irritability) are evaluated with structured questionnaires or sleep diaries. Subjective sleep quality is most commonly worsened by insomnia symptoms (e.g., difficulty initiating or maintaining sleep, or too early morning awakening) but sometimes by sleep disordered breathing (SDB) or restless legs syndrome (RLS) as well. One or more insomnia symptoms which occur at least three times per week during at least 1 month with daytime symptoms are required for the definition of insomnia disorder [35]. Generally, older age, female sex, and lower socioeconomic status, as well as previously diagnosed insomnia, positive family history of insomnia, and poor perceived mental and general health are risk factors for insomnia [36–39]. Also several systemic diseases and the use of medicaments may induce sleep disturbances [40, 41].

Sleep can be objectively measured with polysomnography (PSG), which consists of an electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG). Sleep is divided into wake, non-rapid eye movement (NREM) sleep, and REM sleep. NREM is further divided into stages N1–N3 (former S1–S4). N3 (former S3 and S4) is also called as slow-wave sleep (SWS) [42–44] (Fig. 17.1). In addition to the percentages of sleep stages and total sleep time, sleep latency, sleep efficiency, slow-wave activity (SWA), and the number of arousals and awakenings are typically determined from PSG-measured sleep. The optimal average sleep duration in order to maintain good health ranges from 7 to 8 h [45]. Shorter and longer sleep durations have been associated with increased morbidity and mortality in general populations [46–49]. The basic challenge for evaluating sleep quality and sleep disorders is that the correspondence between subjectively and objectively measured sleep is not unambiguous [50–53]. However, the individual's perceptions of sleep disturbance and daytime consequences are more likely to direct diagnosis and treatment.

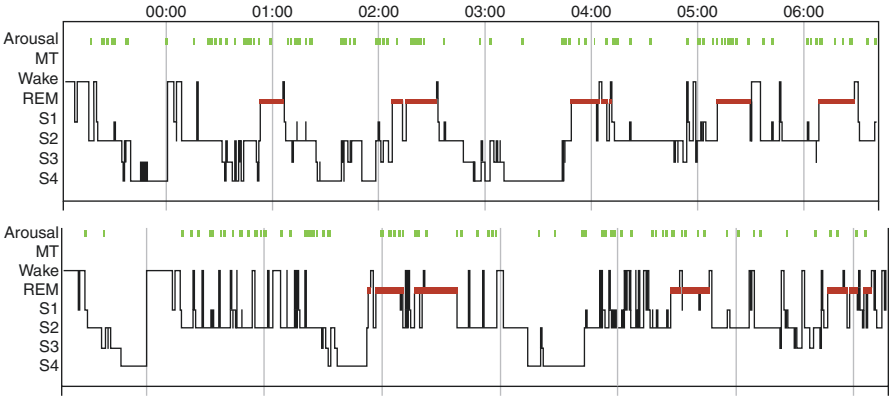

Fig. 17.1 Hypnograms derived from the polysomnograms of the same woman. Premenopausal situation (upper hypnogram) and perimenopausal situation 6 years later (lower hypnogram). Note especially the sleep fragmentation. *MT* movement time, *S1* stage 1 non-REM sleep, *S2* stage 2 NREM sleep, *S3* stage 3 NREM sleep, *S4* stage 4 NREM sleep. *Data from Lampio* et al., *2017*

17.3 Subjective Sleep Quality and Insomnia Symptoms in Climacteric

Sleep disturbances, especially insomnia symptoms, are one of the most bothersome symptoms in climacteric, being reported by 40–60% of climacteric women [54]. Both cross-sectional [55–59] and longitudinal [60–63] studies confirm that the prevalence of perceived sleep disturbances increases in the menopausal transition, even after controlling for age. A meta-analysis of 24 cross-sectional studies reported higher odds of experiencing sleep disturbance relative to premenopause in perimenopausal (1.60), postmenopausal (1.67), and surgically menopausal (2.17) women [64]. The most common sleep-related complaint is nighttime awakenings [55, 58, 61, 63], although also difficulty falling asleep increases across the menopausal transition [55, 58, 61, 63]. The increase in early morning awakening is shown to level off from late perimenopause to postmenopause [55, 58, 61, 63]. Although the insomnia symptoms inevitably increase in climacteric, the research about insomnia disorder in climacteric is limited. The phone interview of nearly 1000 women showed that 26% of perimenopausal women qualified for a DSM-IV diagnosis of insomnia, with difficulty maintaining sleep the most common symptom [65]. As for increasing follicle-stimulating hormone (FSH), the association with greater odds of waking up several times was found, whereas decreasing estradiol (E_2) was associated with higher odds of difficulty falling and staying asleep [61]. Despite this clear increase in poor sleep quality as women enter climacteric, the severity and persistence of poor sleep, as well as the extent of impairment in daytime function, vary between women.

17.4 Sleep Architecture in Climacteric

Even though the evidence for declining subjective sleep quality in climacteric is strong, polysomnographic (PSG) studies have generally not found a corresponding negative change in sleep architecture. The observed mismatch between subjective and objective sleep quality [66] has been explained by a possible influence of psychological state on sleep quality judgments by affecting the sleep appraisal process rather than sleep itself [67]. Also, most PSG studies have been cross-sectional with small sample sizes and differences in definitions of menopausal stages, age ranges, presence of systemic diseases and sleep disorders, and sleep-recording techniques. Some studies have found no differences in sleep architecture between pre- and postmenopausal women [68–72], while a few studies have reported more slow-wave sleep (SWS) in peri- and postmenopausal women than premenopausal women [59, 73–76]. More SWS could be interpreted as reflecting a better sleep pattern, on the one hand, but alternatively could reflect a recovery response to sleep deprivation. A single study has found more time spent awake and lower sleep efficiency in peri- and postmenopausal women compared to premenopausal women, but all studied women were insomnia patients [77].

Few studies have investigated the association between serum concentration of FSH and PSG measures. A cross-sectional study of women mostly in the early menopausal transition without sleep complaints found that higher FSH concentrations were associated with more wakefulness after sleep onset, awakenings, and arousals, after adjusting for age and BMI [78]. However, in women with insomnia symptoms, PSG measures did not correlate with FSH, whereas they were associated with anxiety and symptoms of depression [78]. In a small study with a group of pre- and postmenopausal women with diagnoses of depression, FSH concentration was positively associated with wakefulness after sleep onset and negatively associated with SWS [79]. Further, in another cross-sectional study, a more rapid rate of FSH change over the previous few years was associated with higher amount of SWS and longer total sleep time during a subsequent sleep study [80]. In the only longitudinal, 6-year follow-up study addressing changes in PSG measures across the menopausal transition, at follow-up, women had a shorter total sleep time, lower sleep efficiency, more wakefulness after sleep onset, and more awakenings after adjusting for vasomotor symptoms, BMI, and mood (Fig. 17.1). These changes in sleep were linked with advancing age rather than increased FSH levels. Increasing FSH was associated with a greater proportion of SWS, presumably reflecting an adaptive change to counteract the age-related sleep fragmentation [73] (Table 17.1).

Only limited work about PSG measures in climacteric women with insomnia disorder exists. One study showed substantial objective sleep disruption, with a poorer sleep efficiency, more wakefulness after sleep onset, and shorter total sleep time, matching the subjective poor sleep quality in this group compared to women without insomnia [81]. Further, women with insomnia were more likely to have objectively measured hot flashes, and the presence of hot flashes predicted the number

Table 17.1 Polysomnography sleep studies in menopausal transition

Authors	Study design	Sample characteristics	Findings	Comments
Shaver et al. 1988 [72]	Cross-sectional	Pre-, peri-, and postmenopausal women aged 40–59 y (n = 76)	No differences in sleep parameters between the groups	Peri- and postmenopausal women experiencing hot flashes had longer REM latency and tended to have lower SE compared to women without hot flashes
Young et al. 2003 [59]	Observational epidemiologic study	Pre-, peri-, and postmenopausal women, mean age 46.3 y, SD 8.1 (n = 589)	Peri- and postmenopausal women had more SWS, and postmenopausal women had less S2, and higher SE compared to premenopausal women	Peri- and postmenopausal women were more dissatisfied with their sleep quality compared to premenopausal women. No adaptation night
Sharkey et al. 2003 [76]	Cross-sectional	Pre- and postmenopausal women aged 45–56 y (n = 25)	Postmenopausal women had more SWS and less S1	No difference in subjective sleep quality. Two consecutive laboratory nights
Freedman et al. 2004 [71]	Cross-sectional	Pre- and postmenopausal women with and without hot flashes, aged 46–51 y (n = 31)	No differences in sleep parameters	Most awakenings preceded a hot flash, but not vice versa in the three consecutive laboratory nights
Kalleinen et al. 2008 [70]	Cross-sectional	Young (aged 20–26 y), premenopausal (aged 45–51 y) and postmenopausal (aged 59–71 y) (n = 61)	No differences between pre- and postmenopausal women. Young women had longer TST, higher SE and SWA, more SWS, and less WASO compared to pre- and postmenopausal women	Postmenopausal women were less satisfied with their sleep quality compared to premenopausal women. Two consecutive laboratory nights

(continued)

Table 17.1 (continued)

Authors	Study design	Sample characteristics	Findings	Comments
Sowers et al. 2008 [80]	Sleep was studied cross-sectionally and FSH annually 7 y prior the sleep study	At the time of the sleep study, women were premenopausal, early or late perimenopausal, and postmenopausal, median age 52 y (n = 365)	More rapid rate of FSH change was associated with more SWS and longer TST	More rapid rate of FSH change was associated with poorer subjective sleep quality. Two nights of in-home PSG
Hachul et al. 2009 [69]	Cross-sectional	Early and late postmenopausal women aged 50–65 y (n = 30)	No differences in sleep parameters	Two consecutive laboratory nights
Hachul et al. 2010 [75]	Cross-sectional	Reproductive (mean age 38.8 y [SD 10.4]) and postmenopausal (55.9 y [SD 7.9]) women (n = 931)	More SWS, less S2 and REM in postmenopausal women compared to reproductive women; after adjustment of age and BMI, only greater chance of having AHI >5 for postmenopausal	No adaptation night
Campbell et al. 2011 [68]	Cross-sectional	Pre-, early peri-, late peri-, and postmenopausal women aged 48–59 y (n = 321)	No differences in PSG measures. Beta EEG power, indicating arousal, ↑ in late peri- and postmenopausal women, but no difference in delta EEG power	Beta EEG power was related to hot flash frequency. Three consecutive in-home PSG-measurement nights. Results adjusted with age and other covariates
Xu et al. 2011 [77]	Cross-sectional	Pre-, peri-, and postmenopausal women aged 40–59 y (n = 74)	Longer total wake time and lower SE in peri- and postmenopausal women compared to premenopausal women	All subjects were insomnia patients. No differences in subjective sleep quality. Three consecutive laboratory nights

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Table 17.1 (continued)

Authors	Study design	Sample characteristics	Findings	Comments
de Zambotti et al. 2015 [78]	Cross-sectional	Young (aged 18–27 y) and perimenopausal women with and without insomnia (aged 43–52 y) (n = 44)	FSH ↑ was associated with WASO, awakenings and arousals ↑ in perimenopausal non-insomniacs, but not in insomnia patients in young women FSH ↑ was related to WASO and N1 ↑	In perimenopausal insomniacs TST correlated with anxiety and depression. No adaptation night
Hachul et al. 2015 [74]	Cross-sectional	Reproductive (mean age 34.6 y, (SD 8.4)), early (5.22 y (5.3)), and late (63.3 y (8.6)) postmenopausal women (n = 535)	More N3, higher AHI, and lower SaO_2 in postmenopausal women compared to premenopausal, no difference between early and late postmenopausal women	Wide age range (20–80 y), results were adjusted with age, BMI, blood pressure. No adaptation night
Lampio et al. 2017 [73]	6-year follow-up	At baseline all women (mean age 46 y, SD 0.9) were premenopausal and at the follow-up in different stages of menopausal transition (n = 60)	Increase in FSH associated with SWS ↑, after controlling for BMI, vasomotor and depressive symptoms	Aging was associated with shorter TST, lower SE, increased transitions from SWS to wake, increased WASO and amount of awakenings after controlling for confounding factors

n number, *y* year, *REM* rapid-eye movement sleep, *SD* standard deviation, *SWS* slow-wave sleep, *S2* stage 2 non-rapid eye movement (NREM) sleep, *SE* sleep efficiency, *S1* stage 1 NREM sleep, *FSH* follicle-stimulating hormone, *TST* total sleep time, *PSG* polysomnography, *WASO* wake after sleep onset, *N1* stage 1 NREM sleep, *N3* stage 3 NREM sleep, *SD* standard deviation, *EEG* electroencephalogram, *AHI* apnea-hypopnea index

of PSG awakenings per hour of sleep [81]. According to another study, where subjective sleep quality and PSG measures were compared between premenopausal and peri-/postmenopausal women with insomnia disorder, subjective sleep quality and depression were similar between the two groups, whereas peri-/postmenopausal women had a longer PSG-defined total wake time and lower sleep efficiency, suggesting that PSG measures of sleep quality are impacted to a greater extent in peri-/postmenopausal than in premenopausal women with insomnia disorder [77].

17.5 Primary Sleep Disorders in Climacteric

Sleep disturbances may arise in climacteric in association with primary sleep disorders, such as sleep disordered breathing (SDB), restless legs syndrome (RLS), and periodic limb movement disorder (PLMD) [21, 82]. SDB is characterized by snoring, upper airway obstruction, inspiratory flow limitation, and excessive daytime sleepiness [83]. An apnea-hypopnea index (AHI) of five or more per hour of sleep indicates SDB [83]. The prevalence of SDB is higher in men than in women before menopause [84]; however, the prevalence increases in women following menopausal transition [85–89]. The postmenopausal women have shown to be 2.6 times more likely to have an AHI $\geq$ 5 per hour and 3.5 times more likely to have an AHI $\geq$ 15 per hour, compared with premenopausal women, after adjusting for confounding factors (age, BMI, and smoking) [88]. In the recent longitudinal analyses of the same data, AHI increased from premenopause to peri- and postmenopause, independent of age and changes in body habitus, although these factors were also associated with AHI [85]. Furthermore, in a large follow-up study, the hazard ratio for OSA in women with surgical menopause was 1.27 compared in women with natural menopause independently of age at menopause. The increased OSA risk due to surgical menopause persisted for over 15 years into the postmenopausal period and was more pronounced in leaner women, as well as among women who never used menopausal hormone therapy (MHT). OSA risk associated with surgical menopause was attenuated among physically more active women [90]. The greater prevalence of SDB after menopause might, in part, be due to the loss of the protective effects of female reproductive steroid hormones, especially progesterone, which have shown to have respiratory stimulative effects [88, 89], as well as changes in fat distribution after menopause [86]. The clinical picture of SDB in women usually differs from that of men, and therefore women are probably more likely to be undiagnosed. Women are more symptomatic with lower AHI compared to men, and they have more prolonged partial upper airway obstruction and report insomnia as a symptom of SDB more frequently [91, 92]. Of importance, patients with SDB and insomnia-like symptoms have higher burden of cardiovascular, pulmonary, and psychiatric comorbidity and lower adherence to continuous positive airway pressure treatment compared to patients with traditional sleepy phenotype despite less severe SDB in terms of AHI [92].

The prevalence of RLS and PLMD increases with age, and RLS is more common in women [93]. Freedman et al. found periodic limb movements and apneas to be the best predictors for poorer sleep efficiency in peri- and postmenopausal women reporting sleep disturbances [94]. However, in a group of asymptomatic postmenopausal women, the incidence of periodic limb movements was unrelated to E_2 or FSH levels [95], suggesting that the increase in prevalence of RLS and PLMD after menopause may be related more to aging than to hormonal changes.

In addition to primary sleep disorders, other medical disorders, as well as use of medications, become more common with advancing age and may affect sleep in midlife women [41, 96, 97]. In one of the few prospective studies assessing predictors for menopausal sleep disturbances, medical diseases and use of prescribed

medication predicted future sleep disturbances [98]. In another prospective study, depressive symptoms, personal crises, use of medications affecting the CNS, and perceived impaired general health already 5 years before menopause predicted various sleep disturbances in menopausal transition [99].

17.6 Contributing Factors for Sleep Disturbances in Climacteric

17.6.1 Vasomotor Symptoms (Hot Flashes and Sweating)

Several factors contribute for sleep disturbances in climacteric (Fig. 17.2). Nocturnal hot flashes and sweating are an important component of sleep disturbance during midlife: self-reported vasomotor symptoms are consistently associated with poorer self-reported sleep quality and chronic insomnia [57, 61, 65, 100]. Women with

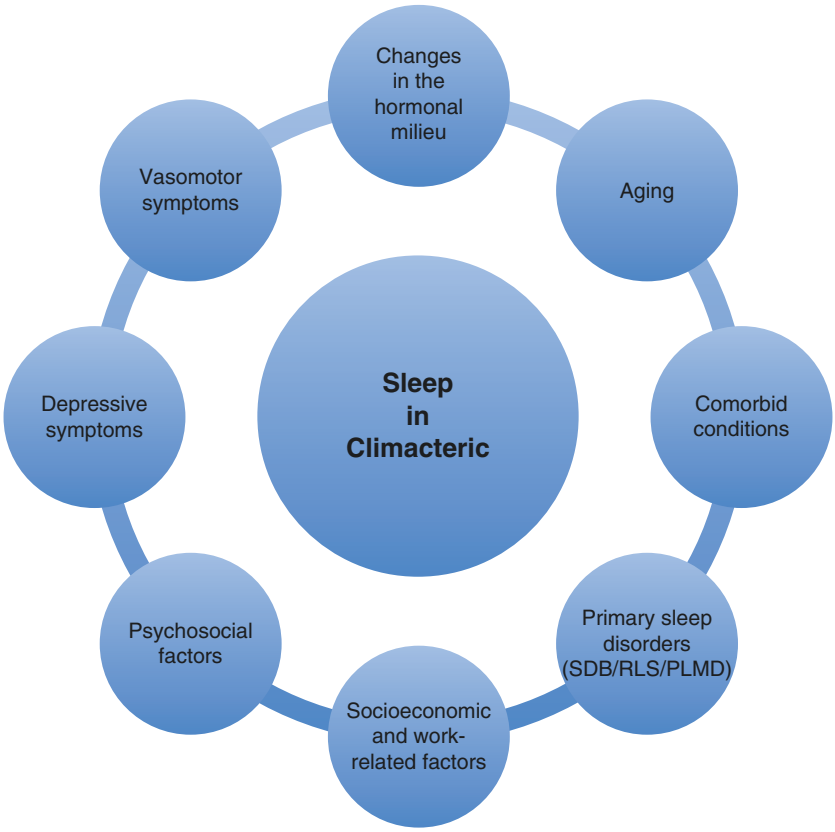

Fig. 17.2 Factors contributing for sleep quality and sleep disorders in climacteric. *SDB* sleep-disordered breathing, *PLMD* periodic limb movement disorder, *RLS* restless legs syndrome

moderate-severe hot flashes are almost three times more likely to report frequent nocturnal awakenings compared to women without hot flashes [101]. However, studies that investigated relationships between reported vasomotor symptoms and objectively measured sleep (with actigraphy or PSG) have produced conflicting results, with no relationship [59, 71] or with association between hot flashes and disrupted sleep [102–104].

Objectively measured vasomotor symptoms have been linked to sleep disruption in some [102, 103, 105, 106], but not all [71, 94, 104] studies. Differences between studies might relate to the classification of hot flashes in association with awakenings [102], as well as between-women variability in the impact of hot flashes on sleep. In an experimental model of new-onset hot flashes in young premenopausal women treated with a gonadotropin-releasing hormone agonist, hot flashes were linked with more PSG awakenings, more wakefulness after sleep onset, and more stage 1 sleep [107], providing a link between hot flashes and disturbed sleep. In an analysis of the overall impact of hot flashes on sleep architecture, wake time attributed to hot flashes was responsible for, on average, 27% of objective wakefulness after sleep onset, although there was wide variability in hot flash impact between women [102]. Additionally, an awakening occurred simultaneously with the majority (69%) of hot flashes. The strong overlap in timing between hot flash onset and awakenings suggests that these events may be driven by a common mechanism within the central nervous system in response to fluctuating estrogen levels, although sweating triggered by a hot flash may still contribute to or extend the interval of waking [102].

17.6.2 Depressive Symptoms

Risk for depression increases in climacteric, independently of other factors [108–111]. Women have been reported to be two to four times more likely to develop major depressive disorder in the menopausal transition and early postmenopause compared to premenopause, after adjusting for confounding factors [109].

Mood and sleep disturbances act in a bidirectional relationship [112, 113]. This relationship has also been documented in climacteric women [114–116]. In a longitudinal study, depressive symptoms were unrelated to menopausal status or annual change in E_2 but were associated with hot flashes and sleep disturbance [117]. Further, in another longitudinal study, the presence of subjective sleep problems at baseline was an important predictor of persistent/recurrent major depressive disorder at follow-up [118]. Studies about the association between sleep architecture and depressive symptoms have produced, however, conflicting results. In one study, more depressive symptoms were associated with lower sleep efficiency and shorter total sleep time in perimenopausal women and with a higher percentage of REM sleep in postmenopausal women [116]. In contrast, in another study, mood symptoms were not independently related to sleep architecture, but anxiety symptoms were related to longer sleep onset latency and lower sleep efficiency; however, this was found only in women who

also reported vasomotor symptoms [119]. Moreover, hot flashes and depressive symptoms have shown to be associated with different sleep disturbance patterns, with hot flashes being exclusively associated with frequent awakenings whereas depression was uniquely associated with difficulty falling asleep and too early morning awakening [120]. In addition, an intervention study in depressive perimenopausal women found that improvement in depression was predicted by improved sleep and increasing E_2, but not by alleviation of vasomotor symptoms [121].

17.6.3 Psychosocial and Sociodemographic Factors

In midlife, women face several challenges and personal life stressors, including changing family roles, loss of significant others, health concerns and worries about getting old, as well as alterations and increasing demands at work or retirement [122]. Life stressors and experiencing stress may contribute to sleep disturbances [122–124]. Indeed, perceived stress and poor perceived health have been associated with subjective sleep disturbances in midlife women [63, 97]. Furthermore, midlife women with higher chronic stress exposure over a 9-year follow-up period were more likely to have insomnia and more wake in objectively measured sleep than participants with moderate stress exposure [125]. Concerning work stress with sleep disturbances, a recent prospective study with over 24,000 participants (82% women, mean age 44 years) showed that the disappearance of job strain was associated with lower odds of insomnia symptoms [126]. In a study of 131 Egyptian teachers in the menopausal transition (aged 46–59 years), the most important menopausal symptoms that affected their work capacity and performance were tiredness (83%) and sleep disturbances (64%) [127]. A larger study of 961 midlife women found that insomnia symptoms were the most problematic menopausal symptoms to affect daily life and working performance [128]. As for work stress and sleep disorders in climacteric, postmenopausal women had worse sleep than premenopausal women during working days, but few differences during leisure days, showing an existing coping mechanism of work stress after menopause and the requirement of enough rest [129].

Some socioeconomic factors are protective against the development of sleep disturbances in climacteric; higher educational level [100], lower financial strain [130], and satisfactory marriage [131, 132] are all related to fewer sleep disturbances. Further, the prevalence of menopausal sleep disturbances is influenced by race and ethnicity: Caucasian women have higher rates, while Hispanic women have lower rates of sleep disturbances [61]. A study assessing the burden of menopausal sleep disturbances on societal costs concluded that menopausal chronic insomnia, characterized by nighttime awakenings, was linked with increased healthcare utilization and associated costs, decreased work productivity, and decreased health-related quality of life after adjustment for demographics and comorbidity [22].

17.7 Management of Sleep Disturbances in Climacteric

As the reasons for sleep disturbances in climacteric are potentially multiple, and sometimes overlapping, before prescription of the treatment, the causes behind should be accurately evaluated. For note is that for some women, sleep disturbances may be transient and thus not requiring any active treatment, whereas for other women, sleep disturbances may be severe, with a significant impact on daytime functioning and quality of life and thus necessity for treatment. In addition, occasionally combined treatments may be required, such as for women who have depression in addition to severe vasomotor symptoms and sleep problems. The cornerstone of management of sleep disorders is good sleep hygiene: appropriate sleeping environment, regular sleep-wake rhythm, sufficient exercise, and avoidance of stimulants, i.e., coffee, especially too late in the evening. Treatment options include MHT, non-hormonal pharmacological medications, and non-pharmacological and self-management strategies (Table 17.2).

17.7.1 Menopausal Hormone Therapy

Several studies have evaluated the effect of MHT on sleep; however, findings are mixed and difficult to compare, given the heterogeneity in study populations and tools to evaluate sleep and various MHT preparations (formulation, dose, and type of administration). According to a recent meta-analysis, MHT modestly improves subjectively evaluated sleep disturbance [133]. In most studies, improved sleep quality has co-occurred with improvement of vasomotor symptom [133–137]. However, there are also some data of enhanced sleep quality with MHT without the report of vasomotor symptoms [135]. PSG studies examining the effect of MHT

Table 17.2 Treatment of climacteric sleep disturbances

Non-pharmacological treatment
Sleep hygiene
Appropriate sleeping environment (calm, dark, appropriate temperature; comfortable bed)
Regular sleep-wake rhythm
Reducement of daytime stimulants
Regular daytime exercise
Relaxation techniques
Behavioral techniques, i.e., stimulus control or sleep restriction
Cognitive-behavioral treatment of insomnia (CBT-I)
Menopausal hormone therapy
Antidepressants (i.e., low-dose selective serotonin/serotonin noradrenaline reuptake inhibitors, mirtazapin)
Gabapentin
Melatonin
H1-antihistamin
Sleep medication (i.e., intermediate-acting benzodiazepines, “Z-drugs”)

on sleep architecture in menopausal women share the same problems with study design as the studies evaluating subjective sleep quality and MHT. In addition, those studies are rare, and the results are conflicting. Some studies have observed positive changes in sleep architecture with MHT [138–141], mainly decreasing wake after sleep onset, although other studies found no improvement [142–144].

17.7.2 Non-hormonal Pharmacological Medications

Of other treatment options, low-dose selective serotonin/serotonin norepinephrine reuptake inhibitors have shown to reduce hot flashes to some extent and modestly reduce insomnia symptoms in women with hot flashes [145–147], although the adverse-effect profiles of these medications need to be carefully considered. Evidence from a single trial shows that gabapentin improves sleep quality in perimenopausal women with hot flashes and insomnia [148]. As for sleep medication, melatonin, antihistamine, intermediate-acting benzodiazepines, and so-called Z-drugs can be used, although especially the two latter with short-term only.

17.7.3 Cognitive-Behavioral Treatment and Other Non-pharmacological Treatments

Cognitive-behavioral treatment of insomnia (CBT-I) is considered the primary intervention for patients with chronic insomnia [149], and it is superior to sleep medication alone in the long term [150]. Recently, a study using CBT-I during the menopausal transition in a randomized clinical trial of peri- and postmenopausal women with insomnia symptoms and daily hot flashes showed that 8 weeks of CBT-I led to a greater reduction in insomnia symptoms, with improvements maintained at 6 months posttreatment [151]. An open trial of CBT-I in women with menopausal sleep problems also found a reduction in insomnia (and depression) symptoms posttreatment [152].

Other non-pharmacological approaches for treating menopausal insomnia, like acupuncture, yoga, massage, exercise, and nutritional supplements containing soy isoflavones, have been used, with mixed effects [153].

17.8 Conclusion

Sleep quality decreases and sleep disturbances increase in climacteric. Sleep problems may be severe and thus deteriorate daytime functioning and quality of life in part of the women, having often also long-term consequences for mental and physical health. Climacteric symptoms, especially vasomotor symptoms, typically interfere with sleep and are strongly associated with reports of sleep disturbances as well as PSG-measured wakefulness. However, also other factors directly related to climacteric (e.g., hormonal changes), as well as a variety of health and/or life

circumstances (e.g., SDB or movement disorders, mood disturbances, presence of medical conditions, or life stressors), have an impact and thus should be evaluated. Given the presence of distinctive sleep-disruptive factors (e.g., hot flashes) and the multifactorial nature of sleep disturbances in climacteric women, treatment needs to be tailored.

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