



Sleep in post-menopausal women: Differences between early and late post-menopause

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ABSTRACT

Objective: The aim of this study was to evaluate the differences in sleep between women of early and late post-menopause.

Study design: Thirty post-menopausal women who came to the climacteric service of their own volition were selected. Fourteen were in early post-menopause (less than 5 years after menopause), and sixteen were in late post-menopause (more than 5 years since menopause). None of the women were suffering from any other clinical diseases. Participants had no previous history of hormone therapy or hypnotic drug use. These patients were not previously selected with regard to any sleep complaints. All participants answered a sleep questionnaire and underwent a polysomnography recording.

Results: Subjective complaints included body pain, bruxism, anxiety, depression, lack of concentration, and sleepiness (measured by the Epworth Sleepiness Scale). These complaints were more frequent in the late post-menopause group. In contrast, complaints of memory impairment were more frequent in the early post-menopause group ($p \leq 0.05$). Polysomnographic findings revealed no differences between the early and late post-menopause groups.

Conclusions: Although early menopause is associated with several symptoms, complaints related to sleep were higher in the late post-menopausal group.

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1. Introduction

Insomnia is a health concern for post-menopausal women. Previous studies have reported the incidence of this issue to be between 28% and 63% in post-menopausal women [1,2]. In fact, this condition often presents as subjective insomnia of 61% and objective insomnia of 83% [3]. Some authors reported that weight gain and aging may be factors that increase the occurrence of snoring and apnoea during the post-menopausal period [4,5]. Climacteric syndrome is more frequent in the first years of post-menopause (early), while other clinical problems, such as bone alterations, are seen more often during late post-menopause. Early post-menopause is defined as the 5 years immediately following the final menstrual period [6]. Polysomnographic studies have demonstrated sleep changes in post-menopausal women [7]. In addition, vasomotor symptoms are the most frequent and

prominent menopausal symptoms during the early phase of post-menopause [6], which may influence sleep disturbances. It is currently not clear whether the sleep alterations are due to aging, which could alter sleep quality by itself, or to the menopausal status. There are two aspects of sleep disturbance, the subjective and the objective. A subjective sleep disturbance is a self-reported complaint of non-restorative sleep, difficulty falling asleep, frequent awakenings, or waking too early from sleep in the morning; while objective sleep disturbance refers to reduced sleep efficiency or abnormalities in sleep architecture that can be measured with polysomnography (PSG) [8]. Studies have found that there is a lower sleep efficiency [9], longer sleep latency [10], and an accentuated difficulty in maintaining sleep [11] in post-menopausal relative to pre-menopausal women. There is some evidence that insomnia is related to vasomotor symptom intensity [12]. Some studies have shown that women who experience hot flashes also experience more waking episodes. This association is not unequivocally accepted as the primary cause of sleep disturbance during menopause [12]. Other studies suggest that mood swings observed in post-menopausal women could result from sleep disorders caused by hot flashes that take place during sleep [13]. Baker et al. [9] reported increases in the number and

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length of waking episodes during peri-menopause that are associated with high levels of anxiety, which may be experienced during mood changes. Among other symptoms, sleep disturbance is a common complaint in these women, and they report difficulty falling asleep and frequent awakenings with difficulty falling back asleep. As reported previously, a large proportion of such women indeed present with sleep-related respiratory disorders [14,15]. Young et al. [16] found no association between HT use and better sleep quality, whereas Sarti et al. [17] did. We have previously published that hormone therapy decreased the prevalence of arousal and PLM [18].

Recently, Elsabagh et al. [19] studied cognitive function in late versus early post-menopausal stages. They observed that women in the late post-menopausal stage performed significantly worse than women in the early post-menopausal stage on tests of executive function. There were no differences between the groups in their ratings of mood or habitual sleepiness or feeling of sleepiness at the start of testing. By the end of testing, the women in the late post-menopausal stage rated themselves as feeling sleepier than the women in the early post-menopausal stage. This change was independent of differences in age, suggesting that hormonal changes between the early and late post-menopausal stages may be responsible for this finding. Because age is a significant factor in sleep quality, well-controlled age-matched studies on the effect of natural menopause are difficult to perform [8]. In this study, we analyzed the sleep parameters (subjective and objective) of women in early and late post-menopause.

The aim of this survey was to determine whether there were any differences in sleep between early and late post-menopausal women with regard to complaints and polysomnographic findings.

2. Methods

2.1. Subjects

We selected 42 patients out of 90 volunteers. However, 12 patients did not complete the polysomnography study, and were therefore not included in this study. Thus, thirty women who came to our gynaecology clinic of their own volition were evaluated. These patients were not previously selected with regard to any sleep complaints. Their ages ranged between 50 and 65 years. They all had at least 1 year of amenorrhoea, serum FSH levels above 30 mIU/ml, and a Body Mass Index (BMI) of 30 or less. They had never received hormone therapy (HT) or sleep-inducing medication.

Women with uncontrolled diabetes mellitus, recent heart attack, thromboembolytic diseases, severe hypertension, severe or active liver failure, as well as those with endometrial echos above 5 mm at ultrasound evaluation and/or a positive progesterone test or endometrial cancer, were excluded from the sample. In addition, women with atypical mammary hyperplasia or breast cancer were also excluded. All women gave written consent after a detailed explanation of the study. The resulting protocol was approved by the Ethics Committee of the Univ Fed Sao Paulo (CEP#153/00).

2.2. Study design

All patients were submitted to a standardized examination performed in the Climacteric Section that included anamnesis; Kupperman Menopausal Index (KI) classification as mild, moderate, or severe; anthropometric measurements (waist/hip and BMI); complete gynaecological and haematological examinations; assessment of fasting blood glucose levels; determination of FSH, LH, and estradiol levels; bilateral mammography; pelvic ultrasound; bone densitometry; determination of total cholesterol levels and its fractions, triglycerides, TSH levels, and serum

calcium, phosphorus, alkaline phosphatase, and creatinine levels; urine evaluation; urine culture; calcium levels in 24 h urine; cervix-vaginal oncotic cytology; and a progesterone test.

In all cases, a full polysomnography (PSG) was performed at the onset of the study following one night's adaptation. All patients also answered a sleep questionnaire. The sleep questionnaire consisted of a standardized instrument [20] designed to quantify subjective sleep quality assessments and contained a variety of questions about sleep quality that addressed items such as frequent arousals, nocturnal leg movements, bruxism, snoring, and apnoea. This questionnaire also included questions regarding attention and/or memory impairment and anxiety and/or depression. The severity of subjective sleepiness was estimated by ESS scores (a score over 9 suggests significant daytime sleepiness [21]).

Polysomnography was performed between 9:00 PM and 7:00 AM (the lights-out time was close to the subjects' habitual sleeping time) and consisted of a Sleep Analyzer Computer (SAC version 9.3 – Oxford Instruments, Inc.). The sleep state was recorded with three channels of an electroencephalogram (EEG: C3-A2; C4-A1; O2-A1), two channels of an electrooculogram (EOG), one submental and one tibial electromyogram, and one electrocardiogram.

Subjects' breathing was assessed by monitoring movements of the chest wall and abdomen using strain-gauge pneumographs and nasal and oral flows using thermistors. The arterial oxygen saturation was measured using a pulse oximeter. The sleep onset latency was measured as the time between lights-out to the start of sleep stage 2 (including any intervening period of wakefulness). Sleep recordings were scored in 30-s intervals according to standard criteria [22]. Apnoea was defined as a reduction in airflow of at least 80% for >10 s. The Apnoea Hypopnoea Index (AHI) was defined as the number of apnoea-hypopnoea episodes per hour of sleep. Arousals were defined as abrupt shifts in EEG frequency lasting from 3 to 15 s, according to the criteria published by the American Sleep Disorders Association (ASDA-1992) [23]. The arousal index was calculated as the number of arousals per hour of sleep. The necessary alterations for respiratory events were incorporated according to the criteria established by the American Academy of Sleep Medicine Committee (1999) [24], whereas assessment of wakefulness and periodic leg movements followed the guidelines of the American Sleep Disorders Association [23,25]. The other sleep characteristics investigated were sleep latency, defined as the interval between lights-off and sleep onset, and final latency, defined as time spent between waking and lights-on.

2.3. Statistical analysis

Comparisons between groups was performed using a chi-squared test, following Cochran's restrictions, and with Fisher's test. The chi-squared test was also used to compare independent samples within groups for sleep complaints. The power calculation shows that, with twenty patients per group, there was 85% power.

The clinical data and polysomnographic parameters were analyzed using unpaired Student's "t" tests. We also used the Mann-Whitney Test for to analyze the number of arousals, number of arousals per hour of sleep, number of awakenings, and WASO. The level of significance was set at $p < 0.05$. The descriptive statistics and p -values were calculated and presented for all measures.

3. Results

Data in Table 1 demonstrate clinical differences between groups. Only time since menopause onset (less than 5 years and more than 5 years of post-menopause) and Kupperman's Index showed differences, suggesting that early post-menopausal women were more symptomatic than late post-menopausal women were. The average age was not different between groups.

Table 1

Comparison between clinical parameters in short-term postmenopause group and long-term postmenopause group.

	Early postmenopause (<5 years, n = 14)	Late postmenopause (>5 years, n = 16)	p
Kupperman Menopausal Index	19.0 ± 8.7	13.1 ± 6.0	0.04*
Age	54.9 ± 3.9	57.4 ± 4.3	0.112
Years after menopause	3.7 ± 1.2	10.5 ± 5.4	<0.01
BMI	26.5 ± 3	26.7 ± 3	0.85
Waist (cm)	88.5 ± 9.3	91.2 ± 10.4	0.46
HIP (cm)	100.2 ± 8.2	99.8 ± 8.9	0.89
Waist/hip	0.88 ± 0.07	0.90 ± 0.06	0.66
Estradiol (pg/ml)	21.5 ± 6.5	22.5 ± 11.3	0.77
Parabasal epithelial vaginal cells (%)	62 ± 37.3	43.3 ± 40.6	0.20
Intermediate epithelial vaginal cells (%)	46.6 ± 56.4	50.5 ± 33.5	0.23
Superficial epithelial vaginal cells (%)	4.5 ± 11.5	7.2 ± 7.5	0.45

Complaints of difficulty in falling asleep were frequent in both groups (nearly 50%), but there was no difference between groups. Frequent awakenings were also a complaint in 50% of women in both groups (Table 2).

The complaint of body pain was present in 50% and 75% of early and late post-menopause cases, respectively. In addition to being highly prevalent, this complaint was significantly more frequent in the late post-menopause group.

Complaint of leg movements was frequent, while the PLMI was low in both groups, but there was no difference between the two groups. Subjective complaints of body pain, bruxism, anxiety, depression, lack of concentration, and sleepiness (measured by Epworth Sleepiness Scale) were more frequent in the late post-menopause group.

However, complaints of lack of memory were more frequent in the early post-menopause group ($p \leq 0.05$) (Table 2).

Objective findings (observed when comparing PSG between groups) revealed no differences between the early and late post-menopause groups (Table 3).

4. Discussion

This study compared objective and subjective sleep quality in both early and late post-menopausal women. Despite the finding that early post-menopausal women were more symptomatic, differences were not revealed by PSG, and the late group had more complaints related to sleep.

In light of the large number of women experiencing menopausal symptoms and the intense endocrinological research into ways of alleviating these symptoms, including sleep-related

Table 3

Comparison between polysomnographic parameters in early postmenopause group and late postmenopause group.

	Early postmenopause (less than 5 years)	Late postmenopause (more than 5 years)	p
Initial latency (min)	10.6 ± 10.3	19.9 ± 22.4	NS
Final latency (min)	5.3 ± 8.9	4.7 ± 8.3	NS
Stage 0 (%TST)	13.8 ± 5.3	15.9 ± 8.4	NS
REM latency (min)	93.5 ± 35.7	90.6 ± 48.5	NS
Stage 1 (%TST)	8.7 ± 4.5	8.7 ± 5.3	NS
Stage 2 (%TST)	54.2 ± 8	48.8 ± 7.6	NS
Stages 3 and 4 (%TST)	17.1 ± 7.2	20.6 ± 6.2	NS
Sleep efficiency (%)	83.5 ± 7.7	81.6 ± 8.3	NS
REM (%TST)	19.8 ± 5.1	21.6 ± 4.9	NS
TST (min)	356.1 ± 71	349.1 ± 61.2	NS
Basal saturation O2 (%)	83.2 ± 4.8	82.0 ± 6.2	NS
AHI (number/h)	5.9 ± 3.8	5.6 ± 4.5	NS
PLM (number/h)	6.5 ± 8.7	4.3 ± 3.9	NS
Arousals (number)	66.6 ± 80.9	59.4 ± 51.1	NS
Microarousals index (number/h)	12.8 ± 13.9	12.1 ± 11.6	NS
Sleep stage shifts (number)	93 ± 51.2	91.3 ± 42.7	NS
Awakenings (number)	17.6 ± 8	19.5 ± 9.2	NS
WASO (min)	44.6 ± 36.9	45.4 ± 28.6	NS

TST: total sleep time; AHI: apnoea-hypopnoea index; PLMI: periodic leg movements; sleep efficiency: TST/TRI (total registered time); WASO: wake after sleep onset.

respiratory disorders [14,15], there is a surprising paucity of literature that addresses sleep difficulties in menopausal women.

Self-reports of sleep disturbance may reflect subjective distress rather than objective sleep disruption. A study by Young et al. [16] and a study by Freedman and Roehrs [26] found that sleep quality was not low in these women, even among those with menopausal symptoms. The authors of the latter study reported that hot flashes did not result in alterations of sleep architecture, sleepiness, fatigue, or psychomotor performance in post-menopausal women. They excluded more than one-third of the subjects because they had sleep disorders unrelated to menopause. By rigorously screening the study participants, they were able to minimize the effect of potential confounding factors.

In the present study, KI scores were higher in the early post-menopause group. Nevertheless, this group did not report more complaints regarding sleep quality. Indeed, both groups presented a high prevalence of sleep complaints, especially the complaints of difficulty falling asleep and frequent awakenings.

Subjective complaints of body pain, bruxism, anxiety, depression, lack of concentration, and sleepiness (measured by Epworth Scale) were more frequent in late post-menopause group. One explanation for this is that sleep disturbance may be related to age or to long-term effects of hypoestrogenism status on the nervous system centre [27].

Table 2

Comparison between sleep and cognition complaints in early postmenopause group and late postmenopause group.

	Early postmenopause (<5 years, n = 14)	Late postmenopause (>5, n = 16)	p	RR
Difficulty in falling sleep	42.85%	50%	NS	0.87 (0.66 to 1.15)
Several awakenings	50%	50%	NS	1 (0.76 to 1.32)
Body pain	50%	75%	0.002	0.6 (0.46 to 0.78)
Leg movements	50%	37.5%	NS	1.3 (0.96 to 1.68)
Bruxism	0	18.75%	0.0001	0.02 (0.001 to 0.35)
Snoring	57.14%	56.25%	NS	0.99 (0.75 to 1.32)
Apnea	21.42%	18.75%	NS	1.09 (0.78 to 1.52)
Lack of memory	71.42%	56.25%	0.01	1.41 (1.02 to 1.94)
Anxiety	35.71%	68.75%	0.0001	0.51 (0.37 to 0.69)
Depression	14.28%	43.75%	0.0001	0.43 (0.26 to 0.69)
Lack of attention	42.85%	37.5%	NS	1.11 (0.84 to 1.46)
Lack of concentration	42.85%	56.25%	0.04	0.75 (0.57 to 1.00)
Epworth > 9	35.7%	50%	0.03	0.75 (0.55 to 0.99)

Complaints of lack of memory were more frequent in the early post-menopause group. In addition, in line with the findings of the present study, the findings of Elsabagh et al. [19] showed that in the late post-menopausal stage, women rated themselves as feeling sleepier than the women in the early post-menopausal stage.

Previous studies have shown little alteration in objective parameters as far as hormonal therapy was concerned. Young et al. [16] also concluded that menopause was not associated with diminished sleep quality, as measured by polysomnography. They stated that although peri-menopausal and post-menopausal women were less satisfied with their sleep relative to pre-menopausal women, menopause was not a strong predictor of specific sleep-disorder symptoms.

Shin et al. [28] studied the prevalence of insomnia and its relationship to menopausal status in middle-aged Korean women, and found that insomnia was significantly associated with the menopausal transition. The prevalence of insomnia increased significantly with the transition from pre-menopause to perimenopause, but not with the transition to post-menopause. To our knowledge, no other study has compared sleep differences between early and late post-menopause.

The number of subjects was limited to allow us to identify differences in the objective measures of this study, and this may have somehow affected the results. It was difficult to maintain the volunteers in their different places for the sleep tests and for the volunteers to adequately complete the analysis. Another limitation of the study was the fact that we used a thermistor instead of a nasal cannula with pressure transducer. It is known that the thermistor is less sensitive. This could have affected the results, because with the thermistor, the flow limitation (partial obstruction) may be missed, and women with low AHI frequently have partial obstruction, especially after menopause [29,30]. In this sense, we could have missed a diagnoses of partial obstruction. Nevertheless, the study of subjective complaints revealed important findings. Although early menopause was associated with several symptoms due to hypoestrogenism (Climacteric Syndrome), subjective complaints related to sleep, such as anxiety, depression, lack of concentration, and sleepiness, were more frequent in the late post-menopause group. This finding was not related to the age of the patient, but rather to years after menopause. Another possibility is the deleterious long-term effect of hypoestrogenism in late post-menopause. Therefore, more attention should be paid to identifying potential differences in symptoms among women at different post-menopausal phases, and future studies should include complete investigations of both subjective and objective measures of sleep disturbance.

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