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Sleep quality and related factors in postmenopausal women

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ABSTRACT

Sleep disorders, resulting from hormonal changes and vasomotor symptoms, are common in both peri- and postmenopausal women. Poor sleep quality is associated with increased metabolic and cardiovascular risk, depression and a global impairment in health status.

Objectives: Our study aimed to assess sleep quality in a sample of postmenopausal women and to identify the factors associated with poor sleep quality. It also considered the negative impact of sleep disorders such as insomnia, hypersomnia and breathing disturbances.

Subjects & methods: Data came from a cross-sectional study of 195 postmenopausal women conducted at the Italian Hospital of Buenos Aires, Argentina. Their sociodemographic, gynecological and clinical characteristics were recorded and sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), and the Oviedo Sleep Questionnaire (Cuestionario Oviedo de Sueño, COS).

Results: The mean PSQI score was 6.90 ± 4.43. Sleep problems were common, with 46.7% of participants scoring over 5 on the PSQI. Snoring was reported by 13% of the patients (PSQI item 10 A). While 10% of the poor sleepers reported episodes of apnea during rest (PSQI item 10B), 7.1% reported leg spasm (PSQ I item 10C). The mean total COS score was 17.57 ± 7. According to COS item 1, all the subjects reported some dissatisfaction with the quality of their sleep. According to the COS, the prevalence of insomnia was 3.6% using ICD-10 criteria and 15.4% using DSM-IV criteria. The mean ESS score was 6.12 ± 4.09.

Conclusion: Postmenopausal women are likely to complain of disturbed sleep. Almost half of the women in this survey said their sleep quality was impaired, and most of that group would benefit from medical attention.

1. Introduction

Postmenopausal women commonly complain of poor sleep quality, night awakenings, insufficient sleep, hypersomnia, snoring, and apnea. Sleep disorders often begin during the menopausal transition, and their prevalence increases after the definitive cessation of menses [1]. Several studies have attempted to identify the causes of impairments in sleep quality, which may be affected by hormonal changes and the natural process of aging. The reported prevalence of sleep disorders varies from 39% to 47% among perimenopausal women and from 35% to 60% in postmenopausal women [2].

During menopause, the GABA-ergic, serotonergic (5HT), noradrenergic (NA) and dopaminergic (DA) systems undergo changes which impact sleep regulation. Fluctuations in serotonin levels, for instance, during the transition to menopause may be responsible for changes in sleep, mood and memory. Experimental models confirm that the depletion of 5HT in the brain may cause insomnia [3]. Thyroid dysfunction and obesity also influence climacteric women's sleep quality [4–7]. Conversely, some authors have found that a history of sleep disturbances prior to menopause is the best predictor of peri- and postmenopausal sleep disorders [8]. Moreover, it is not often easy to assess the influence of other risk factors such as anxiety, stress and depression on sleep disturbances [9].

Recent data suggest that the duration of sleep has a strong influence on health [10]. Insufficient sleep has been related to an increase in ghrelin and a reduction in leptin production, which favor overweight, central obesity, insulin resistance and ultimately the development of diabetes [11]. Poor-quality sleep and inadequate sleep duration, less

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than 6 h per night, are associated with 4-fold higher risk of stroke [12]. In addition, poor sleep quality is related to lower bone mineral density and to an increase in the risk of fracture [13]. The mechanisms by which sleep duration affects bone turnover are unknown; however, changes in rhythmicity of bone cells, sex steroid and cortisol levels and an increase in sympathetic tone might have an impact on the association between sleep patterns and bone turnover [14].

Present data are consistent with an association between sleep disorders, depressed mood and hot flashes [15]. Some authors have found that the risk of depressive symptoms during perimenopause for women with nocturnal hot flashes without a history of depression is twice as high as it is for such women not experiencing hot flashes [16]. So far, there has been scant research into sleep quality and menopause in Latin American countries. Blumel et al reported that vasomotor symptoms were related to insomnia and poor sleep quality in their survey of Latin American women [17].

2. Subjects and methods

2.1. Patients

We enrolled 195 women, aged 40–59 years, at the Italian Hospital, in Buenos Aires, Argentina. They were recruited through personal interviews, as well as the distribution of leaflets and posters, among other methods. Our research was conducted over 43 months, from December 1st, 2012 to June 30th, 2016.

Once the women had given their written informed consent to participate in the survey, their reproductive and medical records were collected. None of them had had premature menopause. Subjects who met any of the following criteria were excluded: (a) a significant hepatic, hematological, cardiovascular or renal disease that limited daily activity and impaired quality of life; (b) a skeletal muscle condition, neuromuscular or neurophysiological disease that could affect sleep quality; (c) difficulty understanding their mother tongue and/or illiteracy.

2.2. Study design

The sample size was based on the fact that menopause, our field of study, is a normal condition that all women experience, typically between 40 and 59 years of age. It was also taken into account that it is difficult to ascertain the extent to which sleep quality is linked to menopause, aging or hot flashes. A statistical software program was used to calculate the sample size for a population size of 9.533 women and an expected minimum frequency of symptoms of 55%, effect size 0.40, with a maximum acceptable error of 5%. That calculation indicated a sample size of 111 women with a 95% confidence interval. Therefore, a total of 226 women were asked to take part in our study. Of the 226 women who underwent the screening, 195 met the inclusion criteria and were enrolled in our research. All the women with an intact uterus had had their last menstrual period at least one year before taking part in our study. Women who had undergone hysterectomy and bilateral oophorectomy were considered menopausal from the date of operation. In case of surgical menopause or diagnostic doubt, an FSH level higher than 40 mIU / ml and an estradiol level lower than 20 pg / ml were required.

We recorded the participants' socio-economic variables, such as their partner's status, their place of residence (urban or rural), their work, physical activity and number of children. Also, their body mass index (BMI) was assessed. We also gathered information about hypertension, thyroid disease, dyslipidemia, tobacco consumption, and use of psychotropic drugs (including antidepressants and benzodiazepines), melatonin, phytotherapy and menopausal hormone therapy.

2.3. Questionnaires

A specific questionnaire was designed to assess the frequency and intensity of hot flashes. The Oviedo Questionnaire, the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale were used to assess sleep quality.

The hot flashes questionnaire was part of a sleep diary that all women completed over the course of one week. The diary form included definitions for mild, moderate, and severe hot flashes and night sweats taken from the NIH hot flash workshop [18].

The Oviedo Questionnaire (Cuestionario Oviedo de Sueño, COS) [19] has 15 items. It provides a subjective assessment of satisfaction with sleep and indicates the presence of insomnia and hypersomnia according to the criteria of the International Classification of Diseases (ICD-10) and of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Other COS items provide additional information on snoring (COS 10.1), apneas (COS 10.2) and leg movements (COS 10.3), nightmares (COS 10.4) (nightmares occurring on three or more nights a week was considered positive) and the use of aids such as herbs or drugs to sleep (COS 11).

The Pittsburgh Sleep Quality Index (PSQI) [20,21] assesses the subjective quality of sleep, sleep duration, sleep efficiency, sleep disturbances, use of hypnotics and diurnal dysfunction. People who score higher than 5 are categorized as bad sleepers and those whose score is 5 or less as good sleepers. Thus a score under 5 suggests no serious sleep problems but a score from 5 to 7 is an indication of the need for medical assessment; a score from 8 to 14 indicates the need for care and medical treatment; and a score from 14 to 21 suggests a serious sleep problem. In this study, the Spanish version of the PSQI was used. On items 10A (absence or presence of snoring), 10B (absence or presence of respiratory apneas) and 10C (absence or presence of leg spasms while sleeping) a score of 0 was considered negative and a score of ≥ 1 positive.

The Epworth Sleepiness Scale (ESD) [22] provides information about somnolence in the adult population. A score higher than 10 reflects daytime sleepiness.

2.4. Statistical analysis

For qualitative variables, results are expressed as frequencies and percentages, while for quantitative variables, means and standard deviations are reported. Measures of central tendency and distribution were used to describe the groups and to test for homoscedasticity. The Shapiro-Wilk test and the Kolmogorov-Smirnov test were used to check the normality of distribution.

Either the *t*-test or the Mann-Whitney *U* test were used to analyze the continuous variables, according to the homogeneity of the variance, measured with the Bartlett test. Chi-square tests were used to compare qualitative variables. All statistical analyses were performed using the Statistical Package for the Social Sciences (version 25.0; SPSS Inc., Headquarters, 233 South Wacker Drive, 11th Floor, Chicago, IL 60606, USA), and a 5% significance level was used.

3. Results

Of the 226 women evaluated, 195 patients met the inclusion criteria seven of whom had undergone hysterectomy. Participants' mean age was 54.6 ± 4.4. Table 1 shows the sociodemographic variables. The mean BMI was 25.2 ± 4 and the prevalence of obesity (BMI > 30) was 9.7%. The mean time elapsed since menopause was 4.9 ± 2.9 (range 1–10 years). The prevalence rates of hypertension, dyslipidemia and thyroid dysfunction were 23.6%, 34.9% and 26.2% respectively. Benzodiazepines were taken by 14.3% of participants, antidepressants by 14.3% and hormone therapy by 11.2%. Hot flashes were reported by 34.9% of the women, with a mean frequency of 4.9 ± 2.9 per week. The PSQI global score was 6.9 ± 4.43 (impaired sleep quality

Table 1
Clinical and sociodemographic data of the study sample. Results are expressed as mean ± standard deviation or total numbers (percentages).

General Characteristics	
Age	54.6 ± 4.4
Number of children	2 ± 1
Weight	65.1 ± 10.7
Size	1.6 ± 0.1
BMI	25.2 ± 4
Years of menopause	4.9 ± 2.9
Number of hot flashes per week	3.2 ± 3
PSQI global score	6.90 ± 4.4
COS GRAV_INS	17.57 ± 7.38
Epworth Somnolence Scale score	6.12 ± 4.09
Stable relationship (n/%)	162 (83.1)
Resident in urban area (n/%)	194 (99.5)
Employed (n/%)	160 (82.1)
Smokers (n/%)	33 (16.9)
Physical active (n/%)	140 (71.7)
Obesity (BMI ≥ 30 kg/mts^2)	19 (9.7)
High blood pressure (n/%)	46 (23.6)
Dyslipidemia (n/%)	68 (34.9)
Thyroid dysfunction (n/%)	51 (26.2)
Benzodiapines for sleep (n/%)	28 (14.3)
Melatonin 3 mg or more for sleep (n/%)	5 (2.5)
Antidepressant with hypnotic effects (n/%)	8 (4.1)
Treatment with antidepressant (n/%)	20 (10.2)
Hormone replacement therapy (n/%)	22 (11.2)

BMI: Body Mass Index: weight over squared height.

when < 5), and the total scores on the COS for insomnia severity (COS GI) and on the ESS were 17.57 ± 7.38 and 6.12 ± 4.09 respectively (Table 1).

Table 2 shows the scores on all three questionnaires. The mean total hours of sleep for the present sample was 6,5 ± 1,3. Nearly half (46.7%) of the women had a global PSQI score over 5, which suggests the need for medical attention. The prevalence rates of snoring (PSQI item 10 A), apnea (PSQI item 10B) and leg spams (PSQI item 10C) were 13%, 5,7% and 7,1% respectively.

The mean COS score for insomnia severity (COS GI) was 17.57 ± 7.38 and for hypersomnia 5.10 ± 2.35. According to the COS, 100% of the participants reported sleep dissatisfaction. However, the incidence of insomnia differed with the criteria used. In our sample, it was 15.4% for ICD-10 and 3.6% for DSM-IV. A third of the sample reported daytime sleepiness on the ESS.

The presence of hot flashes was associated with poor sleep quality and higher PSQI scores (p = 0.0128) and with excessive daytime sleepiness according to the ESS (p = 0.0497) (the greater the number of hot flashes, the higher was the ESS score). However, the frequency and the intensity of hot flashes were not associated with insomnia, when using either the ICD criteria (p = 0.937) or the DSM criteria (p = 0.141). Data regarding the incidence and severity of hot flashes are shown in Table 3. The women who had been menopausal for five or more years had a lower prevalence of hot flashes (p = 0.0007).

Table 3
Characteristics of hot flashes (Chi square).

Hot flashes	< 5 years of menopause		≥5 years of menopause		P
	n	%	N	%	
Hot flashes present (n:68)	47	24.1	21	10.8	0.166
Hot flashes absent (n:32)	13	6.7	19	9.7	0.021
Hot flashes mild (n:33)	22	11,3	11	5,6	
Hot flashes moderate (n:21)	16	8.2	5	2.6	
Hot flashes severe (n:8)	3	1.5	5	2.6	
Night sweats (n:35)	25	12.8	10	5.1	0.158

4. Discussion

The present study explored sleep quality and the relationship between sleep disorders and their related factors within a large sample of midlife postmenopausal women. It is noteworthy that all the subjects included in our research reported some degree of sleep dissatisfaction and that more than half complained about their poor sleep quality as well as symptoms such as snoring and apnea.

The physiological changes of menopause may affect a woman's health and quality of life [23]. Sleep disturbances are some of the most bothersome menopausal symptoms, reported by 40–60% of postmenopausal women [24]. Chronic difficulty falling asleep, non-restorative sleep, global sleep dissatisfaction, and a diagnosis of insomnia are more frequent among peri- and postmenopausal women than among premenopausal women [25]. A major factor in the increased prevalence of insomnia in midlife women appears to be hot flashes; experiencing hot flashes has been strongly associated with a diagnosis of insomnia, along with chronic pain and impaired health.

It is important to discriminate between subjective sleep quality (self-reported data) and objective sleep quality (polysomnographic data). Regarding self-reported sleep quality, a recent meta-analysis of cross-sectional data from 24 studies reported higher odds of experiencing sleep disturbance in perimenopause (1.60), postmenopause (1.67), and after surgical menopause (2.17) compared with women who are premenopausal [26]. In a 7-year follow-up of 3045 women, the Study of Women's Health Across the Nation (SWAN) reported an increase in difficulty falling asleep across the menopause transition but a decrease in early-morning awakening from late perimenopause to postmenopause [27]. That study also found that FSH level was associated with higher odds of nocturnal awakening, whereas a lower level of estrogen was associated with greater difficulty in falling and staying asleep [27]. The most common sleep-related complaint is night-time

Table 2
Sleep characteristics as recorded on the different questionnaires. Women distributed according time since menopause.

Sleep questionnaires	< 5 years of menopause		≥5 years of menopause		P
	n	%	n	%	P
Satisfaction with sleep (COS#1) < 3	122	62.9	72	37.1	0.59
Insomnia according to ICD criteria (COS)	24	12.3	6	3.1	0.023
Insomnia according to DSM criteria (COS)	5	2.6	2	1	0.475
Hypersomnia (COS)	122	5.34	73	16.9	0.067
ESS < 10	65	33.3	8	4.1	0.13
PSQI < 5	58	29.7	33	16.9	0.43
Snoring (PSQI question item 10A)	43	22.1	25	12.8	0.99
Respiratory pauses (PSQI item 10B)	15	7.6	11	5.7	0.26
Spasms / leg movements (PSQI question item 10C)	28	14.4	14	7.1	0.54
Hours of sleep (PSQI)	122	6.50 ± 1.2	71	6.39 ± 1.39	0.55

awakening [28]. Evidence for declining self-reported sleep quality in the menopausal period is strong; however, polysomnographic (PSG) studies have not generally found a corresponding negative change in sleep architecture [29]. Nonetheless, a few studies have reported more slow-wave sleep (SWS) in perimenopausal and postmenopausal than in premenopausal women [30], which reflects a recovery response to sleep deprivation. At the same time, postmenopausal women have been reported to have a higher apnea-hypopnea index (AHI) and lower arterial oxyhemoglobin saturation [30]. The association between FSH, as an endocrine marker of transitioning menopause, and SWS is still unclear. SWAN researchers found that the more rapid the increase in FSH, the greater is the amount of SWS and the longer is the total sleep time (TST) [31]. However, another cross-sectional study of women aged 43–52 years found that in those with insomnia, PSG measures did not correlate with FSH levels and instead were associated with symptoms of anxiety and depression [32]. In summary, PSG studies have shown few consistent effects of menopause on sleep architecture.

We found there is a strong relationship between hot flashes and insomnia. Vasomotor symptoms affect up to 80% of women during menopause [33,34]. The precise mechanism of vasomotor symptoms is poorly understood; however, it has been hypothesized that they result from a disruption of the hypothalamic temperature-regulating system. Thus, the hot flashes would be triggered by central temperature elevations acting within a greatly narrowed thermoneutral zone [35], with GnRH being a hypothalamic link between pituitary gonadotropins, hot flashes and insomnia [36].

The National Sleep Foundation recommends that sleep lasts from 7 to 9 h [37]; however, the mean sleeping time in our sample was 6.5 ± 1.2 h per night. Moreover, almost half of the present sample had impaired quality of sleep, according to the PSQI, which suggests the need for medical attention. Also, it is interesting to note that 14.7% of our sample were taking benzodiazepine and 4.1% hypnotic antidepressants.

After menopause, with increasing age, the risk of developing a primary sleep disorder, such as sleep-disordered breathing (SDB), is increased. In a survey by Freedman, which included midlife women with sleep complaints, 53% presented with sleep apnea, periodic limb movement disorder, or both [38]. The major predictors of poor sleep efficiency previously described are apnea-hypopnea index, periodic limb movement index, arousals associated with these disorders, and total number of arousals, whereas the presence of hot flashes was not a significant predictor of objective sleep efficiency in the polysomnographic study [38]. In our study, 18.7% of the sample reported snoring according to the PSQI and 18.5% reported leg spams as possible causes of arousal and sleep disturbances.

Sleep disturbances may produce distress and disability, reduce quality of life, and increase health-care utilization and costs; they also increase the risk of cardiovascular events, hypertension, weight gain, type 2 diabetes and depression [39–43]. This picture may be related to elevated levels of inflammatory biomarkers, which makes women, especially, vulnerable to the inflammatory impact of sleep disturbance. It demonstrates that greater increases in IL-6 and CRP associated with sleep disturbance in men can also affect women [44]. A recently published study examined the association between sleep continuity and duration with inflammatory biomarkers among 304 women transitioning through the menopause [45]. The median total sleep time was similar to that reported by our sample, at around 6 h, and time awake after sleep onset was on average 42 min, which indicates short and disrupted sleep. Data from this study also revealed that lower sleep efficiency was associated with higher circulating levels of interleukin-6 and that lower sleep efficiency and more minutes awake after sleep onset were independently associated with higher circulating levels of von Willebrand factor antigen. These findings suggest that sleep disturbances are associated with inflammation in midlife women, which may have implications for the development of chronic diseases in which inflammation plays a major role, such as cardiovascular disease [45].

One of the major limitations of the present study is the nature of the instruments used. Data obtained from questionnaires such as the COS, PSQI and ESS are essentially subjective, whereas those obtained by polysomnography are objective; however, the large size of the sample, and the strict inclusion/exclusion criteria and data collection support the validity of our results.

In conclusion, dissatisfaction with sleep is a common complaint during the postmenopausal years and almost half of the sample of women reported impaired sleep quality, which in most cases would warrant medical attention. Further research into sleep disorders during the climacteric and beyond is warranted due to their prevalence and the related impaired quality of life.

Contributors

Stella Maris Valiensi designed the study, and contributed to the analysis and interpretation of data, and revision of the manuscript.

María Alejandra Belardo designed the study, and took part in patient selection.

Susana Pilnik took part in patient selection, and contributed to the analysis and interpretation of data, and revision of the manuscript.

Gustavo Izbizky contributed to the analysis and interpretation of data, and revision of the manuscript.

Agustina Paula Starvaggi took part in patient selection, and contributed to the analysis and interpretation of data, and revision of the manuscript.

Camil Castelo Branco contributed to the analysis and interpretation of data, and revision of the manuscript.

All authors saw and approved the final version of the manuscript. All authors had full access to all of the data in the study (including statistical reports and tables) and can take responsibility for the integrity of the data and accuracy of the data analysis.

Conflict of interest

The authors declare that they have no conflict of interest.

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The authors of the present original study declare that they worked independently, without any funder.

Ethical approval

The study was approved by the Ethics Committee of the Italian Hospital of Buenos Aires, Argentina, 12 April 2013, ref. no. 2018.

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration)

Data are accessible at Mendeley for download under the CC BY 0.4 license. Title of the dataset: Sleep Quality
https://data.mendeley.com/datasets/tn2pv7dc4b/draft?a=ba94a770-83f7-41ff-915d-c59919a3fbde915d-c59919a3fbde.

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