Severe Hot Flashes Are Associated With Chronic Insomnia

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Background: Because hot flashes can occur during the night, their presence has been frequently associated with insomnia in women with symptoms of menopause. However, many factors other than hot flashes or menopause can be responsible for insomnia, and several factors associated with insomnia in the general population are also commonly observed in perimenopausal and postmenopausal women who have hot flashes.

Methods: A random sample of 3243 subjects (aged ≥18 years) representative of the California population was interviewed by telephone. Included were 982 women aged 35 to 65 years. Women were divided into 3 groups according to menopausal status: premenopause (57.2%), perimenopause (22.3%), and postmenopause (20.5%). Hot flashes were counted if they were present for at least 3 days per week during the last month and were classified as mild, moderate, or severe according to their effect on daily functioning. Chronic insomnia was defined as global sleep dissatisfaction, difficulty initiating sleep, difficulty maintaining sleep, or nonrestorative sleep, for at least 6 months. Diagnoses of insomnia were assessed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, classification.

Results: Prevalence of hot flashes was 12.5% in premenopause, 79.0% in perimenopause, and 39.3% in postmenopause. Prevalence of chronic insomnia was reported as 36.5% in premenopause, 56.6% in perimenopause, and 50.7% in postmenopause (P < .001). Prevalence of symptoms of chronic insomnia increased with the severity of hot flashes, reaching more than 80% in perimenopausal women and postmenopausal women who had severe hot flashes. In multivariate analyses, severe hot flashes were significantly associated with symptoms and a diagnosis of chronic insomnia. Poor health, chronic pain, and sleep apnea were other significant factors associated with chronic insomnia.

Conclusions: Severe hot flashes are strongly associated with chronic insomnia in midlife women. The presence of hot flashes should be systematically investigated in women with insomnia. Treating hot flashes could improve sleep quality and minimize the deleterious consequences of chronic insomnia.

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The purpose of this study, performed in a general population, was to assess the prevalence and severity of hot flashes in premenopausal, perimenopausal, and postmenopausal women aged 35 to 65 years and to determine whether hot flashes remain associated with insomnia after controlling for variables commonly associated with insomnia.

METHODS

SAMPLE

The study was performed from June 2003 to April 2004. The target population was the 24 million adults (aged ≥18 years) living in California. Of 3787 eligible individuals, 3243 subjects (85.6%) participated in the survey.

PROCEDURES

In the first stage, telephone numbers were pulled proportional to the population of each county in California. In the second stage, during the telephone contact, the Kish method was used to select 1 respondent per household. This method allowed for selection of a respondent on the basis of age and sex to maintain a sample representative of these 2 variables.

Interviewers explained the goals of the study to potential participants and requested verbal consent before conducting the interview. The study was reviewed by the Stanford University Institutional Review Board, Stanford, Calif.

Subjects who declined to participate or who stopped answering questions before completing half of the interview were classified as refusing to participate. Excluded from the study were subjects who were not fluent in English, who had a hearing or speech impairment, or who had an illness that precluded their being interviewed. Telephone numbers were discarded and replaced only after a minimum of 10 unsuccessful telephone attempts. In the final sample, 21.4% of telephone numbers were unlisted.

The mean (±SD) duration of the interviews was 74.5 (±37.8) minutes. An interview could be completed with more than 1 telephone call if it exceeded 60 minutes or at the request of the participant.

INSTRUMENT

Interviewers used the Sleep-EVAL 21,22 knowledge-based, expert system. This computer software is specially designed to administer questionnaires and conduct epidemiologic studies in the general population. The interview begins with a questionnaire administered to all participants. It includes, in order, sociodemographic information, sleep-wake schedule, sleeping habits, sleep disturbance symptoms, medical and paramedical consultations and hospitalizations during the last 12 months, physical disease information, use of prescribed and nonprescribed drugs, health quality assessment scale, alimentation information, fatigue scale, pain questionnaire, and information about height, weight, and, for women, questions about menopause. After this information is collected, the system begins the diagnostic exploration of sleep and mental disorders. On the basis of responses provided by a subject, the system formulates an initial diagnostic hypotheses that it attempts to confirm or reject by asking supplemental questions or by deduction. Concurrent diagnoses are allowed in accordance with the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,25 and The International Classification of Sleep Disorders, Revised: Diagnostic and Coding Manual.26 The system terminates the interview when all diagnostic possibilities have been exhausted. The system has been tested in various contexts, including clinical psychiatry and sleep disorders clinics.25-28 In psychiatry, values have ranged from 0.44 (schizophrenia disorders) to 0.78 (major depressive disorders)25,26 and, in sleep medicine, values have ranged from 0.68 to 0.92.27,28

DEFINITIONS

Menopausal status was classified in accord with the World Health Organization29 definition, as follows:

- Premenopause: Women aged 35 years or older who reported having regular menstrual cycles in the last year.
- Perimenopause: Women who reported irregular menstrual cycles during the last year and had at least 1 menstrual bleeding in the previous year.
- Postmenopause: Women who reported no menstrual bleeding during the last 12 months.

Hot flashes had to occur at least 3 days per week during the last month. Severity of hot flashes was defined as follows:

- Mild: Most of the time, hot flashes are limited to a sensation of heat without sweating.
- Moderate: Most of the time, hot flashes are a sensation of heat with sweating, but not enough to prevent the pursuit of an activity.
- Severe: Most of the time, hot flashes are a sensation of heat with sweating causing the woman to stop her activity.

Symptoms of insomnia were defined as difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), or nonrestorative sleep (NRS). Global sleep dissatisfaction (GSD)30 was defined as a complaint about sleep quality or quantity. It was required for all these symptoms to be present at the time of the interview at least 3 nights per week for at least the past 6 months. Chronic insomnia was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, classification, with the exception that insomnia duration was set at 6 months rather than 1 month.

OTHER VARIABLES ASSESSED

The following data were also collected:

- Sociodemographic variables: age, sex, marital status, race/ethnicity, occupation, and income.
- Health status variables: subjective assessment of health quality (from very poor to excellent), physical diseases at the time of the interview, chronic pain (lasting at least 6 months), blood pressure, medications (prescribed or not prescribed, including hormone therapy), and medical consultations during the previous year.
- Height and weight, to calculate body mass index (calculated as weight in kilograms divided by the square of height in meters). The body mass index categories were defined as recommended by the National Heart, Lung, and Blood Institute.31
- Breathing pauses during sleep lasting some seconds were coded as present when the subject reported a frequency of at least 3 nights per week.

STATISTICAL ANALYSES

Bivariate analyses were performed using the χ2 test or the Fisher exact test when n values were smaller than 5. Logistic regressions were used to compute the odds ratios (ORs) associated with reports of insomnia. Reported differences were significant at P≤ .05. All data are reported as mean (±SD) unless otherwise indicated.
The sample included 982 women aged 35 to 65 years. Of these women, 57.2% (n = 562) were premenopausal, 22.3% (n = 219) were perimenopausal, and 20.5% (n = 201) were postmenopausal. Demographic characteristics of these 3 groups are given in Table 1. Premenopausal women were younger and more likely to be working than were women in the other 2 groups. Postmenopausal women were more likely to be overweight than were women in the other 2 groups.

Menopause had begun at the age of 40 years or younger in 13.6% of women, between 41 and 44 years in 9.3%, at 45 or 46 years in 12.2%, at 47 or 48 years in 16.5%, at 49 or 50 years in 25.5%, at 51 or 52 years in 10%, and at 53 years or older in 11.9%. The mean age at natural menopause was 50.3 (±3.0) years. Hormone therapy was taken by 20.8% of perimenopausal women and 13.2% of postmenopausal women.

PREVALENCE OF HOT FLASHES

A total of 32.8% of the women reported having hot flashes. The prevalence was 12.5% in the group of premenopausal women, rose to 79.0% in the perimenopausal group, and decreased to 39.3% in the postmenopausal group (P < 0.001). Figure 1 shows this prevalence according to the severity of hot flashes. About half of the women experienced mild hot flashes, nearly one third experienced moderate hot flashes, and 15.3% experienced severe hot flashes. Half (50.9%) of the women experienced night sweats in addition to daytime hot flashes. The median duration of hot flashes was 2 years for premenopausal women, 5 years for perimenopausal women, and 13 years for postmenopausal women.

PREVALENCE OF SYMPTOMS OF CHRONIC INSOMNIA

The presence of chronic insomnia was examined in association with the severity of hot flashes and menopausal status. Chronic insomnia dramatically increased among women with severe hot flashes (Table 2). Of women with severe hot flashes, 81.3% had symptoms of chronic insomnia. Difficulty initiating sleep, NRS, and GSD significantly increased in women with severe hot flashes but were comparable in women with mild hot flashes and those without hot flashes. Chronic DMS increased with the severity of hot flashes.

When chronic insomnia was examined in relationship to menopausal status, chronic DIS, NRS, and GSD were more frequent among perimenopausal women. Difficulty maintaining sleep was lower among premenopausal women. One third (31.8%) of perimenopausal and postmenopausal women also reported that, in their opinion, insomnia was related to the development of menopause. Perimenopausal women with hot flashes were more likely to associate insomnia with menopause than were women without hot flashes. This association was not observed, however, in postmenopausal women (Figure 2).
When examining the temporal relationship between insomnia and hot flashes, it was found that insomnia predated menopause in 53.1% of perimenopausal women who reported symptoms of insomnia and 21.4% of postmenopausal women ($P < .001$) (Figure 3).

MULTIVARIATE MODELS

Several factors are likely to affect the bivariate associations observed among insomnia, hot flashes, and menopausal status. Therefore, logistic regression analyses were performed to account for other variables that may have independent effects on chronic insomnia (Table 3).

Chronic insomnia symptoms were entered as dependent variables. More specifically, 5 models were calculated: chronic DIS, chronic DMS, chronic NRS, at least 1 symptom of chronic insomnia, and GSD. The choice of independent variables was made in conjunction with their positive association with insomnia in bivariate analyses. The models included marital status, occupation, race/ethnicity, severity of hot flashes, menopausal status, perceived health quality, body mass index, hypertension, physical disease, chronic pain, major depressive disorder and anxiety disorders, stress, smoking, alcohol and coffee intake, breathing pauses during sleep, restless legs syndrome, and periodic limb movement symptoms. Age was not entered because of its strong correlation with menopausal status.

The likelihood of having chronic DIS, chronic NRS, or at least 1 symptom of chronic insomnia increased with ethnicity, severity of hot flashes, menopausal status, perceived health quality, body mass index, hypertension, physical disease, chronic pain, major depressive disorder and anxiety disorders, stress, smoking, alcohol and coffee intake, breathing pauses during sleep, restless legs syndrome, and periodic limb movement symptoms. Age was not entered because of its strong correlation with menopausal status.

Table 2. Insomnia by Severity of Hot Flashes and Menopausal Status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Insomnia Symptoms = 6 mo</th>
<th>DSM-IV Insomnia Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DIS</td>
<td>DMS</td>
</tr>
<tr>
<td>Hot flashes, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (n = 673)</td>
<td>7.7</td>
<td>30.5</td>
</tr>
<tr>
<td>Mild (n = 172)</td>
<td>11.6</td>
<td>47.1</td>
</tr>
<tr>
<td>Moderate (n = 89)</td>
<td>19.1</td>
<td>56.2</td>
</tr>
<tr>
<td>Severe (n = 48)</td>
<td>35.4*</td>
<td>68.8*</td>
</tr>
<tr>
<td>Menopausal status, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopause (n = 562)</td>
<td>9.4</td>
<td>30.2*</td>
</tr>
<tr>
<td>Perimenopause (n = 219)</td>
<td>16.0†</td>
<td>49.8</td>
</tr>
<tr>
<td>Postmenopause (n = 201)</td>
<td>9.0</td>
<td>44.8</td>
</tr>
</tbody>
</table>

Abbreviations: DIS, difficulty initiating sleep; DMS, difficulty maintaining sleep; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; GSD, global sleep dissatisfaction; NRS, nonrestorative sleep.

* $P < .001$.
† $P < .05$ between severity of hot flashes or between menopausal status.
‡ $P < .01$.

Figure 2. Association between severity of hot flashes (HF) and insomnia. For a definition of the severity of HF and menopausal status, see the “Definitions” subsection of the “Methods” section.

Figure 3. Temporal relationship between symptoms of insomnia and onset of menopause. Due to rounding percentages do not total 100%.
the severity of hot flashes. Menopausal status was significant only for chronic DMS; postmenopausal women were most likely to report chronic DMS. Other variables significantly associated with insomnia were perception of health as poor, breathing pauses during sleep, and chronic pain. Major depressive disorder was significant only in the model in which at least 1 symptom of chronic insomnia was the dependent variable (Table 3). Similarly, white race was significant only for chronic DMS; postmenopausal women were older. Chronic pain (OR, 2.2; 95% CI, 1.2-3.9; P = .01) and moderate (OR, 2.8; 95% CI, 1.3-6.4; P = .01) or severe (OR, 3.2; 95% CI, 1.6-6.4; P = .001) hot flashes were associated with chronic insomnia occurring around or after menopause.

This study provides evidence that severe hot flashes are associated with chronic insomnia in women aged 35 to 65 years. In general, severe hot flashes increased the likelihood of reporting GSD, chronic DIS, and chronic NRS.

Menopausal status was associated with insomnia only for chronic DMS and GSD. The multiplicity of factors associated with insomnia illustrates the multifactorial aspects of chronic insomnia in women.

Compared with previous epidemiologic studies conducted in women in midlife, this study is unique in several aspects. First, the severity of hot flashes was studied. The dramatic increase in insomnia in women with severe hot flashes indicates that severity of hot flashes should be routinely assessed in all studies of menopause. Second, symptoms of insomnia were defined in terms of frequency and chronicity. This strict definition permitted limitation of the evaluation to the most enduring aspects of insomnia and not transitory phenomena. Third, the variables assessed covered a broad

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chronic DIS</th>
<th>Chronic DMS</th>
<th>Chronic NRS</th>
<th>At Least 1 Symptom</th>
<th>GSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mild</td>
<td>1.6 (0.8-3.2)</td>
<td>1.6 (1.0-2.5)†</td>
<td>1.5 (0.8-2.8)</td>
<td>1.6 (1.1-2.5)†</td>
<td>1.8 (1.0-3.1)‡</td>
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<tr>
<td>Moderate</td>
<td>2.0 (1.0-4.2)</td>
<td>1.8 (1.0-2.3)¶</td>
<td>2.1 (1.0-4.1)¶</td>
<td>2.1 (1.2-3.7)¶</td>
<td>2.8 (1.5-5.2)*</td>
</tr>
<tr>
<td>Severe</td>
<td>2.3 (1.0-5.6)†</td>
<td>1.8 (0.8-3.7)</td>
<td>2.5 (1.5-5.6)†</td>
<td>2.7 (1.2-6.2)†</td>
<td>2.7 (1.2-5.9)‡</td>
</tr>
</tbody>
</table>

Menopausal status

<table>
<thead>
<tr>
<th>Category</th>
<th>Odds Ratio* (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopause</td>
<td>1.0 (1.0-2.0)</td>
</tr>
<tr>
<td>Perimenopause</td>
<td>0.9 (0.5-1.8)</td>
</tr>
<tr>
<td>Postmenopause</td>
<td>0.8 (0.4-1.6)</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>1.4 (0.8-2.3)</td>
</tr>
</tbody>
</table>

Health status

<table>
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<tr>
<th>Category</th>
<th>Odds Ratio* (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>1.0 (1.0-2.0)</td>
</tr>
<tr>
<td>Average</td>
<td>2.1 (1.2-3.6)</td>
</tr>
<tr>
<td>Poor</td>
<td>2.2 (1.1-4.4)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.2 (0.6-2.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>Odds Ratio* (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSM-IV major depressive disorder</td>
<td>1.9 (1.0-3.9)</td>
</tr>
<tr>
<td>Breathing pauses during sleep</td>
<td>6.0 (2.3-15.7)†</td>
</tr>
</tbody>
</table>

Abbreviations: DIS, difficulty initiating sleep; DMS, difficulty maintaining sleep; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; GSD, global sleep dissatisfaction; NRS, nonrestorative sleep.

*Odds ratios after adjusting for other predictors in the models. Nonsignificant variables for all 4 insomnia symptom models were marital status, occupation, body mass index, anxiety disorders, level of stress, smoking, alcohol and coffee intake, restless legs syndrome, and periodic limb movement.

†P < .05.
‡P < .01.
§P < .001.

| Category of reference is the absence of the condition. |
range of potential factors associated with insomnia. Most epidemiologic studies had used a limited set of confounding variables to evaluate the association between hot flashes or menopausal status and insomnia.

The prevalence of hot flashes observed in menopausal women in our present study is comparable to that reported in other epidemiologic studies performed in the United States.2-5 Similar prevalence of hot flashes was also reported in Europe,6 Australia,7 and Asia.8-9 In this sample, the age at natural menopause was comparable to that reported in other US studies.32-34

It was found that 56.6% of perimenopausal women and 50.7% of postmenopausal women had at least 1 symptom of chronic insomnia. This is higher than the rate reported in studies that evaluated difficulty sleeping with a single yes-no question. For example, Kravitz et al.15 found that 39.6% to 45.4% of perimenopausal and postmenopausal women in the United States reported difficulty sleeping during the 2 weeks before the interview. Another US study reported a rate of about 40% in perimenopausal and postmenopausal women.2 An Australian study found rates between 44% and 52% in perimenopausal and postmenopausal women,7 and a study from China found a rate of about 21% of trouble sleeping in premenopausal, perimenopausal, and postmenopausal women.14

Results showed that chronic insomnia considerably increased in perimenopausal and postmenopausal women compared with premenopausal women; more than half of the women reported DIS, DMS, or NRS. Several studies have attributed the increase in sleep disturbances to hot flashes during perimenopause.10,35 However, this may be too simplistic, because many other factors, such as chronic pain and poor health, also increased with age. Both of these factors are closely related to insomnia. Their importance is illustrated in the multivariate models; the association between chronic insomnia and menopausal status considerably diminished and even disappeared for DIS and NRS, whereas chronic pain and poor health remained significant. Postmenopausal women still had a higher probability of reporting DMS. A possible explanation is that, because postmenopausal women are older than the other 2 groups of women, this association is mainly due to aging rather than menopausal status. Other sleep disorders, such as periodic limb movements, restless legs syndrome, and obstructive sleep apnea, are known to increase with age and to be associated with insomnia. Periodic limb movements and restless legs syndrome did not reach significant levels in the multivariate models; however, their inclusion decreased the odds between hot flashes and insomnia. When the temporal sequence between menopause and insomnia was examined, it was observed that insomnia predated menopause in about 50% of perimenopausal women and about 20% of postmenopausal women. Moderate and severe hot flashes remained strongly associated with chronic insomnia occurring around or after menopause.

Objective polysomnographic measures of sleep disturbances in menopausal women have yielded conflicting results. Some studies have demonstrated a significant correlation between the occurrence of hot flashes and waking during sleep,36-38 while others found no evidence that hot flashes disturb sleep in healthy women.39-41 Several factors for the lack of association may have influenced the results. Most of these polysomnographic studies are based on samples of fewer than 20 women, with 2 exceptions.39,41 Therefore, it was difficult to examine the data using different factors such as the severity of hot flashes or the report of frequent nocturnal awakenings. As the results illustrated, about 55% of women with hot flashes had DMS and the number of women with insomnia increased with severe hot flashes. Furthermore, the complaint may not be DMS but other insomnia symptoms such as NRS. It is likely that hot flashes occurring during the night have different levels of severity and cause more or less discomfort, leading to different complaints or no complaint.

This was a cross-sectional study and, therefore, provides a picture of the population at a given point in time. For example, it was possible to identify the association between the severity of hot flashes and chronic insomnia, but the ability to determine whether causality existed was limited. Another limitation is that data are based on self-reports. Measurement of hot flashes relied on individual perceptions and experiences. However, studies that compared subjective and objective measurements of hot flashes found that women reliably described their hot flashes.32,44

**CONCLUSIONS**

The results of this study indicate that insomnia in perimenopausal, perimenopausal, and postmenopausal women is influenced by several factors, such as chronic pain, poor health, and sleep apnea, which are not related specifically to menopausal status but to aging. On the other hand, hot flashes remain an important factor in insomnia in women in midlife, independent of their menopausal status. Treating hot flashes could improve sleep quality and minimize the deleterious consequences of chronic insomnia.

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**REFERENCES**


