Are hot flashes associated with sleep disturbance during midlife?

Hanna Xu, BS[a], **Rebecca C. Thurston, PhD**[b], **Karen A. Matthews, PhD**[b], **Cindy L. Bryce, PhD**[b], **Ron D. Hays, PhD**[c], **Wishwa N. Kapoor, MD, MPH**[b], **Roberta B. Ness, MD, MPH**[d], and **Rachel Hess, MD, MS**[b]

[a]Temple University School of Medicine, Philadelphia, PA

[b]The University of Pittsburgh School of Medicine, 230 McKee Place Suite 600 Pittsburgh, PA, 15213

[c]University of California at Los Angeles School of Medicine, Los Angeles, CA

[d]University of Texas School of Public Health, Houston, TX

Abstract

Objective—Sleep disturbance and hot flashes are common during menopause, but their association is not well understood. We sought to understand the associations among sleep disturbance and the frequency, bothersomeness, and interference of hot flashes in mid-life women.

Study Design—STRIDE is a study of women ages 40–65 years at varied menopausal stages. We examined the cross-sectional associations of sleep disturbance with the frequency and bothersomeness of hot flashes, and interference of hot flashes with work, social, and leisure activities during the 2nd year of STRIDE.

Main Outcome Measure—Self-reported sleep disturbance

Results—Of the 623 women with complete data, 370 (59%) reported having hot flashes. Bivariate analyses showed that reporting hot flashes with bother, but not hot flashes alone, was associated with sleep disturbance (odds ratio [OR] [95% confidence interval (CI)]: 2.8[2.0–4.0] and 1.3[0.7–2.5], respectively). In multivariable models, women reporting bothersome hot flashes were more likely to report sleep disturbance (OR [95% CI]: 2.1 [1.4–3.2]) compared to women who reported no hot flashes. When the perceived interference of hot flashes with work, social activities, and leisure activities were included in the model, the relationships between bothersome hot flashes and sleep disturbance disappeared.

Conclusions—Hot flashes are not associated with sleep disturbance, unless they are bothersome. Mid-life patients should routinely be queried about the bothersomeness of their hot flashes.

Correspondence and requests for reprints should be addressed to: Rachel Hess, MD, MS, 230 McKee Place, Suite 600, Pittsburgh, PA 15213, rah67@pitt.edu, 412-692-2025, 412-692-4838.

Keywords

Menopause; hot flashes; sleep disturbance

1. INTRODUCTION

Vasomotor symptoms (hot flashes and night sweats) are reported by up to 75% of women during menopause and are considered to be a hallmark of menopause. However, among women who experience hot flashes, not all find them bothersome or that they interfere with their lives.(1) It is estimated that 40% to 64% of all peri-or postmenopausal women report disturbed sleep.(2–5) While hot flashes and sleep disturbance are both commonly reported during menopause, their association with each other is not well understood.

While some studies have shown an association between the severity of hot flashes and insomnia symptoms,(6, 7) others have found that mid-life sleep disturbance is related more to psychological well-being and life stressors than to physiologically-assessed menopausal hot flashes.(8, 9)The concept of "bothersomeness" of hot flashes may help explain these disparate findings, yet there are scant data examining the relationship between a woman's perception of how bothersome her hot flashes are and her sleep.

This study examines associations between several hot flash-related indices (perceived frequency, bothersomeness, and interference) and aspects of sleep disturbance (difficulty falling asleep, waking up several times a night, and/or waking up earlier than planned and being unable to fall back asleep) in mid-life women. We hypothesized that women with more frequent, bothersome hot flashes, and interfering hot flashes would report more sleep disturbance.

2. METHODS

2.1 Participants

Do Stage Transitions Result in Detectable Effects (STRIDE) is an ongoing cohort study of 732 women ages 40 to 65 years between January and December 2005 enrolled from a single university-based general internal medicine practice. Briefly, all women ages 40–65 who presented to the practice were asked to participate in a study examining the impact of menopause on health-related quality of life. All women who were in this age range, spoke English, and consented to participate were enrolled in the study. The enrollment of the cohort has been described in more detail previously.(10) Of the 732 participants enrolled in STRIDE, 677 (93%) completed the second year questionnaire that included questions about sleep and hot flash interference; 623 had complete data and formed the analytic sample for these cross-sectional analyses (Table 1). The project was approved by the University of Pittsburgh Institutional Review Board (#0407165) and registered with clinicaltrials.gov (#NCT00097994).

2.2 Measures

In STRIDE, women completed annual questionnaires. Women could self-complete the questionnaires on the study website from home or over the telephone with trained research staff. If questionnaires were completed over the telephone, answers were directly entered into the Internet-based forms by the research staff. Questionnaires included information regarding demographics, menopausal status and menopausal symptoms, hormone therapy use, medical comorbidities, tobacco and alcohol use, physical activity, and health-related

quality of life. In the second year of the study, women also answered questions related to sleep and the interference of hot flashes in their daily life.

2.2.1 Sleep Disturbance—Beginning in the second year of the study, women were asked to report about their sleep over the past two weeks. Women who reported any of the following at least 3–4 times a week were classified as having sleep disturbance: (1) trouble falling asleep, (2) waking up several times a night, and (3) waking up earlier than planned and unable to fall back asleep again.(11, 12)

2.2.2 Hot Flashes, Hot flash-associated Bother, and Hot Flash Interference—In the annual STRIDE questionnaire, women were asked about the frequency and bothersomeness of hot flashes in the last four weeks. Women reported the frequency of hot flashes on a 5-point scale ranging from 0 (*none of the time*) to 4 (*all of the time*). Women who reported experiencing hot flashes at least some of the time (a rating of 2 or above) were asked to rate the bothersomeness of hot flashes using the same 5-point scale. Based on these responses, we constructed a summary symptom plus bother variable. Women were classified as: (1) not having hot flashes (frequency of *none* or *a little of the time*), (2) having hot flashes at least *some of the time* but not bothered by them (bothered *none* or *a little of the time*), or (3) having hot flashes at least *some of the time* and being bothered by them at least *some of the time*.

Beginning in the second year of STRIDE, all women, regardless of reporting hot flashes, were asked about interference of their hot flashes with work, social activities, and leisure activities in the last two weeks on three questions using a 10-point response scale ranging from *do not interfere* to *completely interfere*. These questions, derived from Carpenter's Hot Flash Daily Interference Scale, was considered an alternative marker of hot flash severity. (13) We defined 0–1 as *does not interfere* and 2–10 as *interferes* based on the distribution of responses. Of note, some women who reported hot flashes less than *some of the time* (and were therefore classified for these analyses as not having hot flashes) still reported at least some interference.

2.2.3 Other Variables—Menopausal status was classified as pre-, early peri-, late peri-, early post-, or late postmenopausal based on bleeding patterns using a modification of the Stages of Reproductive Aging Workshop.(14, 15) Women who previously had hysterectomies or were taking oral contraceptive pills could not be classified based on bleeding patterns and were placed into separate categories.

Race was dichotomized as white and non-white. Smoking status, hormone therapy use (any exogenous hormone use), and hazardous drinking (defined as more than 7 drinks per week or more than 4 drinks on any one occasion) (NIAAA, www.niaaa.nih.gov/) were dichotomized as "yes" or "no." Education was categorized as "less than or equal to high school," "some college," "completed college," and "graduate degree."

Women reported the presence or absence of nine comorbid medical conditions: heart disease, heart failure, depression, diabetes, emphysema or lung disease, stroke, arthritis, cancer (other than skin cancer), and high blood pressure. Women were placed into comorbidity categories of: "none," "1–2 conditions," or "≥3 conditions." Marital status was categorized as either "married," or "single," "widowed," or "divorced." Baseline age was calculated from participant's date of birth and body mass index (BMI: weight in kilograms divided by height in meters squared) was abstracted from the participant's medical record.

We used the RAND-36 emotional well-being scale as an indicator of depressive symptoms. (16) The population average RAND-36 emotional well-being score is 50.(16) Participants

were classified as physically active or inactive based on self-report of participation in at least 30 minutes of moderate physical activity five days a week.(17)

2.3 Statistical Analyses

We excluded 54 women with incomplete information for the predictors, outcomes, or covariates. We next summarized participants' baseline characteristics using frequencies and measures of central tendencies.

We used logistic regression models to examine the associations between the frequency and bothersomeness of hot flashes and sleep disturbance. Covariables were selected a priori for inclusion in the initial multivariable models based on their relationship to hot flashes and/or sleep disturbance in the literature. Covariables included age, race, education, marital status, menopausal status, hormone therapy use, medical comorbidities, tobacco and alcohol use, physical activity, and emotional well-being. For example, African American women, older age, and lower levels of educational attainment have been associated with more hot flashes. (18)

A second set of multivariable models were then constructed to understand whether associations between the frequency and bothersomeness of hot flashes and sleep disturbance remained when the perceived interference of hot flashes with work, leisure, and social activities were included in the models. The proportional odds assumption was confirmed in all models. All analyses were conducted using STATA version 10 (Stata Corp, College Station, TX). We considered a p-value of <0.05 to be significant.

3. RESULTS

3.1 Participant characteristics

Of the 623 participants, 22% were premenopausal, 18% were perimenopausal, 39% were postmenopausal, and 21% reported having a hysterectomy. Six percent of women reported hot flashes without bother while 32% reported bothersome hot flashes. Prevalence of hormone therapy use was low. The majority of participants were white, married, reported 1–2 comorbid medical conditions, and reported engaging in moderate physical activity for 30 minutes at least five days per week. On average women were 53 years old with a BMI in the obese range (30) and with a mean emotional well-being score of 46 (Table 1) slightly below the population mean score of 50.(15) Three hundred thirty-eight women were classified as having disturbed sleep.

3.2 Hot flashes and sleep disturbance

In bivariate analyses (Table 1), reporting bothersome hot flashes, but not hot flashes without bother was associated with sleep disturbance (odds ratio (OR)[95% confidence interval (CI)]: 2.8 [2.0–4.0] and 1.3 [0.7–2.5], respectively). In multivariable models, reporting bothersome hot flashes remained associated significantly with reporting sleep difficulty (Table 2).

3.2.1 Associations among the frequency and bothersomeness of hot flashes, perceived interference of hot flashes and sleep disturbance—We next investigated whether the association between the frequency and bothersomeness of hot flashes and sleep disturbance was attenuated by perceived interference of hot flashes with: (1) work, (2) social activities, or (3) leisure activities. It is notable that only 9% of women who reported vasomotor symptoms reported interference from hot flashes *never* or *rarely*.

As expected, having any hot flashes (even those that were not rated as bothersome) were related to perceived interference of hot flashes with work, social activities, and leisure activities (p<0.01). Perceived hot flash interference with work, social activities, and leisure activities was also associated with increasing sleep disturbance as compared to women who did not perceive their hot flashes as interfering (p<0.001 for all comparisons).

Including perceived interference of hot flashes in multivariable models testing associations between hot flashes and sleep disturbance, only hot flash-associated interference with leisure activities remained significantly associated with sleep disturbance (OR [95% CI]: 4.0 [1.3–12]). Reporting bothersome hot flashes was no longer significantly associated with sleep disturbance in this model (OR [95% CI]: 1.2 [0.7–2.0]).

4. DISCUSSION

We tested the associations between both the frequency and perceived bothersomeness of hot flashes with subjective sleep disturbance in mid-life women. We also examined the role of the perceived interference of these hot flashes on work, social activities, and leisure activities in the relationship between hot flashes and sleep disturbance. We found associations among bothersomeness of hot flashes, perceived interference of hot flashes and self-reported sleep disturbance. These findings add to the current literature that is beginning to disentangle the relationship between the occurrence of hot flashes, the perception and perceived bothersomeness of hot flashes, and how women describe hot flashes as interfering with their lives. The findings may help shed light on the role that sleep and perceived interference play in women's perception of a hot flash as "bothersome."

In addition, it adds to the literature of mid-life women, hot flashes, and sleep disturbance by tying the association between bothersome hot flashes and interference of these hot flashes with sleep disturbance. Though many studies have hypothesized that hot flashes and vasomotor symptoms are associated with sleep disturbance in perimenopausal and postmenopausal women, this study expands on this idea. Our study found that rather than hot flashes per se, it was the bothersome hot flashes perceived as interfering with life, especially leisure activities, that were most associated with sleep disturbance. It may be that the women who tend to notice that their hot flashes are bothersome during their leisure activities, when they are resting or relaxing, may also be more bothered at night during sleep. The direction of this association needs to be evaluated in future studies.

This study has several limitations that are worth noting. While we have adjusted for many potential confounders including medical comorbidities and emotional well being, STRIDE does not include detailed information about participant's medication use and depression, both of which have been implicated in sleep disturbance and hot flashes. The time frame of our questions regarding hot flashes and sleep disturbance is different. STRIDE's information about sleep and hot flashes is based on self-report only, and it is possible that common reporting factors may underlie the relations observed here. In addition, we did not ask women what time of the day they were reporting hot flashes or bothersome hot flashes. It would also be interesting to understand if there is an association between the timing of day that women have subjective reports of bothersome hot flashes and sleep disturbance at night. Only six-percent of women with hot flashes at least some of the time did not find their hot flashes bothersome; the absolute number of women in our study in this group was also small, limiting our ability to draw conclusions about this group of women. Further, we did not record method of survey administration (i.e., telephone vs. Internet), which may influence response.(19) Finally, this is a cross-sectional observational investigation of sleep and hot flashes, and therefore the temporal or causal nature of these relations cannot be determined here.

Further research examining the longitudinal relationship between bothersome and interfering hot flashes with sleep disturbance would help shed light on the directionality of these associations, as well as their joint or independent patterns of change over time. Particularly of interest would be studies that can examine a closer temporal relationship between hot flashes and sleep disturbance by asking women if they experienced hot flashes or sleep disturbance last night or using physiologic measures of both hot flashes and sleep in conjunction with questionnaire assessments. Studies incorporating physiologic measures of both sleep and hot flashes would further assist in teasing out relations between reporting versus the physiologic occurrence of each of these symptoms.

5. CONCLUSION

Bothersome hot flashes were associated with increased sleep disturbance in midlife women. This may be due to hot flash interference nature of hot flashes particularly with leisure activities. Midlife women with complaints of either hot flashes or sleep disturbance should be queried regarding hot flashes, sleep quality, and the bothersome and interfering nature of these symptoms.

Acknowledgments

References

1. Thurston RC, Bromberger JT, Joffe H, Avis NE, Hess R, Crandall CJ, et al. Beyond frequency: who is most bothered by vasomotor symptoms? Menopause. 2008 Sep-Oct; 15(5):841–7.

2. Kravitz HM, Zhao X, Bromberger JT, Gold EB, Hall MH, Matthews KA, et al. Sleep disturbance during the menopausal transition in a multi-ethnic community sample of women. Sleep. 2008 Jul 1; 31(7):979–90. [PubMed: 18652093]

3. Kuh DL, Wadsworth M, Hardy R. Women's health in midlife: the influence of the menopause, social factors and health in earlier life. Br J Obstet Gynaecol. 1997 Aug; 104(8):923–33. [PubMed: 9255084]

4. Ledesert B, Ringa V, Breart G. Menopause and perceived health status among the women of the French GAZEL cohort. Maturitas. 1995 Dec; 20(2–3):113–20. [PubMed: 7715462]

5. Owens JF, Matthews KA. Sleep disturbance in healthy middle-aged women. Maturitas. 1998 Sep 20; 30(1):41–50. [PubMed: 9819782]

6. Ensrud KE, Stone KL, Blackwell TL, Sawaya GF, Tagliaferri M, Diem SJ, et al. Frequency and severity of hot flashes and sleep disturbance in postmenopausal women with hot flashes. Menopause. 2009 Mar-Apr; 16(2):286–92. [PubMed: 19002015]

7. Ohayon MM. Severe hot flashes are associated with chronic insomnia. Arch Intern Med. 2006 Jun 26; 166(12):1262–8. [PubMed: 16801508]

8. Freedman RR, Roehrs TA. Sleep disturbance in menopause. Menopause. 2007 Sep-Oct; 14(5):826–9. [PubMed: 17486023]

9. Thurston RC, Blumenthal JA, Babyak MA, Sherwood A. Association between hot flashes, sleep complaints, and psychological functioning among healthy menopausal women. Int J Behav Med. 2006; 13(2):163–72. [PubMed: 16712434]

10. Hess R, Olshansky E, Ness R, Bryce CL, Dillon S, Kapoor W, et al. Pregnancy and birth history influence women's experience of menopause. Menopause. 2008 Jan 9; 15(5):435–41. [PubMed: 18188135]

11. Edinger JD, Bonnet MH, Bootzin RR, Doghramji K, Dorsey CM, Espie CA, et al. Derivation of research diagnostic criteria for insomnia: report of an American Academy of Sleep Medicine Work Group. Sleep. 2004 Dec 15; 27(8):1567–96. [PubMed: 15683149]

12. Lichstein KL, Durrence HH, Taylor DJ, Bush AJ, Riedel BW. Quantitative criteria for insomnia. Behav Res Ther. 2003 Apr; 41(4):427–45. [PubMed: 12643966]

13. Carpenter JS. The Hot Flash Related Daily Interference Scale: a tool for assessing the impact of hot flashes on quality of life following breast cancer. J Pain Symptom Manage. 2001 Dec; 22(6):979–89. [PubMed: 11738160]

14. Hess, R.; Avis, N.; Chang, Y.; Thurston, R.; Bromberger, J.; Greendale, G., et al. Relationship Quality is Associated with Sexual Functioning in Midlife Women: Results From the Study of Women's Health Across the Nation. International Society for the Study of Women's Sexual Health; Florence, Italy: 2009.

15. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, et al. Executive summary: Stages of Reproductive Aging Workshop (STRAW). Menopause. 2001 Nov-Dec; 8(6):402–7. [PubMed: 21141649]

16. Hays, RD.; Prince-Embury, S.; Chen, H. RAND-36: Health Status Inventory. San Antonio, TX: The Psychological Corporation; 1998.

17. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. Jama. 1995 Feb 1; 273(5):402–7. [PubMed: 7823386]

18. Gold EB, Colvin A, Avis N, Bromberger J, Greendale GA, Powell L, et al. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. Am J Public Health. 2006 Jul; 96(7):1226–35. [PubMed: 16735636]

19. Hays RD, Kim S, Spritzer KL, Kaplan RM, Tally S, Feeny D, et al. Effects of mode and order of administration on generic health-related quality of life scores. Value Health. 2009 Sep; 12(6):1035–9. [PubMed: 19473334]

Table 1

Baseline characteristics of the participants overall and population comparisons for sleep difficulty (N=623)

	Total (n=623) n(%)[a]	Women reporting sleep difficulty (n= 338) n(%)[a]	Odds (95% Confidence Interval) of reporting sleep difficulty	p-value
Menopausal Status				
Premenopausal	137 (22)	50 (15)	1	<0.001
Early Perimenopausal	71 (11)	42 (12)	2.5 (1.4-4.5)	
Late Perimenopausal	40 (6)	22 (7)	2.1 (1.0-4.3)	
Early Postmenopausal	111 (18)	60 (18)	2.0 (1.2-3.4)	
Late Postmenopausal	131 (21)	77 (21)	2.5 (1.5-4.1)	
Hysterectomy	133 (21)	87 (21)	3.3 (2.0-5.4)	
Hot Flashes and Bother				
Neither	385 (62)	177 (52)	1	<0.001
Hot flashes without bother	38 (6)	20 (6)	1.3 (0.7-2.5)	
Hot flashes with bother	200 (32)	141 (42)	2.8 (2.0-4.0)	
Hot flash-associated Work Interference (yes)	152 (24)	118 (35)	4.0 (2.6-6.0)	<0.001
Hot flash- associated Social Activities (yes)	134 (22)	107 (32)	4.4 (2.8-7.0)	<0.001
Hot flash- associated Leisure Activities (yes)	135 (22)	111 (33)	5.3 (3.3-8.6)	<0.001
Race (non-white)	163 (26)	86 (25)	0.9 (0.6-1.3)	NS[b]
Tobacco use (yes)	95 (15)	71 (21)	2.9 (1.8-4.7)	<0.001
Education				
<= High School	94 (15)	63 (19)	1	<0.001
Some College	172 (28)	107 (32)	0.8 (0.5-1.4)	
Completed College	146 (23)	70 (21)	0.5 (0.3-0.8)	
Graduate Degree	211 (34)	98 (29)	0.4 (0.3-0.7)	
Medical comorbidities				
0	155 (25)	71 (21)	1	0.04
1-2	347 (56)	192 (57)	1.4 (1.0-2.1)	
≥3	121 (19)	74 (22)	1.8 (1.1-2.9)	
Hormone Therapy use (yes)	52 (8)	35 (10)	1.8 (1.0-3.3)	<0.05
Marital Status (not married)	261 (42)	155 (46)	1.4 (1.0-2.0)	0.03
Hazardous drinking (yes)	58 (9)	38 (11)	1.8 (1.0-3.0)	NS[b]
Physical activity (yes)	394 (63)	205 (61)	0.8 (0.6-1.1)	NS[b]
Age (mean (sd[c]))	53 (6)	54 (6)	1.0 (1.0-1.0)	NS[b]

	Total (n=623) n(%)[a]	Women reporting sleep difficulty (n= 338) n(%)[a]	Odds (95% Confidence Interval) of reporting sleep difficulty	p-value
Emotional well being (mean (sd[c]))	46 (11)	44 (11)	0.9 (0.9-1.0)	<0.001
Body Mass Index (mean (sd[c]))	30 (8)	30 (8)	1.0 (1.0-1.0)	NS[b]

[a] N(%): number with percentage unless indicated with mean(sd);

[b] NS: non-significant;

[c] sd: standard deviation

Table 2

Multivariable analysis sleep difficulty with hot flashes (Odds ratio (95% confidence interval))

	Sleep difficulty[a]	p-value
Menopausal Status		
Premenopausal (ref[c])	1	
Early Perimenopausal	3.0 (1.6-5.6)	0.001
Late Perimenopausal	2.0 (0.9-4.4)	NS[b]
Early Postmenopausal	2.4 (1.3-4.6)	0.008
Late Postmenopausal	4.2 (1.9-9)	<0.001
Hysterectomy	3.9 (1.9-7.7)	<0.001
Hot Flashes and Bother		
Neither (ref)	1	
Hot flashes without bother	1.1 (0.5-2.2)	NS
Hot flashes with bother	2.1 (1.4-3.2)	<0.001
Race (non-white)	0.6 (0.4-0.9)	0.01
Tobacco use (yes)	1.9 (1.1-3.4)	0.03
Education		
<= High School (ref)	1	
Some College	1.0 (0.5-1.8)	NS
Completed College	0.7 (0.4-1.3)	NS
Graduate Degree	0.6 (0.3-1.2)	NS
Medical comorbidities		
0 (ref)	1	
1-2	0.8 (0.5-1.3)	NS
≥3	0.7 (0.4-1.4)	NS
Hormone Therapy use (yes)	1.4 (0.7-2.8)	NS
Marital Status (not married)	1.3 (0.9-1.9)	NS
Hazardous drinking (yes)	1.3 (0.7-2.4)	NS
Physical activity (yes)	0.9 (0.6-1.4)	NS
Age	1.0 (0.9-1.0)	NS
Emotional well being	**1.0 (0.9-1.0)**	<0.001
Body Mass Index	1.0 (1.0-1.0)	NS

[a]Sleep difficulty: no vs. yes

[b]NS: non-significant

[c]ref: referent group