

Sleep-disordered Breathing and the Menopausal Transition Among Participants in the Sleep in Midlife Women Study

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ABSTRACT

Objective: Menopause is widely believed to be an established cause of sleep disorders, but evidence for this theory is inconclusive. Attributing any sleep problem to normal processes of menopause may lead to underdiagnosis of treatable sleep disorders in midlife women. This study uses detailed longitudinal data on sleep and menopausal health from participants in the Sleep in Midlife Women Study to investigate whether risk and severity of sleep-disordered breathing increase with progression through menopause, accounting for changes in age and body habitus.

Methods: A total of 219 women aged 38 to 62 years were recruited from participants in the Wisconsin Sleep Cohort Study. Menopause status was determined from daily diaries in which participants reported menstrual flow, hot flashes, and use of hormonal medications. Each participant underwent in-home polysomnography studies every 6 months, to measure the apnea-hypopnea index (AHI) (N = 1,667 studies). Linear models with empirical standard errors were fit for logarithm of AHI on menopause status and years in menopause, adjusting for age, body mass index, waist girth, and neck girth.

Results: Compared with women in premenopause, AHI was 21% higher among participants in perimenopause (95% CI, -4 to 54), 31% higher among participants in postmenopause (95% CI, 2-68), and 41% higher among participants whose menopausal stage could not be distinguished between peri- and postmenopause (95% CI, 8-82). Among women who had begun perimenopause, each additional year in menopause was associated with 4% greater AHI (95% CI, 2-6).

Conclusions: Progression through menopause is associated with greater sleep-disordered breathing severity. This association is independent of aging and changes in body habitus.

Age at Natural Menopause Genetic Risk Score in Relation to Age at Natural Menopause and Primary open-angle Glaucoma in a US-based sample

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ABSTRACT

Objective: Several attributes of female reproductive history, including age at natural menopause (ANM), have been related to primary open-angle glaucoma (POAG). We assembled 18 previously reported common genetic variants that predict ANM to determine their association with ANM or POAG.

Methods: Using data from the Nurses' Health Study (7,143 women), we validated the ANM weighted genetic risk score in relation to self-reported ANM. Subsequently, to assess the relation with POAG, we used data from 2,160 female POAG cases and 29,110 controls in the National Eye Institute Glaucoma Human Genetics Collaboration Heritable Overall Operational Database (NEIGHBORHOOD), which consists of 8 datasets with imputed genotypes to 5.6+ million markers. Associations with POAG were assessed in each dataset, and site-specific results were meta-analyzed using the inverse weighted variance method.

Results: The genetic risk score was associated with self-reported ANM ($P = 2.2 \times 10^{-77}$) and predicted 4.8% of the variance in ANM. The ANM genetic risk score was not associated with POAG (Odds Ratio (OR) = 1.002; 95% Confidence Interval (CI): 0.998,

1.007; $P = 0.28$). No single genetic variant in the panel achieved nominal association with POAG ($P \geq 0.20$). Compared to the middle 80 percent, there was also no association with the lowest 10th percentile or highest 90th percentile of genetic risk score with POAG (OR = 0.75; 95% CI: 0.47, 1.21; $P = 0.23$ and OR = 1.10; 95% CI: 0.72, 1.69; $P = 0.65$, respectively).

Conclusions: A genetic risk score predicting 4.8% of ANM variation was not related to POAG; thus, genetic determinants of ANM are unlikely to explain the previously reported association between the two phenotypes.

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Cultural Issues in Menopause: An Exploratory Qualitative Study of Macedonian Women in Australia

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ABSTRACT

Objective: This study explored the attitudes to, and experience of, menopause among Macedonian women living in Australia, including attitudes and responses to hormone therapy (HT) and complementary therapies, as well as related psycho-sexual, relationship and other midlife issues.

Methods: Using qualitative methodology, the study was based on seven unstructured, nondirective group discussions. Natural social groups were recruited, meeting wherever each group felt most at home. A total of 81 participants ranged in age from 45 to 75 years. The women included both first-generation immigrants and women born in Australia to Macedonian parents. A bilingual Macedonian researcher conducted the fieldwork.

Results: Participants typically claimed they lacked information about menopause in their native language, and their knowledge of HT was highly variable. Some women only felt comfortable approaching Macedonian doctors. Others reported an easing of symptoms when they revisited their homeland. Deeply religious participants claimed their faith helped them through this phase of life, and that they were as likely to consult a priest as a doctor. A recurring theme was that Macedonian men tended to regard their wives differently after menopause, sometimes treating them as "non-sexual." Women regarded this shift in male attitudes as a precipitating factor in domestic violence, extramarital affairs and divorce. Symptoms such as hot flashes and mood swings were associated with negative attitudes toward menopause.

Conclusions: Culturally determined attitudes appear to affect the perception and experience of menopause. Other influencing factors include migration, women's roles, marital status, religion, use of herbal and traditional remedies, social situation, access to information, knowledge and experience of menopausal symptoms.

Vaginal Erbium Laser as Second-Generation Thermotherapy for the Genitourinary Syndrome of Menopause: A Pilot Study in Breast Cancer Survivors

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ABSTRACT

Objective: The aim of this study was to evaluate the efficacy and acceptability of a second generation of vaginal laser treatment, the vaginal erbium laser, as a nonablative photothermal therapy for the management of genitourinary syndrome of menopause in postmenopausal breast cancer survivors.

Methods: The study was performed using an erbium laser crystal yttrium-aluminum-garnet (XS Fotona Smooth, Fotona, Ljubljana, Slovenia) with a wavelength of 2,940 nm. Forty-three postmenopausal breast cancer survivors were treated with

three laser applications every 30 days. Symptoms were assessed before the treatment and after 1, 3, 6, 12, and 18 months, using two methods, subjective Visual Analog Scale (VAS) and objective Vaginal Health Index Score (VHIS). The procedures were performed on an outpatient basis without anesthesia or drug use before or after the intervention.

Results: From baseline values of 8.5 +/- 1.0 cm, vaginal dryness VAS scores were 4.4 +/- 1.2 cm after the third treatment and 5.5 +/- 1.5 cm 12 months after the treatment ($P < 0.01$ vs basal values), whereas they were 7.5 +/- 1.8 cm after 18 months from the last laser application (NS vs basal values). From baseline values of 7.5 +/- 1.5 cm, dyspareunia VAS values decreased to 4.2 +/- 0.9 cm after the third treatment and 5.1 +/- 1.8 cm 12 months from the last laser application ($P < 0.01$ vs basal values), whereas they were 6.5 +/- 1.8 cm after 18 months from the last laser application (NS vs basal values). VHIS, from baseline values of 8.1 +/- 1.3, was 21.0 +/- 1.4 after the third treatment and 18 +/- 1.8 12 months from the last laser application ($P < 0.01$ vs basal values), whereas they were 14.8 +/- 1.5 cm after 18 months from the last laser application (NS vs basal values). No adverse events were recorded during the study.

Conclusions: This study suggests that the vaginal erbium laser is effective and safe for the treatment of genitourinary syndrome of menopause in breast cancer survivors.

Association of Genetic Variation in the Tachykinin Receptor 3 Locus with Hot Flashes and Night Sweats in the Women's Health Initiative Study

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ABSTRACT

Objective: Vasomotor symptoms (VMS, ie, hot flashes or night sweats) are reported by many, but not all, women. The extent to which VMS are genetically determined is unknown. We evaluated the relationship of genetic variation and VMS.

Methods: In this observational study, we accessed data from three genome-wide association studies (GWAS) (SNP Health Association Resource cohort [SHARe], WHI Memory Study cohort [WHIMS+], and Genome-Wide Association Studies of Treatment Response in Randomized Clinical Trials [GARNET] studies, total $n = 17,695$) of European American, African American, and Hispanic American postmenopausal women aged 50 to 79 years at baseline in the Women's Health Initiative Study. We examined genetic variation in relation to VMS (yes/no) in each study and using trans-ethnic inverse variance fixed-effects meta-analysis. A total of 11,078,977 single-nucleotide polymorphisms (SNPs) met the quality criteria.

Results: After adjustment for covariates and population structure, three SNPs (on chromosomes 3 and 11) were associated with VMS at the genome-wide threshold of 5×10^{-8} in the African American SHARe GWAS, but were not associated in the other cohorts. In the meta-analysis, 14 SNPs, all located on chromosome 4 in the tachykinin receptor 3 (TACR3) locus, however, had $P < 5 \times 10^{-8}$. These SNPs' effect sizes were similar across studies/participants' ancestry (odds ratio ~1.5).

Conclusions: Genetic variation in TACR3 may contribute to the risk of VMS. To our knowledge, this is the first GWAS to examine SNPs associated with VMS. These results support the biological hypothesis of a role for TACR3 in VMS, which was previously hypothesized from animal and human studies. Further study of these variants may lead to new insights into the biological pathways involved in VMS, which are poorly understood.

Effects of Aerobic Exercise Training on Ace and Adrb2 Gene Expression, Plasma Angiotensin II Level, and Flow-Mediated Dilation: A Study on Obese Postmenopausal Women with Prehypertension

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ABSTRACT

Objective: The purpose of this study is to determine the effect of 10 weeks of moderate-intensity aerobic exercise training (MIET) on blood pressure (BP), angiotensin-converting enzyme (ACE) and [beta]2-adrenergic receptor (ADRB2) gene expression

in leukocytes, plasma angiotensin II (Ang II), and flow-mediated dilation (FMD) in obese postmenopausal women (PMW) with prehypertension.

Methods: Twenty-four obese prehypertensive PMW (aged 50-70 y; body mass index ≥ 30 kg/m²) randomly assigned to control (n = 12) and exercise (n = 12) groups. Exercise group performed MIET (25-40 min/d, 3 d/wk at 50%-70% of heart rate reserve) for 10 weeks. Control group maintained their normal daily physical activity level. Body composition, VO₂max, BP, ACE and ADRB2 gene expression, plasma Ang II, and FMD were measured before and after the training program.

Results: After MIET, systolic and diastolic BPs decreased by 4.6% and 2.4%, respectively (P < 0.001). Plasma Ang II level decreased by 45.7%, whereas FMD increased by 86% in the exercise group (P < 0.001). Exercise training resulted in a threefold increase in ADRB2 and a fourfold decrease in ACE gene expressions (P < 0.05). Training-induced changes in BP inversely associated with the changes in FMD and ADRB2 (r values range -0.55 to -0.78), and positively associated with Ang II and ACE (r values range 0.68-0.86) (P < 0.001).

Conclusions: Ten weeks of MIET modulates ACE and ADRB2 gene expression, decreases Ang II plasma levels, and improves endothelial function in obese PMW, and these alterations are associated with reduction in BP.

Association Between Maternal Age at Childbirth and Metabolic Syndrome in Postmenopausal Women: Korea National Health and Nutrition Examination Survey 2010 To 2012

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ABSTRACT

Objective: The aim of this study was to evaluate the relationship between maternal age at childbirth and metabolic syndrome in postmenopausal women.

Methods: We carried out a cross-sectional study on 3,956 Korean postmenopausal women who participated in the Korea National Health and Nutrition Examination Survey from 2010 to 2012. Multivariate logistic regression was used to evaluate the association between maternal age at first and last childbirth and metabolic syndrome, with adjustment for potential confounding variables.

Results: Women with metabolic syndrome had younger age at first delivery (23.3 +/- 0.1 vs 24.4 +/- 0.1 y, P < 0.001) and an older age at last delivery (30.8 +/- 0.1 vs 30.3 +/- 0.1 y, P = 0.011) than those without metabolic syndrome. After adjustments for confounding factors, earlier ages of first and last childbirth were positively associated with metabolic syndrome. The odds ratio (OR) was 2.157 (95% CI 1.256-3.705) for age at first childbirth, and 1.639 (95% CI 1.118-2.403) for age at last childbirth. Among the components of metabolic syndrome, only fasting glucose was positively associated with early age at first childbirth (OR 1.86; 95% CI 1.065-3.249) and early age at last childbirth (OR 1.71; 95% CI 1.197-2.444).

Conclusions: A younger maternal age at first and last childbirth was independently associated with a higher risk of metabolic syndrome in postmenopausal women. Advanced maternal age at last childbirth was, however, not an independent risk factor for metabolic syndrome.

Effect of Gua Sha Therapy on Perimenopausal Syndrome: A Randomized Controlled Trial

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ABSTRACT

Objective: This study aims to evaluate the effectiveness and safety of Gua sha therapy on perimenopausal symptoms, quality of life, and serum female hormones in participants with perimenopausal syndrome.

Methods: A prospective, randomized, controlled clinical trial was conducted at the First Affiliated Hospital of Nanjing University of Chinese Medicine in China. Eighty women with perimenopausal syndrome were recruited and randomized into an intervention group or a control group. Participants in the intervention group received 15-minute Gua sha treatment sessions once a week plus conventional treatment for 8 weeks, whereas participants in the control group received conventional treatment alone. The primary outcome was the change in perimenopausal symptoms and quality of life as obtained through the modified Kupperman Index (KI) and the Menopause-Specific Quality of Life. The secondary outcome was the change of serum female hormones including estrogen, follicle-stimulating hormone, and luteinizing hormone.

Results: Seventy-five out of 80 participants (93.8%) completed the study-38 in the intervention group and 37 in the control group. The baseline levels of demographic and outcome measurements were comparable between the two groups. After eight sessions of intervention, the reduction in the total modified KI score was, however, 16.32 +/- 4.38 in the intervention group and 11.46 +/- 5.96 in the control group, with a difference of 4.86 +/- 6.15 ($P < 0.01$) between the two groups. Also the reductions of hot flash/sweating, paresthesia, insomnia, nervousness, melancholia, fatigue, and headache were greater in the intervention group than in the control group ($P < 0.05$). The reduction in the total Menopause-Specific Quality of Life score was 17.87 +/- 3.84 in the intervention group and 13.62 +/- 7.40 in the control group, with a difference of 4.46 +/- 7.52 ($P < 0.01$) between the two groups. And the scores for vasomotor, psychosocial, and physical domains in the intervention group were significantly lower than those in the control group ($P < 0.05$). There were no significant differences in serum estrogen, follicle-stimulating hormone, and luteinizing hormone between the two groups.

Conclusions: The results of this study suggest that Gua sha therapy was effective and safe in relieving perimenopausal symptoms and improving the quality of life in participants with perimenopausal syndrome. The therapy may serve as a promising, effective, nondrug treatment for perimenopausal syndrome in clinical work. Additional research is needed to better understand its effectiveness and examine its mechanism for treating perimenopausal syndrome.

An Investigation of Life Circumstances Associated with the Experience of Hot Flashes In Campeche Mexico

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ABSTRACT

Objective: The purpose of this study was to better understand the experience of calores (hot flashes) in the state of Campeche, Mexico, and characteristics of women's lives. This study was carried out to understand the sociocultural context of women's lives before conducting a larger semistructured survey in the same communities.

Methods: Eighty-five women from rural and urban settings participated in open-ended interviews about the menopausal transition, with particular attention to hot flashes. Univariate and logistic regression analyses identified potential determinants of hot flashes. Qualitative responses were analyzed for central themes from the 40 women who experienced "calores" associated with menopause at the time of interview.

Results: The word "calores" was used to describe a variety of sensations and experiences related to the hot climate, infections, going in and out of air-conditioning, emotional stress, and physical exertion, as well as the symptom associated with menopause. In quantitative analyses, the likelihood of experiencing hot flashes varied by menopause status and rural/urban residence. In qualitative analyses, themes that characterized the lives of women with hot flashes were as follows: the search for, and the availability of, biomedical care; presence or absence of networks of social support; marital status and quality of the relationship; and occupational stress.

Conclusions: Hot flash questionnaires can elicit different symptom frequencies depending on the language used and the sociocultural context of women's lives. Qualitative findings suggest that the themes most likely to influence the perception and experience of hot flashes in Campeche are biomedicine, social support, marriage, and stress.