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Review

Vasomotor symptoms in women and cardiovascular risk markers: Systematic review and meta-analysis

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ABSTRACT

We performed a systematic review and meta-analysis of the observational or interventional studies assessing the association of vasomotor symptoms (hot flushes and night sweats) with various cardiovascular risk markers (systolic (SBP) and diastolic blood pressure (DBP), hypertension, total cholesterol, body mass index (BMI), and measures of subclinical atherosclerosis), in peri-menopausal, menopausal, or postmenopausal women. Eleven unique studies were identified with data available on 19,667 non-overlapping participants. Pooled analysis showed that women with hot flushes, compared to those without, tended to have significant higher levels of SBP (mean difference (MD): 1.95 mmHg (95%CI, 0.27 to 33.63)), and DBP (MD 1.17 mmHg (95%CI, −0.21 to 2.54)) and higher odds of having hypertension (OR: 1.18, 95%CI: 0.93 to 1.51), albeit non-significant. Similarly, women who reported night sweats compared to those who did not, had significant higher levels of SBP, (MD: 1.33 mmHg (95%CI, 0.63 to 2.03)), DBP (MD: 0.55 mmHg (95%CI, 0.19 to 0.91)), total cholesterol (MD: 0.17 mmHg (95%CI, 0.03 to 0.31)) and BMI (MD: 0.64 mmHg (95%CI, 0.47 to 0.80)). Vasomotor symptoms in women were not associated with measures of subclinical atherosclerosis. Women with vasomotor symptoms may have an unfavorable cardiovascular risk profile compared to women without vasomotor complaints.

Contents

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1. Introduction

Menopause has been linked to increased risk of cardiovascular disease (CVD) among older women [1–3]. During their menopausal transition, women commonly report vasomotor symptoms (VMS), which typically include hot flushes along with night sweats [4]. VMS are known to impair the quality of life [5,6] principally owing to irritability, fatigue, a generally depressed mood [4,7] and disturbed sleep [8]. Up to 80% of women experience hot flashes and night sweats, mainly in the peri-menopausal and early postmenopausal period [9]. VMS remain the leading reason menopausal women seek menopause-related healthcare [8,10,11].

In addition to a decreasing quality of life in menopausal women, a growing body of evidence suggests a link between VMS and cardiovascular risk profile [12–17]. Although many studies have reported associations between VMS and adverse cardiovascular risk profile [15,16], others either failed to show such associations [18–21] or point towards a favorable link between VMS and cardiovascular parameters [22–24]. Although the relation between VMS and cardiovascular risk is an area of active inquiry, interpretation of the often conflicting findings remains a challenge. As CVD remains the leading cause of death for women worldwide [25–27], and poses a substantial economic burden [55], assessing the published evidence on VMS and cardiovascular risk markers in a systematic manner is of particular importance.

In the present study, we have synthesized all available evidence of VMS in relationship with various conventional cardiovascular risk factors such as systolic (SBP) and diastolic blood pressure (DBP), hypertension, total cholesterol, body mass index (BMI) and measures of subclinical atherosclerosis.

2. Methods

2.1. Data sources, search strategy and eligibility criteria

This review was conducted using a predefined protocol and in accordance with the PRISMA and MOOSE guidelines [28,29] (eAppendix A and B). Relevant studies, published before February 12th, 2015 (date last searched) were identified by two independent authors, through electronic searches without language restriction in MEDLINE, EMBASE, and Web of Science databases. Electronic searches were supplemented by scanning reference lists of articles identified for all relevant studies (including review articles), by hand searching of relevant journals and by correspondence with study investigators and experts in the field. The computer-based searches combined terms related to the exposure (e.g., *hot flushes, night sweats*) and outcomes (e.g., *blood pressure, cholesterol, coronary artery calcification (CAC)*). Details on the search strategy are provided in Appendix C. Studies were sought that had reported on associations of vasomotor symptoms (defined as hot flushes and/or night sweats) with cardiovascular risk markers, including SBP, DBP, hypertension, serum total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, BMI, CAC and carotid intima-media thickness (IMT).

2.2. Study selection

Observational or interventional studies in humans with relevant data were eligible for inclusion if they reported on associations of any VMS (defined above) with cardiovascular risk factors in peri-menopausal, menopausal, or postmenopausal women. Two independent reviewers working in pairs screened the titles and abstracts of all initially identified studies according to the selection criteria. A third reviewer was available in case of disagreements. Full texts were retrieved from studies that satisfied all selection criteria. Reference lists of selected studies and relevant reviews identified on the topic were searched for additional publications.

2.3. Data extraction

Data were extracted by two independent authors and a consensus was reached with involvement of a third. A predesigned data extraction form was used to collect relevant information. This included questions on study size; study design; baseline population; location; age at baseline; duration of follow-up (for cohort studies); reported degree of adjustment (defined as '+' when risk estimates were adjusted for age and/or sex; '++' further adjustment for established vascular risk factors (e.g., age, sex, BMI, smoking status, lipids, hypertension, history of cardiometabolic disease); type of outcome and reported risk estimates (mean differences for continuous outcomes and odds ratios for categorical outcomes). Additionally, in the case of multiple publications, the most up-to-date or comprehensive publication was included.

2.4. Assessing the risk of bias

Bias within each individual study was evaluated using the validated Newcastle-Ottawa Scale [30], a semi-quantitative scale designed to evaluate the quality of nonrandomized studies. Study quality was judged by two independent reviewers based on the selection criteria of participants, comparability of cases and controls, and exposure and outcome assessment. Studies that received a score of nine stars were judged to be of at low risk of bias; studies that scored seven or eight stars were considered at medium risk; those that scored six or less were considered at high risk of bias.

2.5. Statistical analysis

The inverse variance weighted method was used to combine mean differences (for continuous outcomes) and odds ratios (for categorical outcomes) to produce pooled respective estimates using random effects models to allow for between-study heterogeneity. Heterogeneity was assessed using the Cochrane χ^2 statistic and the I^2 statistic. Publication bias was evaluated through a funnel plot and Egger's test. All tests were two-tailed and p-values of 0.05 or less were considered significant. STATA release 12 (Stata Corp, College Station, Texas) was used for all statistical analyses.