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Review

The association between vasomotor symptoms and depression during perimenopause: A systematic review

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ABSTRACT

There is a high incidence of depression in women presenting to menopause clinics. The aim of this review was to determine if there is an association between depressive symptoms or major depressive disorder (MDD) and vasomotor symptoms (VMS). A systematic review of the literature was conducted according to PRISMA guidelines. 33 relevant publications were found, 12 from three large studies. Overall, we found that there is a bidirectional association between VMS and depressive symptoms. This has been established in well-conducted, large observational studies. There does not appear to be a relationship between VMS and MDD. However, studies examining VMS and MDD were prone to bias making it difficult to draw any conclusions.

Contents

1. Introduction

Vasomotor and psychological symptoms cause a significant burden for many women during and following the menopause transition [1,2], impacting on their quality of life [3], work ability [4] and relationships [5]. The incidence and severity of vasomotor symptoms (VMS) increases in the menopause transition and after menopause [6]. There is universal acceptance that the biological changes associated with the menopause are the cause of hot flushes and night sweats. Debate exists about the extent to which other symptoms in particular mood disturbance, relates to the menopause transition. The perimenopause has been described as a 'window of vulnerability' for depression [7], though not all authors agree with this notion [8]. In clinical practice, many women presenting to menopause clinics feel depressed and attribute their symptoms to menopausal changes. There is a high incidence of both self reported depressive symptoms and clinically diagnosed depression in these women [9–12].

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The objective of this review was to examine evidence for an association between VMS and self-reported depressive symptoms or major depressive disorder (MDD) in otherwise healthy perimenopausal women.

2. Methods

The review was conducted according to PRISMA guidelines [13]. Longitudinal and cross-sectional studies published in English were considered without any restriction on publication date. Studies were considered eligible if they involved: (1) perimenopausal women (as defined by pattern of menstrual bleeding and/or serum FSH measure), (2) women without major illness (other than depression), (3) at least one measure of VMS, and (4) a validated measure of depression. Studies were excluded if the sample included only premenopausal or postmenopausal women, or only women with a medical illness such as breast cancer. Clinical trials were also excluded.

Cochrane reviews and published peer reviews in the area were searched to identify relevant search terms. Ovid Medline, EMBASE, CINAHL and PsychInfo were searched using combinations of the following terms: hot flashes, hot flushes, night sweats, vasomotor symptoms, depression, mood disorders, depressive disorders, climacteric, menopause, perimenopause, menopause transition, cohort studies, epidemiological studies, cross sectional studies, longitudinal studies, retrospective studies, prospective studies. After combining search terms the following limits were used: human, female, English language. The search strategy for Medline is shown in Appendix I. The last search was run on 2 July 2013. Papers from different databases were collated in EndNote, allowing automatic detection and then manual deletion of duplicate articles. The title list was then manually reviewed again for duplicates.

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.maturitas.2013.11.007.

Data retrieved from eligible studies included: study design; number of participants; whether sampling was random or used convenience methods; the setting participants were recruited from (community or clinical); type of VMS measure used; which validated depression measure was used and the cut off score used to define depressive symptoms; the relationship found, in particular, an odds ratio. Where possible, the data extracted was specific to perimenopausal women within each study.

Depression is very broad concept, from transient mood changes through to persistent debilitating melancholic depression with neurovegetative symptoms. Hence the term “depressive disorders” is used to encompass a number of conditions with the common symptom of lowered mood. A commonly used, highly validated classification system of depressive disorders is the Diagnostic and Statistical Manual (DSM) version 5 [14]. The criteria for the diagnosis of MDD requires five or more of the following symptoms to be present for at least 2 weeks: depressed mood, diminished interest, significant weight changes, sleep pattern changes, psychomotor agitation or retardation, loss of energy, feeling worthless or inappropriate guilt, decreased concentration, suicidal ideation or attempts. Exclusion criteria include recent losses or other causal factors such as substance use or a medical illness, the presence of manic episodes, or the diagnosis of psychotic disorders. In research settings MDD is diagnosed using a validated clinical interview, undertaken by a skilled clinical rater, such as the Structured Clinical Interview for the DSM (SCID) [15].

There are many depressive symptoms that cause considerable suffering for the individual but do not meet the diagnostic criteria for MDD. Subsyndromal symptoms can be just as debilitating as MDD. Examples of such symptoms include fluctuating anger, irritability, anxiety, suicidality, cognitive changes, paranoia, loss of libido, transient changes in sleep and appetite and low energy. Screening for depressive symptoms in the general population with self-rating scales such as the Center for Epidemiological Studies Depression Scale (CES-D) [16] can yield very different results compared to diagnosing MDD with the SCID [17]. Therefore, the results of included studies have been divided into those measuring depressive symptoms, and those that examine formally diagnosed MDD.

An assessment of the risk of bias was conducted on all included studies using the 11-item tool validated by Hoy [18]. This tool includes items that assess the external and internal validity of prevalence studies, with an overall rating of low (L), moderate (M) or high (H) risk of bias. Studies rated as M or H are less likely to accurately reflect the actual prevalence of any particular outcome in the general or target population [18]. The full bias assessment for each study is included in Appendix II.

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3. Results

The search of Medline, PsychInfo, CINAHL and Embase retrieved 326 articles. After title screening, 107 papers remained and all abstracts were then reviewed. After reviewing abstracts 66 papers remained for which the full text was read. Of these 31 met inclusion criteria. A further 3 papers were found through searching the bibliographies of included studies. Three large longitudinal studies accounted for a large number of the included publications; 5 from The Study of Women’s Health Across the Nation (SWAN); 4 from the Seattle Midlife Women’s Health Study (SMWH); and 3 from the Penn Ovarian Aging Study (POA). Different publications from the same studies have been included in the following tables, as different aspects of the association between VMS and depression have been assessed. It should be noted that multiple publications from one study do not represent independent analyses as the same women are being reanalyzed. Therefore, it has been clearly identified where a publication has been derived from SWAN, SMWH or POA.

3.1. Studies that have reported on VMS and depressive symptoms

Cross-sectional studies can provide evidence for an association but not directionality so cross-sectional and longitudinal studies are reported separately below.

3.1.1. Cross-sectional studies that have reported on VMS and depressive symptoms

Seventeen cross-sectional studies that assessed depressive symptoms and VMS were found (Table 1). Eleven studies involved community dwelling women and seven involved women in clinical settings. The studies ranged in size from 70 to 1280 participants, with a total of 9615 women across all studies. In four studies data specific to perimenopausal women was extracted, whereas other studies presented analyses based on pooled data of women from multiple menopausal stages.

Six cross-sectional studies found no relationship between VMS and depressive symptoms [19–24]. Two studies performed a factor analysis finding only a weak relationship [25,26]. A statistically significant relationship was found in 9 of 17 studies [27–34] with odds ratios ranging between 1.27 (1.08–1.51) [35] and 8.1 (2.5–26.4) [28]. Estimates of odds ratios were lower (1.27–1.76) in studies that controlled for multiple factors known to be associated with VMS or depression such as demographics, menopausal status and insomnia [29,30,33,35].