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Review

Menopause and depression: Is there a link?

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ABSTRACT

Aim: Depression is common and may have significant implications for the individual, their families and work and for the health care system. The menopause transition (MT) may be an 'at risk' time for the development of depression. This review aims to explore the relationship between depression and MT and the complex interaction between the biological, psychological and social factors that inform it.
Methods: The literature on depressive disorders and MT is reviewed.
Results and conclusions: Longitudinal studies have demonstrated an association between the menopause transition (MT) and an increase in depressive symptoms. A trend towards higher rates of depressive disorders during the MT, has also been shown, although not always reaching statistical significance. Risk factors for the development of depressive symptoms and depression in the MT include the presence of vasomotor symptoms (VMS), a personal history of depression (particularly depression that is related to pregnancy or hormonal changes through the menstrual cycle), surgical menopause, adverse life events, and negative attitudes to menopause and ageing. A treatment approach to depression during the MT exploits the biological as well as the psychosocial factors that are likely to be contributing in an individual.

Contents

1. Introduction

Depression is the most common illness worldwide, with around 350 million people affected [1] and the burden of depression is rising globally. It can have detrimental effects on an individual's relationships, capacity to work in or outside the home, financial status as well a risk of self-harm and suicide. In addition to the impact

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on the psychosocial wellbeing, depression has serious implication for physical health. Morbidity and mortality associated with ischaemic heart disease, and cancer are increased in individuals diagnosed with concurrent depression [2,3].

Depression is around twice as common in women as in men [4,5], and it has been widely suggested women may be at increased risk during periods of hormonal change such as puberty, pregnancy and the menopause transition [6]. While a clear association between specific hormonal changes and depression has not been established, these observations suggest that these are times of "risk" during a woman's life.

The menopause transition (MT) is the period from infrequent and irregular periods until the final menstruation, this marking the beginning of the post-menopausal period [7]. The MT lasts for 3–9 years and is characterised by fluctuations in sex steroid levels, vasomotor symptoms (VMS), vaginal dryness and loss of libido. It coincides with the Midlife, generally defined as between the age of 45 and 55 years [8] which may be associated with increasing physical health concerns, changing social, work and family roles [9]. As a result, the MT has long been considered a time of physical as well as psychological and social change. More recently there has been increasing interest in prevention of depression, emphasising the importance of knowing which women are at increased risk for depression at menopause so that targeted prevention interventions could be developed. In combination with an ageing population in Australia and many other resource-rich countries, it is important to establish whether the menopause transition is a period of vulnerability to depression, and if so what are the personal and environmental factors that contribute to risk. Further, it is important to know whether the increased risk of depression is confined to the MT or whether it persists in postmenopausal women. This review aims to explore this relationship between MT and depression and the biological, psychological and social factors that inform it.

2. Sources and selection criteria

We searched Medline and Pubmed, used personal archives of references, and consulted with other experts to inform this manuscript. When available, data from systematic reviews and randomised controlled trials were used. We also used expert guidelines [9].

3. Depressive symptoms and menopause transition

Depressive symptoms, measured using depression scales such as the CES-D, have been widely studied as a surrogate for the relationship between MT and depressive disorders [10]. They differ in the duration, severity and impact on function. More widely, the CES-D scale is used as a screening tool for individuals who may have a depressive disorder and require further assessment [11]. As a result, depressive symptoms encompass depressive disorders as well as depressive symptoms, which do not persistently impact negatively on function across a range of areas of life. Quality of life however, may be affected by the presence of depressive symptoms in the absence of a depressive disorder. Cross-sectional studies have been varied in their results, with some, finding an association between MT and depressive symptoms [12–15] and in others, no association has been found [16,17].

More recently, longitudinal studies looking at depressive symptoms, using the CES-D score (a score of >16 signifies a high level of depressive symptoms) and other validated measures, through the MT into the post-menopausal period have found a positive association, independent of other risk factors for depression [18–21]. The Study of Women's Health Across the Nation (SWAN), a large multiethnic study of 3302 women through MT, found increasing risk of CES-D score >16 as women progressed through the MT, independent of demographic, psychosocial and behavioural factors [18]. At 5 years of follow-up, the odds of developing depressive symptoms was significantly higher in the early perimenopausal (OR 1.3), the late perimenopausal (OR 1.7)and postmenopaual (OR 1.57) compared to the premenopausal period. This suggests that depressive symptoms increase during the MT, and may persist after the menopause. However, this finding has not been replicated by other longitudinal studies [20,21]. The nature of this relationship between the postmenopausal period and depressive disorders remains unclear.

The Pennsylvanian Ovarian Aging Study (PENN study), a cohort study with 436 participants, found that depressive symptoms were highest during the MT compared to both pre-menopausal and post-menopausal stages [19,20]. But in the Seattle Midlife Women's Health study, of 302 women, only the late MT was significantly associated with an increase in depressive symptoms when compared to the premenopause [21]. Variations in study design, measures of depressive symptoms used, and assessment of potential confounders in the relationship between depressive symptoms and MT impact on the comparisons that can be made between studies. While commonly used as a screening tool for depressive disorders in the community, we cannot assume that the presence of depressive symptoms in this population necessarily implies an increased risk of depressive disorder. The cross over between symptoms of the MT (sleep disturbances, sexual dysfunction) and those of depression may further complicate the usefulness of measures of depressive symptoms such as the CES-D, in the context of the MT.

4. Menopause transition and depression

Three large longitudinal studies all in the United States of America (USA), addressing the relationship between the menopause transition and depressive disorder have reached conflicting conclusions [19,22,23]. Bromberger et al. applied structured clinical interviews to diagnosis depressive disorders in 221 woman, from one site of the SWAN study – a multicultural longitudinal cohort study of women transitioning the menopause [22]. Demographics, a history of depressive disorders, and other psychosocial risk factors were recorded at the beginning of the study. Structured clinical interviews were administered annually to determine the presence of current or recent depressive disorders, as well risk factors for depressive disorders such as stressful life events, and the presence of VMS. After adjusting for psychosocial risk factors and menopausal symptoms, depressive disorders were twice as likely in the menopause transition, and almost four times more common in the post-menopause when compared to the premenopausal period [22]. These findings in the postmenopausal period have not been replicated by other longitudinal studies, which have limited their investigation to depressive disorders in the MT [19,23]. Further study is needed to delineate how the hormonal changes of the post-menopausal period impact on mood.

Two studies, both of which were also part of larger longitudinal cohorts, looked at new-onset depressive disorders through the MT, and found depressive disorders were approximately twice as common in the MT compared to the pre-menopause [19,23]. In the study by Freeman et al. while depressive symptoms were significantly associated with the MT, depressive disorders were not, after adjusting for risk factors [19]. The primary outcome in this study was depressive symptoms, rather than a diagnosis of a depressive disorder. As a result, there were a small number of women diagnosed with a depressive disorder ($n = 42$). This may have contributed to its not reaching significance. In the study by