

Menopausal depression - state of art

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Summary

It is believed that major depression is currently the leading cause of disease related disability among women in the world. In this review the authors analyzed the features and associations between menopause, the hormones associated during this stage, and their influence on depression..

Key words: Menopause; Peri-menopausal period; Depression; Hormones; Hormone replacement therapy.

Introduction

There is extensive literature addressing the phenomenon of depression in women during menopause. Changes in mood have been observed in those who are about to undergo, currently undergoing, and have undergone menopause. During this transition time, it has been globally observed that with these physiologic changes, women can experience a myriad of symptoms [1]. These symptoms can vary in type and severity. The most commonly observed include, however are not limited to: hot flashes, sweating, mood changes, and insomnia [2].

During reproductive senescence, in addition to symptoms of menopause, a woman's quality of life may also change. In one study on predictors of quality of life in the perimenopausal period, it was found that women reported having somatic symptoms, as well as a loss of sense of attractiveness [3]. This decrease in quality of life could contribute to a depressed mood that some women experience during menopause.

The aim of this review is to analyze the features and associations between menopause, the hormones associated during this stage, and their influence on depression. It has long been proposed that changes in hormones during the transition and time of menopause could be the reason for changes in mood [4]. It is believed that major depression is currently the leading cause of disease-related disability among women in the world [5]. Therefore it is necessary that the phenomenon of menopausal depression and associated risk factors be further studied.

Reasoning behind hormonal effects

There have been published articles indicating that hormonal fluctuations affect neurochemical pathways to depression [6]. This may be a leading factor as to why women are more susceptible to depression. Unlike men, women continuously undergo hormonal changes throughout their life, however some of the most profound changes are during pregnancy and menopause; this may be due to the varying levels of estrogen and progesterone [7-9].

Hormonal changes and their effects on depression are believed to be explained by the neuro-modulating effects of estrogen within interactions of the neurotransmitting systems [10]. They are believed to have a contribution in dysregulation of serotonergic, noradrenergic, cholinergic, and opioid systems. This in turn would affect mood and behaviour of an individual [11].

Hormonal effects on depression during various life stages

Women with postmenopausal depression typically display lower levels of estradiol and serotonin. It is reported that hormonal replacement therapy can protect these women from the depressive symptoms in addition to the symptomatic treatment of menopause. Although hormonal replacement therapy may be protective in postmenopausal women, there is little evidence indicating that it may be beneficial in woman currently undergoing menopause. It was also noted that women who began taking hormonal replacement at an earlier age were more likely to develop

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postmenopausal depression; this however may be due to a decreased number of reproductive years [12]. On the contrary, it was also noted that hormonal replacement therapy might enhance cognition and mood if given during menopause rather than during post-menopause [13].

In a study conducted on Korean woman, there was a statistically significant trend relating to the total number of reproductive years to the onset of depression post-menopause ($p < 0.001$). An odds ratio of 0.41 (95% CI: 0.27-0.62) was noted in a group of woman with a total number of reproductive years higher than 35 compared to those with less than 30. While the age of menarche onset showed no significance in the onset of depression, it was noted that women who underwent menopause at 52 years of age or greater, had an odds ratio of 0.35 (95% CI: 0.22-0.55) compared to those woman who underwent menopause before 46 years of age [12].

Factors outside of hormonal influence on depression

Various factors outside hormonal influences can affect mood and contribute to depression occurring during menopause. For example, the quality of life experienced may play a role in the mood of menopausal women. According to WHO, quality of life is complex and is affected by a person's psychological state, physical health, social relationships, the environment around them, and their own personal beliefs [14].

In one study, WHO's quality of life questionnaire was used to assess the quality of life of healthy Japanese women aged 40-55. The following dimensions were evaluated: depressive mood, somatic symptoms, anxiety, attractiveness, memory/concentration, sexual behaviour, vasomotor symptoms, and sleeping problems [3]. The researchers found that as menopausal symptoms intensified, there was a decrease in quality of life [15].

It has been observed that increased vasomotor symptoms have been closely associated with depression in so called "domino effect" [16]. In addition to this, one study demonstrated that 20% of surveyed women with psychosocial risk factors reported a triad of depressed mood, sleep disturbances, and sexual problems [17].

Vulnerability based on prior events

There is evidence suggesting an increased risk in perimenopausal depression in women who have experienced depression during a prior reproductive event [18]. Conversely it was found that women with a prior history of major depressive disorder were more likely to undergo an earlier transition to menopause or premature ovarian failure [19]. In a population based cohort study of early perimenopausal woman (ages 35- to 47-years-old at the time of enrollment), it was observed that women whom displayed premenstrual syndrome (at the time of enrollment)

were more likely to experience a depressed mood compared to those that did not [18]. This is likely due to the physiological gonadal hormone fluctuations during menses. The vulnerability to depression onset and continuation during these hormonal fluctuations may be increased with ovarian aging [20]. Moreover women in perimenopause who had larger fluctuations in gonadal hormones were more likely to report menopausal symptoms than their counterparts [21]. Interestingly, a study found that surgically menopausal women have an increased risk of depressive symptoms when compared to women undergoing natural menopause [22].

Treatment

Hormonal replacement therapy, including menopausal hormone therapy and oral contraceptives may be a great way to decrease hormonal fluctuations in women. Menopausal hormone therapy improves the clinical status of the depressed patient. It acts both directly through the estrogen effect on the serotonergic and noradrenergic systems and indirectly alleviating vasomotor symptoms.

Although oral contraceptives may play a role in causing depressive symptoms, the risk is small [23] and thus might be a suitable alternative to help women decrease future outcomes of menopausal depression. In addition to controlling these hormonal fluctuations, oral contraceptives can help alleviate the physiological symptoms of premenstrual syndrome. This in turn may help to reduce somatic and psychological symptoms and improve the patient's overall wellbeing.

When choosing a treatment plan for depression in women, it is important to take into account her reproductive status. It has been noted that pre-menopausal women respond better to serotonergic antidepressants than males [24]. However, when post-menopausal women received selective serotonin reuptake inhibitors (SSRI), the response was poorer in comparison to when they were given an SSRI in combination with estrogen therapy [25]. These findings suggest that female hormones may positively influence the efficacy of SSRI's [24].

Conclusion

There are many different factors which can predispose women to depression during their life. Whether the factors are physiological, pathological or psychological, it appears that external stressors have the greatest impact on depression onset during the early reproductive years [26]. However, it appears that physiological and prior psychological factors influence the onset of depression during the menopausal period of life [27]. It is difficult to assess specific relations between menopause and depression as there are many different factors to address. It can however be noted that a high quality of overall health, with regular vis-

its to the primary care physician, can be influential in reducing future menopausal depression. Maintaining a healthy and balanced physiological and psychological state may be the key factor to reducing depressive outcomes in women undergoing menopausal stages. In addition to proper physician compliance and psychological support throughout the patient's life, it is important to ensure that women who are transitioning to menopause receive frequent visits. This will help diagnose, assess, and treat the physiologic, psychological, and somatic symptoms these women may experience.

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