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Depression in women

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Abstract

Depression is the leading cause of disease-related disability in women. Epidemiological studies have shown that the lifetime prevalence of a major depressive disorder in women (21.3%) is almost twice that in men (12.7%). This ratio has been documented in different countries and ethnic groups. Sex differences relating to depression vary with age, with male and female children showing similar incidence rates. National comorbidity data reveal that sex differences in prevalence first appear around the age of 10 years and persist until midlife, after which they disappear. Therefore, women have the greatest risk for developing depressive disorders during their child-bearing years. Several biological processes are thought to be involved in the predisposition of women to depression, including genetically determined vulnerability, hormonal fluctuations related to various aspects of reproductive function, and an undue sensitivity to such hormonal fluctuations in brain systems that mediate depressive states. Psychosocial events such as role-stress, victimization, sex-specific socialization, internalization coping style, and disadvantaged social status have all been considered to be contributors to the increased vulnerability of women to depression. Women are more susceptible than men to stress-induced depression and to changes in photoperiod (more than 80% of individuals with seasonal affective disorder are women). Depression in women may develop during different phases of the reproductive cycle (premenstrual dysphoric disorder, depression during pregnancy, postpartum depressive conditions, and menopausal depression). Other reproductive events such as infertility, miscarriage, oral contraceptives, and hormone replacement treatment have been reported to cause depression in women.

1. Introduction

Data from the National Comorbidity Survey, a population-based epidemiological study, show that the prevalence of a major depressive disorder (MDD) is 21.3% in women and 12.7% in men [1]. This sex gap begins in adolescence and continues to midlife, approximating the span of the childbearing years in women [1]. Similar female/male prevalence ratios have been documented across different countries and ethnic groups [2]. Data from a cross-national epidemiological study disclose a higher rate of MDD in women in the 10 countries surveyed (United States, Canada, Puerto Rico, France, West Germany, Italy, Lebanon, Taiwan, Korea, and New Zealand) [2].

2. Reproductive mood disorders in women

2.1. Premenstrual syndrome and premenstrual dysphoric disorder

2.1.1. Prevalence

The American College of Obstetricians and Gynecologists states that as many as 20% to 40% of women of reproductive age experience difficulties during the period just preceding menstruation [3]. Such difficulties include depressed mood, irritability, anxiety, and emotional lability [4]. Roughly 2% to 10% of women report a severe disruption of work or interpersonal relationships during the luteal phase of their menstrual cycle, thereby meeting the *Diagnostic and Statistical Manual of Mental Disorders*, *Fourth Edition*, criteria for premenstrual dysphoric disorder (PMDD)—a condition more severe than the premenstrual syndrome [3,5].

2.1.2. Changes in the balance of sex hormones

Premenstrual syndrome occurs during the luteal phase (progesterone) of a woman's cycle and disappears during the follicular phase (estrogen). Hence, it has been theorized that hormonal fluctuations contribute to mood changes [6]. A strong similarity has been found among affects reported during the premenstrual period, during menopause, and as a side effect of oral contraceptives—a similarity that has been interpreted as providing support for the existence of a biological component of the depression that can occur at such times [7]. This idea is supported by the fact that the syndrome is absent during anovulatory cycles [8].

But the degree to which a women experiences premenstrual complaints is probably not dependent on the amount

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of estrogen and progesterone produced by the ovaries, but rather, on how sensitive the brain is to the influence of these hormones [6]. This hypothesis is supported by the observation that treatment with estrogen and gestagen-containing oral contraceptives, which results in a replacement of the endogenous sex steroids by exogenous hormones, usually does not lead to a reduction in symptoms [7]. Administration of gestagens (or estrogen) during the latter part of the luteal phase does not reduce symptoms of PMDD [7]. Of importance in this area is also a recent study showing that administration of female sex steroids may cause a relapse in symptomology in women with PMDD who had become symptom free during treatment with an ovulation inhibitor [6,8].

2.1.3. Role of serotonin

During the past decade, many reports have shown that the neurotransmitter serotonin may be involved in the pathophysiology of PMDD [9,10]. Although there are as yet no clear findings suggesting that patients with PMDD differ from controls with respect to brain serotonergic activity, the indirect evidence supporting an involvement of serotonin is very strong [6].

First, animal experiments have established that brain serotonergic neurons mainly modulate aspects of behavior that are also regulated by sex steroids [10]. Women with PMDD have been assumed to be under serotonergic control [10]. Second, it is known that estrogen, progesterone, and testosterone influence brain serotonergic activity [11,12]. Third, women with PMDD differ from controls with respect to a number of biological markers believed to reflect brain serotonergic transmission. These include platelet monoamine oxidase activity [13]; density of serotonin transporters in platelets [14]; ratios between the dopamine metabolite, homovanillic acid, and the serotonin metabolite; 5-hydroxyindoleacetic acid in the cerebrospinal fluid [15], and serotonin-mediated release of prolactin [9]. The fourth and most cogent argument for involvement of serotonergic neurons in the pathophysiology of PMDD is the report that pharmacologic agents facilitating brain serotonergic transmission effectively relieve PMDD symptoms in most patients [16].

2.2. Depression during pregnancy

Typical signs of depression—changes in sleep, changes in appetite, fatigue, decreased libido—are often difficult to distinguish from the normal physiological changes of pregnancy [17]. However, it has been shown that the prevalence of depression during pregnancy is approximately 25% to 35%, with about 10% of women meeting the criteria for an MDD (equal to that in nonpregnant women) [18,19]. Depressive symptoms most commonly occur during the first or third trimester.

One of the major risk factors for depression during pregnancy is a history of depression, especially if antidepressant treatment was discontinued before the pregnancy [20,21]. Other risk factors may include younger age, limited social support (especially from the child's father), living alone, a greater number of children, marital conflict, ambivalence about the pregnancy, comorbid illness, closely spaced pregnancies, illness or death of a significant other, death of previous children, and chronic illness [21-23]. There is a considerable risk to the mother and the fetus of not treating depression during pregnancy. However, there is no Food and Drug Administration–approved antidepressant for use during pregnancy. In mild-to-moderate cases, psychotherapy must be considered, and if an antidepressant must be used, it is advisable to wait until after the first trimester [24].

2.3. Postpartum blues

A short-lived cluster of depressive symptoms often occurs in new mothers during the first 2 weeks after delivery [25]. The usual complaints are depressed mood, tearfulness, anxiety, irritability, emotional lability, sleep disturbance, and decreased appetite. Because approximately 50% to 80% of women experience varying degrees of postpartum blues, this syndrome does not indicate psychopathology [25]. However, up to 25% of those affected will experience postpartum depression [23]; therefore, patients with postpartum blues require careful monitoring. Risk factors include employment status, interpersonal difficulties, stressful life events, personal or family history of depression, history of premenstrual depression, depression during pregnancy, labor occurring at night, and sleep disturbance late in pregnancy [25,26]. Most cases resolve spontaneously [18].

2.4. Postpartum depression

2.4.1. Prevalence and psychosocial aspects

Postpartum depression includes feelings of extreme loneliness, irritability, fear of going crazy, and a sense of "loss of self" [27-29]. Women with postpartum depression may also experience suicidal ideas and obsessive thoughts. Suicide and infanticide occur infrequently, but are more likely during episodes of severe postpartum depression [30]. Postpartum depression has also been linked to several psychosocial factors, including limited educational attainment, psychological distress, social isolation, poor social support during pregnancy, long interval between marriage and first pregnancy, marital discord, history of major depression, and unplanned or unwanted pregnancy [31-33].

2.4.2. Postpartum changes in reproductive hormone levels

The rapid decline in reproductive hormone levels that occurs immediately after delivery is thought to be the primary cause of postpartum depression [34]. However, the evidence in support of an association of changes in estrogen, cortisol, and prolactin with postpartum depression is equivocal [35,36]. During pregnancy, maternal levels of estrogen, progesterone, cortisol, prolactin, β endorphin, and human chorionic gonadotropin rise steadily and then decline

rapidly after birth has taken place. Therefore, the normal rapid withdrawal of estrogen and other hormones occurring at this time may trigger the onset of postpartum depression [37]. However, as in PMDD, estrogen modulates neurotransmitter systems (including serotonin) that control mood during the postpartum period [38]. It seems likely that the brain's sensitivity to hormonal changes—modulated by any or all of a number of as yet poorly understood factors such as genetic vulnerability and degree of emotional stability—determine whether a given patient will develop postpartum depression [39].

Antidepressants typically require 3 to 4 weeks of use before efficacy can be demonstrated. Decision about prophylaxis against recurrent illness with antidepressants should weigh the risk of recurrent illness against the risk of medication use in the late third trimester and during lactation [24].

2.5. Postpartum psychosis

This syndrome is considered to be a variant of bipolar disorder, with prominent cognitive impairment and bizarre behavior [33,38,39]. Symptoms include severe dysphoria or elevated mood, emotional lability, disorganized behavior, delusions, hallucinations, feelings of depersonalization, confusion, disorientation, and agitation. Women who suffer from this syndrome pose a threat to themselves and their infants, and almost always require hospitalization and treatment. The incidence of this condition is 0.1% to 0.2% of new mothers, with 78% of cases occurring after the first delivery. Risk factors for this condition include a personal or family history of psychosis or major affective disorder, especially bipolar disorder [27].

2.6. Menopause and depression

2.6.1. Prevalence and predisposing factors

An increased tendency to depression has been reported in women during perimenopause and menopause. Perimenopause is the period during which the transition from regular ovarian cycles to complete cessation of menstruation takes place. Absence of menses for 12 or more months denotes menopause. Demographic studies show that in 1990, there were 467 million postmenopausal women in the world. Population projections on the basis of these demographic studies predict that by the year 2030, the number of postmenopausal women will increase to 1.2 billion [40]. At this time, approximately 47 million women will be entering menopause each year. The median age of menopause in the Massachusetts Women's Health Study of 2570 women was 51.3 years [40]. Symptoms include depression, hot flashes, night sweats, headaches, vaginal dryness, sleep disturbances, fatigue, irritability, and changes in appetite and libido. Factors that affect vulnerability to depression during menopause include marital status, educational background, socioeconomic status, race, smoking, exposure to toxic substances, nutrition, and history of previous depression [35].

2.6.2. Hormonal changes during menopause

Perimenopause is a time during which large fluctuations in hormone levels occur. The daily production rate of estrogen (which may have antidepressant properties) falls nearly 8-fold, to an output of approximately 48 μg per 24 hours [35,36]. It has been debated whether the incidence of depressive symptoms or MDD increases in association with the drop in estradiol levels accompanying the transition [35,36]. Further changes in levels of follicle-stimulating hormone, inhibin, activin, follistatin, insulin-like growth factors, luteinizing hormone, progesterone, androgens (testosterone and androstenedione), and gonadotropin-releasing hormone have been reported [36]. Such hormonal changes may affect the behavior of serotonin-specific neuronal systems in a fashion similar to that seen in postpartum depression [38] and PMDD [6].

3. Conclusion

Women are more prone than men to depression, and this increased vulnerability has been ascribed to events arising from changes in the endocrine control of the reproductive system. These changes occur during the menstrual cycle (premenstrual syndrome and PMDD), after parturition (postpartum depression), and during the menopause (perimenopausal and menopausal syndrome). Because the serious mood disorders that sometimes accompany these syndromes cannot be explained by changes in sex hormone balance alone, increasing attention has been given to the notion that women who develop these disorders are, for various reasons (psychosocial and/or metabolic), especially susceptible to changes in hormonal balance, which in turn are believed to affect the activity of certain neuronal systems (particularly the serotonin-specific ones). This interpretation is favored by evidence indicating the existence of a powerful effect of the sex hormones on serotonin-specific neurotransmitter function, and on mood.

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