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Review

Mood and anxiety disorders in women with PCOS

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ABSTRACT

Women with polycystic ovary syndrome have gynecologic, reproductive and metabolic co-morbidities that span their entire lifespan. More recently a higher risk of mood and anxiety disorders has been reported in women with PCOS. Women with PCOS have higher depression scores and a higher risk of depression independent of BMI. Although clinical features of hyperandrogenism affect health related quality of life, the association between hirsutism, acne, body image and depression is currently unclear. Similarly there is limited data on the association between variables such as biochemical hyperandrogenism or infertility and depression. Women with PCOS are also at risk for symptoms of generalized anxiety disorder. There is insufficient data examining the risk of other anxiety disorders such as social phobia, obsessive compulsive disorders and panic disorder. In a number of patients some of these disorders coexist increasing the health burden. These data underscore the need to screen all women with PCOS for mood and anxiety disorders and adequately treat women who are diagnosed with these conditions.

Contents

1. Introduction

Polycystic ovary syndrome (PCOS), a common endocrine disorder in reproductive age, is associated with a number of metabolic co-morbidities including obesity, hypertension, dyslipidemia, insulin resistance, impaired glucose tolerance and diabetes [1]. In addition, a recent systematic review reported a negative impact of PCOS on health related quality of life (HRQoL) measures [2]. Physical symptoms associated with PCOS, such as weight gain, hirsutism and acne have been shown to cause a reduction in psychosocial well-being and sexual satisfaction [3]. This may result in feelings of frustration and negatively impact HRQoL [4–6]. We have recently reported in two meta-analyses that PCOS is also associated with increased risk for depressive and anxiety symptoms [7,8]. The burden of healthcare costs related to PCOS is known to be high [9] and these estimates do not include costs related to metabolic syndrome, mood and anxiety disorders which are known to be considerable. This paper will review the evidence for increased risk of depressive and anxiety symptoms in women with PCOS and discuss possible etiologies.

2. Mood disorders

Mood disorders include Major Depressive Disorder (MDD), Dysthymic Disorder, and Depression Not Otherwise Specified based on

Abbreviations: GAD, generalized anxiety disorder; CVD, cardiovascular disease; HRQoL, health related quality of life; MDD, major depressive disorder; BDI, Beck Depression Inventory; CAD, coronary artery disease.

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the Diagnostic and Statistical Manual IV (DSM-IV) [10]. Major Depressive Disorder affects nearly 14.8 million American adults each year and is more prevalent in women [11]. In a US survey the prevalence of MDD in women 18–44 years ranged from 12–14% with the mean age of onset of 30.4 years [12]. Surveys of adults living in the community in 10 countries (Brazil, Canada, Chile, Czech Republic, Germany, Japan, Mexico, Netherlands, Turkey, and the United States) found that the lifetime prevalence of major depression varied from as low as 3 percent in Japan to 17 percent in the US, with most rates in the range of 8 to 12 percent [13]. Compared to men, women with major depression tend to have an earlier age of onset, a greater family history of affective disorders, poorer social adjustment and quality of life [14]. Up to 25% of women will satisfy the criteria for MDD during their lifetime. The overall prevalence of depressive disorders in a large multicenter study of obstetric-gynecologic patients was reported to be approximately 12% (6% rate for Major Depressive Disorder and 6% for Other Depression) [15]. These data underscore the importance of timely identification of depression in all reproductive age women.

Based on the DSM IV definition we previously reported an increased prevalence of depression in women with NICHD defined PCOS compared with geographically matched controls (35% versus 10.7%) after adjusting for body mass index (BMI), family history of depression, and history of infertility (adjusted OR 4.23 {95% CI 1.49–11.98; $P<.01$}) [16]. Subjects were screened using a validated screening tool (PRIME-MD PHQ) and those subjects with a positive screen were subsequently interviewed by a psychiatrist. Of the 103 PCOS subjects 21.6% were newly diagnosed with depression (major and other) and another 13% were being treated for depression. In comparison 2.9% of the controls were newly diagnosed with depression and 7% were being treated for depression. We found daily fatigue and sleep disturbances to be the two most common symptoms in the affected women, followed by appetite changes and diminished interest in doing things.

More recently we published a systematic review and meta-analysis reporting a fourfold increased prevalence of depressive symptoms in women with well-defined PCOS compared to age matched controls (OR 4.03, 95% CI 2.96–5.5) [7]. The meta-analysis included 10 studies from several countries and a sub-analysis of 5 BMI-matched studies also showed an increased risk of depressive symptoms in women with PCOS (OR 4.09, 95% CI 2.62–6.41). A variety of validated screening tools were used in these studies including Patient Health Questionnaire (PHQ), PRIME-MD PHQ – Primary Care Evaluation of Mental Disorders PHQ, Psychiatric Neuropsychological Interview (MINI NPI), Symptom check list (SCL – German version), Depression Adjective Check List (DACL), Minnesota Multiphasic Personality inventory (MMPI) and Becks Depression Inventory (BDI). Although the lack of a single screening tool may be seen as a limitation, it likely supports the wider applicability of these results. Only 3 studies had a psychologist/psychiatrist follow up with subjects who had a positive screen. This is a limitation of the other studies as they reported increased abnormal depression scores but did not confirm the diagnosis of depression.

3. Possible etiologies for increased risk of depression

Major depression is a multi-factorial disorder with many etiologic variables that are interrelated through developmental pathways. In a comprehensive developmental model for risk of depression in women three broad pathways reflecting internalizing symptoms, externalizing symptoms, and psychosocial adversity were identified [17]. In addition depression is associated with endocrine and metabolic illnesses such as hypothyroidism and diabetes. Most women with PCOS have clinical or biochemical hyperandrogenism and the relationship between androgens and mood disorders in women remains controversial. We did not observe any significant differences in total or free testosterone levels or in the adrenal androgen DHEAS between depressed women with PCOS and non-depressed women with PCOS [16]. Although a few small studies suggest a correlation between depressive symptoms and serum androgens [18,19] other studies have failed to demonstrate this association [20]. It has been suggested that the physical manifestations of hyperandrogenism cause lower self-esteem and negative self images and are associated with a decrease in HRQoL measures [4]. This was most common in areas of social and emotional functioning, decreased sexual satisfaction, and increased emotional distress. These physical symptoms, however, do not account independently for the increased mood disturbances observed among patients with PCOS.

4. Infertility and mood disorders

The data regarding risk of depressive disorders in PCOS women with infertility is controversial and limited [16,21]. There is some evidence that during the time that couples attempt to conceive, women with fertility problems experience more negative emotional feelings compared to women who conceive spontaneously [22]. Although infertility is a feature of PCOS, a majority of women with PCOS will respond to ovulation induction medications and achieve a pregnancy. In a large internet based study, infertility was found to interact with PCOS status for depression and infertility patients with PCOS had significantly lower quality of life scores compared to controls [23] The influence of variables such as cause of infertility, duration of infertility, type of treatment (oral agents versus IVF) on depression has not been fully examined.

5. Obesity and mood disorders

Depressive symptoms and mood disorders are common in persons of all ages seeking treatment for obesity [24]. Obesity has been associated with increased odds of past-year MDD among women (OR 1.37, 95% CI 1.09–1.73) [25]. Given the increasing prevalence of obesity in the US there is a strong probability that obesity and depression will occur together. It is unclear how much of the clinical overlap between mood disorders and obesity is due to co-occurrence of two common disorders or inherited pathogenic factors. Based on the current literature MDD with atypical features (namely binge eating disorder), MDD with juvenile onset and bipolar disorder are associated with overweight and obesity [26]. Our meta-analysis detected a high risk of depressive symptoms independent of BMI in women with PCOS [7]. Our previous data suggests an association between depression scores as measured by BDI and BMI [16] however; this association was not strong enough to fully account for the increased risk of depressive disorders.

6. Follow up of PCOS women with mood disorders

There are limited data on the longitudinal follow-up of women with PCOS who have been diagnosed with mood disorders. We examined the prevalence of depression in women with PCOS over a 2 year time period and reported a persistent high rate of depression in young women with PCOS [27]. The prevalence of depression was 35% (n = 103) in the first survey [16] and 40% in the second survey (n = 60) compared to 10% in controls. Although 7 women reported symptomatic improvement, 10 new cases of depression were diagnosed at the time of the second survey. Therefore the detection rate of new cases in the follow up study (19%) was similar to that in the first survey (21%). In addition, we continued to detect a high prevalence of anxiety and eating disorders in this