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Psychiatric disorders related to polycystic ovary syndrome

Zaburzenia psychiczne związane z zespołem policystycznych jajników

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Abstract

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age. The psychiatric disorders accompanying the clinical symptoms and hormonal abnormalities are important, but underestimated, aspects in PCOS. Obesity, hirsutism, acne, menstrual disturbances and infertility play important roles in lowering the quality of life in women with PCOS. Depression and anxiety are more often observed in patients with PCOS than in healthy women. Some authors consider that there is a relationship between valproic acid treatment of bipolar disease and PCOS. There have been reports that in women with PCOS anorexia nervosa, bulimia nervosa and other unspecified eating disorders are found more often than in the general population. **(Endokrynol Pol 2012; 63 (6): 488–491)**

Key words: *PCOS, quality of life, depression, bipolar disease, eating disorders*

Streszczenie

Zespół wielotobielowatych (policystycznych) jajników (PCOS, *polycystic ovary syndrome*) jest częstym schorzeniem endokrynologicznym występującym u kobiet w wieku rozrodczym. Ważnym, choć niedocenianym, aspektem są zaburzenia psychiczne towarzyszące objawom klinicznym i nieprawidłowościom hormonalnym istniejącym w tym zespole. Otyłość, hirsutyzm, trądzik, zaburzenia miesiączkowania oraz niepłodność istotnie wpływają na obniżenie jakości życia kobiet z PCOS. U pacjentek z tym zespołem, częściej niż w populacji zdrowych kobiet, rozpoznawana jest depresja i zaburzenia lękowe. Ponadto uważa się, że istnieje związek między stosowaniem kwasu walproinowego w chorobie dwubiegunowej a rozwojem PCOS. Istnieją również doniesienia o częstszym występowaniu zaburzeń odżywiania u kobiet z PCOS, takich jak: bulimia, jadłowstręt psychiczny i niespecyficzne zaburzenia jedzenia. **(Endokrynol Pol 2012; 63 (6): 488–491)**

Słowa kluczowe: *PCOS, jakość życia, depresja, choroba dwubiegunowa, zaburzenia odżywiania*

Polycystic ovary syndrome (PCOS) is one of the commonest endocrine disorders in women of reproductive age. For the diagnosis of this syndrome the Rotterdam Criteria are used: polycystic ovary syndrome is diagnosed in the presence of at least two of three criteria: menstrual disorders or amenorrhoea with chronic lack of ovulation, clinical and/or biochemical features of hyperandrogenism, and the presence of polycystic ovaries in ultrasonography after the exclusion of other endocrine disorders [1].

The prevalence of PCOS varies depending on the criteria for diagnosis. According to most studies which engage the NIH criteria it concerns 5–10% of premenopausal women [1]. There are reports that the incidence of PCOS diagnosed on the basis of other criteria is much more frequent. In a study aimed at assessing the incidence of PCOS in 728 women from South Australia, PCOS was shown in 8.7% of the women according to the NIH criteria, in 17.8% according to the Rotterdam criteria, and in 12% according to the AES criteria [2]. There are some metabolic complications included in the clinical picture of PCOS, such as obesity, insulin resistance, type 2 diabetes, dyslipidaemia and increased risk of developing cardiovascular disease. The relationship of PCOS with psychiatric disorders is less well known and we believe has been underestimated, although a reduced quality of life, depression, anxiety disorders and eating disorders occur in women with PCOS with increased frequency compared to the general population [3–10].

Reduced quality of life indicators

According to the WHO definition of 1948, health is a state of physical, mental and social well-being and not merely the absence of disease. There is also a term 'quality of life', introduced by Schipper, which is related to the above definition of health [11]. Quality of life depending on health (HRQOL, Health Related Quality of Life) enables the assessment of the therapeutic process from the perspective of the patient. A HRQOL survey is carried out by means of questionnaires, general and specific to a given disease. General questionnaires assess the overall relation-

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ships between patient health status and factors such as emotional state, family relations, and professional activity. Specific questionnaires are divided into two categories, focusing on specific areas of patient functioning and around the phenomena arising from the disease itself [11, 12].

The symptoms of polycystic ovary syndrome, such as hirsutism, acne, menstrual disturbances, infertility and obesity are strong factors that can influence the quality of life. A series of studies, using both questionnaires general and specific for PCOS, has been carried out mainly in Great Britain, the United States and Germany. The most commonly used questionnaires were the Short Form-36 (SF-36), and the only available one specific to polycystic ovary syndrome, PCOSQ [12]. All of these studies, mostly case-controlled, have shown that PCOS significantly reduces quality of life compared to healthy women [3, 4, 6, 7, 13] or patients with other mild gynaecological problems [10, 14]. Another case-control, the study by Coffey et al., has shown that women with PCOS have a 20% lower quality of life than patients with asthma, diabetes mellitus, epilepsy and chronic back pain [5].

According to most studies, obesity is the most noticeable factor that lowers the quality of life in PCOS patients. On a scale where 1 means the worst quality of life, and 7 the best, obesity reaches an average value of 2.1 [5], 2.33 [15], 2.85 [7], 2.86 [4] and 2.94 [10].

Infertility is the second most important factor influencing negatively the quality of life in women with PCOS. Trent et al. studied 97 adolescents with this syndrome and compared them to 186 healthy women matched for age [16]. Patients with PCOS significantly more often (3.4 times) had concerns about their ability to become pregnant in the future, which corresponded to the reduced quality of life indicators.

Hirsutism is another symptom of PCOS that plays a significant role in reducing quality of life in women with this syndrome. Lipton et al. studied 88 women with hirsutism localised on the face and found a reduction in quality of life in the field of social life and interpersonal relationships [17]. The studied patients spent an average of 104 minutes a week checking the degree of hair excess: two thirds by looking in the mirror and 76% by touch.

Cultural factors have an important influence on the relationship between the individual components or symptoms of PCOS and deterioration in quality of life. Hashimoto's study showed that in Brazilian women (102 women with PCOS) compared to Austrian ones (31 women with PCOS), infertility had a greater impact on HRQL than obesity [18]. In turn, Schmid has shown that Muslim women suffered more from infertility than obesity [19].

Depression

Depressive disorders are defined as a deep and persistent lowering of mood. According to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) major depression, dystymia and unspecified depressive disorders can be distinguished. According to the data from the NIH (National Institutes of Health), depression affects about 5% of the population in a year, and 13% of people during their whole life. Almost half of people with depression have suicidal thoughts, and one third attempt suicide. Depression occurs most frequently between the ages of 20 and 40. A review of the literature from 1965 to 2008, made by Accortt et al., has shown that women suffer from it almost twice as often as men [20]. These findings suggest the need for greater recognition of depression, especially in groups of increased risk, which include PCOS patients.

Many researchers in longitudinal studies have shown an increased incidence of depression in women with PCOS [10, 21, 22], and some have even reported a seven-fold increase in the incidence of suicide among women with this syndrome [13]. Kerchner et al. found depression in 40% of 60 women diagnosed with PCOS [21]. In this group, ten women met the criteria for the diagnosis of depression, while 14 others had already been receiving antidepressants. After comparing these findings with the results from previous studies in the same group of women, it appeared that within an average of 22 months 19% (11 of 60) of women with PCOS have developed depression. Hollinrake et al. assessed the prevalence of depression among 103 women with PCOS compared to an equally-sized control group [22]. Depression, both previously diagnosed and treated, and newly found during the study, concerned 35% of patients with PCOS, compared to 10.7% of women in the control group. Fatigue (96%) and sleep disturbances (88%) were the most commonly reported symptoms of depression. The risk of depressive disorders in a subgroup of obese women with PCOS was assessed as 44% compared to 14.7% in obese women from the control group. Women with PCOS and depression had higher BMI and lower values of insulin sensitivity indices compared to PCOS patients without depression.

Anxiety disorders often coexist with depression. On the basis of a questionnaire study, Benson et al. found anxiety disorders in 34% of 448 women with PCOS. These symptoms were associated mainly with acne and fertility problems [23].

The same disorders found in PCOS that are associated with decreased quality of life contribute to the manifestation of depression. Among them are obesity, infertility, hirsutism and acne. Furthermore, it is be-

lieved that increased levels of testosterone, which is one of the key abnormalities in PCOS, is associated with an increased risk of developing depression [24].

Bipolar disorder

Bipolar disorders are characterised by the alternating occurrence of periods of mania and depression. They are divided into bipolar disorder I (full-blown mania and major depression), bipolar disorder II (hypomania and episodes of major depression) and unspecified bipolar disorder (bipolar symptoms that do not meet criteria I or II). The incidence of bipolar disorder is about 1%. Women are more prone to bipolar disorder II [25].

There is little evidence on the relationship of bipolar disorder and PCOS. Opinions of the authors concerning the links between these conditions are divergent. Some of them claim that the development of PCOS is influenced by the valproic acid (VPA) itself, which is used to treat bipolar disorder. Others believe that there is a direct relationship between both these diseases, and they explain it by disturbances that are common to PCOS and bipolar disorder at the hypothalamic-pituitary-ovary level [26] and the similarity of metabolic abnormalities in these diseases [26, 27]. Only a few studies have focused on the impact of the drugs used to treat bipolar disease, especially valproic acid, on the occurrence of menstrual disturbances [27–29]. McIntyre et al. compared 18 women treated with VPA with 20 female patients treated with lithium, and they found a higher incidence of menstrual disturbances in the first group (50% versus 15%) [29]. In addition, patients treated with VPA had significantly higher levels of androgens (total testosterone, free testosterone and androstenedione), more atherogenic lipid profile (higher total cholesterol, LDL cholesterol and triglycerides, and lower HDL cholesterol levels) and higher serum leptin concentrations. In another study concerning 80 women with bipolar disorder, PCOS was diagnosed in 6% of patients treated with VPA and in none treated with other antipsychotic drugs [28].

Klipstein et al. studied the incidence of bipolar disorder in 78 patients previously diagnosed with PCOS: 28% of the women had been diagnosed with bipolar disorder or met the criteria for the diagnosis according to the MDS questionnaire (Mood Disorders Questionnaire) [26]. Ninety seven per cent of patients in whom bipolar disorder was diagnosed before or during the study had not been treated with valproic acid before the time of diagnosis of PCOS. So, valproic acid therapy alone cannot explain the linkage between bipolar disorder and PCOS. Due to the coexistence of metabolic disturbances such as insulin resistance, obesity or hyperglycaemia, found in both these diseases, a common pathogenic background seems possible [26].

Eating disorders

According to DSM-IV, three types of eating disorders are distinguished: anorexia nervosa, bulimia nervosa, and periodic overeating (BED, binge-eating disorder). In addition, subgroups of non-specific eating disorders (EDNOS, Eating Disorders Not Otherwise Specified) are recognised. Ninety per cent of eating disorders occur in women, mainly in teenagers and young women. Bulimia occurs in 1.1 to 4.2% of young women, anorexia nervosa in 0.5 to 3.7% and BED concerns 26% of women. EDNOS is the commonest eating disorder: it concerns approximately 60% of people presenting to psychiatric clinics because of problems with eating [30]. As dissatisfaction with self-appearance is often associated with PCOS and plays an important role in the pathogenesis of eating disorders, a relationship between these two diseases seems likely.

McCluskey et al. found that one third of 153 studied women with PCOS fulfilled the diagnostic criteria for eating disorders, and bulimia was diagnosed in 6% of them [31]. Other studies have shown an increased incidence of polycystic ovaries on ultrasound image in women with bulimia, and even the normalisation of these changes after recovery from bulimia [9]. Morgan et al. studied the prevalence of eating disorders in a group of 80 women with hirsutism, including 68 patients with PCOS [32]. In 36.3% of the women, eating disorders were diagnosed (all the women were from the PCOS group): in 22.5% EDNOS was recognised, in 12.6% bulimia nervosa and in 1.3% anorexia nervosa.

In contrast to the abovementioned results, Michelmore et al. found no association between PCOS or polycystic ovaries on the ultrasound image and eating disorders [33]. They studied a group of 230 young women. Picture of polycystic ovaries in ultrasound was found in 74 women (33%), and 59 of them were diagnosed with PCOS. Thirty per cent of the participants admitted to episodes of binge eating, while 4% had used extreme methods to maintain body weight. In two women bulimia was diagnosed: one of them had normal ovaries on ultrasound scanning, in the other an ultrasound examination was not performed. In five women (three with PCOS and two with normal ovaries), BED was diagnosed. No statistically significant differences between the incidence of eating disorders in women with PCOS and women with normal ovaries were found.

Summary

PCOS is the commonest endocrine disorder in premenopausal women. More and more is known about the relationship between PCOS and impaired mental

health. However, it seems that clinicians still attach too little importance to this aspect of the disease. It should be remembered that significantly reduced quality of life and the more frequent occurrence of depression and eating disorders may be associated with this condition.

References

1. Azziz R, Carmina E, Dewailly D et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force. Fertil Steril 2009; 91: 456-488.
2. March WA, Moore VM, Willson KJ et al. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010; 25: 544–551.
3. Barnard L, Ferriday D, Guenther N et al. Quality of life and psychological well being in polycystic ovary syndrome. Hum Reprod 2007; 22: 2279–2286.
4. Ching HL, Burke V, Stuckey BGA. Quality of life and psychological morbidity in women with polycystic ovary syndrome: body mass index, age and the provision of patient information are significant modifiers. Clin Endocrinol (Oxf) 2007; 66: 373–379.
5. Coffey S, Bano G, Mason HD. Health-related quality of life in women with polycystic ovary syndrome: a comparison with the general population using the Polycystic Ovary Syndrome Questionnaire (PCOSQ) and the Short Form-36 (SF-36). Gynecol Endocrinol 2006; 22: 80–86.
6. Elsenbruch S, Hahn S, Kowalsky D et al. Quality of Life, Psychosocial Well-Being, and Sexual Satisfaction in Women with Polycystic Ovary Syndrome. J Clin Endocrinol Metab 2003; 88: 5801–5807.
7. Guyatt G, Weaver B, Cronin L et al. Health-related quality of life in women with polycystic ovary syndrome, a self-administered questionnaire, was validated. J Clin Epidemiol 2004; 57: 1279–1287.
8. Hahn S, Janssen OE, Tan S et al. Clinical and psychological correlates of quality-of-life in polycystic ovary syndrome. Eur J Endocrinol 2005; 153: 853–860
9. Himelein MJ, Thatcher SS. Polycystic Ovary Syndrome and Mental Health: A Review. Obstet Gynec Surv 2006; 61: 723–732.
10. Jones GL, Hall JM, Balen AH et al. Health-related quality of life measurement in women with polycystic ovary syndrome: a systematic review. Hum Reprod Update 2008; 14:15–25.
11. Schipper H, Clinch J, Powell V. Quality of life studies: definitions and conceptual isues. In: Spilker B, eds.: Quality of life and pharmacoeconomics in clinical trials. Philadelphia, Lippincott-Raven 1996; 1–24.
12. Cronin L, Guyatt G, Griffith L et al. Development of a Health-Related Quality-of-Life Questionnaire (PCOSQ) for Women with Polycystic Ovary Syndrome (PCOS). J Clin Endocrinol Metab 1998; 83: 1976-87.
13. Mansson M, Holte J, Landin-Wilhelmsen K et al. Women with polycystic ovary syndrome are often depressed or anxious — a case control study. Psychoneuroendocrinology 2008; 33: 1132–1138.
14. Trent ME, Rich M, Austin SB, et al. Quality of life in adolescent girls with polycystic ovary syndrome. Arch Pediatr Adolesc Med 2002; 156: 556–560.
15. McCook JG, Reame NE, Thatcher SS. Health-related quality of life issues in women with polycystic ovary syndrome. J Obstet Gynecol Neonatal Nurs 2005; 34: 12–20.
16. Trent ME, Rich M, Austin SB et al. Fertility concerns and sexual behavior in adolescent girls with polycystic ovary syndrome: implications for quality of life. J Pediatr Adolesc Gynecol 2003; 16: 33–37.
17. Lipton MG, Sherr L, Elford J et al. Women living with facial hair: the psychological and behavioral burden. J Psychosom Res 2006; 61: 161–168.
18. Hashimoto DM, Schmid J, Martins FM et al. The impact of the weight status on subjective symptomatology of the Polycystic Ovary Syndrome: a cross-cultural comparison between Brazilian and Austrian women. Anthropol Anz 2003; 61: 297–310.
19. Schmid J, Kirchengast S, Vytiska-Binstorfer E et al. Infertility caused by PCOS-health-related quality of life among Austrian and Moslem immigrant women in Austria Hum Reprod 2004; 19: 2251–2257.
20. Accortt EE, Freeman MP, Allen JJ. Women and major depressive disorder: clinical perspectives on causal pathways. J Womens Health (Larchmt) 2008; 17: 1583–1590.
21. Kerchner A, Lester W, Stuart SP et al. Risk of depression and other mental health disorders in women with polycystic ovary syndrome: a longitudinal study. Fertil Steril 2009; 91: 207–12.
22. Hollinrake E, Abreu A, Maifeld M et al. Increased risk of depressive disorders in women with polycystic ovary syndrome. Fertil Steril 2007; 87: 1369–1376.
23. Benson S, Arck PC, Tan S et al. Disturbed stress responses in women with polycystic ovary syndrome. Psychoneuroendocrinology 2009; 34: 727–35.
24. Rohr UD. The impact of testosterone imbalance on depression and women's health. Maturitas 2002; 15: 41 (Suppl. 1):S25–46.
25. Miller CJ, Johnson SL, Eisner. Assessment Tools for Adult Bipolar Disorder. Clin Psychol (New York) 2009; 16: 188–201.
26. Klipstein KG, Goldberg J F. Screening for bipolar disorder in women with polycystic ovary syndrome: A pilot study. J Affect Disord 2006; 91: 205–209.
27. Freeman MP, Gelenberg AJ. Bipolar disorder in women: reproductive events and treatment considerations. Acta Psychiatr Scand 2005; 112: 88–96.
28. Rasgon NL, Altshuler LL, Fairbanks L et al. Reproductive function and risk for PCOS in women treated for bipolar disorder. Bipolar Disord 2005; 7: 246–259.
29. McIntyre RS, Mancini DA, McCann S et al. Valproate, bipolar disorder and polycystic ovarian syndrome. Bipolar Disord 2003; 5: 28–35.
30. Keel PK, Brown TA. Update on course and outcome in eating disorders. Int J Eat Disord 2010; 43: 195–204.
31. McCluskey S, Evans C, Lacey JH et al. Polycystic ovary syndrome and bulimia. Fertil Steril 1991; 55: 287–291.
32. Morgan JF, McCluskey SE, Brunton JN et al. Polycystic ovarian morphology and bulimia nervosa: a 9-year follow-up study. Fertil Steril 2002; 77: 928–931.
33. Michelmore KF, Balen AH, Dunger DB. Polycystic ovaries and eating disorders: Are they related? Hum Reprod 2001; 16: 765–769.