

Editorial

A New Classification System For Pcos: Could It Work?

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We want to mention about a feasible classification system for polycystic ovary syndrome (PCOS) which is the most common female endocrinopathy, affecting 5–10% of the female population. It is an etiologically heterogeneous condition which involves over production of ovarian androgens leading to a wide range of symptoms including hirsutism, acne, anovulation and infertility [1]. It is also associated with insulin resistance, obesity, dyslipidemia, hypertension, hypercoagulable state and abnormal vascular function [2,3]. Unfortunately there is no consensus for a definition and diagnosis of PCOS yet. After first definition of PCO by Stein and Levental, the National Institutes of Health (NIH) Conference on PCOS firstly recommended diagnostic criteria in 1990 that include both evidence of hyperandrogenism and ovulatory dysfunction, without any regard to the morphological diagnosis of PCO by ultrasonography [4]. However there are some limitations of NIH criteria. If only the NIH criteria would be considered, a group of women who are affected by only hyperandrogenism or oligoamenorrhoea with or without PCO, and who might benefit from medical therapy, would be underdiagnosed. Because of phenotypic heterogeneity of the syndrome, correct diagnosis of the disease is crucial due to prevention of both short term complications and the long-term health risks associated with the syndrome: diabetes, cardiovascular disease and endometrial cancer [5-7]. In 2003, in the Rotterdam ESHRE/ASRM Consensus workshop, ultrasound PCO appearance was added to the other NIH criteria (clinical and biochemical criteria) and the presence of two of three of the following criteria were required for the diagnosis of PCOS: (i) oligo and/or anovulation, (ii) clinical and/or biochemical signs of hyperandrogenism and (iii) echographic PCO, after the exclusion of other pathologies having a similar clinical presentation [8]. According to the Rotterdam consensus, PCO is defined as presence of one of the following two criteria: either 12 or more follicles measuring 2–9 mm in diameter or increased ovarian volume (>10 cm³). The presence of a single polycystic ovary is also sufficient to provide the diagnosis [8]. However some weaknesses also exist for these criteria. The Rotterdam criteria encompasses a higher proportion of women due to those women who show only one clinical symptom (anovulation or hyperandrogenism) associated with an ultrasound PCO morphology being considered as having the disease, meaning an increased number of women accepted as having the disease, resulting in a high sensitivity but low specificity. As a result, use of these criteria for diagnosis may lead unnecessary

intervention and anxiety in patients without the disease or milder forms of the syndrome. In 2006 a new approach for definition of the disease was accepted by the Androgen Excess Society (AES). The AES taskforce in its final recommendations concluded that current evidence supported the following criteria for PCOS: a) clinical and/or biochemical hyperandrogenism; b) ovarian dysfunction, including ovulation dysfunction and/or polycystic ovaries, and c) the exclusion of related disorders. Patients with PCOS would have all three features. The taskforce also affirmed the recognition that PCOS is a hyperandrogenic disorder [9]. Consideration of AES criteria for diagnosis would cause exclusion of a group of women who are affected only PCO morphology with ovulatory dysfunction or with hyperandrogenism. So some women who might benefit from medical therapy would be underdiagnosed. Due to the dissidence about definition of diagnostic criteria, the actual prevalence of PCOS in a given population is the subject of a continuing debate. PCOS prevalence based on the NIH criteria is estimated to be about 6–8%. With use of the Rotterdam criteria, the prevalence increased to 15–25%, while the use of AES recommendations put PCOS prevalence at about 10–15% [10]. These findings suggest that despite many different criteria, optimal diagnosis with high sensitivity and specificity is not possible, disagreement still continues about criteria. The diagnostic criteria of PCOS are formed mainly by biochemical and clinical hormonal parameters and PCO morphology. Women with PCOS might have different degrees of hyperandrogenemia and hypothalamic-pituitary-ovarian axis dysfunction. Besides cases with similar hormonal results might have different phenotypic features due to discrepancy of receptor function, receptor sensitivity and post-receptor signaling. We know that as much as half of patients with PCOS have obesity, insulin resistance and dyslipidemia. Insulin resistance and resistance to some adipokines such as leptin lead to important metabolic changes in different tissues (fat, liver, muscle, skin and ovaries), thus leading to a some phenotypical changes in PCOS and modifying severity of the disease. Although presence of obesity and insulin resistance change management of the present and long term complications of PCOS, these are not included the diagnostic criteria. Since PCOS is a syndromehavinga cluster of symptoms and since a common etiologic factor which could explain pathophysiological pathway cannot be found, primary prevention and exact treatment are not possible currently. Confusion and difference in opinion for diagnostic parameters of PCOS make everything more difficult. So we must focus on treatment of present problems and prevention of future complications. If we assess this syndrome by this way, we could form a new classification system which is formed according to management strategies and prevention of both endocrinologic and metabolic complications. This new system might also prevent over diagnosis and unnecessary intervention. The classification of PCOS women as below might prevent confusion in treatment and follow up in some extent:

- Asymptomatic form: women with only PCO morphology
- Mild form: PCO morphology + anovulation

- Classical form: Hyperandrogenism + ovarian dysfunction (Anovulation and / or PCO).
- Metabolic form: Combination of mild and classical forms with presence of obesity and/or insulin resistance (abdominal obesity, insulin resistance, raised waist / hip ratio, etc).

This definition of sub classification would lead to more case-oriented treatment. Also searches in the area of PCOS would be more accurate because of more homogenous distribution of patients with similar characteristics. So results would be more precise. The logic behind this classification is that although etiopathogenesis similar between these subgroups there might be some minor differences in terms of receptor and hormone sensitivity between these groups. For example in asymptomatic women with only PCO morphology, local increase of androgen exposure in ovarian microenvironment might be responsible from the development of arrested antral follicles. This amount of androgen might be not high enough to produce other symptoms and signs of the disease. The mild form of the PCOS is represent milder form of hormonal disturbance showing itself as only anovulation together with PCO. When hormonal disturbance high enough, we would see classical form of the syndrome which consists of hyperandrogenism + anovulation +/- PCO. Presence of obesity and insulin resistance together with PCOS increase severity by changing serum hormone levels and binding proteins, by increase local IGF levels, and sensitivity to them. Also mitogenic and metabolic effects of insulin modify the syndrome by potentiation of ovarian androgen production and effects of it on the peripheral tissue.

In asymptomatic form, to give recommendation about life style, prevention of weight gain and advice about admission of in case of appearance of other classical symptoms would be enough. In mild and classical form in addition to these recommendations about life style, use of gestagens, oral contraceptives, antiandrogens or ovulation induction agents (for patients desiring pregnancy) would be needed. But in metabolic form treatment strategies must focus on weight loss and correction of insulin resistance in addition to the treatments mentioned above. Even only losing weight to get normal

BMI might correct problem and prevent future complications in most cases. Although metabolic form of PCOS is the most difficult one to manage, it is the most successful group in terms of treatment if they can achieve normal BMI. Dietary, medical and surgical treatment alternatives must be considered in this group. Optimal management for these cases could be improved by interdisciplinary approach.

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