Polycystic ovary syndrome: A misnomer?

Anita Sharma

Polycystic ovary syndrome (PCOS) is the commonest endocrinopathy affecting women of child-bearing age with reproductive, metabolic and emotional sequelae. There is currently discussion among consumer groups and professional bodies that it would be appropriate to replace PCOS with a term that reflects the complex features of the syndrome and removes the emphasis on ovarian cysts, which is neither necessary nor sufficient for diagnosis. One of the proposed alternative names is "metabolic reproductive syndrome". The clinical implications of PCOS are associated with poor health outcomes across the life span: this calls for a paradigm shift to early diagnosis and a multidisciplinary care approach to management. This article will cover the diagnosis, aetiology and management of PCOS.

Polycystic ovary syndrome (PCOS) is the commonest endocrinopathy affecting women of child-bearing age with reproductive, metabolic and emotional sequelae and affects 12–21% of Australian reproductive-aged women, depending on the diagnostic criteria and the population studied. PCOS has consequences for reproduction (e.g. menstrual irregularities and subfertility), metabolism (e.g. obesity, impaired glucose tolerance, type 2 diabetes metabolic syndrome and cardiovascular disease) and psycho-social (depression, anxiety and eating disorders).

As illustrated, PCOS is a heterogenous condition which can result in misdiagnosis, delayed diagnosis and suboptimal care. Diagnostic dilemmas exist because of multiple guidelines and over-reliance on the presence of ovarian cysts for diagnosis. Psychological needs are often ignored and there is little recognition of the importance of early lifestyle interventions, as treatment and management tends to focus on fertility alone. Treatment needs to address both short-term and long-term reproductive, metabolic and psychological aspects of this syndrome, incorporating lifestyle and drug interventions.

Diagnosis

In Australia, almost 70% of women with PCOS remain undiagnosed, even though most women have seen, on average, three doctors at the time of diagnosis and experience high levels of dissatisfaction. In 2010, the anticipated economic burden of PCOS in Australia was $400 million annually, representing a major health cost (Teede et al, 2010).

Aetiology

The aetiology of PCOS is complex and involves an interplay of genetics and environment, which explains the heterogeneity of the syndrome (*Figure 1*). There are probably 160 candidate genes implicated in PCOS. Some of these genes may be related to insulin secretion and action, contributing to insulin resistance (IR) and obesity (Shaikh et al, 2014), which are risk factors for type 2 diabetes. IR in PCOS contributes to both metabolic and reproductive features. Hyperinsulinaemia caused by IR drives hyperandrogenism, which is in turn exacerbated by obesity (Shaikh et al, 2014).

Diagnosis of PCOS

The Rotterdam consensus criteria, which are inclusive of the original National Health Institute (NIH) criteria, are the most widely used diagnostic tool for PCOS. Diagnosis of PCOS requires the presentation of two of three

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Article points

1. Polycystic ovary syndrome is a condition with a complex aetiology, which affects multiple systems in the body. There is discussion that a name change that better encapsulates the aetiology would be more appropriate.
2. Early recognition and a focus on metabolic, reproductive and emotional aspects of the syndrome through a holistic, multidisciplinary team is crucial.

Key words

- Endocrinology
- Polycystic ovary syndrome
- Reproduction

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"Management of polycystic ovary syndrome should address both the short- and long-term reproductive, metabolic and psychological features and needs to be individualised to address the symptoms most relevant to the patient."

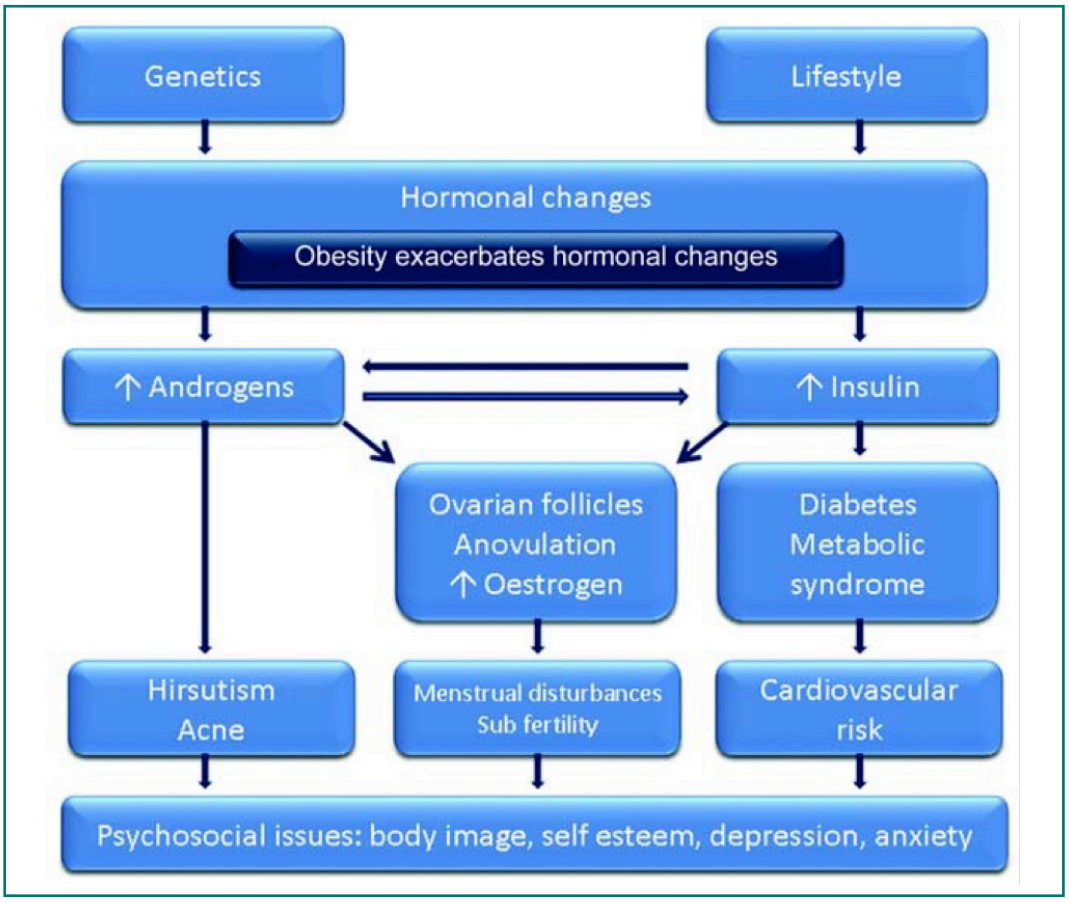

Figure 1. The hormonal, clinical and psychosocial features of polycystic ovary syndrome. Adapted and reproduced from Teede (2016) with permission from The Royal Australian College of General Practitioners.

key features: oligo- or anovulation, clinical and/or biochemical hyper-androgenism and polycystic ovaries on ultrasound, and the exclusion of other endocrine disorders (Rotterdam ESHRE/ASRM PCOS Consensus Workshop Group, 2004). In a survey of 1380 women with PCOS, their symptoms were reported and the prevalence was calculated (Hart et al, 2015):

- Difficulty losing weight (56.2%).
- Irregular menstrual cycles (52.3%).
- Infertility (44.4%).
- Insulin resistance (35.6%).
- Excess hair growth (35.2%).
- Increased tendency to weight gain (31.3%).
- Anxiety and/or depression (24.4%).
- Increased metabolic risk (13.9%).
- Scalp hair loss (11.4%).
- Pregnancy complications (11%).
- Ovarian cysts (10.7%).

Variations in presentation are common among ethnicities. Women of Asian ethnicity may have milder hyperandrogenic symptoms but greater metabolic complications, while hirsutism is more common among women of Middle Eastern and Mediterranean heratige (Ogilvie, 2014).

Management of PCOS

Management of PCOS should address both the short- and long-term reproductive, metabolic and psychological features and needs to be individualised to address the symptoms most relevant to the patient. It is crucial to focus on psychological issues early in diagnosis to promote self-care in terms of lifestyle interventions, which are the cornerstone of management. Lifestyle interventions that achieve modest weight loss of 5–10% improve many features of PCOS

and can be used alone, or in conjunction with targeted medical therapies.

Hyperandrogenism

Androgenic symptoms, which are particularly distressing to patients, can be treated with combined oral contraceptive pill (COCP) treatment, or other anti-androgenic agents like spironolactone. In the case of spironolactone, effective contraception, and renal function and potassium monitoring are required. Vaniqa® (eflonorthine hydrochloride), a prescription topical cream, may be effective in preventing new hair growth.

Fertility

Women with PCOS should not be defined as infertile, rather that they are at risk of subfertility. Fertility outcomes can be improved by achieving a BMI in normal range at preconception. Clomid is a first-line treatment for anovulatory PCOS (achieving 60% cumulative pregnancy rate over 6 months). It is cost effective and relatively non-invasive (Milsom et al, 2002). Other options include Femara® (letrozole), which induces ovulation with increased FSH, or IVF.

Endometrial protection

The hyperoestrogenic environment in PCOS puts women at risk of endometrial hyperplasia and carcinoma. The COCP has good evidence for endometrial protection. The Mirena® device (levonorgestrel-releasing intrauterine system) and Provera® (medroxyprogesterone acetate) are alternatives for women who cannot use the COCP (Vessey and Painter, 2004).

Psychological symptoms

Women with PCOS have higher rates of anxiety, depression, eating disorders and psycho-sexual issues than women without PCOS and so should be screened at initial diagnosis and subsequently. As weight gain is a symptom of PCOS, there needs to be an index of suspicion for eating disorders, especially when women lose an excessive amount of weight (Veltman-Verhulst et al, 2012).

Impaired glucose tolerance

Given that IR is central to the aetiology of PCOS, lifestyle assessment and modification is a key element. Sustainable, long-term changes that reduce weight (or prevent weight gain) through a multidisciplinary team of dietitians and psychologists should be implemented.

Metformin has been used widely for the management of PCOS. While there is good data supporting its use in impaired glucose tolerance, data for its use for its effects on the other symptoms of PCOS are not clear (Diabetes Prevention Program Research Group, 2002). Metformin suppresses hepatic glucose production, but it is not a true insulin sensitiser and lowers insulin by decreasing glucose. Furthermore, it has no effect on insulin sensitivity in the absence of weight loss. However, it has a weak anti-androgenic effect by decreasing basal androstenedione and progesterone production from theca cells, which may help with androgenic symptoms in some women. Compared to placebo, metformin may help to regulate the menstrual cycle in about 50% of women and may assist some women with weight loss (or prevention of weight gain). However, it is difficult to predict which women will respond. Metformin is essentially a second-line agent that is best used in combination with lifestyle interventions for optimum results.

Thiazolidinediones are insulin-sensitising oral medicines that have been proposed, along with metformin, for the long-term treatment of PCOS. They are not considered primary therapy and caution should be given due to effects on weight, bone health and their associated risks in pregnancy (Li et al, 2011).

Bariatric surgery is perhaps an option for the morbidly obese but needs careful evaluation by a specialist multidisciplinary team. It may be effective in achieving significant weight loss, reducing cardiovascular risk and improving pregnancy outcomes; however, the predicted benefits need to be balanced against the short- and long-term risks (Malik and Traub, 2012).

Page points

1. Women with polycystic ovary syndrome (PCOS) should not be defined as infertile, rather that they are at risk of subfertility.
2. Women with PCOS have higher rates of anxiety, depression, eating disorders and psycho-sexual issues than women without PCOS and so should be screened at initial diagnosis and subsequently.
3. Insulin resistance is central to the aetiology of PCOS; therefore, lifestyle assessment and modification is a key element of managing the condition.

"Early recognition and focus on the metabolic, reproductive and emotional aspects of polycystic ovary syndrome through a holistic, multidisciplinary team is crucial."

Conclusion

PCOS is a "metabolic disease", hence, the term "metabolic reproductive syndrome" may better reflect the impact of this syndrome (Teede, 2016). Early recognition and focus on metabolic, reproductive and emotional aspects of the syndrome through a holistic, multidisciplinary team is crucial. Future research that focuses on early identification of the predisposing risk factors in PCOS, the factors that modify environmental factors in order to mitigate the risk and better guidance on individualising therapy will perhaps bring about greater doctor and patient satisfaction in treating this complex syndrome (Pasquali et al, 2011). ■

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