NEW column

Treating PCOS

Professor Helena Teede
MBBS, PhD, FRACP

Research Director, Jean Hailes Foundation for Women's Health, and Chair, Women's Health at Monash University

POLYCYSTIC ovary syndrome (PCOS) is the most common endocrine abnormality in women of reproductive age and has psychological, reproductive and metabolic manifestations.

PCOS affects 5%-10% of women of reproductive age or 400,000 women in Australia.[1]

In 2006 the estimated economic burden of PCOS in Australia was $40 million (menstrual dysfunction 31%, infertility 12% and PCOS-associated diabetes 40%), representing a major health and economic burden.[1]

CLINICAL MANIFESTATIONS

1. Psychological: anxiety, poor self-esteem, reduced quality of life.
2. Reproductive: hyperandrogenism, ovulatory and menstrual dysfunction, infertility, pregnancy complications including early pregnancy loss, gestational diabetes, pregnancy-induced hypertensive disorders and neonatal complications.
3. Metabolic: insulin resistance, metabolic syndrome including lipid abnormalities, increased risk of impaired glucose tolerance, type II diabetes and potentially cardiovascular disease.[2,3]

DIAGNOSIS

The diagnosis remains controversial, but is based on the presence of two of three reproductive criteria – ovulatory disturbance, hyperandrogenism and polycystic ovaries on ultrasound in the absence of other causes.

In the majority of both lean and overweight women with PCOS, insulin resistance is central to the pathogenesis of the syndrome, with hyperinsulinaemia driving reproductive and metabolic features.[4-7]

Insulin resistance is both genetic and lifestyle-related. Obesity exacerbates psychological, reproductive and metabolic features of PCOS and as obesity increases in the community, the prevalence of the PCOS phenotype and associated glucose intolerance and diabetes are expected to rise significantly.

ASSESSMENT

There is no single diagnostic test. Ensure the patient is not taking an oral contraceptive before hormone testing.

Investigations include: testosterone, sex hormone binding globulin, free-androgen index, prolactin and thyroid-stimulating hormone.

Other optional investigations include a pelvic ultrasound for ovarian morphology and endometrial thickness.

An oral glucose tolerance test and lipid profiles should be performed in all women at diagnosis and regularly thereafter in those who are overweight or at increased risk of diabetes (1-2 yearly). Fasting glucose is inadequate in these women.

There is no role in clinical practice for measuring insulin levels as the assays are inaccurate and highly variable.

Insulin resistance is best reflected by features of metabolic syndrome and abnormalities on the oral glucose tolerance test.

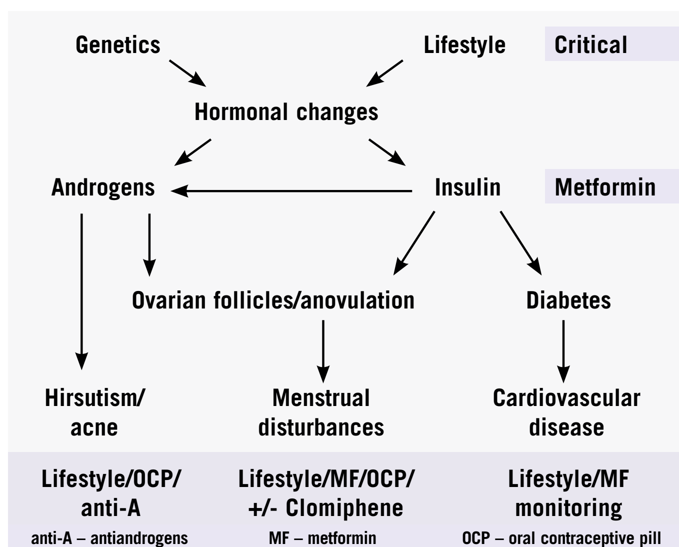


Figure 1: Targeted treatment options for the clinical features related to hyperandrogenism, menstrual disturbance (including infertility) and metabolic features.
Source: Teede, H et al, RACGP CHECK Program: Polycystic ovary syndrome, 2008. Reproduced with permission.

TREATMENT

Treatment needs to be individualised and underpinned by education on both short and long term sequelae.

Psychological features need to be discussed and counselling considered as women with PCOS are unlikely to sustain lifestyle changes unless psychosocial issues are addressed.

LIFESTYLE INTERVENTION

Lifestyle change is first-line therapy and is critical in all overweight women with PCOS. Prevention of weight gain is also important.

Weight loss of 5%-10% has major clinical benefits, including improving psychological outcomes,[8] reproductive features (menstrual cyclicity, ovulation and fertility)[9,10] and metabolic outcomes (insulin resistance, metabolic syndrome).[9-13]

It is critical to counsel patients that small, achievable goals make a large clinical impact, even though subjects may remain clinically overweight or obese.[9,14,15]

Lifestyle change is paramount as no specific dietary regimen has been proven superior in PCOS and although a low-glycaemic-index diet may offer theoretical advantages, it is yet to be adequately researched in PCOS.

Structured moderate exercise (three times per week for 40 minutes) is more effective than diet alone, inducing greater improvements in androgens, insulin resistance and ovulation, and a trend to increased pregnancy rate, despite a greater weight loss with diet alone.

Translation of current evidence into practice suggests a combination of exercise with overall sustainable reduction in caloric intake through long-term behavioural change.

TARGETED THERAPY

Treatment options for the reproductive and metabolic implications of PCOS are varied and need to be tailored to the clinical presentation (see chart).

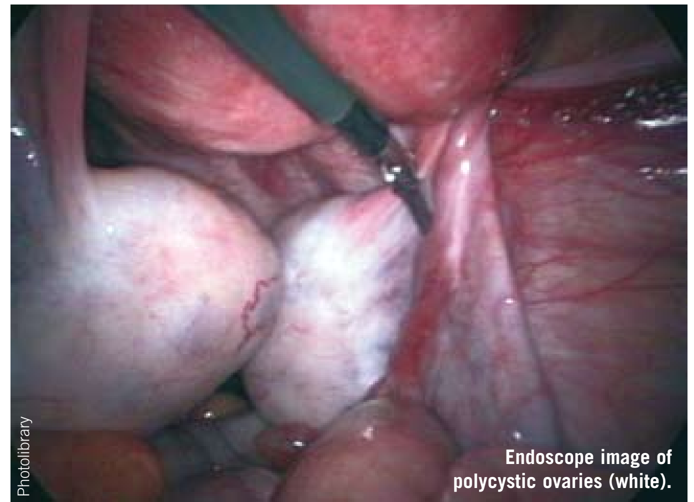
In addition to healthy lifestyle changes, options include cyclic progestin to induce withdrawal bleeds (2-3 monthly), the oral contraceptive pill, metformin and targeted infertility therapies (see chart and box).

SUMMARY

PCOS is common and is a major health and economic burden. It is associated with psychological, reproductive and metabolic features and in the majority of cases is underpinned by insulin resistance.

Management should focus on education, lifestyle and targeted medical therapy as required.

Monitoring for longer term metabolic complications, including glucose intolerance and hyperlipidaemia, is also important.



Endoscope image of polycystic ovaries (white).

Targeted treatment options in PCOS

Hirsutism/acne secondary to hyperandrogenism

- Lifestyle changes and 5%-10% weight loss
- Combined oral contraceptive pills increase sex hormone binding globulin and reduce androgens (lower dose 20 g OCPs may be preferable as higher dose OCPs increase insulin resistance)
- Metformin* 1-2 g slow release given at night has equivalent efficacy to OCPs[11]
- Cosmetic therapy (for example, electrolysis and laser)
- Topical anti-androgens (for example, eflornithine [Vaniqa])
- Anti-androgens can be added to OCPs (spironolactone 50 mg bd or cyproterone acetate 25 mg/day for days 1-10 of the active OCP tablets), take for about six months, both anti-androgens **must** be taken with the OCP to prevent abnormal menstrual bleeding and adverse effects in pregnancy.

Irregular cycles

- Lifestyle changes aiming for sustainable 5%-10% weight loss, including structured exercise three times a week
- Cyclic progestins (for example, 10 mg medroxyprogesterone [Provera], 14 days every 2-3 months), decreases risk of endometrial hyperplasia/ carcinoma
- The OCP, as above.

Infertility

- Obesity independently causes infertility and should be addressed with healthy lifestyle (lifestyle change is critical – even small changes in weight have major benefits)
- Be wary of age-related infertility and advise patients to plan a family before age 35 if possible
- Other effective therapies are available and include clomiphene, metformin* and gonadotrophins.

Metabolic syndrome, prediabetes, diabetes and cardiovascular disease risk

- Obesity independently causes metabolic complications and should be addressed
- Lifestyle change with a 5% weight loss reduces diabetes risk by 60% in high-risk groups
- Metformin* reduces the risk of diabetes by 60% in high-risk groups.

**The use of metformin in PCOS is supported by Level I evidence including a Cochrane review and multiple randomised controlled trials, as well as by relevant professional bodies including the Endocrine Society of Australia. However no application has yet been lodged with the Therapeutics Goods Administration so it has not been approved for use in PCOS and prescriptions are off-label. A TGA application is underway.*

References available at **www.medicalobserver.com.au**

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