

Polycystic ovarian syndrome (PCOS)

Diagnosis

There is now agreement about the diagnosis of PCOS. This was reached after discussion in a meeting in Rotterdam in 2003 and was universally endorsed by both the European society of human reproduction and the American society for Reproductive Medicine in 2008. It now universally sets the standard for diagnosis and allows some uniformity in the various trials carried out for treatment of some or all symptoms/signs of PCOS.

Patients now require evidence of 2 of the following 3 signs or symptoms

1. Oligomenorrhoea (scant and irregular periods) - or anovulation (no ovulation).
2. Clinical and/or biochemical signs of hyperandrogenism- signs such as increased facial hair or acne. Blood tests showing higher levels of androgens such as testosterone
3. Polycystic ovaries and exclusion of other aetiologies (congenital adrenal hyperplasia, androgen-secreting tumours, Cushing's syndrome). Ovaries should have:

“Presence of 12 or more follicles in each ovary measuring 2 -9 mm in diameter, and/or increased ovarian volume (>10 mL)” when examined by ultrasound, usually transvaginal.

High Leutinising hormone levels and metabolic syndrome (insulin resistance) are important factors in the condition but are not considered in the diagnosis.

Patients with insulin resistance have impaired fertility. This is directly linked with obesity. Tests should include a glucose tolerance test. The assessment of insulin resistance is not necessary to make the diagnosis of PCOS and it does not affect the selection of treatment for PCOS.

The long-term potential consequences of PCOS are not discussed here as they are not important in the management of infertility. The need is here and now as often the most important factor is non-ovulation and is required immediately for fertility treatments to succeed.

Management

Management of PCOS depends upon the symptom that the woman wishes to improve. The discussion below concentrates on fertility only. Clearly although facial hair or acne may improve with variants of the contraceptive pill this management is inappropriate for fertility

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improvement. The discussion below summarised the current consensus views of both the European society of human reproduction and the American society for Reproductive Medicine published in March 2008.

The management concentrated on 6 areas

- 1) Lifestyle changes
- 2) Ovulation induction with Clomiphene
- 3) Insulin sensitising agents
- 4) Gonadotrophins treatment
- 5) Laparoscopic ovarian diathermy
- 6) Assisted conception

Lifestyle change

The most important factor is obesity. This leads to both a reduction in ovulation and an increase in miscarriage. Weight loss before conception improves live birth rates in women with PCOS, even without medication and is recommended as the first line treatment. A diet with very low carbohydrate may be the best. Variants of the Atkins diet may be the best to try. These reduce glycaemic load and may be beneficial in improving the excess insulin production that some women with PCOS may have. Your diet should be calculated as your daily requirement in kilocalories minus 500 kilocalories.

Patients with an excess of central body fat are the most affected.

Any calorie restricting diet that achieves a 5% reduction in body weight may help, 10% is ideal. There is good evidence that the ovaries also become less polycystic looking and function better as weight decreases.

Other general lifestyle improvements such as exercise and cessation of smoking are always going to increase the chance of conception. Exercise alone is not likely to reduce weight. Many women with PCOS already have a lower baseline activity than control women.

Treatments to reduce absorption or suppress appetite may be effective here. In serious cases bariatric surgery has been shown to be effective but carries serious risks. It is worth considering if your BMI is over 40 and may help you health in general if its over 50.

Ovulation induction with Clomiphene

This drug remains the treatment of choice for inducing ovulation in women with PCOS. It should be used ideally after weight loss rather than during.

To be effective a woman needs a normal Follicle Stimulating Hormone (FSH) level, as its mode

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of action is to entice the pituitary gland to secrete more FSH and therefore stimulate the ovary with it. Approximately 75-80% of women with PCOS will ovulate and the conception rate is up to 22% per cycle - about 50%-60% after 6 cycles. Treatment should be limited to 6 cycles in the first instance. A further 6 cycles can be given after further investigation and discussion. No more than 12 cycles of treatment would be used and pregnancies are rare after this time.

Treatment should be monitored to ensure the dose used achieves ovulation. After that is determined no further monitoring is necessary unless women do not wish to take any risk of multiple pregnancy- in which case see ovulation induction section.

If the side effects of Clomiphene are not tolerable, then the drug Tamoxifen or Letrozole may be used (see information sheets). The drugs are not licensed for fertility use but is widely used with a similar success rate and comparable side effects.

Adding metformin or dexamethasone (a steroid) to treatment confers NO benefit to patients unless there is evidence of glucose intolerance.

In a few women the source of the raised androgens (usually DHEA) is the adrenal gland. They may benefit from corticosteroids to suppress the adrenal gland. They will usually need an ovulation induction agent ie clomiphene or similar as well.

Insulin Sensitising Agents

These are used for treatment of diabetes. The consensus view was that drugs such as Metformin should only be used where there is evidence of glucose intolerance. Metformin alone is less effective than Clomiphene in inducing ovulation. It has been used to improve weight loss but the results are disappointing. It does reduce the risk of multiple pregnancy as there is more single ovulations. This has to be contrasted with the lower pregnancy rate.

Gonadotrophins

These are injectable drugs containing either FSH alone or in combination with LH. The injections are subcutaneous. A set protocol is essential as the risk of an excessive response is significant. It is a highly effective treatment in patients who have not responded to Clomiphene especially in those under 35.

Intensive monitoring is mandatory and consists of ultrasound scans and if necessary blood tests.

The medication is highly effective. The risk of over stimulation is much higher than with Clomiphene. A number of treatments may be cancelled due to over response. Over response may result in an extra risk of multiple pregnancy and also the ovarian hyperstimulation syndrome.

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This is a serious medical condition.

A maximum of 6 cycles of treatment should be used.

Combination with GnRH analogues has been suggested to reduce Leutinising hormone (LH) levels but there is no evidence to support an improvement in outcome.

Laparoscopic Ovarian Diathermy

This treatment requires a laparoscopy, which is an operation, carried out under a general anaesthetic. The ovary is diathermised using an electrical device, a laser or an instrument that delivers heat via friction. The idea is to damage the ovary with a heat modality. This seems to have the effect of temporarily resetting the ovarian response and ovulation sometimes ensues.

It may work well in conjunction with Clomiphene.

It is an alternative to gonadotrophins treatment.

It may be especially useful in women who need a laparoscopy as a test of their fallopian tube function anyway. It could therefore be carried out at the same time as the diagnostic laparoscopy carried out for testing tubal patency.

Intensive monitoring is not required as if ovulation happens it is usually a single ovulation.

If not carried out when a diagnostic laparoscopy was already scheduled the additional risks of laparoscopy should be considered.

Assisted Reproduction Techniques

IVF

In principal anovulation or PCOD is not an indication for IVF. If however ovulation induction fails to achieve conception then it may be. If ovulation cannot be achieved by any therapy then there is little point in trying IVF as some degree of ovarian response is necessary.

IVF should be only considered after all the above techniques have failed or are deemed not appropriate. There is an increase in the rate of ovarian hyperstimulation syndrome

Pregnancy rates for women with PCOS are similar to those without PCOS if matched for weight. Implantation is not thought to be compromised in PCOS but miscarriage rates may be higher. This is largely due to the increased risk of miscarriage with increasing BMIs over 28-30.

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There is an increased abandonment rate of treatment in PCOS. This is either for non-response or over response that might or does result in ovarian hyperstimulation Syndrome.

Intrauterine Insemination

Research in this area is poor (for PCOS). Single insemination may be indicated if the response to ovulation induction is good but no pregnancy ensues. Usually it is only used where there is either a psychosexual problem or an erectile problem

Antimullerian Hormone

This is used as a test of ovarian reserve. PCOS patients often have a very high level of antimullerian hormone (AMH). If the level is high then the risk of hyperstimulation is also high and the dose of gonadotrophin adjusted. In IVF it may be prudent to use an antagonist cycle stimulation regimen.

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