

PCOS and Fertility Issues: Management of Subfertility



This department covers selected points from the 2009 Endocrine Update: A CME Day from the Division of Endocrinology and Metabolism at McMaster University and the University of Western Ontario.
Program Chairs: Aliya Khan, MD, FRCPC, FACP, FACE and Terri Paul, MD, MSc, FRCPC



Stephen Power, MD, PhD, FRCSC; and Sultan Chaudhry, BHSc

Polycystic ovarian syndrome (PCOS) is one of the most common hormonal disorders among women of reproductive age and is the leading cause of infertility.¹ Women with PCOS are anovulatory or oligo-ovulatory as a result of hypothalamic-pituitary-ovarian dysfunction. One in two women with PCOS are often obese. The major goal of fertility promotion for women affected with PCOS is a singleton gestation without complications and a vaginal delivery at term. The treatments should optimize maternal health, minimize maternal and embryonic/fetal/neonatal morbidity and the risk of premature delivery.

PCOS is one of the most common hormonal disorders among women of reproductive age and is the leading cause of infertility.

Slim women with PCOS have normal BMI, classic PCO-type ovaries (multiple small follicles at the periphery of the ovary) and luteinizing

hormone (LH)/follicle-stimulating hormone (FSH) ratio > 2:3 with elevated LH levels. The elevated LH causes mitotic arrest of early antral follicles and blocks FSH induction of folliculogenesis.² The obese women with PCOS do not present with classic PCO-type ovaries and the LH/FSH ratio may be > 1 with decreased FSH levels. Inadequate levels of FSH from the pituitary result in disruption of folliculogenesis and endometrial receptivity.² The obese woman with PCOS may also manifest insulin resistance and altered adipokine levels.³

Therapeutic strategies to achieve pregnancy for the slim women with PCOS include:

- ovulation induction with timed intercourse or intrauterine insemination and
- controlled ovarian stimulation with *in vitro* fertilization (IVF) technologies.

For the obese women, high emphasis should be placed on weight loss. These women present at a time in their lives when significant lifestyle changes may produce results that prevent metabolic and cardiac disease in the future. Strategies for weight loss are often ineffective. Thereafter, similar ovulation induction protocols as for the slim woman are adopted. Preferably, better strategies for weight loss need to be developed and implemented.

Clomiphene citrate and aromatase inhibitors are the first-line oral ovulation-inducing agents for slim women. If these agents fail, subcutaneous FSH (purified from urine of postmenopausal women or produced from recombinant molecular technologies) can be used. The use of all ovulation-inducing agents can result in multiple gestations. Women using FSH should be monitored closely to assess response to therapy and limit grand multiples. Metformin, an insulin-enhancing agent, is now being used to enhance the action of ovulation-inducing agents as well as increase the frequency of spontaneous ovulations in obese women with PCOS. Fifty per cent of obese women with PCOS will improve cyclicity with metformin alone⁴ but higher pregnancy rates per cycle are achieved with clomiphene citrate therapy.

Women using FSH should be monitored closely to assess response to therapy and limit grand multiples.


If pregnancies are not achieved with the aforementioned strategies, women may opt to proceed with IVF technologies. FSH is administered with doses aimed at stimulating up to 20 follicles per

Dr. Power is an Associate Professor, Department of Obstetrics and Gynaecology, Schulich School of Medicine & Dentistry, University of Western Ontario, London, Ontario.

Dr. Chaudhry is an MD/PhD Candidate, the Michael G. DeGroote School of Medicine & Medical Sciences, McMaster University, Hamilton, Ontario.

cycle. About eight to 12 oocytes are retrieved. About 70% to 80% of the oocytes will be fertilized with IVF techniques, of which 50% will develop into embryos suitable for transfer either on luteal day three (six to 10 cells) or luteal day five (the blastocyst stage).⁵ Both slim and obese women with PCOS pose a challenge with respect to finding the “right” dose of FSH for stimulation. Slim women may hyperstimulate excessively and develop ovarian hyperstimulation syndrome. Obese women may require higher doses of FSH.

Collaborative model of care should be utilized to provide care for women with PCOS which may include:

- infertility specialists,
- endocrinologists,
- dieticians and
- psychologists. 

References

1. Azziz R, Woods KS, Reyna R, et al: The Prevalence And Features Of The Polycystic Ovary Syndrome In An Unselected Population. *J Clin Endocrinol Metab* 2004; 89(6):2745-9.
2. Taylor AE, McCourt B, Martin KA, et al: Determinants Of Abnormal Gonadotropin Secretion In Clinically Defined Women With Polycystic Ovary Syndrome. *J Clin Endocrinol Metab* 1997; 82(7):2248-56.
3. DeUgarte CM, Bartolucci AA, Azziz R: Prevalence Of Insulin Resistance In The Polycystic Ovary Syndrome Using The Homeostasis Model Assessment. *Fertil Steril* 2005; 83(5):1454-60.
4. Bailey CJ, Turner RC: Metformin. *N Engl J Med* 1996; 334(9):574-9.
5. Fedorcsák P, Dale PO, Storeng R, et al: The Effect Of Metformin On Ovarian Stimulation And In Vitro Fertilization In Insulin-Resistant Women With Polycystic Ovary Syndrome: An Open-Label Randomized Cross-Over Trial. *Gynecol Endocrinol* 2003; 17(3):207-14.