

Clinical Fertility Management in Polycystic Ovarian Syndrome Patients



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Abstract

Polycystic Ovarian Syndrome affects 5-20% of women of reproductive age in the United States¹. It is a complex endocrine disorder that affects female fertility, insulin resistance, and produces symptoms of hyperandrogenism including cystic acne, hirsutism, and abdominal weight gain. Patients with PCOS who want to conceive should be treated with a multi-layered approach which can include lifestyle modification, pharmaceutical therapy, or surgery.

Introduction

Polycystic Ovarian Syndrome (PCOS) is the most common endocrine disorder among women of reproductive age. Myriad aspects of this condition remain widely under-researched and poorly understood. PCOS is a complex diagnosis that has a profound effect on the physical and mental health of patients as it is commonly associated with eating disorders, insulin resistance, hypertension, and infertility. While there are well-established guidelines for hypertension and diabetes management in PCOS patients, a major concern that requires greater patient education and follow up on behalf of the clinician is infertility. Infertility is defined as the inability to conceive after 12 months of unprotected intercourse or insemination in women under the age of 35. For women over age 35, it is after only 6 months². Infertility in PCOS patients requires a multi-dimensional approach that includes lifestyle modification with thorough patient education, behavioral therapy, and use of pharmaceutical agents including letrozole and clomiphene citrate when indicated.



Clinical Presentation and Diagnostics

Clinical Presentation

- Woman of reproductive age (typically from menarche to 4th decade of life)
- Obesity
- Irregular menstruation (amenorrhea or oligomenorrhea)
- Male-pattern hair distribution (i.e. terminal hairs on jawline, umbilicus, or shoulders)
- Cystic acne

Once there is clinical suspicion of PCOS, the Rotterdam Criteria can be used which requires 2 of 3 of the following criteria for an official diagnosis: Oligo-anovulation, polycystic ovarian morphology, or hyperandrogenism³. Ovarian morphology is best diagnosed by transvaginal ultrasound; however, polycystic morphology is rarely seen. Important labs to order in an initial work up for infertility secondary to PCOS include hemoglobin A1C, complete metabolic panel, complete blood count, follicle stimulating hormone, luteinizing hormone, serum prolactin, thyroid panel, progesterone, and dehydroepiandrosterone (DHEA). Commonly, Hgb A1C and DHEA will be elevated⁴. Additionally, it is important to consider other factors affecting conception such as sperm count and motility, effective timing and method of intercourse, and current medications when completing a thorough evaluation.

Lifestyle Modification

- patients who are clinically overweight or obese should have a 5-10% decrease in weight⁵.
- A high-protein diet has the greatest effect on ovulation and menstruation producing the greatest increase in relative fertility for patients. This diet should not be considered for women with renal damage.
- Aerobic exercise recommendations for PCOS patients follow the American Heart Association guidelines of 150-300 minutes per week of moderate-intensity activity or 75-150 minutes weekly of vigorous activity⁷.
- patients should perform strengthening exercises two times per week and decrease the amount of time sitting daily.
- Additionally, it has been suggested that women with PCOS who participate in at least 135 minutes of moderate activity for 3 months have a 60% increase in ovulation.
- Patients with PCOS, especially those struggling with infertility, should be screened for anxiety and depression at each visit. Positive screening results should lead the clinician to discuss treatment with the patient including behavioral therapy or pharmaceutical management with SSRIs.

Pharmaceutical Intervention

Clomiphene citrate (CC) is an estrogen receptor modulator which blocks the negative feedback loop, increases the secretion of progesterone during the luteal phase, and leads to a more predictable menstrual cycle. A negative pregnancy test and pelvic exam should be performed prior to initiating therapy. A fasting lipid panel should be obtained and monitored every 6-8 weeks to assess for high triglyceride levels. Perform a transvaginal ultrasound to visualize any follicle development 11-12 days into the patient's menstrual cycle after initiating treatment and urine LH test or blood progesterone test should be monitored for increased values. 15% of women with PCOS are resistant to the medication and should progress to second line therapy. Contraindications include abnormal vaginal bleeding, decreased liver function, poorly controlled adrenal or thyroid dysfunction, patients who are currently breastfeeding or pregnant, and endometrial cancer¹¹. Adverse effects include flushing, mood changes, nausea, vaginal dryness, and ovarian hyperstimulation syndrome. Symptoms for OHS include diarrhea, abdominal distention, shortness of breath, chest pain, and urinary hesitancy which appear 7 days into the luteal phase and can be treated with increased hydration in mild cases or may require IV fluids.

Letrozole is second line treatment and an aromatase inhibitor with decreased risk of developing multiple follicles compared to CC. Letrozole is considered first line treatment for women with a BMI greater than 30 kg/m² who have failed effective weight management. Adverse effects and contraindications are the same as CC.

The third line pharmaceutical treatment is gonadotropin therapy which entails low dose therapy with follicular stimulating hormone (FSH) or human menopausal gonadotropin (HMG). This option is considered for women who failed CC and letrozole therapy and are not interested in more invasive measures for fertility management. Unfortunately, this method is high cost to the patient and requires serum LH monitoring 40 minutes after each administration which can lead to low patient compliance. Additionally, there is increased risk of multiple pregnancies with this method compared to the first and second line treatments.

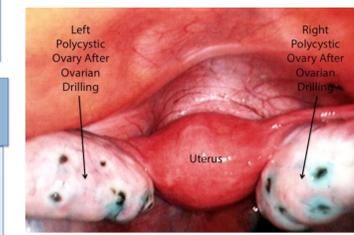
Surgical Intervention

Ovarian Drilling

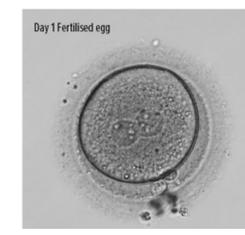
- Optimal for patients undergoing abdominal laparoscopic procedure for an alternative reason
- Procedure: monopolar energy is used to create perforations in each ovary
- Benefit: minimally invasive, high success rate
- Disadvantages: risk for adhesions, damage to the ovaries, or premature ovarian failure

In Vitro Fertilization

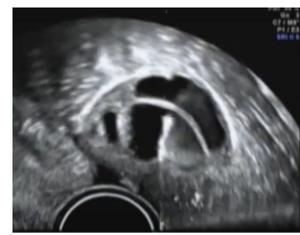
- Indicated for women who have failed all other therapies
- Procedure: Ovulation stimulation, egg retrieval, fertilization, then embryo transfer. Refer to Fertility for management and discussion of outcomes
- Benefit: Option for women who have failed all other measures
- Disadvantage: high cost, risk of multiple gestations, OHSS, relatively low success rate with women with PCOS



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Conclusion

Fertility management in PCOS patients is a complex issue that requires proper patient education and lifestyle modification. The clinical approach to managing these patients requires primarily realistic expectations and proper education on dietary changes and physical activity recommendations. Patients who are unable to achieve weight loss goals or are unable to conceive despite a 5 to 10 % weight loss should be recommended pharmaceutical treatment beginning with clomiphene citrate. If CC is unsuccessful, then letrozole should be given as an option. If the patient is still unable to conceive, options of laparoscopic ovarian drilling or gonadotropin therapy is the next step. Finally, IVF is the last-resort option for patients who have failed all of the above treatments. Regardless of treatment method, a major obstacle patients face is discontinuation of treatment due to low morale or lack of proper education and reasonable goals. It is crucial for providers to be emotionally supportive during the treatment period and establish realistic next steps in treatment. This can be achieved through creating a network of specialists including a dietitian, physical therapist, and mental health professional if the patient desires additional support. Through a team-oriented approach, patients with polycystic ovarian syndrome have a better opportunity to conceive a viable pregnancy.

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