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MEDICAL UPDATE

PCOS: Treating Women Trying to Conceive

Polycystic ovary syndrome (PCOS) makes up 85 percent of all ovulatory disorders, affecting nearly 15 percent of reproductive-age women.[1] Over the past several years, treatment recommendations for women with PCOS have changed. As a result, there are many questions about how best to treat women with PCOS who are trying to conceive.

Diagnosing PCOS through Exclusion

One of the greatest challenges with PCOS is not treating the disorder, rather diagnosing it. Currently, there is no single diagnostic test that can be used to positively identify PCOS. As a result, physicians must approach a diagnosis through the presence of symptoms and exclusion of other disorders. According to the Rotterdam Criteria, established in 2003 by the European Society of Human Reproduction and Embryology (ESHRE) along with the American Society for Reproductive Medicine (ASRM), a diagnosis of PCOS requires two of the following three symptoms to be present along with the exclusion other causes of those symptoms:

HYPERANDROGENISM OR HYPERANDROGENEMIA: acne, excessive hair growth, alopecia, or elevated androgen levels in the blood.

MENSTRUAL DISTURBANCES: oligo/amenorrhea

POLYCYSTIC APPEARING OVARIES ON ULTRASOUND

EXCLUDE: thyroid disease, hyperprolactinemia, hypothalamic suppression, premature ovarian failure, androgen secreting tumors, and congenital adrenal hyperplasia.

Letrozole vs. Clomiphene Citrate

Clomiphene citrate (a selective estrogen receptor modulator, or SERM) functions by blocking the body's ability to "see" and respond to estrogen. As a result, the ovaries respond by recruiting, growing, and ovulating a follicle so that conception can occur. But due to the body's inability to see estrogen, many women experience a thinning of the uterine lining that can ultimately impact the ability for an embryo to implant.

Over the last several years, letrozole has been explored as an alternative to clomiphene citrate. The primary difference between the two relates to how they manipulate the body's response to estrogen. Letrozole (an aromatase inhibitor) lowers the amount of estrogen produced rather than blocking the ability to respond to it. As a result, thinning of the uterine lining is not as severe. Studies have found that women with PCOS using letrozole experience a greater frequency of ovulation and live births compared with those using clomiphene (27.5% vs 19.7% live birth rate with letrozole vs. clomid).[2] Although studies show a higher live birth rate in letrozole compared to clomiphene citrate, it is important to note that the use of letrozole for ovulation induction is not FDA approved.

MEDICATION RECOMMENDATION

	CLOMIPHENE CITRATE	LETROZOLE
Cycle 1- days 3-7 or 5-9	50 mg QD	2.5 mg QD
Cycle 2*- days 3-7 or 5-9	100 mg QD	5.0 mg QD
Cycle 3*- days 3-7 or 5-9	150 mg QD	7.5 mg QD

**If ovulation has not occurred, confirmed by either no menstrual period at the end of the cycle or a progesterone level under 3 mg/mL on approximately day 21 of the cycle or 1 week after positive ovulation predictor kit.*

If using clomiphene citrate or letrozole for ovulation induction in a patient with PCOS, it is important to confirm tubal patency (with hysterosalpingogram, or HSG) and presence of adequate sperm in the male partner (with semen analysis) prior to starting treatment.

Current Recommendation for Metformin Use

While there is a place for metformin in the treatment of women with PCOS, it is no longer recommended for the sole purpose to regulate a woman's menstrual cycle or induce ovulation. Other options such as clomiphene citrate or letrozole are more appropriate (and effective) for ovulation induction.

Treatment with metformin should be considered in women with PCOS who are found to have impaired glucose tolerance, pre-diabetes, or diabetes. It is also reasonable to use metformin for women with PCOS who are overweight or obese as it is associated with a 5% decrease in body weight.[3]

1. Sirmans S, Pate K. Epidemiology, diagnosis, and management of polycystic ovary syndrome. *Clin Epidemiol.* 2014; 6: 1–13. doi: 10.2147/CLEP.S37559
2. Legro R, Brzyski R, Diamond M, et al. Letrozole versus Clomiphene for Infertility in the Polycystic Ovary Syndrome. *N Engl J Med.* 2014; 371: 119-129. doi: 10.1056/NEJMoa1313517
3. The effect of orlistat versus metformin on body composition and insulin resistance in obese premenopausal women: 3-month randomized prospective open-label study. AU Kujawska-uczak M, Musialik K, Szuli ska M, Swora-Cwynar E, Kargulewicz A, Grzymis awska M, Pupek-Musialik D, Bogda ski P SO Arch Med Sci. 2017;13(4):725. Epub 2016 Aug 29 PMID: 28721138

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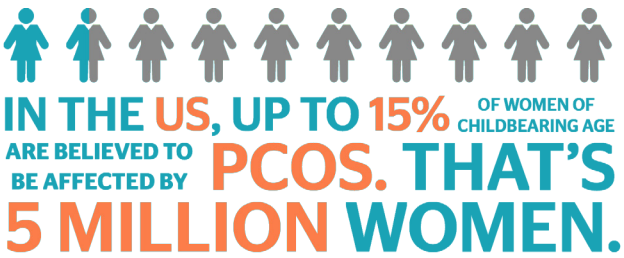
Referring a Patient with Suspected or Diagnosed PCOS

Physicians can refer their patients who are actively trying to conceive at any point whether PCOS is suspected or diagnosed. If first-line treatments such as clomiphene citrate or letrozole have not been successful after three cycles, a referral is highly recommended. This allows patients to progress to treatment options usually only available with a fertility specialist such as intrauterine insemination (IUI) or in vitro fertilization (IVF). An early referral will give women more treatment options and a greater chance of success.

LEARN MORE ABOUT DIAGNOSING AND TREATING PCOS ▶



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