

Co-treatment with Letrozole during ovarian stimulation for IVF/ICSI: a systematic review and meta-analysis

Letrozole reduces serum estradiol by inhibiting the aromatase enzyme and has growing clinical indications in fertility. This systematic review and meta-analysis were aimed to assess the effect of letrozole co-treatment in ovarian stimulation for In vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI).

Study overview

- Systematic review and meta-analysis of 31 studies including 16 randomized controlled trials (RCTs) & 15 observational studies
- N = 3952 women (poor, normal, high responders)
- >6,000 IVF/ICSI cycles

Key findings

Parameter	Effect of Letrozole Co-treatment	Significance
Live Birth Rate (Poor Responders)	Increased by 7%	$p = 0.03$
Gonadotropin Dose	Reduced significantly	Reduced cost burden
Oocytes Retrieved (Normal Responders)	Increased with 1.8 oocytes	$p = 0.01$

Conclusion

Letrozole co-treatment may enhance outcomes in poor responders by improving ovarian efficiency and optimizing stimulation with fewer gonadotropins and comparable safety.

Ref: Bülow, Nathalie Söderhamn et al. "Co-treatment with letrozole during ovarian stimulation for IVF/ICSI: a systematic review and meta-analysis." Reproductive biomedicine online vol. 44,4 (2022): 717-736. doi:10.1016/j.rbmo.2021.12.006

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Drug Review

Anovulation & Infertility

- ♀ Anovulation is a common cause of infertility. It's caused by hormonal imbalances, and the main sign of it is having irregular periods. Anovulation can often be treated with lifestyle changes and/or medication.
- ♀ In general, infertility is defined as not being able to get pregnant (conceive) after one year (or longer) of unprotected intercourse. Because fertility in women is known to decline steadily with age, some providers evaluate and treat women aged 35 years or older after 6 months of unprotected intercourse.

Guideline Recommendations

-  Letrozole Should be considered as first line therapy for OI in Patients with PCOS & BMI > 30 because of increased LBR Compared to Clomiphene Citrate .
-  Letrozole should be first line pharmacological therapy to improve fertility outcome in women with PCOS & an ovulatory infertility with no other infertility factors.
-  Letrozole as the first line treatment due to its higher ovulation pregnancy & Live birth rate as well as lower multiple pregnancy rate.
-  Letrozole are first line treatment of anovulatory infertility in women with PCOS

Hope for Anovulatory Infertility of PCOS Patient

- ♀ Letrozole is an orally-active aromatase inhibitor, with good potential for ovulation induction. Many researchers have studied this drug as an option for ovulation induction.
- ♀ Inhibition of aromatase enzyme leads to decrease in estrogen levels, resulting in more follicle stimulating hormone (FSH) release, which results in follicular growth.
- ♀ Aromatase enzyme inhibitors also cause a local increase of ovarian androgens which increases the follicular sensitivity to FSH and stimulation of insulin-like growth factor (IGF)-I. FSH and IGF-I are both essential for follicular maturation.

Evidence Based Result

- ♀ Better pregnancy outcomes and higher live births compared to CC in PCOS patients
- ♀ Effective even in patients with CC-resistant PCOS
- ♀ No anti-estrogenic effects on endometrium & cervical mucus (reduces hot flashes & other perimenopausal symptoms)
- ♀ Mono-follicular development and lower multiple pregnancies
- ♀ Safety established in clinical studies
- ♀ Maintains physiological FSH levels and lowers multiple pregnancy rates

Ref.: 1. <https://www.sciencedirect.com/science/article/pii/S1110569018300554> 2. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3148573/> 3. <https://www.ijrcog.org/index.php/ijrcog/article/view/7154>