LETROZOLE ALONE OR WITH METFORMIN FOR OVULATION INDUCTION IN PATIENTS WITH PCOS

Authors: Valdez-Sinon AN (1), Schmiech KV (2), Moragianni VA (2)

Affiliations: (1) Department of Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Baltimore, MD, USA; (2) Division of Reproductive Endocrinology and Infertility, Department of Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Background

Polycystic ovarian syndrome (PCOS) has a prevalence of 10-13% and is characterized by insulin resistance, with many patients experiencing infertility secondary to anovulation. When comparing ovulation induction (OI) agents in PCOS, there is an established superiority of letrozole over clomid, with improved ovulation and increased live birth rates. Clomid has been evaluated alone or in combination with metformin for OI. However, the impact of metformin on fertility outcomes has not been studied when combined with letrozole. Given the large number of PCOS patients seeking fertility care, it is important to have evidence for pharmacologic regimens that maximize fertility outcomes.

Objective

To determine if use of letrozole combined with metformin for OI in patients with PCOS is associated with improved fertility outcomes compared to use of letrozole alone.

Materials and Methods

This study is a retrospective cohort chart review of patients with PCOS who presented for care at an academic fertility center between 2020-2024 and underwent letrozole OI. Of the 214 charts identified by EPIC query, 67 patients had confirmed PCOS based upon Rotterdam criteria. Patients with endometriosis, uterine cavity abnormalities, AMH <1, and use of metformin for >1-year were excluded. Data gathered during chart review included demographics, metformin use, number of cycles of OI with letrozole for either timed intercourse (TIC) or intrauterine insemination (IUI). For each cycle, information was collected on number of follicles >14mm and cycle outcomes. Data was compared between patients who used metformin during OI and those who did not. Categorical variables were compared and analyzed with the chi-squared test. A sub analysis of cycle outcomes was performed with stratification of patients based upon having a BMI of <30 or $\geq$30.

Results

Information was gathered from 203 cycles (105 TIC and 98 IUI). Clinical pregnancy was achieved in 18.9% (28/148) of OI cycles with letrozole alone. Use of metformin was associated with a significantly higher clinical pregnancy rate of 32.7% (18/55, $p < 0.05$). The outcomes of clinical pregnancies were not different with metformin use. Live birth rate for letrozole alone was 10.8% of total cycles compared to 18.2% of total cycles with concurrent use of metformin. Follicle growth and number of cycles to first clinical pregnancy were unchanged with use of metformin. Upon stratification of patients by BMI, the significant increase in clinical pregnancy

rate with metformin use was only noted in patients with BMI <30 (16.8% vs 34.4%, p<0.05). Metformin use in patients with BMI ≥30 was associated with an increase in live birth rate (26.1% versus 13.2%)- but was not statistically significant.

Conclusions

In this study of patients with PCOS undergoing OI with letrozole, concurrent use of metformin was associated with a significant increase in clinical pregnancy rates. When stratified by BMI, the increased clinical pregnancy rate was only significant in patients with a BMI <30. While there was a trend towards increased live birth rates with metformin use, this was not statistically significant. Larger studies are warranted to further elucidate benefits of metformin use with letrozole during OI.

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