

*Research Article***A aromatase enzyme inhibitor versus gonadotropin for induction of ovulation in patients with polycystic ovary syndrome resistant to clomiphene citrate a randomized controlled trial****Hossam Eldin Sh. Abd-Allah, Haitham A. Bahaa El-Din****Alaa G. Abd El-Azeem and Osama A. Abd El Aziz**

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**Abstract**

**Introduction:** Clomiphene citrate (CC) is the first drug used to induce ovulation in patients with polycystic ovary syndrome (PCOS). Although 70–80% of such women ovulate when treated with CC, only 40% become pregnant (van Wely et al., 2005). Women who do not ovulate with increasing doses of CC are CC-resistant (Amin et al., 2003). So a different modality of treatment for such patients was required. **Aim of the work:** The aim of the present work is to compare the effects of letrozole versus gonadotropin for induction of ovulation in patients with polycystic ovary syndrome resistant to clomiphene citrate. **Patients and Methods:** The present study is a randomized clinical trial. The study was conducted at infertility clinic of Minia general hospital, Minia, Egypt; throughout the duration of 18 months from January 2017 to June 2018. **Results:** Letrozole groups showed a statistically significant higher incidence of ovulation compared to gonadotropins group yet no difference in pregnancy rate was detected between the two groups. **Discussion:** Most studies comparing letrozole and gonadotropins in women with CC-resistant PCOS were either retrospective or in the context of intra uterine insemination presenting the need for studying letrozole versus gonadotropins in the context of induction of ovulation and timed intercourse. **Summary:** Letrozole is a cost effective modality for induction of ovulation in patients with PCOS resistant to CC.

**Keywords:** Clomiphene citrate, Aromatase enzyme, polycystic ovary syndrome**Introduction**

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, with an incidence of 5–10% (Erol, Karaagac, & Kounis, 2014). PCOS manifestations range from mild menstrual irregularities to severe endocrine and reproductive dysfunction.

Clomiphene citrate (CC) is the first drug used to induce ovulation in patients with PCOS. Although 70–80% of such women ovulate when treated with CC, only 40% become pregnant (van Wely et al., 2005). Women who do not ovulate with increasing doses of CC are CC-resistant (Amin et al., 2003). So a different modality of treatment for such patients was required

**Aim of the work**

The aim of the present work is to compare the effects of letrozole versus gonadotropin for

induction of ovulation in patients with polycystic ovary syndrome resistant to CC

**Patients and Methods**

150 eligible patients were randomized into two groups the first group received letrozole 2.5 tablets twice daily for five days starting at third day of spontaneous menstrual cycle or progesterone induced withdrawal bleeding the second group received gonadotropin hormones in the form of highly purified FSH with a starting dose of 75-150 IU according to BMI, age and previous exposure given intramuscular in day three of spontaneous menstrual cycle or progesterone induced withdrawal bleeding, another TVUS was performed on day seven and repeated dose adjustment of gonadotropins in the form of 75-150 (IU) – maximum dose of 300IU/cycle – may be required according to the ovarian response

Both groups underwent transvaginal ultrasound

scan (TVUS) /48 to assess ovarian maturation with a leading follicle >17 mm, when ovarian maturation was confirmed human chorionic gonadotropin (HCG) 10,000IU was given for triggering of ovulation.

Quantitative  $\beta$ -human chorionic gonadotrophin ( $\beta$ -hcg) was measured on day 14 after triggering and patient considered pregnant if serum level is >50 mIU/ml.

In the presence of a positive  $\beta$ -hcg test, an intrauterine gestational sac was confirmed by ultrasound at 5 weeks of gestation.

### Results

There was a non-significance difference ( $P>0.05$ ) between the two groups as regards Age, BMI, Duration of infertility, Type of infertility and Previous ovarian drilling.

The results of this study showed a statistically significant higher incidence of confirmed ovulation in letrozole group compared to gonadotropin group. For letrozole group incidence of confirmed ovulation was 82.67% compared to 66.67% for gonadotropin group with P value of 0.024.

The average number of cycles needed to achieve ovulation was lower in letrozole group (1.95) compared to (2.98) for gonadotropin group with a P value less than (0.001).

The incidence of confirmed pregnancy was higher in letrozole group 18.67% compared to 13.34% for gonadotropin group however the difference was statistically non-significant P value 0.37.

The number of cycles needed to achieve pregnancy was lower in letrozole group 2.41 compared to 3.25 for gonadotropin group with a significant P value of 0.018.

The cost of ovulation induction medication per cycle was significantly lower in letrozole group 185LE/cycle compared to 410LE/cycle for gonadotropin group.

### Discussion

Most studies comparing letrozole and gonadotropins in women with PCOS resistant to cc were either retrospective (Dahan, 2007) or

investigated women undergoing intra-uterine insemination (IUI) (Ganesh et al., 2009)

Ganesh et al., published a RCT study in 2009 comparing the effect of letrozole with continuous gonadotropins and clomiphene-gonadotropin combination for ovulation induction in 1387 PCOS women after clomiphene citrate failure, this study showed that the PR in letrozole group 23.39 was observed to be slightly higher, though not statistically significant, as compared to gonadotropin group (PR= 17.92%).

Ganesh et al., study is similar to our study in the type of infertility and the dose of letrozole used and reported a similar result as our study in PR however Ganesh et al., study was different in gonadotropins form and dose also it was conducted in the context of IUI and added a third group treated with CC and gonadotropin but showed lower PR (14.35%).

### Conclusion

The use of letrozole for induction of ovulation in patients with PCOS resistant to CC is showed higher incidence of ovulation and no difference in pregnancy rate compared to gonadotropins. Letrozole is a cost-effective modality for induction of ovulation in patients with PCOS resistant to CC.

### Recommendations

- The need for prolonged randomized controlled trial (RCT) to compare the effect of letrozole versus gonadotropins considering take home babies as the index for successful treatment.
- More RCT comparing letrozole versus different forms and induction protocols of gonadotropins in the context of ovulation induction and timed intercourse and not in the context of intra uterine insemination.

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