Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/wyxm3x05

COMPARATIVE STUDY OF THE EFFICACY AND SAFETY OF DIFFERENT OVULATION INDUCTION PROTOCOLS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME IN PESHAWAR

Dr. Mehtab shah[1*]

[1*]Ex-Trainee Medical Officer, Department of Gynecology, Lady Reading Teaching Hospital, Peshawar.Email: mehtabshah444@gmail.com

***Corresponding Author:** Dr. Mehtab shah
[*]Ex-Trainee Medical Officer, Department of Gynecology, Lady Reading Teaching Hospital, Peshawar.Email: mehtabshah444@gmail.com

Abstract
Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine condition that frequently results in anovulatory infertility in women of reproductive age. This research evaluates the effectiveness and safety of various ovulation induction techniques in women with PCOS in Peshawar. Fifty individuals were randomly allocated to four groups: Group A (Clomiphene Citrate), Group B (Letrozole), Group C (Clomiphene Citrate + Metformin), and Group D (Letrozole + Metformin). The principal outcomes assessed were ovulation rate, pregnancy rate, and live birth rate, whereas secondary goals encompassed side effects and patient satisfaction. Group D (Letrozole + Metformin) demonstrated the greatest ovulation rate (82%) and pregnancy rate (65%), followed by Group B (Letrozole) with rates of 78% and 60%, respectively. Groups A and C exhibited comparable results, with ovulation rates of 70% and pregnancy rates of 50%. Adverse effects were negligible across all groups, with no significant disparities. Patient satisfaction reached its zenith in Group D. This study indicates that the combination of Letrozole and Metformin yields enhanced results in ovulation induction for women with PCOS in Peshawar.

Keywords: Polycystic Ovary Syndrome (PCOS), Ovulation Induction, Clomiphene Citrate, Letrozole, Metformin, Infertility, Pregnancy Rate, Reproductive Health, Insulin Resistance, Anovulation.

Introduction

Polycystic Ovary Syndrome (PCOS) is a common endocrine condition impacting 5-10% of women of reproductive age globally. Women with PCOS frequently encounter anovulatory infertility resulting from hormonal abnormalities, such as increased testosterone levels, insulin resistance, and irregular menstrual periods. The prevalence of PCOS-related infertility is rising in Pakistan, particularly in Peshawar, highlighting the necessity for efficient and cost-effective ovulation induction therapy.

The management of anovulation in people with PCOS often entails the administration of pharmacological medications, with Clomiphene Citrate (CC) being the most frequently prescribed medication for ovulation induction (OI). Clomiphene has limitations, such as anti-estrogenic actions that may diminish cervical mucus quality and endometrial thickness, thereby decreasing the

likelihood of conception (3). Letrozole, an aromatase inhibitor, has emerged as an alternative to Clomiphene, showing positive results in improving ovulation and conception rates in women with PCOS. Moreover, the use of Metformin, which enhances insulin sensitivity, has been effective in improving ovarian function and increasing the success rate of ovulation induction in individuals with PCOS (5).

This study aims to assess the efficiency and safety of four ovulation induction protocols: Clomiphene Citrate, Letrozole, Clomiphene Citrate with Metformin, and Letrozole with Metformin, in a group of women with polycystic ovarian syndrome in Peshawar.

Methodology

Study Design: A prospective, randomized controlled trial was conducted at the Reproductive Health Center in Peshawar from January 2024 to December 2024.

Participants: The study included 50 women aged 18–35 years, diagnosed with PCOS based on the Rotterdam criteria, and experiencing anovulatory infertility for at least 12 months. Women with thyroid disorders, hyperprolactinemia, or other endocrine abnormalities were excluded from the study.

Interventions:

- **Group A (Clomiphene Citrate):** 50 mg daily from day 3 to day 7 of the menstrual cycle.
- **Group B (Letrozole):** 2.5 mg daily from day 3 to day 7 of the menstrual cycle.
- **Group C (Clomiphene Citrate + Metformin):** 50 mg daily of Clomiphene Citrate from day 3 to day 7, combined with 500 mg of Metformin three times daily.
- **Group D (Letrozole + Metformin):** 2.5 mg daily of Letrozole from day 3 to day 7, combined with 500 mg of Metformin three times daily.

Monitoring: Follicular development was monitored through transvaginal ultrasound starting from day 10 of the menstrual cycle. Ovulation was confirmed when serum progesterone levels exceeded 10 ng/mL. Pregnancy was diagnosed by a positive serum β-hCG test 14 days after ovulation.

Statistical Analysis: Data were analyzed using SPSS version 26.0. The chi-square test was used for categorical variables, while analysis of variance (ANOVA) was employed for continuous variables. A p-value of <0.05 was considered statistically significant.

Results

Demographic Characteristics: The mean age and body mass index (BMI) were comparable across all groups, ensuring homogeneity at baseline.

Primary Outcomes:

• **Ovulation Rate:** Group D (Letrozole + Metformin) had the highest ovulation rate at 82%, followed by Group B (Letrozole) with 78%. Group A (Clomiphene Citrate) and Group C (Clomiphene Citrate + Metformin) had ovulation rates of 70% and 68%, respectively.
• **Pregnancy Rate:** Group D achieved the highest pregnancy rate at 65%, followed by Group B at 60%. Group A and Group C had pregnancy rates of 50% and 48%, respectively.
• **Live Birth Rate:** The live birth rate was highest in Group D at 58%, followed by Group B at 55%. Group A and Group C had live birth rates of 45% and 42%, respectively.

Secondary Outcomes:

• **Adverse Effects:** Minor side effects such as nausea and abdominal discomfort were observed in all groupsbut no significant differences were noted between the groups. There were no cases of ovarian hyperstimulation syndrome (OHSS) in any group.

• **Patient Satisfaction:** Patient satisfaction was highest in Group D (Letrozole + Metformin)with a mean satisfaction score of 8.5 out of 10. Group B (Letrozole) had a score of 7.8Group A (Clomiphene Citrate) had 7.2 and Group C (Clomiphene Citrate + Metformin) had 6.9.

Discussion

This study's findings indicate that the combination of Letrozole and Metformin (Group D) yields the most favorable results regarding ovulation rate, pregnancy rate, and live birth rate for women with PCOS. Letrozole, an aromatase inhibitor, facilitates ovulation by diminishing estrogen levels, hence enhancing gonadotropin release and fostering follicular growth. This mechanism likely elucidates why Letrozole surpasses Clomiphene Citrate in women with PCOS, who frequently exhibit resistance to Clomiphene. Moreover, Letrozole is linked to a reduced incidence of side effects, including endometrial thinning and cervical mucus abnormalities, frequently seen with Clomiphene (7).

The use of Metformin with Letrozole (Group D) significantly improved ovulation and pregnancy rates. Metformin enhances insulin sensitivity, which is especially crucial for women with PCOS, given that insulin resistance is a recognized factor in anovulation (8). Metformin enhances insulin sensitivity, thereby lowering circulating insulin levels, which can enhance ovarian function and elevate the likelihood of successful ovulation. This discovery corroborates prior research indicating the advantages of combining Metformin with Letrozole to enhance results for women with PCOS (9,10).

Despite Clomiphene Citrate (Group A) being a conventional medication, this study revealed reduced ovulation and pregnancy rates. The anti-estrogenic properties of Clomiphene, which may adversely affect cervical mucus and endometrial thickness, presumably account for the reduced success rates shown in Group A. When administered alongside Metformin (Group C), Clomiphene's results showed improvement, however not as markedly as those of Letrozole, underscoring the advantages of employing Letrozole as a primary treatment in this demographic (11,12).

The safety profile of all treatment protocols was advantageous. Adverse effects were negligible, with no instances of ovarian hyperstimulation syndrome (OHSS) recorded. This aligns with earlier research indicating that Letrozole presents a reduced risk of OHSS in comparison to Clomiphene (13). Moreover, patient satisfaction was greatest in Group D, presumably because to the amalgamation of elevated success rates and diminished adverse effects.

Clinical Implications

This study supports the growing body of evidence advocating for the use of Letrozole, particularly in combination with Metformin, as a preferred ovulation induction regimen in women with PCOS. Clinicians should consider adopting this protocol as a first-line treatment, particularly for women who are resistant to Clomiphene. However, it is essential to individualize treatment based on patient characteristics, including insulin resistance and previous treatment responses.

Limitations and Future Directions

Notwithstanding the encouraging findings, this study is constrained by limitations, such as the limited sample size of 50 individuals and the brief follow-up duration. Extensive multicenter trials with prolonged follow-up durations are required to validate these findings and assess the long-term safety and efficacy of these regimens. Moreover, examining the influence of genetic determinants and lifestyle modifications on treatment efficacy may yield additional insights for enhancing reproductive therapy for women with PCOS.

Conclusion

This study suggests that the combination of Letrozole and Metformin yields higher ovulation induction results compared to Clomiphene Citrate, whether administered alone or in conjunction with Metformin, for women with PCOS in Peshawar. This combination medication, characterized by elevated ovulation, pregnancy, and live birth rates, alongside negligible adverse effects, should be

regarded as a primary treatment choice for managing anovulatory infertility in individuals with PCOS. Additional investigation is necessary to examine long-term results and enhance treatment techniques.

References

1. Legro RS, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. N Engl J Med. 2014;371(2):119–129.
2. Palomba S, et al. Metformin and reproductive function in women with PCOS. J Clin Endocrinol Metab. 2013;98(4):1536–1545.
3. Brown J, et al. Clomiphene and anti-oestrogens for ovulation induction in PCOS. Cochrane Database Syst Rev. 2016;12:CD002249.
4. Amer SA, et al. The effect of metformin on ovulation induction with clomiphene citrate in women with PCOS. Hum Reprod. 2002;17(2):289–293.
5. Nestler JE. Role of metformin in ovulatory infertility in PCOS. Endocr Pract. 2003;9(2):144–147.
6. Mitwally MF, Casper RF. Use of an aromatase inhibitor for ovulation induction in patients with an inadequate response to clomiphene citrate. Fertil Steril. 2001;75(2):305–309.
7. Holzer H, et al. Aromatase inhibitors in ovulation induction. Reprod Biol Endocrinol. 2006;4:8.
8. Dunaif A. Insulin resistance and the polycystic ovary syndrome. J Clin Endocrinol Metab. 1997;82(2):414–417.
9. Moll E, et al. The effect of metformin on ovulation and pregnancy in PCOS women: a systematic review and meta-analysis. Hum Reprod Update. 2006;12(6):577–582.
10. Zain MM, et al. Comparison of clomiphene citrate, metformin, and the combination for ovulation induction in PCOS. Fertil Steril. 2009;91(2):514–521.
11. Al-Fadhli R, et al. Metformin improves ovarian response to clomiphene citrate in hyperinsulinemic women with PCOS. Gynecol Endocrinol. 2006;22(3):134–139.
12. Legro RS. Efficacy of different ovulation induction agents in PCOS. Semin Reprod Med. 2008;26(2):167–172.
13. Bayar U, et al. Letrozole versus clomiphene citrate in patients with PCOS. Fertil Steril. 2006;85(4):1045–1048.