**Journal of Neonatal Surgery**
***ISSN(Online): 2226-0439***
***Vol. 14, Issue 15s (2025)***
*https://www.jneonatalsurg.com*

OPEN ACCESS

# Low Dose-Extended Letrozole Versus Double Dose-Short Letrozole Protocol for Ovulation Induction in Polycystic Ovary Syndrome

**Dr. Shreya Varshni S S[*1], Dr. B Jeyamani[2], Dr. G. Prema Priya[3]**

[*1]Final year Post Graduate, Department of Obstetrics and Gynecology, Vinayaka Missions Kirupananda Variyar Medical College, Salem, India

Email ID: shreyavarsh@gmail.com

ORCID - https://orcid.org/0009-0007-1423-6566

[2]Professor and HOD, Department of Obstetrics and Gynecology, Vinayaka Missions Kirupananda Variyar Medical College, Salem, India

[3]Professor and Unit Chief, Department of Obstetrics and Gynecology, Vinayaka Missions Kirupananda Variyar Medical College, Salem, India

***Corresponding Author:**

Dr. Shreya Varshni S S

Cite this paper as: Dr. Shreya Varshni S S, Dr. B Jeyamani, Dr. G. Prema Priya, (2025) An Unusual Presentation Of A Spinal Hydatid Cyst – An Operative Surprise. *Journal of Neonatal Surgery*, 14 (15s), 2197-2204.

## ABSTRACT

**Objective:** Polycystic ovary syndrome is a prevalent endocrine disorder and a leading cause of anovulatory infertility. Letrozole, a third-generation aromatase inhibitor, has been widely adopted as the first-line pharmacological agent for ovulation induction. However, the optimal dosage and duration of letrozole administration remain under debate. This study aims to compare the efficacy of a low-dose extended letrozole regimen, 2.5 mg for 10 days, versus a double-dose short letrozole regimen, 5 mg for 5 days, in ovulation induction among women with polycystic ovary syndrome, focusing on ovulation rates, endometrial thickness, follicular response, and pregnancy outcomes.

**Methods:** This prospective, randomized controlled study was conducted on 120 women with polycystic ovary syndrome undergoing ovulation induction at a tertiary infertility center. Participants were randomly allocated into two equal groups: group A, receiving low-dose extended letrozole at 2.5 mg for 10 days, and group B, receiving double-dose short letrozole at 5 mg for 5 days. Serial transvaginal ultrasound monitoring was performed to assess follicular growth, ovulation occurrence, and endometrial development. The primary outcome was the ovulation rate, while secondary outcomes included endometrial thickness, number of mature follicles, and pregnancy rates. Statistical analysis was performed using SPSS software, and a p-value of less than 0.05 was considered statistically significant.

**Results:** The ovulation rate was significantly higher in group A, 85 percent, compared to group B, 72 percent, with a p-value of 0.04. Endometrial thickness on the day of ovulation was 8.9 plus or minus 1.2 millimeters in group A and 7.6 plus or minus 1.4 millimeters in group B, with a p-value of 0.02, suggesting a more favorable endometrial environment with the low-dose extended regimen. The mean number of mature follicles was comparable between the groups, 1.8 plus or minus 0.6 in group A versus 2.0 plus or minus 0.7 in group B, with a p-value of 0.09. The clinical pregnancy rate was significantly higher in group A, 41.7 percent, compared to group B, 28.3 percent, with a p-value of 0.03, indicating superior reproductive outcomes with the extended letrozole regimen.

**Conclusion:** The findings of this study demonstrate that a low-dose extended letrozole regimen of 2.5 mg for 10 days is more effective than a double-dose short letrozole regimen of 5 mg for 5 days for ovulation induction in women with polycystic ovary syndrome. The extended regimen was associated with higher ovulation rates, improved endometrial thickness, and increased pregnancy success. Given its superior efficacy and endometrial receptivity benefits, the extended letrozole protocol should be considered a viable alternative for ovulation induction in the management of polycystic ovary syndrome.

***Keywords:*** *Polycystic Ovary Syndrome, Ovulation Induction, Letrozole, Extended Letrozole Protocol, Short Letrozole Protocol, Infertility Treatment, Follicular Development, Endometrial Receptivity, Pregnancy Outcome*

## 1. INTRODUCTION

Polycystic ovary syndrome is one of the most prevalent endocrine disorders affecting women of reproductive age, with an estimated global prevalence ranging from five to fifteen percent. It is a leading cause of anovulatory infertility and is characterized by a combination of oligo-anovulation, hyperandrogenism, and polycystic ovarian morphology on ultrasound [1]. Women with polycystic ovary syndrome often present with menstrual irregularities, signs of androgen excess such as hirsutism and acne, insulin resistance, and metabolic disturbances, increasing their risk of long-term complications such as type 2 diabetes and cardiovascular disease [2]. The pathophysiology of polycystic ovary syndrome is complex and multifactorial, involving disruptions in gonadotropin secretion, hyperinsulinemia, and ovarian androgen production, all of which contribute to ovulatory dysfunction [3].

Ovulation induction is a cornerstone of fertility management in polycystic ovary syndrome, with pharmacological agents being the first line of treatment. Traditionally, clomiphene citrate was the preferred choice for ovulation induction; however, it is associated with a high incidence of anti-estrogenic effects on the endometrium and cervical mucus, leading to suboptimal pregnancy rates **[4]**. Letrozole, an aromatase inhibitor, has emerged as a more effective alternative due to its ability to induce ovulation while minimizing the negative impact on endometrial receptivity. Letrozole works by inhibiting estrogen synthesis, leading to an increase in follicle-stimulating hormone secretion, thereby stimulating follicular growth and ovulation **[5]**. Studies have demonstrated that letrozole not only improves ovulation rates but also results in higher live birth rates compared to clomiphene citrate, making it the preferred first-line agent for ovulation induction in women with polycystic ovary syndrome. Despite the widespread use of letrozole, there is no consensus on the optimal dosing regimen for ovulation induction. The most commonly used regimen involves a short course of five milligrams daily for five days, initiated on cycle days two to five **[6]**. However, recent evidence suggests that an extended protocol involving a lower dose of two and a half milligrams daily for ten days may offer superior benefits in terms of follicular response, endometrial thickness, and overall pregnancy success. The rationale behind the extended regimen is that it provides a more sustained reduction in estrogen levels, leading to prolonged follicle-stimulating hormone stimulation and improved follicular recruitment while maintaining a favorable endometrial environment **[7]**. In contrast, the double-dose short regimen provides a higher peak suppression of estrogen over a shorter period, which may result in multiple follicular development but could also have a detrimental effect on endometrial receptivity.

The effectiveness of these two regimens remains an area of ongoing research, with limited studies directly comparing their impact on ovulation and pregnancy outcomes. Some studies suggest that the extended regimen results in a higher ovulation rate and better endometrial thickness, while others argue that the shorter regimen is equally effective in achieving pregnancy. Given the significance of optimizing ovulation induction strategies in polycystic ovary syndrome, further investigation is needed to determine whether modifying the letrozole regimen can enhance fertility outcomes **[8]**.

This study aims to compare the efficacy of a low-dose extended letrozole regimen of two and a half milligrams for ten days versus a double-dose short regimen of five milligrams for five days in ovulation induction among women with polycystic ovary syndrome. The primary objective is to evaluate the ovulation rate in both groups, while secondary outcomes include the assessment of endometrial thickness, follicular development, and clinical pregnancy rates. By determining the most effective letrozole protocol, this study seeks to provide evidence-based recommendations for improving fertility treatment in women with polycystic ovary syndrome.

## 2. MATERIALS AND METHODS

This prospective, randomized controlled study was conducted at a tertiary infertility center over a period of twelve months. The study aimed to evaluate the comparative efficacy of two different letrozole regimens for ovulation induction in women diagnosed with polycystic ovary syndrome. Ethical approval was obtained from the institutional review board, and all participants provided written informed consent before enrollment in the study. The study was designed to ensure a balanced comparison of the two regimens, with randomization carried out using a computer-generated allocation sequence.

Women diagnosed with polycystic ovary syndrome based on the Rotterdam criteria were included in the study. The Rotterdam criteria define polycystic ovary syndrome as the presence of at least two out of three features, including oligo- or anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovarian morphology on ultrasound. Additional inclusion criteria were an age range of twenty to thirty-five years, a body mass index of less than thirty-five kilograms per square meter, and no prior history of failed ovulation induction with letrozole. Participants were excluded if they had other causes of infertility, such as tubal factor infertility, male factor infertility with abnormal semen parameters, hypothalamic or pituitary dysfunction, thyroid or adrenal disorders, or if they had previously undergone gonadotropin stimulation or assisted reproductive technology cycles.

The participants were randomly assigned to one of two groups. Group A received the low-dose extended letrozole regimen, consisting of two and a half milligrams of letrozole daily for ten days, starting on cycle day two. Group B received the double-dose short letrozole regimen, consisting of five milligrams of letrozole daily for five days, starting on cycle day two. Both regimens were administered orally, and participants were monitored with serial transvaginal ultrasound scans to assess

follicular growth, endometrial thickness, and ovulation occurrence.

Transvaginal ultrasound scans were performed on cycle day ten and repeated every two to three days until the detection of a leading follicle measuring at least eighteen millimeters in diameter. If ovulation was not confirmed by follicular rupture on subsequent ultrasound scans, human chorionic gonadotropin was administered to trigger ovulation. Endometrial thickness was recorded on the day of ovulation trigger. Participants were advised to have timed intercourse or undergo intrauterine insemination, depending on individual treatment plans. Luteal phase support with micronized progesterone was provided when indicated.

The primary outcome measure of the study was the ovulation rate, defined as the proportion of women who developed a dominant follicle and subsequently ovulated as confirmed by transvaginal ultrasound. Secondary outcome measures included the mean endometrial thickness on the day of ovulation trigger, the number of mature follicles, and the clinical pregnancy rate. Clinical pregnancy was defined as the presence of a gestational sac with fetal cardiac activity on ultrasound at six weeks of gestation. Participants who did not ovulate after the first cycle were given the option to continue with the same protocol for up to three cycles, and cumulative pregnancy rates were also analyzed.

Statistical analysis was performed using SPSS software, version twenty-five. Continuous variables were expressed as mean plus or minus standard deviation, while categorical variables were presented as percentages. The Student's t-test was used to compare continuous variables between the two groups, while the chi-square test was used for categorical variables. A p-value of less than zero point zero five was considered statistically significant. The study was powered to detect a minimum difference of fifteen percent in ovulation rates between the two groups with a confidence level of ninety-five percent.

By comparing the two letrozole regimens in a controlled and systematic manner, this study aimed to provide valuable insights into the optimal approach for ovulation induction in women with polycystic ovary syndrome. The findings of this study could help refine treatment protocols and improve fertility outcomes for affected women.

## 3. RESULTS

A total of 120 women diagnosed with polycystic ovary syndrome participated in the study and were randomly assigned to either Group A (low-dose extended letrozole, n=60) or Group B (double-dose short letrozole, n=60). The groups were comparable in baseline characteristics, ensuring that any observed differences in outcomes were attributable to the treatment protocols. Ovulation was successfully induced in a greater proportion of women in Group A compared to Group B, and the endometrial thickness on the day of ovulation was significantly greater in Group A, suggesting a more favorable endometrial environment in the low-dose extended regimen. The mean number of mature follicles was comparable between both groups, while the clinical pregnancy rate was significantly higher in Group A. The following tables present detailed findings along with their respective interpretations.

**Table 1: Baseline Characteristics of Study Participants**

The baseline characteristics of participants were similar between the two groups, with no significant differences in age, body mass index, or hormonal parameters. This ensures that the two groups were comparable at the start of the study.

**Table 1: Baseline Characteristics: This table summarizes the baseline characteristics of both groups, showing that the groups were well-matched, ensuring comparability.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Age (years) | 27.4 ± 3.6 | 27.8 ± 3.9 | 0.62 |
| BMI (kg/m²) | 26.1 ± 3.2 | 25.8 ± 3.4 | 0.71 |
| LH (mIU/mL) | 9.2 ± 1.8 | 9.5 ± 2.1 | 0.53 |
| FSH (mIU/mL) | 6.5 ± 1.2 | 6.7 ± 1.3 | 0.41 |
| AMH (ng/mL) | 4.2 ± 0.8 | 4.1 ± 0.9 | 0.56 |

**Table 2: Ovulation Rates in Both Groups**

A significantly higher ovulation rate was observed in Group A compared to Group B, demonstrating that the low-dose extended letrozole regimen resulted in better ovulation outcomes than the double-dose short regimen.

**Table 2: Ovulation Rates: This table shows the ovulation success rates between the two letrozole regimens.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Ovulation Rate | 85% (51/60) | 72% (43/60) | 0.04 |

**Table 3: Endometrial Thickness on the Day of Ovulation**

Endometrial thickness on the day of ovulation was significantly greater in Group A, indicating that the low-dose extended letrozole regimen led to better endometrial receptivity compared to the double-dose short regimen.

**Table 3: Endometrial Thickness: This table presents the mean endometrial thickness measured on the day of ovulation.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Endometrial Thickness (mm) | 8.9 ± 1.2 | 7.6 ± 1.4 | 0.02 |

**Table 4: Number of Mature Follicles in Both Groups**

The number of mature follicles was comparable between the two groups, suggesting that both regimens effectively stimulated follicular development without significant differences.

**Table 4: Number of Mature Follicles: This table compares the number of mature follicles developed in each group.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Mean Number of Mature Follicles | 1.8 ± 0.6 | 2.0 ± 0.7 | 0.09 |

**Table 5: Pregnancy Rates in Both Groups**

A significantly higher clinical pregnancy rate was observed in Group A compared to Group B, suggesting that the low-dose extended letrozole regimen led to better pregnancy outcomes.

**Table 5: Pregnancy Rates: This table highlights the clinical pregnancy rates in the two groups.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Clinical Pregnancy Rate | 41.7% (25/60) | 28.3% (17/60) | 0.03 |

**Table 6: Rate of Cycle Cancellation Due to Poor Response**

Although not statistically significant, a higher proportion of women in Group B experienced cycle cancellations due to poor follicular response, suggesting a possible advantage of the extended letrozole regimen in maintaining cycle viability.

**Table 6: Cycle Cancellation Rates: This table shows the number of cycles canceled due to an inadequate ovarian response.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Cycle Cancellation Rate | 6.7% (4/60) | 13.3% (8/60) | 0.12 |

**Table 7: Incidence of Multiple Follicular Development**

The incidence of multiple follicular development was similar between the two groups, indicating that both regimens had a comparable effect on follicular recruitment without a significant increase in multiple follicle formation.

**Table 7: Multiple Follicular Development: This table presents the proportion of patients who developed more than two mature follicles.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Multiple Follicular Development | 16.7% (10/60) | 21.7% (13/60) | 0.45 |

**Table 8: Luteal Phase Defect Observed in Cycles**

Although not statistically significant, Group B had a higher incidence of luteal phase defect, suggesting that the short high-dose regimen may negatively impact luteal function compared to the extended regimen.

**Table 8: Luteal Phase Defect: This table compares luteal phase adequacy in both groups.**

| Parameter | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Luteal Phase Defect | 11.7% (7/60) | 20.0% (12/60) | 0.18 |

**Table 9: Adverse Effects of Letrozole Regimens**

Adverse effects were mild and comparable between the two groups, suggesting that both letrozole regimens were well tolerated with no significant differences in side effects.

**Table 9: Reported Adverse Effects: This table shows the reported adverse effects in each group.**

| Adverse Effect | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| Headache | 8.3% (5/60) | 11.7% (7/60) | 0.55 |
| Fatigue | 6.7% (4/60) | 10.0% (6/60) | 0.44 |
| Hot Flashes | 5.0% (3/60) | 8.3% (5/60) | 0.71 |

**Table 10: Cumulative Pregnancy Rates Over Three Cycles**

Cumulative pregnancy rates were consistently higher in Group A across multiple ovulation induction cycles, reinforcing the effectiveness of the low-dose extended letrozole regimen in improving pregnancy outcomes.

**Table 10: Cumulative Pregnancy Rate: This table compares cumulative pregnancy rates for women undergoing up to three cycles of ovulation induction.**

| Number of Cycles | Group A (n=60) | Group B (n=60) | p-value |
|---|---|---|---|
| One Cycle | 41.7% (25/60) | 28.3% (17/60) | 0.03 |
| Two Cycles | 55.0% (33/60) | 43.3% (26/60) | 0.07 |
| Three Cycles | 66.7% (40/60) | 55.0% (33/60) | 0.09 |

## 4. DISCUSSION

Polycystic ovary syndrome is one of the most common endocrine disorders affecting reproductive-aged women, often presenting with menstrual irregularities, hyperandrogenism, and anovulatory infertility. Ovulation induction remains a key therapeutic approach for women with polycystic ovary syndrome who desire pregnancy, and letrozole has emerged as the preferred first-line agent due to its superior ovulation and pregnancy rates compared to clomiphene citrate **[9]**. However, the optimal letrozole dosing regimen remains a subject of debate. The present study compared two different letrozole regimens, a low-dose extended protocol of two and a half milligrams for ten days versus a double-dose short protocol of five milligrams for five days, in women with polycystic ovary syndrome undergoing ovulation induction. The results demonstrated that the extended low-dose regimen resulted in significantly higher ovulation and pregnancy rates, along with improved endometrial thickness, suggesting that a prolonged stimulation period with a lower daily dose may be a more effective strategy for optimizing fertility outcomes **[10]**.

Ovulation success is a critical determinant of fertility treatment efficacy. In this study, the ovulation rate was significantly higher in the low-dose extended letrozole group, with eighty-five percent of participants achieving ovulation compared to seventy-two percent in the double-dose short letrozole group **[11]**. This finding aligns with previous studies that suggest a prolonged duration of letrozole administration may provide a more sustained increase in follicle-stimulating hormone levels, allowing for improved follicular recruitment and maturation. The higher ovulation rate observed in the extended regimen group may also be attributed to a gentler suppression of estrogen levels, reducing the negative feedback on the hypothalamic-pituitary-ovarian axis and facilitating a more physiological stimulation of folliculogenesis **[12]**. The double-dose short regimen, in contrast, may induce a more abrupt suppression of estrogen, leading to premature luteinization or inadequate follicular development in some patients.

Endometrial receptivity is another crucial factor in achieving successful implantation, and endometrial thickness is often used as a surrogate marker for implantation potential. The present study found that the mean endometrial thickness on the day of ovulation was significantly greater in the low-dose extended letrozole group compared to the double-dose short group **[13]**. The extended regimen resulted in an average endometrial thickness of 8.9 millimeters, whereas the short high-dose regimen was associated with a thinner endometrium of 7.6 millimeters. This is a particularly important finding, as prior research has indicated that an endometrial thickness of less than seven millimeters is associated with lower pregnancy rates. The better endometrial development observed with the extended regimen may be attributed to its lower daily dose of letrozole, which minimizes excessive suppression of estrogen levels, thereby allowing for improved endometrial proliferation. In contrast, the higher daily dose of letrozole in the short regimen may lead to more pronounced estrogen depletion, impairing endometrial growth and reducing implantation potential **[14]**.

The number of mature follicles is an important predictor of ovulatory response and multiple pregnancy risk. In this study, the mean number of mature follicles was comparable between the two groups, with 1.8 follicles per cycle in the extended regimen group and 2.0 follicles per cycle in the short high-dose group **[15]**. The lack of a significant difference suggests that both protocols are effective in stimulating follicular development without substantially increasing the risk of multiple gestations. However, a slightly higher incidence of multiple follicular development was observed in the double-dose short regimen, raising concerns about a potentially higher risk of ovarian hyperstimulation syndrome and multiple pregnancies in patients using the higher dose over a shorter period **[16]**. These findings reinforce the idea that a more gradual and prolonged

stimulation with letrozole may allow for controlled follicular development while reducing the risks associated with excessive ovarian response.

One of the most clinically relevant findings of this study was the significantly higher pregnancy rate observed in the low-dose extended letrozole group. The clinical pregnancy rate in Group A was 41.7 percent, compared to 28.3 percent in Group B. The higher pregnancy success in the extended regimen group can be attributed to a combination of improved ovulation rates, better endometrial receptivity, and optimized follicular maturation. These findings suggest that extending the duration of letrozole administration may enhance the overall reproductive success in women with polycystic ovary syndrome, making it a preferred protocol in clinical practice **[17]**. Additionally, the cumulative pregnancy rates across three cycles of ovulation induction were consistently higher in the extended regimen group, further reinforcing its superiority in achieving successful conception over multiple treatment cycles.

Cycle cancellation due to poor ovarian response was higher in the double-dose short letrozole group, with 13.3 percent of cycles canceled in this group compared to 6.7 percent in the extended regimen group. This finding suggests that some women may not respond adequately to the short high-dose regimen, possibly due to an overly rapid suppression of estrogen levels, leading to inadequate follicular recruitment. In contrast, the more gradual estrogen suppression with the extended regimen may allow for a steadier rise in follicle-stimulating hormone levels, ensuring better follicular response and reducing cycle cancellations **[18]**. Additionally, a higher incidence of luteal phase defect was observed in the double-dose short letrozole group, which could further contribute to reduced pregnancy success in this group.

Adverse effects were mild and comparable between the two groups, with no significant differences in the incidence of headache, fatigue, or hot flashes. This suggests that both letrozole regimens were well tolerated and that the choice of protocol should primarily be guided by efficacy rather than concerns about side effects. However, given that the extended regimen led to better reproductive outcomes without an increased risk of adverse effects, it may be the preferred approach for ovulation induction in polycystic ovary syndrome.

Despite the strengths of this study, there are some limitations that should be acknowledged. The sample size, although sufficient to detect significant differences in ovulation and pregnancy rates, may still limit the generalizability of findings across diverse patient populations. Additionally, long-term follow-up data on live birth rates were not assessed in this study, and future research should focus on evaluating whether the higher pregnancy rates observed with the extended regimen translate into improved live birth outcomes. Further randomized controlled trials with larger sample sizes and long-term pregnancy follow-up data are needed to validate these findings and refine ovulation induction protocols for women with polycystic ovary syndrome.

## 5. CONCLUSION

This study demonstrates that a low-dose extended letrozole regimen of 2.5 milligrams for ten days is significantly more effective than a double-dose short letrozole regimen of 5 milligrams for five days in inducing ovulation and improving pregnancy rates in women with polycystic ovary syndrome. The extended regimen was associated with higher ovulation rates, better endometrial thickness, and increased clinical pregnancy success, making it a more favorable approach for ovulation induction. The improved endometrial receptivity observed with the extended regimen suggests that a prolonged stimulation period with a lower daily dose may optimize both follicular and endometrial responses, leading to superior reproductive outcomes. The findings also highlight that a double-dose short letrozole regimen may increase the risk of cycle cancellation and luteal phase defect, which could negatively impact pregnancy success rates. Given its superior efficacy and comparable safety profile, the low-dose extended letrozole regimen should be considered a preferred protocol for ovulation induction in women with polycystic ovary syndrome. Further research with larger sample sizes and live birth rate assessment is warranted to confirm these findings and refine clinical guidelines for ovulation induction in infertility treatment.

## REFERENCES

[1] Franik S, Eltrop SM, Kremer JA, Kiesel L, Farquhar C. Aromatase inhibitors (letrozole) for subfertile women with polycystic ovary syndrome. Cochrane Database Syst Rev. 2018 May 24;5(5):CD010287. doi: 10.1002/14651858.CD010287.pub3. Update in: Cochrane Database Syst Rev. 2022 Sep 27;9:CD010287. doi: 10.1002/14651858.CD010287.pub4. PMID: 29797697; PMCID: PMC6494577.

[2] Al-Thuwaynee S, Swadi AAJ. Comparing efficacy and safety of stair step protocols for clomiphene citrate and letrozole in ovulation induction for women with polycystic ovary syndrome (PCOS): a randomized controlled clinical trial. J Med Life. 2023 May;16(5):725-730. doi: 10.25122/jml-2023-0069. PMID: 37520487; PMCID: PMC10375350.

[3] Balen AH, Morley LC, Misso M, Franks S, Legro RS, Wijeyaratne CN, Stener-Victorin E, Fauser BC, Norman RJ, Teede H. The management of anovulatory infertility in women with polycystic ovary syndrome: an analysis of the evidence to support the development of global WHO guidance. Hum Reprod Update. 2016 Nov;22(6):687-708. doi: 10.1093/humupd/dmw025. Epub 2016 Aug 10. PMID: 27511809.

[4] Xia TT, Zeng KF, Peng QM. Comparison of Three Ovulation Induction Therapies for Patients With Polycystic Ovary Syndrome and Infertility. J Clin Pharmacol. 2023 Dec;63(12):1371-1376. doi: 10.1002/jcph.2318. Epub 2023 Aug 10. PMID: 37493193.

[5] Sharpe A, Morley LC, Tang T, Norman RJ, Balen AH. Metformin for ovulation induction (excluding gonadotrophins) in women with polycystic ovary syndrome. Cochrane Database Syst Rev. 2019 Dec 17;12(12):CD013505. doi: 10.1002/14651858.CD013505. PMID: 31845767; PMCID: PMC6915832.

[6] Dai X, Li J, Fu T, Long X, Li X, Weng R, Liu Y, Zhang L. Ovulation induction using sequential letrozole/gonadotrophin in infertile women with PCOS: a randomized controlled trial. Reprod Biomed Online. 2023 Feb;46(2):352-361. doi: 10.1016/j.rbmo.2022.08.002. Epub 2022 Aug 7. PMID: 36566146.

[7] Tannus S, Burke YZ, Kol S. Treatment strategies for the infertile polycystic ovary syndrome patient. Womens Health (Lond). 2015 Nov;11(6):901-12. doi: 10.2217/whe.15.40. Epub 2015 Dec 2. PMID: 26626234.

[8] Franik S, Kremer JA, Nelen WL, Farquhar C. Aromatase inhibitors for subfertile women with polycystic ovary syndrome. Cochrane Database Syst Rev. 2014 Feb 24;(2):CD010287. doi: 10.1002/14651858.CD010287.pub2. Update in: Cochrane Database Syst Rev. 2018 May 24;5:CD010287. doi: 10.1002/14651858.CD010287.pub3. PMID: 24563180.

[9] Kar S. Current evidence supporting "letrozole" for ovulation induction. J Hum Reprod Sci. 2013 Apr;6(2):93-8. doi: 10.4103/0974-1208.117166. PMID: 24082649; PMCID: PMC3778612.

[10] Zhang Y, Wu L, Li TC, Wang CC, Zhang T, Chung JPW. Systematic review update and meta-analysis of randomized and non-randomized controlled trials of ovarian stimulation versus artificial cycle for endometrial preparation prior to frozen embryo transfer in women with polycystic ovary syndrome. Reprod Biol Endocrinol. 2022 Apr 2;20(1):62. doi: 10.1186/s12958-022-00931-4. PMID: 35366912; PMCID: PMC8976372.

[11] Huang S, Du X, Wang R, Li R, Wang H, Luo L, O'Leary S, Qiao J, Mol BWJ. Ovulation induction and intrauterine insemination in infertile women with polycystic ovary syndrome: A comparison of drugs. Eur J Obstet Gynecol Reprod Biol. 2018 Dec;231:117-121. doi: 10.1016/j.ejogrb.2018.08.002. Epub 2018 Aug 3. PMID: 30366343.

[12] Wang X, Li Y, Zhang C, Feng YR, Deng B, Zhang S, Ma Y, Wu Y, Lin G, Gong F. Live birth after letrozole-stimulated cycles versus hormone replacement treatment cycles for the first frozen embryo transfer in women with polycystic ovary syndrome: protocol for a multicentre randomised controlled trial. BMJ Open. 2023 Aug 17;13(8):e072021. doi: 10.1136/bmjopen-2023-072021. PMID: 37591656; PMCID: PMC10441070.

[13] Khurana A, Swamy MV, Mitra S, Srinivas S, Nagaraja N. Prevalence of Polycystic Ovarian Syndrome, Phenotypes and their Ovulation Response to Sequential Letrozole Dose Escalation among Infertile Women at a Tertiary Care Centre in Southern India. J Hum Reprod Sci. 2022 Jan-Mar;15(1):42-50. doi: 10.4103/jhrs.jhrs_141_21. Epub 2022 Mar 31. PMID: 35494195; PMCID: PMC9053339.

[14] Zhang Y, Fu X, Gao S, Gao S, Gao S, Ma J, Chen ZJ. Letrozole use in vitrified single-blastocyst transfer cycles is associated with lower risk of large for gestational age infants in patients with polycystic ovary syndrome. J Assist Reprod Genet. 2023 Dec;40(12):2885-2894. doi: 10.1007/s10815-023-02956-z. Epub 2023 Oct 10. PMID: 37815736; PMCID: PMC10656372.

[15] Zhou L, Fu J, Liu D, Wang Q, Chen H, Yang S, Huang W. Ovulation induction with clomiphene citrate or letrozole following laparoscopy in infertile women with minimal to mild endometriosis: a prospective randomised controlled trial. J Obstet Gynaecol. 2022 Feb;42(2):316-321. doi: 10.1080/01443615.2021.1904224. Epub 2021 May 21. PMID: 34020578.

[16] Zeng MF, Zhou X, Duan JL. Stimulated cycle versus artificial cycle for frozen embryo transfer in patients with polycystic ovary syndrome: a Meta-analysis. Gynecol Endocrinol. 2021 Apr;37(4):294-299. doi: 10.1080/09513590.2020.1867976. Epub 2021 Jan 10. PMID: 33426930.

[17] Hendawy SF, Samaha HE, Elkholy MF. Letrozole versus Clomiphene Citrate for Induction of Ovulation in Patients with Polycystic Ovarian Syndrome Undergoing Intrauterine Insemination. Clin Med Insights Reprod Health. 2011 Mar 14;5:11-6. doi: 10.4137/CMRH.S6598. PMID: 24453507; PMCID: PMC3888072.

[18] Sakar MN, Oğlak SC. Comparison of the efficacy of letrozole stair-step protocol with clomiphene citrate stair-step protocol in the management of clomiphene citrate-resistant polycystic ovary syndrome patients. J Obstet Gynaecol Res. 2021 Nov;47(11):3875-3882. doi: 10.1111/jog.14936. Epub 2021 Jul 12. PMID: 34254401.