OPTIMIZING THE DIAGNOSIS AND TREATMENT OF INFERTILITY DUE TO CLOMIPHENE RESISTANCE IN POLYCYSTIC OVARY SYNDROME

Sarkisova L.V.[1], Usmonova M.S.[2]
[1]Scientific supervisor, associate professor, Bukhara State Medical Institute
[2]Bukhara State Medical Institute

Received: 11.11.2025
Revised: 12.11.2025
Accepted: 13.11.2025

Keywords:
hormones, thyroid hormones, prolactin, gonadotropins, autoimmune thyroiditis, hormonal contraceptives ion.

Abstract. Polycystic ovary syndrome (PCOS) is one of the most pressing issues in modern gynecology, and the recurrence of polycystic ovaries once again emphasizes the seriousness of this pathology. Functional ovarian cysts are found in 60% of women of reproductive age and show a tendency to increase — from 6–12% up to 25%. Among surgical interventions performed in gynecology departments, this pathology accounts for 25–30%. The treatment methods for the clomiphene-resistant type of infertility caused by PCOS are improving year by year; however, in many cases, the process still ends with surgical intervention, which has been proven to potentially lead to a decrease in ovarian reserve.

Research Objective. To optimize the methods of diagnosis and treatment of infertility associated with clomiphene resistance in patients with polycystic ovary syndrome (PCOS).

Research materials and methods. The diagnosis of polycystic ovary syndrome (PCOS) was established based on the Rotterdam criteria — that is, in women presenting with at least two of the following three features: oligo- or amenorrhea, clinical and/or laboratory signs of hyperandrogenism, and polycystic ovaries. The study was conducted at the Bukhara State Medical Institute Clinic. A total of 30 women diagnosed with clomiphene citrate (CC)–resistant infertility were included. Among them, 17 patients received letrozole plus human menopausal gonadotropin (hMG), while 9 patients were treated with hMG alone. All patients were administered 75 IU of hMG every other day until the dominant follicle matured.

In the third group, gonadotropins were administered according to a “step-up” protocol, starting from a low dose and gradually increasing. If no follicular growth or pregnancy occurred after three cycles of 100 mg CC administered for 5 days, the patients were considered resistant to clomiphene.

In all women, during the early follicular phase, levels of FSH, LH, AMH, estradiol (E_2), total testosterone, free testosterone, cortisol, DHEAS, prolactin (PRL), TSH, free T_4, anti-TPO antibodies, and VEGF were measured. Additionally, transvaginal ultrasonography was performed to determine the number of antral follicles (3–9 mm in diameter) in the ovaries.

Research results. Ovarian stimulation cycles were performed in 30 patients resistant to clomiphene citrate (CC). In 6 (20%) of them, due to the risk of ovarian hyperstimulation, human chorionic gonadotropin (hCG) was not administered; instead, Decapeptyl 0.2 mg was injected subcutaneously as a trigger.

The total dose of human menopausal gonadotropin (hMG, IU) used in the first and second groups (letrozole + hMG and CC + hMG, respectively) was significantly lower than in the third group (hMG only). However, the difference between the first and second groups was not statistically significant.

The ovulation rate was 12 (40%) women in the first group, 10 (30%) in the second group, and 10 (30%) in the third group, with no significant difference between the groups. The rate of monofollicular development was 84.6% in the first group, 66.7% in the second group, and 53.8% in the third group, being significantly higher in the letrozole + hMG group compared with the others ($p < 0.05$).

The number of growing follicles (≥14 mm in diameter) and the frequency of cycle cancellation due to ovarian hyperresponse were lowest in the first group. Serum estradiol levels on the day of trigger administration were also lower in the first group compared to the other groups.

No multiple pregnancies were observed in the first group, whereas one case occurred in the second group and four in the hMG-only group. Mild ovarian hyperstimulation syndrome (OHSS) was more frequent in the hMG-only group compared to the others. No cases of triplet pregnancy or ectopic pregnancy were observed in any group.

Conclusion. In conclusion, the use of a combination of letrozole and human menopausal gonadotropin (hMG) reduces both the duration of stimulation and the total dose of hMG required, making this protocol more cost-effective for patients. Moreover, this approach promotes monomolecular development and helps prevent complications associated with ovulation induction, such as ovarian hyperstimulation syndrome (OHSS) and multiple pregnancy.

REFERENCES

1. Nayimova N.S., Karimova N.N. Disharmony and its correction in premature ovarian insufficiency //Journal of Pharmaceutical Negative Results, Vol. 13 special ISSUE 08 (2022) Scopus. P 3328-3332

2. 26. Gao Y , Chen F , Kong QQ , Ning SF , Yuan HJ , Lian HY , Luo MJ , Tan JH . Stresses on female mice impair oocyte developmental potential: effects of stress severity and duration on oocytes at the growing follicle stage. Reprod Sci. 2016;23(9):1148–1157.

3. Levine S, Muneyyirci-Delale O. Stress-Induced Hyperprolactinemia: Pathophysiology and Clinical Approach. Obstet Gynecol Int. 2018 Dec 3;2018:9253083. doi: 10.1155/2018/9253083. PMID: 30627169; PMCID: PMC6304861.