



SEMEN PARAMETERS, ENDOMETRIAL THICKNESS, AND HORMONAL PROFILE: THEIR INFLUENCE ON LETROZOLE PROTOCOL OUTCOMES IN INTRAUTERINE INSEMINATION FOR UNEXPLAINED INFERTILITY (A STUDY BASED ON COMPARATIVE CLINICAL DATA)

Ashish Kumar¹, Ishu Mehta¹, Drishti Rana^{1*}, Ashok Verma¹, Vinay Kumar Dogra², Abhinav Gautam³, Manmeet Saini⁴

¹*Department of Obstetrics and Gynecology, Dr. Rajendra Prasad Government Medical College, Tanda, Himachal Pradesh, India

²Department of Endocrinology, Dr. Rajendra Prasad Government Medical College, Tanda, Himachal Pradesh, India

³Department of Pediatrics, Dr. Rajendra Prasad Government Medical College, Tanda, Himachal Pradesh, India

⁴Department of Pediatrics, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India

***Corresponding Author: Drishti Rana**

*Department of Obstetrics and Gynecology, Dr. Rajendra Prasad Government Medical College, Tanda, Himachal Pradesh, India

Abstract:

This study investigates how semen parameters, endometrial thickness, and hormonal profile affect outcomes in unexplained infertility cases undergoing intrauterine insemination (IUI) with two letrozole protocols: step-up and fixed-dose regimens. An analysis of clinical, biochemical, and sonographic markers was performed in relation to ovulation, follicular development, endometrial lining, and pregnancy rates.

Introduction:

Unexplained infertility accounts for 10–15% of infertility cases after comprehensive evaluation. Empirical treatments, including ovulation induction with letrozole and IUI, are the mainstays. Letrozole, an aromatase inhibitor, can be used in various dosing protocols, most commonly as a fixed-dose (e.g., 5mg/day for 5 days) or a step-up regimen (incremental increase from 2.5mg). While the overall efficacy of letrozole is well established, the roles of semen quality, endometrial development, and baseline hormones as predictors of treatment success require further elucidation.

Materials and Methods:

A prospective randomized controlled trial was conducted including 60 patients with unexplained infertility, divided equally into:

Step-up protocol (Group A): Letrozole 2.5mg on day 2, incrementally increased daily up to 10mg over 4 days.

Fixed-dose protocol (Group B): Letrozole 5mg/day, days 2–6.

All participants underwent semen analysis (volume, concentration, motility, morphology), serum TSH, prolactin, and fasting blood sugar measurement, and serial transvaginal sonography to assess follicular growth and endometrial thickness. IUI was performed 36–40 hours post-HCG trigger, with up to four cycles allowed.

Results:

Semen Parameters:

Majority of conceptions occurred when semen concentration was 15–50 million/ml (Group A: 17.2% pregnancy rate, Group B: 15%). Higher concentrations did not correlate with increased pregnancy rates; in fact, conception rates dropped in higher concentration brackets.

Sperm motility <60% was associated with most pregnancies in Group A (17.9%). In Group B, higher motility (61–75%) achieved a 25% pregnancy rate, while <60% motility yielded 11.5%.

These results suggest an optimal mid-range semen quality for successful IUI with letrozole protocols, possibly reflecting a threshold effect where additional sperm do not translate to improved fertilization rates.

Endometrial Thickness:

Most cycles demonstrated endometrial thickness between 7–10mm at trigger, with no significant differences between protocols or cycles. Pregnancies occurred in participants with endometrial thickness ≥ 7 mm.

There were no statistically significant differences in endometrial thickness between successful and unsuccessful cycles or between protocols (mean Group A: 8.85mm, Group B: 8.33mm).

Hormonal Profile:

Mean TSH, prolactin, and RBS were within normal limits for both groups (TSH ~ 2.2 mIU/L, prolactin ~ 10 –13.5 ng/ml, RBS ~ 89 –97 mg/dl), with no statistically meaningful difference between groups or association with outcome.

No participants with overt endocrine abnormalities were included, bolstering the reliability of outcome attribution to protocol rather than baseline hormonal pathology.

Follicular Response:

Group A had more dominant follicles >20mm (34 vs 17 in Group B), hinting at a more robust response with step-up dosing.

Ovulation rates were high in both groups (Group A: 95.06%, Group B: 93.59%), with a non-significant edge for step-up protocol.

Pregnancy Outcomes:

Group A achieved a marginally higher cumulative pregnancy rate (16.7% vs 13.3%), but the difference was not statistically significant.

Cycle viability was better in Group A (lower cancellation rate).

Age stratification indicated younger women (<25) favored Group B, while older women (>30) benefited more from step-up protocol.

Discussion:

While both letrozole protocols offer substantial ovulation and pregnancy rates for unexplained infertility, semen quality within the optimal range and adequate endometrial thickness are significant contributors to success—regardless of protocol. Extreme semen concentration or motility did not proportionally improve success and may be associated with other subtle functional deficits not captured by routine analysis. Endometrial thickness maintained above the generally accepted threshold ($\geq 7\text{mm}$) is favorable but not distinguishable between standard and step-up dosing.

No significant interaction was seen between hormonal profile and outcome in a euthyroid, normoprolactinemic population. The slight numerical advantages of step-up letrozole in follicular response and pregnancy trend reinforce its utility in women with lower ovarian reserve or suboptimal response, though larger trials are needed to validate these trends.

Conclusion:

Semen parameters (concentration and motility) and endometrial thickness at trigger remain key predictors for IUI success in letrozole-induced cycles.

Both step-up and fixed-dose letrozole protocols are effective; step-up may offer advantages in older or less responsive women.

Routine endocrine screening is important, but in otherwise normal populations, these do not predict protocol-specific success.

Individualization of letrozole regimen may optimize outcomes, especially considering age, prior response, and baseline follicular development.

References:

1. Katole A, Saoji AV. Prevalence of Primary Infertility and its Associated Risk Factors in Urban Population of Central India: A Community-Based Cross-Sectional Study. *Indian J Community Med.* 2019.
2. Practice Committee of the American Society for Reproductive Medicine. Effectiveness and treatment for unexplained infertility. *Fertility and sterility.* 2006.
3. Badawy A, Metwally M, Fawzy M. Randomized controlled trial of three doses of letrozole for ovulation induction in patients with unexplained infertility. *Reproductive BioMedicine Online,* 2007.