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ORIGINAL RESEARCH

A Novel Letrozole Stair-Step Duration Regimen for Ovulation Induction in Women with Polycystic Ovary Syndrome and Letrozole Resistance

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Background: Letrozole is the first-line treatment for ovulation induction in women with polycystic ovary syndrome (PCOS). However, a subset of patients remains anovulatory despite standard treatment, a condition termed "letrozole resistance". This retrospective cohort study aimed to evaluate the effectiveness and time efficiency of a novel "letrozole stair-step duration regimen", which skips progestin-induced withdrawal bleeding and proceeds directly to an extended letrozole course after anovulatory cycles, compared with a previously established "2-step extended letrozole regimen".

Methods: We analyzed 158 women with PCOS and letrozole resistance who underwent ovulation induction at two university-affiliated reproductive centers between March 2018 and September 2024. Participants received either the stair-step duration regimen (n = 62) or the 2-step extended regimen (n = 96). Outcomes compared included follicular development, hormone profiles, ovulation, and pregnancy outcomes. The primary outcome was the ovulation rate.

Results: Ovulation rates were comparable between groups [95.16% vs 94.79%]. Clinical pregnancy rates [23.73% (14/59) vs 20.88% (19/91), P = 0.681] and live birth rates [16.95% (11/59) vs 18.68% (17/91), P = 0.824] also showed no significant differences. However, the stair-step group achieved ovulation in a significantly shorter time, with a median of 36 days (interquartile range [IQR] 32–54) versus 47 days (IQR 45–51) in the extended regimen group (P < 0.001).

Conclusion: The letrozole stair-step duration regimen is a time-saving and effective ovulation induction protocol for women with PCOS and letrozole resistance, yielding comparable reproductive outcomes in a shorter treatment duration.

Keywords: polycystic ovarian syndrome, ovulation induction, letrozole resistance, letrozole stair-step duration regimen

Introduction

Women with polycystic ovary syndrome (PCOS) account for the majority of the infertile population due to anovulation; these women usually need exogenous medications to induce follicular development. In recent years, letrozole (LE), a third-generation aromatase inhibitor, has become the preferred choice for ovulation induction in women with PCOS.[1–4] However, a proportion of women failed to respond to the conventional LE regimen.[5–15] For these women, the traditional method involves the addition of exogenous gonadotrophin, which is associated with an increased risk of ovarian hyperstimulation (OHSS) and multiple pregnancies due to the development of multiple follicles.[16] Therefore, it is of great clinical significance to explore convenient alternatives to induce ovulation in women with PCOS and LE resistance.

Our team previously introduced a 2-step extended LE regimen,[14] in which LE was administered for 7 days and, if no response occurred, for 10 days in the subsequent cycle after progestin-induced withdrawal bleeding. In a prior study,[14]

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this protocol led to mono- or bi-follicular development in most patients, with an ovulation rate of 92.75% and a live birth rate of 24.63%, while avoiding OHSS and maintaining a low rate of multiple pregnancies. These findings suggested that prolonging LE treatment duration is a viable alternative for ovulation induction in women with PCOS and LE resistance. However, this approach still required withdrawal bleeding between cycles, which increased the treatment time and added costs and patient burden.

To further improve efficiency, we proposed a novel "LE stair-step duration regimen" that omits progestin-induced bleeding between treatment steps.[17] In this protocol, if the patient did not respond to the initial 7-day LE treatment, a 10-day LE treatment was initiated immediately, without waiting for withdrawal bleeding.[17] Unlike previously reported stair-step protocols that increase the dose of LE within a single cycle,[18–21] our novel approach maintains a fixed dose and instead incrementally extends the treatment duration,[17] providing a prolonged FSH window to support follicular recruitment. Herein, we conduct this retrospective study to evaluate: (1) whether the stair-step duration protocol is effective in inducing ovulation in women with PCOS and LE resistance, and (2) whether it shortens the time to ovulation compared to the 2-step extended LE regimen.

Materials and Methods

Study Population and Design

This retrospective cohort study was conducted at the reproductive center of Shanghai First Maternity and Infant Hospital and Shanghai Ninth People's Hospital between March 2018 and September 2024. Women with PCOS who underwent ovulation induction using LE alone were screened for inclusion. This study was approved by the institutional review board of Shanghai First Maternity and Infant Hospital (the number of the approval: KS20301). Informed consent was obtained from all participants prior to LE treatment, and all cases were reported anonymously. PCOS was diagnosed by oligo/anovulation and either the presence of clinical or biochemical signs of hyperandrogenism, or polycystic ovaries, with exclusion of other disorders that mimic PCOS according to a modified version of the Rotterdam criteria.[22] The exclusion criteria were as follows: those older than 40 years; those whose core data were unavailable; those lost to follow-up.

Treatment Protocol

To illustrate the differences between the LE stair-step duration regimen and the 2-step extended LE regimen, schematic diagrams of each ovulation induction protocol are presented in Figure 1. Day 1 was defined as the initiation day of LE treatment. Patients were allocated to treatment groups based on the protocol they received in routine clinical practice. The decision was made collaboratively by the physician and the patient, without the use of randomization or predefined assignment criteria.

For women with PCOS, LE (Yimeishu, Zhejiang Hi Sun Pharmaceutical Co., Ltd., China) 5 mg daily was administered for five consecutive days, beginning on the menstrual cycle (MC) day 3 after spontaneous or progestin-induced menses. Patient response was assessed through ultrasound and serum hormone measurements—including FSH, LH, estradiol (E_2), and progesterone—every two to seven days following the last LE dose. Women were classified as LE-resistant if, 14 days after the last LE dose, they showed no response, defined as: (1) absence of follicles >10 mm, (2) E_2 levels <70 pg/mL, and (3) progesterone levels <1.0 ng/mL. These women were then treated with either the LE stair-step duration regimen or the 2-step extended LE regimen.

LE stair-step duration regimen: for LE-resistant women, an immediate second course of LE 5 mg/day for 7 days was initiated without progestin withdrawal. Hormone testing and ultrasound monitoring were repeated as previously described. If no response was observed 14 days after the last LE dose, a 10-day LE course (5 mg/day) was administered, again without progestin withdrawal. If patients remained unresponsive after the maximum LE duration (10 days), dydrogesterone (Duphaston; Abbott Biologicals B.V., Netherlands) 10 mg/day for 10 days was prescribed to induce withdrawal bleeding.

2-step extended LE regimen: dydrogesterone was first administered to induce withdrawal bleeding. In the subsequent cycle, LE 5 mg/day for 7 days was initiated from MC3. If no ovulation occurred within 14 days after the last LE dose, dydrogesterone was re-administered to induce withdrawal bleeding, followed by LE 5 mg/day for 10 days in the next cycle.

Dominant follicles either ovulated spontaneously or were triggered using human chorionic gonadotropin (hCG) 5000 IU (Lebaode, Lizhu Pharmaceutical Trading Co., China). Successful ovulation was defined by one of the following criteria: (1) disappearance of a follicle >14 mm, accompanied by a >50% decrease in E_2 and a progesterone increase >1.0 ng/mL, or

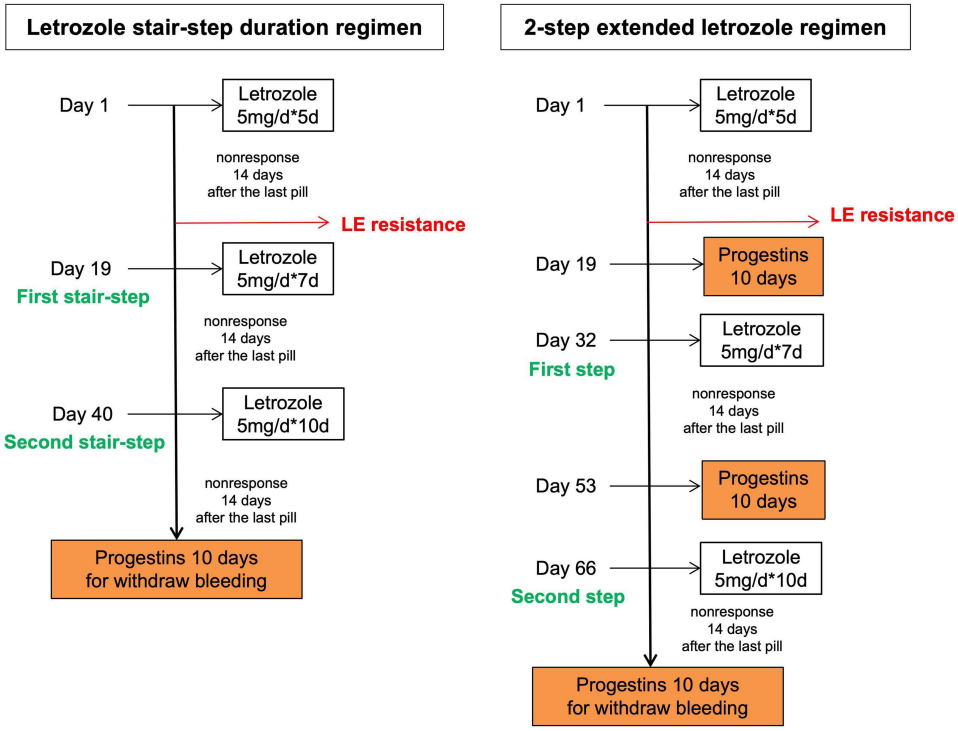

Figure 1 Overview of the letrozole stair-step duration protocol and the 2-step extended letrozole regimen.Note: "*" denotes multiplication (eg, 5 mg/d*5 d = 5 mg per day for 5 days), not statistical significance.

(2) a serum progesterone level >5 ng/mL, followed by either pregnancy or the onset of menses.[14] Couples were advised to engage in regular intercourse every two to four days, with timed intercourse recommended after hCG administration or a detected LH surge.

Outcome Variables

The primary outcome was the ovulation rate. Secondary outcomes included the rates of clinical pregnancies, live births, multiple pregnancies, early miscarriages (defined as the loss of pregnancy before 12 weeks of gestation), spontaneous ovulation (ovulation occurring without the use of exogenous trigger agents), time to ovulation (measured as the number of days from the first LE dose to ovulation), the number of follicles with a diameter exceeding 14 mm, the largest follicle diameter, endometrial thickness, and OHSS rate. Clinical pregnancies were confirmed by the presence of an ectopic pregnancy or the observation of a gestational sac in the uterus via ultrasonography.

Statistical Analyses

The Student's *t*-test was used to compare continuous variables between groups with a normal distribution, while the Mann–Whitney *U*-test was applied for continuous variables with a non-normal distribution. Chi-square (χ^2) or Fisher's exact test was used to assess categorical variables. Statistical analyses were performed using IBM SPSS Statistics for Windows (version 20; release 6.0; IBM Corporation, Armonk, NY, USA). All P values were two-sided, and a P-value < 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 158 patients with PCOS were included in our study (Table 1). Of these, 62 women underwent the LE stair-step duration regimen, and 96 women received the 2-step extended LE regimen. All patients exhibited menstrual dysfunction and polycystic ovaries. The proportion of women with amenorrhea was similar between the two groups. More than half of the women included in

Table 1 Patient Characteristics

Characteristic	Letrozole Stair-Step Duration Regimen	2-Step Extended Letrozole Regimen	P values
No. of patients (n)	62	96	
Maternal age (years)	29.37 ±3.76	29.48 ±3.76	0.86*
BMI (kg/m^2), n (%)	26.37 ±4.4	25.69 ±4.11	0.328*
<18.5	3.23% (2/62)	3.13% (3/96)	
18.5–25	29.03% (18/62)	39.58% (38/96)	
25–30	53.23% (33/62)	42.71% (41/96)	
≥30	14.52% (9/62)	14.58% (14/96)	
Infertility duration (years)	2 (1–3)	2 (1–3.75)	0.19†
AMH (ng/mL)	9.21 (6.87–11.46)	8.31 (5.97–11.22)	0.623†
Type of infertility, n (%)			0.91‡
Primary infertility	74.19% (46/62)	75% (72/96)	
Secondary infertility	25.81% (16/62)	25% (24/96)	
PCOS diagnosis, n (%)			1.000‡
Polycystic ovaries	100% (96/62)	100% (96/96)	
Hyperandrogenism (clinical or laboratory)	0% (0/62)	0% (0/96)	
Menstrual dysfunction	100% (62/62)	100% (96/96)	
Menstrual dysfunction, n (%)			0.53‡
Oligomenorrhea	59.68% (37/62)	64.58% (62/96)	
Amenorrhea	40.32% (25/62)	35.42% (34/96)	
Fallopian tube patency, n (%)			0.638§
One patent tube	6.45% (4/62)	3.13% (3/96)	
Bilateral patent tube	41.94% (26/62)	42.71% (41/96)	
No test records	51.61% (32/62)	54.17% (52/96)	

Notes: Data are presented as n, mean± SD, median (IQR) or n (%). *Student's *t*-test was used to assess continuous variables in normally or near-normally distributed variables. †Mann–Whitney *U*-test was used for continuous variables owing to the non-normality of the variables. ‡Pearson Chi-Square or §Fisher's Exact Test were used for categorical variables.

Abbreviations: AMH, anti-Müllerian hormone; BMI, body mass index; E_2, estradiol; FSH, follicle-stimulating hormone; LH, luteinizing hormone; P, progesterone; PCOS, polycystic ovarian syndrome; T, testosterone.

the study had not undergone a fallopian tube patency test before starting ovulation induction therapy. The mean maternal age, body mass index (BMI), infertility duration, AMH levels, and other baseline characteristics were comparable between the two groups.

Ovulation Outcomes

As shown in Figure 2, in the LE stair-step duration regimen group, 38 patients ovulated after the first stair-step, and 21 patients achieved ovulation after the second stair-step. In the 2-step extended LE regimen group, 84 patients ovulated after the first step, while 7 women achieved ovulation after the second step. The overall ovulation rate in the LE stair-step duration regimen group was 95.16% (59/62), which was comparable to the 2-step extended LE regimen group at 94.79% (91/96).

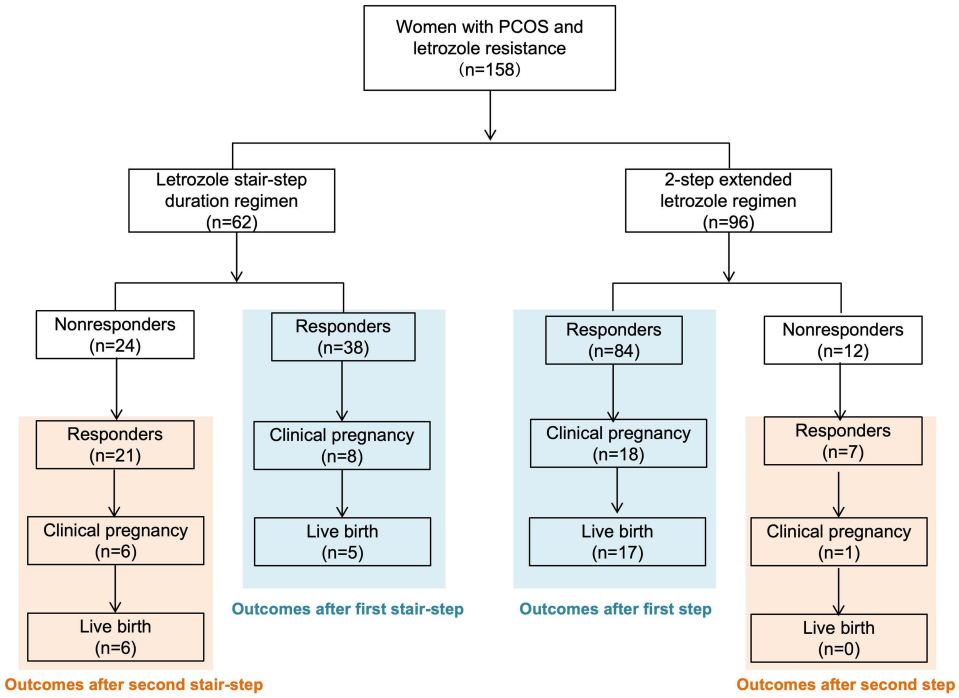

Figure 2 Flowchart of outcomes using the letrozole stair-step duration protocol or the 2-step extended letrozole regimen.

Among ovulated women, 71.19% (42/59) in the LE stair-step duration regimen group exhibited mono-follicular development, which was comparable to 79.12% (72/91) in the 2-step extended LE regimen group (Table 2). The largest follicle diameter recorded before ovulation was 36.4 mm in the LE stair-step duration regimen group and 31.5 mm in the 2-step extended LE regimen group (Figure 3A and Table 2). Endometrial thickness <7 mm was observed in four women from the LE stair-step duration regimen group and three women from the 2-step extended LE regimen group (Figure 3B and Table 2). For women who ovulated after the first increase in LE treatment, the time to ovulation ranged from 26 to 46 days in those without progestin withdrawal, which was significantly shorter than the 41 to 54 days observed in those with progestin withdrawal (Figure 3C). A similar trend was observed in women who required a second increase in LE treatment (51 to 69 days vs 80 to 85 days, respectively) (Figure 3D). Overall, the mean time to ovulation was shorter with the LE stair-step duration regimen

Table 2 Cycle Characteristics in Ovulated Patients

Characteristics	Letrozole Stair-Step Duration Regimen (n=59)	2-Step Extended Letrozole Regimen (n=91)	P values
Mono-follicular rate, % (n)	71.19% (42/59)	79.12% (72/91)	0.266†
Bi-follicular rate, % (n)	28.81% (17/59)	20.88% (19/91)	0.266†
No. of follicles >14 mm (n)	1 (1–2)	1 (1–1)	0.299*
Largest follicle size (mm)	21.65 (19.78–23.75)	21.1 (19.15–23.13)	0.407*
Time to ovulation (days)	36 (32–54)	47 (45–51)	<0.001*
Endometrial thickness (mm)	8.85 (7.3–10)	9.8 (8.5–11.4)	0.001*
Peak E_2 levels (pg/mL)	169.71 (126.7–193.72)	173.89 (134.91–208.96)	0.445*

(*Continued*)

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Table 2 (Continued).

Characteristics	Letrozole Stair-Step Duration Regimen (n=59)	2-Step Extended Letrozole Regimen (n=91)	P values
Spontaneous ovulation (n)	93.22% (55/59)	98.9% (90/91)	0.078‡
Side effects (n)	3.23% (2/62)	2.08% (2/96)	0.646‡
OHSS (n)	0	0	
Biochemical pregnancy rate, % (n)	27.12% (16/59)	23.08% (21/91)	0.575†
Clinical pregnancy rate, % (n)	23.73% (14/59)	20.88% (19/91)	0.681†
Multiple pregnancy rate, % (n)	7.14% (1/14)	0% (0/19)	0.424‡
Ectopic pregnancy rate, % (n)	7.14% (1/14)	0% (0/19)	0.424‡
Early miscarriage rate, % (n)	14.29% (2/14)	0% (0/19)	0.172‡
Live birth rate, % (n)	16.95% (11/59)	18.68% (17/91)	0.824†

Notes: Data are presented as n, mean± SD, median (IQR) or n (%). *Mann–Whitney *U*-test was used for continuous variables owing to the non-normality of the variables. †Pearson Chi-Square or ‡Fisher's Exact Test were used for categorical variables.

Abbreviations: E_2, estradiol; OHSS, ovarian hyperstimulation.

(36 [32–54] days) compared to the 2-step extended LE regimen (47 [45–51] days) (Table 2). With regards to side effects, no cases of OHSS were reported. In the LE stair-step duration regimen group, one woman experienced diarrhea, and one woman reported a mild headache. In the 2-step extended LE regimen group, two women experienced diarrhea (Table 2).

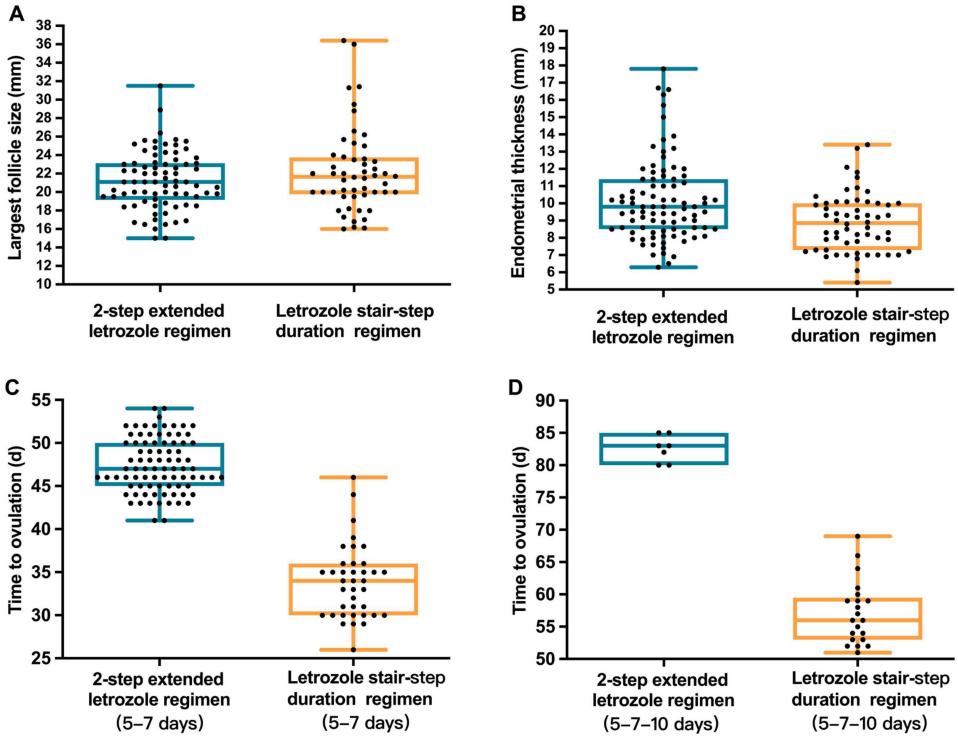

Figure 3 Distribution of women in the two groups with the largest follicle diameter. (**A**), the largest endometrial thickness (**B**), and the time of ovulation in ovulatory cycles after 5–7 days (**C**) or 5–7–10 days (**D**) treatment of letrozole, respectively. Time to ovulation refers to the number of days from the first dose of letrozole administration to ovulation.

Pregnancy Outcomes

In the LE stair-step duration regimen group, 8 women became pregnant after the first stair-step, and 5 achieved a live birth, while 6 women became pregnant after the second stair-step, and all of them yielded a live birth (Figure 2). Among those using the 2-step extended LE regimen, clinical pregnancy occurred in 18 women and live birth occurred in 17 women after the first step. Late miscarriage occurred in one woman due to fetal malformation. Only one woman was pregnant after the second step and experienced late miscarriage owing to cervical insufficiency. The rates of clinical pregnancy [(23.73% (14/59) vs 20.88% (19/91), P = 0.681], and live birth [16.95% (11/59) vs 18.68% (17/91), P = 0.824] did not differ significantly between the treatment groups (Table 2). One pregnant patient in the LE stair-step duration regimen group had twins, who spontaneously labored at 36^{+3} weeks with good neonatal outcomes. Additionally, no early neonatal death or congenital birth defects were detected in the present study.

Hormone Profile During Treatment

Figure 4 shows the dynamic hormone profiles of women who successfully ovulated using the LE stair-step duration regimen. Women were categorized into two groups based on the LE treatment duration: the 5–7 days regimen group and the 5–7–10 days regimen group. Day 1 was defined as the initiation of LE treatment. Following LE administration, there was a slight increase in mean serum FSH and LH levels, which subsequently decreased after ovulation. The 5–7 days regimen group showed slightly higher FSH levels throughout ovulation induction compared to the 5–7–10 days regimen group, though the difference was not statistically significant. Notably, clear LH surges were detected during the ovulation induction process. As follicular development progressed, serum E_2 levels increased and peaked just before ovulation. Serum E_2 levels in the 5–7 days regimen group were slightly higher than those in the 5–7–10 days regimen group, although the difference was not statistically significant. A mild increase in mean progesterone levels was observed before ovulation, followed by a significant rise in progesterone secretion after ovulation.

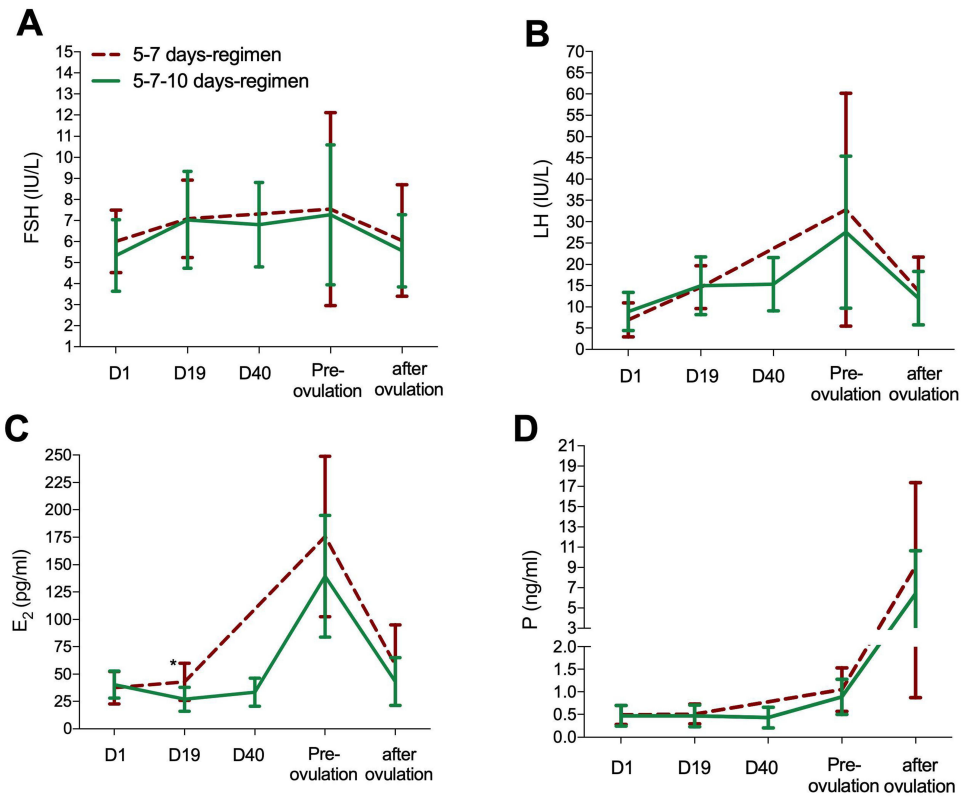

Figure 4 Serum hormone levels during ovulation induction using the LE stair-step duration regimen. Women were categorized into two groups based on the LE treatment duration: the 5–7 days regimen group and the 5–7–10 days regimen group. The day of treatment initiation was recorded as day 1 for each group. (**A**) Changes in follicle-stimulating hormone (FSH) levels over time in the two groups; (**B**) Changes in luteinizing hormone (LH) levels over time in the two groups; (**C**) Changes in estradiol (E_2) levels over time in the two groups; (**D**) Changes in progesterone (P) levels over time in the two groups.

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Discussion

Principal Findings

This is the first study to comprehensively describe the hormonal, follicular, and endometrial dynamics, as well as the ovulation and pregnancy outcomes, of the novel LE stair-step duration regimen in women with PCOS and LE resistance. This approach achieved a remarkable ovulation rate of 95.16% (59/62), with a clinical pregnancy rate of 23.73% (14/59) and a live birth rate of 16.95% (11/59). These findings highlight the LE stair-step duration regimen as a promising and effective strategy for inducing ovulation in women with PCOS and LE resistance.

Comparison with Previous Studies

The conventional LE regimen consists of a 5-day treatment, starting at 2.5 mg per day. If there is no response, the dose is typically increased in 2.5 mg increments in subsequent cycles until ovulation occurs or the maximum daily dose of 7.5 mg is reached.[1–4] In clinical practice, when women with PCOS fail to ovulate with the initial LE dose, it is common to induce endometrial shedding with progestin before escalating the dose for ovulation induction.[1–4] However, the necessity of this routine progestin withdrawal has been increasingly questioned. On one hand, this stepwise approach can take months to confirm LE or clomiphene citrate (CC) resistance, prolonging treatment and contributing to patient anxiety and frustration due to repeated failures and prolonged waiting time.[23,24] On the other hand, studies have reported lower conception (6.6% vs 27.7%) and live birth rates (5.4% vs 19.7%) in women with PCOS who undergo ovulation induction after progestin-induced withdrawal bleeding compared to those who proceed without withdrawal.[24] In response to these challenges, the stair-step protocol was initially proposed using clomiphene citrate,[25–30] and later adapted to letrozole,[18–21] offering an alternative approach for PCOS patients who require successive ovulation induction cycles.

Our novel LE stair-step duration regimen introduces a key innovation compared to previously reported LE stair-step protocols, which typically rely on dose escalation.[18–21] Rather than increasing the daily LE dose in non-responders, we extended the treatment duration, thereby prolonging the "FSH window". This allows additional time for a cohort of antral follicles to become responsive to FSH stimulation.[31] As demonstrated in our study, this approach achieved effective ovulation induction while maintaining safety: mono-follicular development predominated, no patients developed three or more follicles ≥14 mm, only one twin pregnancy occurred, and no cases of OHSS were observed.[14] Our protocol incorporated both hormonal and ultrasound monitoring, enabling a more accurate assessment of ovarian response compared with ultrasound alone. This combined approach reduced the risk of misclassifying patients as non-responders when ovulation occurred between monitoring visits or when corpus luteum formation was not yet apparent. Moreover, unlike previous studies that assessed follicular response only 7 days after the last LE dose,[18–21] we extended the observation window to 14 days. This was based on our earlier findings that ovulation in LE-resistant PCOS patients after a 7-day course of LE (5 mg/day) occurred within 11–23 days from the first day of medication.[12] Extending the monitoring period therefore minimizes the risk of premature re-dosing and provides a more reliable evaluation of treatment response.

Previous studies comparing the LE stair-step dose protocol with the CC stair-step protocol have reported ovulation rates ranging from 83.6% to 96%.[18–20] More recently, a randomized controlled trial by Karakaya et al reported a cumulative ovulation rate of 93% (37/40) with the LE stair-step protocol, which was comparable to the conventional LE regimen requiring progestin-induced withdrawal bleeding (90%, 36/40; P = 1.0).[31] In line with these findings, our study showed the novel LE stair-step duration protocol yielded an overall ovulation rate of 95.16% (59 out of 62) among women with PCOS and LE resistance, which was comparable to that observed with the 2-step extended LE regimen.

When it comes to the time to ovulation, the LE stair-step duration regimen significantly reduced the period (36 days) compared to the 2-step extended LE regimen (47 days), but it took longer than the stair-step protocols with LE[18–21] or CC dose adjustments.[25–30] This may be attributed to differences in the time interval used to determine treatment failure. Follicular development was assessed one week after the last dose of ovulation induction drugs in previous studies,[18–21,25–30] whereas in our study, this period was extended to two weeks. In addition, we favored spontaneous follicular rupture over routine triggering when dominant follicles reached ≥18 mm, recognizing that estradiol levels often remain insufficient to induce an LH surge at that point. Given the short half-life of LE (≈45 hours) but the subsequent rapid rise in E_2 after discontinuation,[32]

additional time may be required before ovulation occurs. As a result, most women in our study ovulated spontaneously without exogenous trigger, which prolonged the time to ovulation but more closely reflects the natural physiological process.

There were concerns that the longer LE treatment duration may result in a higher rate of unruptured follicles, thinner endometrium, and less pregnancy. However, in our study, no significant difference was observed in the rate of spontaneous ovulation between the treatment groups. Although endometrial thickness was slightly lower in women using the LE stair-step duration protocol compared to those on the 2-step extended LE regimen, the rates of clinical pregnancy and live birth were comparable between the groups.

For the risk of experiencing side effects, in the conventional LE regimen, Amer et al reported that 12 out of 80 participants developed minor adverse events during LE treatment.[6] Similarly, in a study by Legro et al, the rates of side effects such as hot flushes, fatigue, and dizziness were 20.3% (73 out of 359), 21.7% (78 out of 359), and 12.3% (44 out of 359), respectively.[5] In contrast, a lower percentage of women experienced side effects when using the LE stair-step protocol varying between 8.2% and 25% across different cohorts.[18–21] In our study, adverse events were infrequent and mild, with one case of diarrhea and one case of headache in the LE stair-step group and two cases of diarrhea in the control group; none required treatment discontinuation. These findings collectively suggest that the stair-step modifications of LE do not increase the risk of side effects and may offer comparable tolerability to conventional regimens.

Strengths and Limitations

We incorporate ultrasound and serum hormone level measurements into a practice to accurately determine whether women are responsive to the current treatment. Our work confirmed it was feasible to skip routine progestins withdrawal for nonresponsive women and proceed directly to increasing the LE duration during ovulation induction. In other words, it is not necessary to induce menses before increasing LE treatment duration in those nonresponsive PCOS patients. The shortened time to ovulation using the stair-step regimen is a clear advantage over traditional progestins withdrawal regimen.

Our study has several limitations. First, it is a retrospective cohort study without randomization, and there was no control group receiving the conventional letrozole regimen. Treatment allocation was based on physician-patient discussions in routine clinical practice, which may have introduced selection bias and affected the generalizability of our findings. Therefore, the study reflects real-world clinical decision-making rather than a controlled experimental setting. To better contextualize the findings and determine the relative efficacy of the novel letrozole stair-step duration regimen, future large-scale randomized controlled trials including a conventional letrozole regimen as a comparator are warranted. Furthermore, as only a single cycle of ovulation induction was analyzed, cumulative pregnancy outcomes were not evaluated. Future prospective studies are needed to assess cumulative live birth rates and long-term offspring outcomes in order to comprehensively evaluate the effectiveness and safety of this regimen.

Conclusion

Our study demonstrates that the LE stair-step duration regimen is effective for inducing ovulation in women with PCOS and LE resistance, and it shortens the time to ovulation compared to the 2-step extended LE regimen. This approach may help women with PCOS conceive more quickly, as the reduced time to ovulation, combined with decreased emotional distress from repeated ovulation failures, may improve outcomes. Further research is needed to identify potential indicators that could predict ovarian response to LE and to explore the mechanisms underlying ovarian sensitivity. These efforts may provide valuable evidence to support the personalized use of LE for ovulation induction in women with PCOS.

Data Sharing Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the institutional review board of Shanghai First Maternity and Infant Hospital (KS20301) and was conducted according to the Declaration of Helsinki for Medical Research. All the women gave informed consent before receiving LE treatment, and cases were reported anonymously in our study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to disclose for this work.

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