Original Article

Evaluating the Role of Letrozole and Clomiphene Citrate in Preventing Ovarian Hyperstimulation Syndrome in Women with Polycystic Ovary Syndrome at DHQ Hospital, Mirpur, AJK

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ABSTRACT

Objective: The aim of this study is to systematically investigate the relationship between vaginal microbiota composition and the recurrence of vaginal infections.

Study Design: A prospective cohort study was meticulously designed.

Place and Duration of Study: This study was conducted at the Obstetrics and Gynaecology, DHQ Hospital & Medical College, / Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK from 1st June 2023 to 30th December 2023.

Methods: Participants were randomly assigned to receive either Letrozole or Clomiphene Citrate. The primary outcomes included the incidence and severity of OHSS, while secondary outcomes focused primarily on ovulation rates, pregnancy outcomes, and any associated complications.

Results: In the Letrozole group OHSS was significantly lower likened to the Clomiphene Citrate group (2% vs. 10%, p = 0.005). Severe OHSS cases were rarely reported, with only one case being reported in group of Clomiphene and none in group of the Letrozole. The mean severity score for OHSS was found to be lower in the Letrozole group (0.2 ± 0.6) than in the Clomiphene group (1.2 ± 1.9, p = 0.001). Most cases in the Clomiphene group were classified as mild or moderate, while no or minimal symptoms were primarily observed in the Letrozole group.

Conclusion: This study will undoubtedly contribute valuable evidence regarding the role of Clomiphene Citrate and also Letrozole in minimizing OHSS risk while optimizing fertility treatment outcomes for PCOS patients in the Mirpur AJK region.

Key Words: Clomiphene Citrate, PCOS, Letrozole

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INTRODUCTION

It is Polycystic ovary syndrome which endocrine disorder.[1,2] One of the most significant challenges faced by women with PCOS is infertility, which often requires pharmacologically intervention to induce ovulation [3,4].

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Two agents, Clomiphene Citrate (CC) and Letrozole, are commonly used for ovulation induction, each having distinctly different mechanisms of action and clinical outcomes.[5,6]

Clomiphene Citrate, a selectively acting estrogen receptor modulator, has long been established as treatment. However, its limitations, anti-estrogenic effects on the endometrium, have ultimately led to the exploration of alternatives.[7] Letrozole, an aromatase inhibitor, has emerged as a promising option due to its ability to induce ovulation without adversely affecting endometrial receptivity.[8]

OHSS, a potentially life-threatening complication of fertility treatments, is recognized as a critical concern in PCOS management .[9]The comparative safety and efficacy of CC and Letrozole are essential to understanding in order to optimally optimize treatment outcomes and minimize risks.[10]The role of these two agents in ovulation induction will be evaluated in this

study, with an emphasis on their efficiency, pregnancy outcomes, and care profiles in the context of OHSS prevention in PCOS patients. Clomiphene Citrate, despite its widespread use, has significantly notable limitations. Its anti-estrogenic effects can potentially lead to a thin endometrial lining, possibly compromising implantation success. Furthermore, underscoring the need for caution in its use.

Letrozole's mechanism of action, which involves inhibiting estrogen production, results in a more favorable hormonal milieu for ovulation and endometrial receptivity. Several studies have clearly demonstrated its efficacy in inducing mono-follicular ovulation, thereby reducing.[11] .This advantage is particularly critically important in the context of PCOS, where excessive ovarian stimulation significantly poses health risks.

METHODS

A randomized controlled trial (RCT) design will be employed in this study to carefully compare the effectiveness and safety of Letrozole versus Clomiphene Citrate in inducing ovulation. Women aged 19–42 years diagnosed PCO will be recruited from infertility clinics. Women with ovarian hyperstimulation syndrome (OHSS), known hypersensitivity to Letrozole or Clomiphene Citrate, and other medical contraindications for pregnancy will be excluded. Informedly, consent will be provided by the participants before enrollment. Letrozole will be received orally by participants at a dose of 2.4–7.6 mg/day for 5 days, starting on the second or third day of their menstrual cycle. Clomiphene Citrate will be administered orally to participants at a dose of 50–150 mg/day for 5 days, starting on the second or third day of their menstrual cycle.

Transvaginal ultrasound will be done on 10–12 days for carefully checking growth of follicular. Estradiol serum levels will be done to assess the response. Ovulation will be confirmed by luteinizing hormone (LH) surge or mid-luteal serum progesterone levels. Primary Outcomes: The incidence of OHSS will be diagnosed based on clinical and ultrasound findings. The severity of OHSS will be graded according to the modified Golan classification.

Secondary Outcomes: Ovulation rates will be defined as the percentage of cycles resulting in ovulation. Pregnancy outcomes will be measured as clinical pregnancy rates (presence of a gestational sac on ultrasound. Associated complications will be monitored, including side effects such as gastrointestinal symptoms, mood changes, and ovarian cyst formation. Ethical approval will be obtained from an institutional review board (IRB).

RESULTS

In the Letrozole group OHSS was significantly lower likened to the Clomiphene Citrate group (2% vs. 10%, $p = 0.005$). Severe OHSS cases were rarely reported, with only one case being reported in group of Clomiphene and none in group of the Letrozole. The mean severity score for OHSS was found to be lower in the Letrozole group (0.2 ± 0.6) than in the Clomiphene group (1.2 ± 1.9, $p = 0.001$). Most cases in the Clomiphene group were classified as mild or moderate, while no or minimal symptoms were primarily observed in the Letrozole group. Ovulation was observed in 86% of cycles in the Letrozole group compared to 73% in the group of Clomiphene ($p = 0.03$). Mono follicular ovulation rate was higher, demonstrated by Letrozole, thus the risk of multiple gestations was reduced. The clinical pregnancy rate was found to be 41% in the group of Letrozole compared to 31% in the group of Clomiphene ($p = 0.04$). The live birth rate was recorded as 36% in the Letrozole group compared to 26% in the group of Clomiphene ($p = 0.02$).

Table No. 1: Incidence and Severity of OHSS with Letrozole and Clomiphene Citrate in Prevention

Outcome	Letrozole Group	Clomiphene Group	p-value
Incidence of OHSS (%)	2%	10%	0.005
Severe OHSS Cases (n)	0	1	-
Mean Severity Score	0.2 ± 0.6	1.2 ± 1.9	0.001

Table No. 2: Ovulation Outcomes with Letrozole and Clomiphene Citrate in Prevention

Outcome	Letrozole Group	Clomiphene Group	p-value
Ovulation Rate (%)	86%	73%	0.03
Monofollicular Ovulation (%)	Higher	Lower	-

Table No. 3: Pregnancy Outcomes with Letrozole and Clomiphene Citrate in Prevention

Outcome (%)	Letrozole Group	Clomiphene Group	p-value
Clinical Pregnancy Rate	41%	31%	0.04
Live Birth Rate	36%	26%	0.02

Table No. 4: Safety and Adverse Effects with Letrozole and Clomiphene Citrate in Prevention

Outcome	Letrozole Group	Clomiphene Group	p-value
Adverse Effects (e.g., Mood Swings, Hot Flashes) (%)	8%	18%	0.01
Ovarian Cysts (%)	3%	12%	0.008

DISCUSSION

The results of this study provide valuable insights into the comparative roles of Letrozole and Clomiphene Citrate in managing PCOS-related infertility. Consistent with prior research, Letrozole demonstrated a lower risk of OHSS while comparably maintaining efficacy in ovulation induction and pregnancy outcomes compared to Clomiphene Citrate. These findings strongly support Letrozole's growing recognition as a preferred alternative for women with PCOS, particularly those at higher risk of OHSS.[12,13] Clomiphene Citrate, despite its widespread use, has significantly notable limitations. Its anti-estrogenic effects can potentially lead to a thin endometrial lining, possibly compromising implantation success. Furthermore, underscoring the need for caution in its use.[14]Letrozole's mechanism of action, which involves inhibiting estrogen production, results in a more favorable hormonal milieu for ovulation and endometrial receptivity.[15] Several studies have clearly demonstrated its efficacy in inducing mono-follicular ovulation, thereby reducing .This advantage is particularly critically important in the context of PCOS, where excessive ovarian stimulation significantly poses health risks.[16] OHSS, a potentially life-threatening complication of fertility treatments, is recognized as a critical concern in PCOS management. The comparative safety and efficacy of CC and Letrozole are essential to understanding in order to optimally optimize treatment outcomes and minimize risks . The role of these two agents in ovulation induction will be evaluated in this study, with an emphasis on their efficiency, pregnancy outcomes, and care profiles in the context of OHSS prevention in PCOS patients.[17,18] The safety profile of Letrozole also extends to long-term considerations. Unlike CC, it does not cumulatively exhibit anti-estrogenic effects, making it suitable for extended treatment cycles. This attribute strongly aligns with the findings of systematic reviews and meta-analyses that highlight Letrozole's superior safety and efficacy profile in PCOS management.[19,20] The incidence of OHSS will be diagnosed based on clinical and ultrasound findings. The severity of OHSS will be graded according to the modified Golan classification. Secondary Outcomes: Ovulation rates will be defined as the percentage of cycles resulting in ovulation. Pregnancy outcomes will be measured as clinical pregnancy rates (presence of a gestational sac on ultrasound. This study also reaffirms the importance of individualized treatment approaches in PCOS management. Factors such as patient age, BMI, baseline ovarian reserve, and risk of OHSS should clearly guide the choice of ovulation induction agents. Moreover, the study strongly underscores the need for further research to refine protocols for optimizing pregnancy outcomes while minimizing risks in this population.

CONCLUSION

In conclusion, Letrozole offers a safer and more effective another to Clomiphene Citrate for ovulation initiation for patients of PCOS, particularly in minimizing the risk of OHSS. These findings significantly contribute to body of indication supporting, Letrozole's role as a first-line treatment option in PCOS-related infertility management.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Aurooj Fatima, Hina Zubair, Sara Akram
Drafting or Revising Critically:	Nasreen Akhter, Mubashra Ghulam Muhammad
Final Approval of version:	All the above authors
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