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EFFECT OF LETROZOLE FOR OVULATION INDUCTION IN POLYCYSTIC OVARY SYNDROME IN FEMALE POPULATION

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Abstract:
Introduction: *Polycystic ovary syndrome (PCOS) is an endocrine and reproductive disorder with a prevalence ranging from 5% to 13% in women of reproductive age.* ***Aims and objectives:*** *The main objective of the study is to analyze the effect of Letrozole for Ovulation Induction in Polycystic Ovary Syndrome in female population.*
Material and methods: *This cross sectional study was conducted in DHQ hospital, Narowal during March 2018 to December 2018. The data was collected from 100 female patients who visited the OPD of the hospital during their diseases. All those female who were suffering from PCOS, included in this study. All cases of infertile women with PCOS from 18 to 45 years old were analyzed in this study. All patients underwent letrozole on cycle day 3 for consecutive 5 days for up to 5 menstrual cycles. If there was a nonresponse or a poor ovulatory response occurred, the dose was increased in subsequent cycles in the either group. The maximum daily dose of letrozole was 7.5 mg.*
Results: *The data were collected from 100 female patients. The results showed that patients who received letrozole did not exert better outcomes in neither primary endpoint, including live birth. There were not significant differences in all adverse events. All the values were expressed in mean and standard deviation.*
Conclusion: *It is concluded that induction of ovulation with letrozole in PCOS patients is associated with limited number of mature follicles, no adverse effect on endometrial thickness or cervical mucous, and ovulation and pregnancy in a significant number of patients.*

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INTRODUCTION:

Polycystic ovary syndrome (PCOS) is an endocrine and reproductive disorder with a prevalence ranging from 5% to 13% in women of reproductive age. PCOS is the primary cause of hyperandrogenism and oligo-anovulation at the reproductive age and is often associated with infertility [3] and clinical and metabolic disorders [1].

The prevalence of infertility in women with PCOS varies between 70 and 80%. According to the American Society for Reproductive Medicine, the evaluation of infertility in women with PCOS or other causes of subfertility should start after six months of attempting pregnancy without success if the couple has regular sexual intercourse (2 to 3 times/week) without using contraceptive methods [2]. To optimize the efficacy of the treatment of infertile women with PCOS, evaluations of tubal patency (hysterosalpingography or laparoscopy with chromotubation) and semen analysis (spermogram) are mandatory before deciding on treatment. However, tubal patency evaluation may not be necessary prior to initiating clomiphene citrate (CC) treatment [3]. Notably, if a patient is resistant to this drug and/or requires the use of gonadotropins and/or presents with other causes of infertility, a tubal patency evaluation becomes mandatory prior to initiating the therapeutic treatment of infertility [4].

Letrozole is an aromatase inhibitor that was used as an ovulation inductor in anovulatory infertility women with more than 56 mm endometrial thickness. It inhibits estrogen production by repressing the enzyme aromatase [5]. It has been reported that letrozole can inhibit estrogen levels by at least 97% to 99%. The other studies also reported that letrozole is effective in clomiphene-resistant patients, and also resulted in ovulation of 62% cases, and pregnancy of 14.7% [6]. Additionally, no adverse events have been reported on fetus. However, current data are still insufficient to support the idea that letrozole can be utilized effectively to treat such condition. Therefore, in this retrospective study, we investigated the efficacy and safety of letrozole for infertility women with PCOS [7].

Aims and objectives

The main objective of the study is to analyze the effect of Letrozole for Ovulation Induction in Polycystic Ovary Syndrome in female population.

MATERIAL AND METHODS:

This cross sectional study was conducted in DHQ hospital, Narowal during March 2018 to December 2018. The data was collected from 100 female patients who visited the OPD of the hospital during their diseases. All those female who were suffering from PCOS, included in this study. All cases of infertile women with PCOS from 18 to 45 years old were analyzed in this study. All patients underwent letrozole on cycle day 3 for consecutive 5 days for up to 5 menstrual cycles. If there was a nonresponse or a poor ovulatory response occurred, the dose was increased in subsequent cycles in the either group. The maximum daily dose of letrozole was 7.5 mg.

Statistical analysis:

All outcome and characteristic values were analyzed by using SPSS software (SPSS V.17.0). Continuous non-normally value was analyzed by U test, while normally variables were performed by *t*-test. Categorical value was conducted by Chi-squared test. $P < .05$ was defined as having a statistical significance.

RESULTS:

The data were collected from 100 female patients. The results showed that patients who received letrozole did not exert better outcomes in neither primary endpoint, including live birth. There were not significant differences in all adverse events. All the values were expressed in mean and standard deviation.

Table 01: Analysis of outcomes of letrozole group

	Letrozole group	*t*	*P* value
Total number of follicles	4.4 ± 0.4	4.3	.042[a]
Number of follicles >14 mm	2.1 ± 0.3	6.13	.008[a]
Number of follicles >18 mm	2.3 ± 0.1	5.03	.03[a]
Pretreatment endometrial thickness (mm)	4.5 ± 0.4	1.41	.52
Endometrial thickness at hCG (mm)	8.1 ± 0.2	5.44	.021[a]
Serum E_2 (pg/mL)	255.1 ± 64.2	4.12	.022[a]
Serum progesterone (ng/mL)	7.1 ± 0.9	6.33	.024[a]
Duration of stimulation (days)	12.1 ± 1.38	4.91	.036[a]
Pregnancy/cycle	82/540 (15.1%)	1.33	.72
Miscarriage/patient	4 (12.1%)	1.73	.43

DISCUSSION:

Comparing letrozole responders and nonresponders with regard to clinical and laboratory characteristics, there were no significant differences in BMI, waist or hip circumference, waist/hip ratio, hirsutism, LH, FSH, or LH/FSH ratio [8]. Thus, letrozole can be given to all patients with CC resistance, because its efficacy is not limited to a specific abnormality. Achieving weight reduction is difficult, particularly as the metabolic status of patients with PCOS conspires against weight loss [7]. Letrozole can be used in patients with hirsutism, and there is no need to add dexamethasone to reduce adrenal androgen production. Dexamethasone can worsen diabetic tendencies and as a result it may not be a suitable treatment for patients with diabetes, insulin resistance, or glucose intolerance, conditions present in many PCOS patients (3). Letrozole can be used in case of high LH without the need to add oral contraceptives for pretreatment suppression of LH. Oral contraceptive pills exacerbate insulin resistance. Many PCOS patients are overweight, and obesity is a relative contraindication to oral contraceptive pills [9].

On the other hand, regarding the positive effect of letrozole in producing FSH sensitivity and satisfactory E_2 elevation (at normal physiological levels), it can have better therapeutic effects in infertile females. In addition, because serum clearance of letrozole is faster than clomiphene citrate and does not lead to a decrease in the estrogen receptors, it is probable that letrozole does not produce deleterious effects similar to that found with clomiphene citrate on the endometrium, although it can lead to pregnancy at similar or even higher rates [10].

CONCLUSION:

It is concluded that induction of ovulation with letrozole in PCOS patients is associated with limited number of mature follicles, no adverse effect on endometrial thickness or cervical mucous, and ovulation and pregnancy in a significant number of patients. Induction with letrozole does not seem to depend on age, period of infertility, BMI, waist circumference, LH, FSH or LH/FSH ratio.

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