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Research Article

**EVALUATION OF OVULATION INDUCTION WITH
LETROZOLE WITH METFORMIN IN FEMALES WITH
POLYCYSTIC OVARIAN SYNDROME**Dr Zunaira Fatima¹, Dr Kaleem Asad², Dr Safi Ullah Sardar³¹Ibne Sina Hospital, Multan²Rural Health Center Dhuman, District Chakwal³District Headquarter Hospital, Kasur

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Abstract:

Objectives of the study: To compare the frequency of Ovulation Induction after administration of Letrozole with metformin in females presenting with Polycystic Ovarian Syndrome. **Methodology of the study:** This descriptive study was conducted at Ibne Sina Hospital, Multan during June 2019 to January 2020. Total 200 females fulfilling the inclusion criteria were recruited from OPD. Then random ordering of females was done in 2 groups by utilizing lottery method. Females in A-group were given Letrozole 2.5mg once a day for three days (from third day to seventh day) for three cycles and metformin 1500mg (500mg 3 times a day) daily for three months, while females in group Both BMI & age were studied for Mean & S.D. Ovulation induction was studied and Percentage along with frequency was calculated. **Results:** In Group-A mean age of women was 28.18±6.58 years. In Group-B mean age of women was 27.08±5.15 years. In Group-A ovulation induction rate was significantly higher as compared to that of Group-B women. i.e. (89% vs. 60%). p-value=0.000. Ovulation induction rate was significantly higher with Letrozole+ Metformin in women who were having normal BMI, overweight & obese as compared to that of Letrozole alone. **Conclusion:** Letrozole with metformin is more effective for the ovulation Induction females presenting with polycystic ovarian Syndrome as compared to letrozole alone.

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INTRODUCTION:

Polycystic ovary syndrome, is considered most prevalent endocrine abnormality in females with much high prevalence.¹ It commonly leads to anovulatory infertility & being responsible for up to 70% of total infertility cases occurring because of anovulation.²

The etiology is somewhat complicated as it is a heterogeneous condition and not understood with variations in phenotype.¹ Clomiphene citrate is still drug used as first preference for ovarian stimulation. But it is also reported that 20–25% of total women become resistant to this and result in failure to ovulate. For these cases, the gonadotropins are opted though these are related with increased chances of multiple pregnancies & ovarian hyperstimulation.³

It was reported recently that Letrozole has good effects on endometrium, so it enhances rates of pregnancy after prospective ovulation induction for subjects suffering with PCOS.⁴ These beneficial advantages are lessened rate for occurrence of multiple pregnancies, no anti estrogenic adverse events, and consequently intensive monitoring is not much needed.⁵ Studies has reported that letrozole effective in ovulation induction from 64.9% to 78.7%.⁶ One study reported very low frequency of ovulation induction with letrozole i.e. 60.78%.⁷ While another reported that letrozole is effective for ovulation induction in 88% cases.⁸ In contrast to that ovulation induction with letrozole in combination with metformin was 90.57%.⁹

The main objective of the study is to evaluate the ovulation induction with letrozole with metformin in females with polycystic ovarian syndrome.

MATERIAL AND METHODS:

This descriptive study was conducted at Ibne Sina Hospital, Multan during June 2019 to January 2020. Total of 200 cases (100 subjects in every group was calculated using 80% power of the test and 5% significance level & taking ovulation induction percentage expected as 90.57% with Letrozole with metformin and 60.78% with Letrozole alone in cases presenting with PCOs) were enrolled by Non-Probability, consecutive Sampling.

Data collection

Woman age 18-39 years, BMI <35, Infertility due to anovulation, Polycystic Ovarian Syndrome (having at the very least any 2 of following as diagnostic criteria: amenorrhea/Oligomenorrhea, Hyper androgenaemia (testosterone ≥ 2.5 nmol/l) or free androgen index ≥ 5 or clinical evidence (acne/hirsutism), Ultrasound evidence of Polycystic Ovarian Syndrome (either ≥ 12 follicle measuring 2-9mm in dia meter or ovarian volume > 10ml)), Normal husband semen analysis (sperm count 20 million/ml, 60% are motile and 30% have normal morphology), Patency of both fallopian tubes by hysteroscopy and laparoscopy, and No recent treatment within six months for induction of ovulation on history were included.

Statistical analysis

SPSS version 20 was used by researchers to analyse the data gathered. Both BMI & age were studied for Mean & S.D. Ovulation induction was studied and Percentage along with frequency was calculated. Chi-square test was conducted taking p value ≤ 0.05 as significant value. Data was stratified for BMI (Normal, overweight and Obese). Chi-Square testing was reapplied with a p value < 0.05 as significant.

RESULTS:

In Group-A mean age of women was 28.18 ± 6.58 years. In Group-B mean age of women was 27.08 ± 5.15 years. In Group-A minimum and maximum age of women was 18 and 39 years while in Group-B this was 18 and 37 years respectively. (Table-1)

In Group-A mean BMI of women was 28.05 ± 2.82 . In Group-B mean BMI of women was 27.54 ± 2.54 Kg/m². In Group-A minimum and maximum BMI of women was 23 and 32 while in Group-B this was 23 and 31.9 respectively. (Table-2)

As per body mass index criteria in Group-A 20(20%) women were having normal BMI, 44(44%) were overweight and 36(36%) were obese. In Group-B 20(20%) women were having normal weight, 59(59%) were overweight and 21(21%) were observed. (Table-3)

TABLE-1: AGE DISTRIBUTION OF PATIENTS

	Group-A	Group-B
<i>n</i>	100	100
<i>Mean</i>	28.18	27.08
<i>SD</i>	6.585	5.154
<i>Minimum</i>	18	18
<i>Maximum</i>	39	37

Group-A= Letrozole + Metformin

Group-B= Letrozole

TABLE-2: DESCRIPTIVE STATISTICS FOR BODY MASS INDEX OF WOMEN

	<i>Group-A</i>	<i>Group-B</i>
<i>n</i>	100	100
<i>Mean</i>	28.059	27.544
<i>SD</i>	2.8211	2.5492
<i>Minimum</i>	23.0	23.0
<i>Maximum</i>	32.0	31.9

TABLE-3: BODY MASS INDEX STATUS OF WOMEN

<i>BMI</i>	<i>Group-A</i>	<i>Group-B</i>	<i>Total</i>
<i>Normal</i>	20(20%)	20(20%)	40
<i>Overweight</i>	44(44%)	59(59%)	103
<i>Obese</i>	36(36%)	21(21%)	57
<i>Total</i>	100	100	200

DISCUSSION:

PCOS is considered one of most prevalent endocrine abnormalities in women who have reached childbearing age (6.8%),¹⁰ and subsequently causes infertility because of ovulation disturbance. 75% of total disturbances are related to PCOS. Ovulation induction is therapy opted for treatment of PCOS. There are many treatment options available for this but none is solely to be considered for therapy. Clomiphene, metformin, letrozole, gonadotropins, ovaries cauterization & wedge resection, gonadotrophin-releasing hormone agonists and reproductive assisted technology.^{11,12}

Almost 50%–70% of total women affected with PCOS have somewhat insulin resistance. Hyperinsulinemia may lead to hyperandrogenism, which causes signs & symptoms of the PCOS.¹³ A biguanide, Metformin treats insulin resistance in cases with co-occurrence of PCOS reducing production of endrogens in ovaries affecting follicular development & ovulation induction. Also, many reports state that the metformin plus CC in case of CC-resistant PCOS is particularly effective in inducing ovulation for 68.6%– 77.7% of subjects.⁶

CONCLUSION:

Letrozole plus metformin is more effective as therapy for the induction of ovulation in females presenting with polycystic ovarian syndrome as compared to letrozole alone.

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