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USE OF LETROZOLE FOR INFERTILITY IN THE POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Introduction: The polycystic ovary syndrome is a common cause of infertility. Letrozole, a third generation aromatase inhibitor, is now considered as the best alternative of clomiphene citrate for the infertility treatment in women with the polycystic ovary syndrome. **Objective**: To observed effect of letrozole therapy in infertile women with polycystic ovary syndrome. **Methodology**: In this cross-sectional study we enrolled 310 infertile women aged 20-35 years diagnosed as polycystic ovary syndrome. Participants who had normal uterine cavity and sperm concentration of at least 20 million/ml of her husband were prescribed letrozole for 6 months. Medication was discontinued when pregnancy was confirmed and participants were followed untill delivery. **Results**: After 6 months treatment 125 (40.5%) patient was conceived. Live birth was 65 (20.9%) of 310 subjects. Among pregnancies multiple (twin) birth was 18 (5.7%). First trimester pregnancy loss was 61(19.5%). After having 6 months of therapy there was no pregnancy in 185 (59.5%) patients. **Conclusions**: Letrozole is safe and cost effective medicine in achieving live birth in infertile women with polycystic ovary syndrome.

KEYWORDS: Letrozole, polycystic ovary synodrome, infertility.

INTRODUCTION

Polycystic ovary syndrome is one of the most common endocrine disorders, affecting about 5-15% of women of reproducitve age.[1,2] The polycystic ovary syndrome, which is diagnosed on the basis of hyperandrogenism oligoovulation with associated oligomenorrhea, and polycystic ovaries on ultrasonography affects 5 to 10% of reproductive-age women[3] and is the most common cause of anovulatory infertility[4] and early pregnancy loss.[5] The cause of polycystic ovary syndrome is not fully understood, but evidence of a genetic component has been recognised in family and twin studies,[6] Oligo-ovulation or an ovulation in women with polycystic ovary syndrome is a major cause of infertility and such women might require ovulation induction or assisted reproductive technology to become pregnant.[7]

Our bodies make oestradiol from cholesterol through a series of chemical changes involving enzymes. Enzymes are able to make a structural change in one of the building blocks of our body. To change cholesterol to oestradiol involves about 10 chemical changes. The last chemical change involves the aromatase enzyme. Letrozole blocks the aromatase enzyme and therefore the production of oestradiol.[8]

Oestradiol does not feedback and more FSH is made The Possible advantage of letrozole is that is its half-life of 45 house (the length of time required for the body to eliminate one half of the drug). It does not buildup in the body and may avoid the negative effects of clomiphene buildup. However, even though letrozole does not block the receptors and doesn't accumulate it may cause a longer depression of oestadiol in some individuals than desired.[8] This can sometimes be avoided by prescribing the letozole earlier in the cycle.[8]

METHODOLOGY

During the period of 2012-2017 a total of 310 participants 20-35 years of age diagnosed as polycystic ovary syndrome by history, ultrasongraphic findings, blood hormone analysis and other causes of infertility were enrolled in a private hospital.

Inclusion criteria: Participants who had normal uterine cavity and sperm concentration of at least 20 million/ml of her husband were included in this study. Participants who trated hyperporolactinemia by bromocriptin, oligomenorrhea by progesterone therapy were also included in this study after completion of treatment.

Exclusion criteria: Participants who had history of taking ovulation inducing agents were excluded from the study.

All the participants were counseled about ovulation induction, letrozole therapy and its side effects. Unsuccessful pregnancy outcome was also informed as well. History of infertility and use of ovulation inducing medicine were recorded.

Participants were prescribed to take letrozole tablet (5mg) five consecutive days from the 2nd day of menstruation. They were instructed to have intercourse every alternate days from the 10th day of menstruation. They also requested to maintain diary to keep records like last menstrual period, vaginal bleeding and symptoms like nausea, vomiting, abdominal cramp, back pain, heardache and hot flush. letrozole was given for at least 6 cycles and medication discontinued when pregnancy was confirmed by viabilitw of fetus documented by ultrasonography and then they were referred for prenatal checkup.

RESULTS

A total of 310 infertile women aged 20-35 years diagnosed as polycystic ovary syndrome were enrolled in this study. Baseline characteristics of the study population has shown in Table- I.

Table-1: Clinical, radiological and laboratory findings.

Biometric features	Mean
Age (year)	25.2±5.0
BMI	30.0±6.3
Waist circumference (cm)	100.0±2.0
Ovarian volume (cm3)	
left ovary	14.8±5.2
Right ovary	13.2±4.3
Fasting blood sugar (mg/dl)	81.0±7.5
LH:FSH-ratio	>3

Participants who had normal uterine cavity and sperm concentration of at least 20 million/ml of her husband were prescribed letrozole for 6 months. Medication was discontinued when pregnancy was confirmed and participants were followed until delivery. A total of 125 (40.5%) subjects became pregnant (conceived), of them pregnancy loss was (61(19.5%), first trimester termination was 37 (11.9%) and second trimester termination was 24 (7.6%) main reasons for pregnancy loss were placenta previa, severe hypertension, LUD etc, After completion of study we found live birth was 65 (20.9%) of them singleton was 47 (15.2%) and twin was 18 (5.7) live birth rate was higher among the women whose BMI was 30 kg/m2 (Table-II).

Table-II: Outcome of the therapy.

Variable	n(%)
Conception	125(40.4)
Pregnancy loss	61 (19.5)
Live birth	65 (19.5)
Singleton	47 (15.2)
Twins	18 (5.7)
Pregnancy loss	
First trimester	37 (11.9)
Second trimester termination	24(7.6)

Several adverse effects of letrozole was found in the study cases. Among them nausea as found in majority of the cases 74 (23.8). Most of the events were also found in normal pregnancy i, e nausea, vomiting, headache etc. All of them were subsequently controlled with advancement of pregnancy. One patient had hemorrhagic corpus luteum cyst was treated by laparotomy and cystectomy, 2 cases treated by laparotomy and cystectomy, 2 cases treated for severe back pain. Serious adverse event before birth were pregnancy loss after 12 weeks of gestation, preeclampsia, preterm delivery, antipartum haemorrhage, premature rupture of memebrance. All above pregnancy complications/ adverse effects of letrozole were treated accordingly (Table III).

Table III: Adverse effects of letrozole.

Adverse effects	n(%)
Serious Adverse effects	
Hemorrhagic corpus luteum cyst	1(0.4)
Back pain	3(0.9)
Other adverse effects	
Nausea	74(23.8)
Stomach discomfort	4 (1.4)
Vomiting	15 (4.7)
Back pain	3 (0.9)
Headache	18 (5.7)
Hot Flashes	22 (7.1)
Adnexal pain	3 (0.9)
Mild preeclampsia	15 (4.7)

DISCUSSION

In our study, we found mean age of the study women was almost similar to other studies.[5,10] Mean BMI was lower comparing other studies but the mean fasting blood glucose was similar to the study and ovarian volume was little higher comparing other study.[5]

In our study live birth was 65 (20.9) which indicates letrozole works better in polycystic ovaries to ovulate and have conception. It is safe and less costly treatment that couple can enter into trial before having in vitro fertilization[3] Singleton live birth rate was lower in our study comparing other study 10.

BMI 30kg/m^2 showed increased live birth rate with letrozole therapy 11.12 Rate of pregnancy loss was higher 61 (19.52%) in the study ndue to inclusion of obese and elder woman.[5]

In our study pregnancy outcome was lower comparing other studies.[5-10] The reason of lower pregnancy outcome may be due to lack of confirmation of fallopian tube patency.

CONCLUSION

Use of letrozole may be considered as the best alternative of clomiphene citarate for the infertility treatment in women with the polycystic ovary syndrome due to its following benefits such as higher ovulation and pregnancy rate, lower rate of multiple pregnancies, less harmful effect on cervical mucus and endometrial and lower miscarriage rate.

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