Use of Clomiphene for Infertility in the Polycystic Ovary Syndrome

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Abstract

Background : The polycystic ovary syndrome is a common cause of infertility. Clomiphene is the current first-line infertility treatment in women with the polycystic ovary syndrome.

Objective : To observed effect of clomiphene therapy in infertile women with polycystic ovary syndrome.

Methodology : In this cross-sectional study we enrolled 210 infertile women aged 25 – 35 years diagnosed as polycystic ovary syndrome. Participants who had normal urine cavity and sperm concentration of at least 20 million/ml of her husband were prescribed clomiphene for 6 months. Medication was discontinued when pregnancy was confirmed and participants were followed until delivery.

Results : After 6 months treatment 85(40.5%) patient was conceived. Live birth was 44(20.9%) of 210 subjects. Among pregnancies multiple (twin) birth was 12(5.7%). First trimester pregnancy loss was 41(19.5%). After having 6 months of therapy there was no pregnancy in125 (59.5%) patients.

Conclusions : Clomiphene is safe and cost effective medicine in achieving live birth in infertile women with polycystic ovary syndrome.

Key words : Clomiphene, polycystic ovary syndrome, infertility.

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Introduction

Polycystic ovary syndrome is one of the most common endocrine disorders, affecting about 5-15% of women of reproductive age.[1,2] The polycystic ovary syndrome, which is diagnosed on the basis of hyperandrogenism, oligo-ovulation 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 anovulation 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] Although the syndrome is a complex reproductive metabolic disorder, the hypothalamic pituitary axis has been the target of first-line ovulation induction therapy. Clomiphene citrate, a selective estrogen-receptor modulator that antagonizes the negative feedback of estrogen at the hypothalamus with a consequent increase in ovarian stimulation by endogenous gonadotropin, has been used for this indication for decades. Along with its advantages it has drawbacks as well, low live birth rate[5], a relatively high multiple pregnancy rate and an undesirable side-effect profile, including mood changes and hot flushes.[5] Serious adverse event of this medicine is haemorrhagic corpus luteum cyst, hyper sensitivity reaction, back pain. Serious adverse events before birth were pregnancy loss after 12 weeks, ectopic pregnancy and preterm labour.

Methods

During the period of 2009 – 2013, a total of 210 participants 25 –35 years of age diagnosed as polycystic ovary syndrome by history, ultrasonographic findings, blood hormone analysis and other causes of infertility were enrolled in a private hospital. Participants who had normal urine cavity and sperm concentration of at least 20 million/ml of her husband were included in this study. Participants who treated hyperprolactinemia by bromocriptin, oligomenorrhea by progesterone therapy were also included in this study after completion of treatment. Participants who had history of taking ovulation inducing agents were excluded from the study. All the participants were

counseled about ovulation induction, clomiphene 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 clomiphene citrate tablet (5mg) five consecutive days from the 3rd day of menstruation. They were instructed to have intercourse every 2 to 3 days from the 6th day after completion of 5 days medication. They also requested to maintain diary to keep records like last menstrual period, vaginal bleeding and symptoms like nausea, vomiting, abdominal cramp, back pain, headache and hot flush. Clomiphene citrate was given for at least 6 cycles and medication discontinued when pregnancy was confirmed by viability of fetus documented by ultrasonography and then they were referred for prenatal cheek up.[8]

Results

A total of 210 infertile women aged 25 – 35 years diagnosed as polycystic ovary syndrome were enrolled in this study. Baseline characteristics of the study population has shown in Table-1.

Table – I : Clinical, radiological and laboratory findings

Biometric features	Mean
Age (year)	26.3 ± 4.0
BMI	30.0 ± 7.2
Waist circumference (cm)	101.0 ± 2.0
Ovarian volume (cm^3)	
Left ovary	14.9 ± 5.2
Right ovary	12.2 ± 4.3
Fasting blood sugar (mg/dl)	82.0 ± 7.6
LH: FSH- ratio	> 3

Participants who had normal urine cavity and sperm concentration of at least 20 million/ml of her husband were prescribed clomiphene for 6 months. Medication was discontinued when pregnancy was confirmed and participants were followed until delivery. A total of 85 (40.5%) subjects became pregnant (conceived), of them pregnancy loss was 41 (19.5%), first trimester termination was 25 (11.9%) and second trimester termination was 16 (7.6%). Main reasons for pregnancy loss were placenta previa, severe hypertension.IUD etc. After completion of study we found live birth was 44 (20.9%), of them singleton was 32 (15.2%) and twin was 12 (5.7). Live birth rate was higher among the women whose BMI was <30 kg/m^2. (Table-2)

Table –II: Outcome of the therapy

Variable	n (%)
Conception	85 (40.4)
Pregnancy loss	41 (19.5)
Live birth	44 (20.9)
Singleton	32 (15.2)
Twins	12 (5.7)
Pregnancy loss	
First trimester termination	25 (11.9)
Second trimester termination	16 (7.6)

Several adverse effects of clomiphene was found in the study cases. Among them nausea was found in majority of the cases 50(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 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 membrane. All above pregnancy complications / adverse effects of clomiphene were treated accordingly (Table 3).

Table III : Adverse effects of clomiphene

Adverse effects	n (%)
Serious adverse effects	
Hemorrhagic corpus luteum cyst	1 (0.4)
Back pain	2 (0.9)
Other adverse effects	
Nausea	50 (23.8)
Stomach discomfort	3 (1.4)
Vomiting	10 (4.7)
Back pain	2 (0.9)
Headache	12 (5.7)
Hot Flashes	15 (7.1)
Adnexal pain	2 (0.9)
Mild preeclampsia	10 (4.7)

Discussion

In our study, we found mean age of the study women was almost similar to other studies.[5,9] Mean BMI was lower comparing other studies[5,9] 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 44 (20.9) which indicates clomiphene 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 fertilisation[3]. Singleton live birth rate was lower in our study comparing other study.[9]

BMI<30kg/m^2 showed increased live birth rate with clomiphene therapy.[10,11] Rate of pregnancy loss was higher 41 (19.52%) in this study due to inclusion of obese and elderly women.[5]

In our study pregnancy outcome was lower comparing other studies.[5,9] The reason of lower pregnancy outcome was due to not done hysterosalpingography to confirm fallopian tube patency.

Conclusions

Use of clomiphene is safe and cost effective medicine in achieving live birth in infertile women with polycystic ovary syndrome.

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