



A PROSPECTIVE OBSERVATIONAL COHORT STUDY ON THE EFFECT OF LAPAROSCOPIC OVARIAN DRILLING ON OVULATION RATE IN WOMEN WITH CLOMIPHENE RESISTANT POLYCYSTIC OVARIAN SYNDROME

Health Science

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ABSTRACT

Background: Laparoscopic ovarian drilling (LOD) is a surgical treatment that can stimulate ovulation in women diagnosed with polycystic ovarian syndrome (PCOS) and especially those with resistance to clomiphene citrate (CC). Our main objective was to observe the effect of LOD on ovulation rate in women with PCOS. **Methods:** The study included fifty CC resistant PCOS women between 24-38 years of age, trying for conception, with patent bilateral fallopian tubes and male factor infertility ruled out. Hormone levels including serum LH, FSH and testosterone were tested on day 2/3 of menstrual cycle before and 1 month after LOD. Patients underwent LOD in between 5th -9th day of the cycle. During the procedure each ovary was drilled using monopolar cautery of 40 W of power at 4 sites, 4mm deep, for 4 seconds. Spontaneous ovulation rate was noted by follicular monitoring done by transvaginal sonography following LOD in the next two menstrual cycles. **Results:** It was observed that serum testosterone levels reduced from 40.24 ± 10.06 ng/dl before LOD to 30.02 ± 10.85 ng/dl after LOD and 80% PCOS women ovulated after ovarian drilling (i.e., 40 out of 50 cases). 8 women conceived following LOD making the cumulative pregnancy rate of 40.28%. **Conclusions:** LOD induces ovulation in PCOS women resistant to CC due to decreasing testosterone levels as seen in this study. So prior to initiation of gonadotropin therapy for CC resistant PCOS, LOD may be used as an alternative treatment in such cases.

KEYWORDS

Ovarian drilling, laparoscopy, clomiphene resistance, PCOS, pregnancy.

INTRODUCTION:

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting 5-10% of reproductive age women and at least 75% of cases with anovulatory infertility.¹ PCOS is diagnosed based on the 2003 ESHRE (Rotterdam criteria) - 1) Clinical and biochemical evidence of increased androgen; 2) Oligomenorrhea or amenorrhea; 3) Ultrasound evidence of polycystic ovaries (20 subcortical follicles of 2-9 mm in diameter with dense stroma and/or increased ovarian volume (more than 10 ml) and ruling out other causes (congenital adrenal hyperplasia, androgen secreting tumours, Cushing syndrome).² A single ovary meeting these criteria is sufficient to affix the polycystic ovarian morphology. The presence of at least two of the three criteria is sufficient to diagnose PCOS.

Chronic anovulation is one of the leading cause of infertility. The first line drug for anovulatory infertility in PCOS is clomiphene citrate (CC), a selective oestrogen receptor modulator.³ It is typically administered in an empiric incremental fashion to identify the lowest effective dosage 50-150 mg daily for 5 days, beginning on cycle day 2 - 6.⁴ CC resistance refers to anovulation even after three cycles of ovulation induction with 150 mg of CC.³ Approximately 20% of patients prove refractory to clomiphene treatment, most of those having severe hyperandrogenism or obesity.⁵ Treatment options in CC resistant PCOS include gonadotrophins or laparoscopic ovarian drilling (LOD). However, gonadotrophins is an expensive treatment and has an additional side effects of ovarian hyperstimulation syndrome (OHSS) and multifetal pregnancy.

Ovarian drilling induces ovulation in PCOS women and especially those resistant to clomiphene citrate. Surgical therapy with LOD may reduce the need for medical ovulation induction, or may facilitate its usefulness.⁶ The present study was undertaken to observe the effect of LOD on ovulation rate in women with PCOS.

MATERIAL AND METHODS:

An observational study was conducted in the department of obstetrics and gynaecology at District Hospital Howrah from December 2020 to May 2021. A prior approval from the institutional ethical committee and informed consent was taken. 50 CC resistant PCOS women were taken as sample size. Women between 24-38 years age group, trying for conception, clinically diagnosed as CC resistant PCOS were enrolled in the study. Other inclusion criteria were normal hysterosalpingography and no male factor infertility. Hormone levels including serum LH, FSH and testosterone were tested on 2nd or 3rd day of menstrual cycle before and 1 month after LOD, which was done

in between 5th-9th day of menstrual cycle. During the procedure each ovary was drilled using monopolar cautery of 40 W power at 4 sites, 4mm deep, for 4 seconds. One month after LOD, same hormone levels were again tested on 2nd or 3rd day of menstrual cycle. Spontaneous ovulation rate was period of cases was range between 3-11 years with the mean of 6.23 ± 2.47 years. Mean waist hip circumference ratio was 0.9 ± 0.05 , which was raised.

Statistical Analysis:

Data analysis was performed using Statistics Package for Social Sciences version 18.0 (SPSS, Chicago, Illinois). Statistically significant differences were determined using Fisher's exact test, χ^2 test, unpaired Wilcoxon test, or Student's t test, as appropriate. A stepwise forward logistic regression model was used to adjust for variables known to be associated with leiomyomas (body mass index (BMI), black ethnicity, parity). A p value ≤ 0.5 was considered statistically significant.

RESULTS:

Table 1: Demographic Data Of Cases (N = 50)

Variables	Mean +/- SD
Age (Years)	26.67 +/- 2.00
BMI (kg/m ²)	29.12 +/- 2.89
Duration of infertility (years)	8.11 +/- 3.00
Waist hip circumference ratio (WC/HC)	0.8 +/- 0.01

Table 1 shows demographic data of cases. Age group of women varied from 26-38 yrs. Mean age was 26.67 ± 2.00 years and mean BMI was 29.12 ± 2.89 kg/m². Infertility period of cases was range between 4-12 years with the mean of 8.11 ± 3.00 years. Mean waist hip circumference ratio was 0.8 ± 0.01 , which was raised.

Table 2: Clinical Parameters (N = 50)

Clinical parameters	Number	Percentage
Menstrual cycle		
-Oligomenorrhea	27	54%
-Amenorrhea	10	20%
Hirsutism	14	28%
Acne	6	12%
Acanthosis Nigricans	6	12%

As shown in table 2, out of 30 cases, 27 (54%) cases had oligomenorrhea and 10 (20%) cases had amenorrhea. Hirsutism was present in 14 (28%) cases and absent in 86 (72%) cases. Acne was present in 6 (12%) cases and acanthosis was present in 6 (12%) cases.

Table 3: Hormonal Profile Pre And Post LOD (N = 30)

Hormones	Pre LOD (Mean +/- SD)	Post LOD (Mean +/- SD)	P Value
LH (IU/L)	10.46 +/- 2.89	9.67 +/- 2.78	0.218
FSH (IU/L)	8.45 +/- 1.67	6.23 +/- 1.20	0.014
LH/FSH	1.13 +/- 0.07	2.11 +/- 0.09	0.256
Testosterone (ng/dl)	50.23 +/- 12.78	40.67 +/- 12.66	0.005

Table 3 shows comparison of mean LH value before (10.46 +/- 2.89) and after LOD (9.67 +/- 2.78 IU/L), the difference was found to be statistically insignificant (p value= 0.218). Mean FSH value before LOD was 8.45 +/- 1.67 IU/L and after LOD was 6.23 +/- 1.20 IU/L. This difference was found to be statistically significant (p value= 0.014). Mean LH/ FSH value before (1.13 +/- 0.07) and after LOD (2.11 +/- 0.09) was found to be statistically insignificant (p value= 0.256). The difference between mean testosterone levels before (50.23 +/- 12.78 ng/dl) and after LOD (40.67 +/- 12.66 ng/dl) was found to be statistically significant (p value 0.005).

Table 4: Ovulation And Pregnancy Rate Post LOD

Categories	Number	Percentage
Ovulation rate (N=50)	40	80%
Pregnancy rate (N=40)	12	30%

Before LOD, all 50 cases were anovulatory (100%). Post LOD, out of 50 cases, 40 (80%) women ovulated spontaneously. However, rest 10 (20%) cases had anovulatory cycles. Total 12 women out of 40 cases conceived during the study period. Cumulative pregnancy rate after the extended follow up at 9 months after LOD was 30% (table 4)

DISCUSSION:

In our study, amongst the 50 patients with CC resistant polycystic ovaries, ovulation occurred in 40 patients (80%) 1 month after LOD. The remaining rest 20% of patients had anovulatory cycles. A study done by Amer et al in 2004 showed that among the 30 patients with CC resistant polycystic ovary, ovulation rate was 78%.⁷ This is similar to the findings seen in our study.

Poujade et al included 74 CC resistant polycystic ovary women and found conception in 47 (63%) patients but this was within 11 months after LOD.⁸ The higher cumulative conception rate in their study could be explained by a longer period of follow up. Similarly, Debras et al found that in 289 women with a mean follow-up of 28.4 months, pregnancy was obtained in at least 137 (47.4%) women after a drilling, and 71 (51.8%) of these pregnancies were spontaneous, 48 (16.6%) women achieved at least two pregnancies after drilling, and 27 (56.3%) of these were spontaneous.⁹ The predictive factors for effectiveness were a normal body mass index (BMI), an infertility period of less than three years, an AFC of less than 50, and an age of less than 35 years.

In our study the serum testosterone levels had a statistically significant reduction (p value 0.005) when compared pre LOD (50.23 +/- 12.78 ng/dl) and post LOD (40.67 +/- 12.66 ng/dl). This finding is similar to a study by Salem et al 2017 which also showed significant (p value =0.05) reduction of testosterone levels post ovarian drilling (from 2.61±1.15 pre LOD to 1.61±0.6 post LOD).¹⁰ This can be explained by destruction of androgen producing ovarian stroma during LOD. It is known that increasing serum levels of testosterone and/or increasing free androgen index (FAI) are associated with a statistically significant reduction of the chances of success of LOD. Furthermore, a subgroup of PCOS women with marked hyperandrogenism (testosterone ≥4.5 nmol/l, FAI ≥15) appeared to be resistant to LOD. Gjonjaess et al in 1994 found that women with low levels of sex hormone binding globulin (i.e. high levels of free testosterone), whether they were of normal weight or overweight, were less likely to respond to LOD.¹¹ Our study demonstrated that there was a reduction in serum testosterone levels post LOD which could have facilitated conception. The risks of LOD are ovarian adhesion formation, reduced ovarian reserve and premature ovarian failure¹²⁻¹⁴

These complications were not seen in our cases which may be because of following precautions taken during LOD: irrigation with saline after electrocautery, avoiding the tubo-ovarian junction, keeping a maximum cautery depth of 4 mm at 4 sites for 4 seconds only, using a minimum power of 40 watts and achieving adequate haemostasis. Laparoscopic treatment is increasingly being recommended as an early treatment option for women with clomiphene resistant PCOS. The reduction in serum androgen levels after LOD is reported to be the main mechanism by which reproductive outcome is improved.¹⁵ Our

study also provides support to the fact the LOD is an effective treatment modality for clomiphene resistant PCOS.

The limitation of our study was single centre study with a smaller sample size and also we have lost some cases in follow up. So we recommended further research with a larger sample size in future.

CONCLUSION:

LOD induces ovulation in PCOS women resistant to CC due to decreasing testosterone levels as seen in this study. So prior to initiation of gonadotropin therapy for CC resistant PCOS, ovarian drilling may be used as an alternative treatment in such cases.

Conflict Of Interest: None.

Disclaimer: Nil.

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