

Frequency of Pregnancy Following Laparoscopic Ovarian Drilling in Patients with Clomiphene Resistant Polycystic Ovarian Syndrome

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ABSTRACT

Aim: To study was to determine the frequency of pregnancy following laparoscopic ovarian drilling in our patients with clomiphene citrate resistant polycystic ovarian syndrome.

Methods: This case series study was carried out in the Department of Obstetrics and Gynaecology, Nishtar Hospital, Multan from January 2014 to December 2014. A total of 100 patients with clomiphene citrate resistant polycystic ovarian syndrome were included in the study.

Results: Total 5327 patients visited Gynaecology OPD during six month study period. Overall frequency of PCOS was 4.84% and among infertility cases frequency was 26.93%. Majority of cases of PCOS were in age group 20-30 years. Out of 258 cases of PCOS, 72% of cases were having primary infertility and 28% were having secondary infertility. 41.86% of cases were resistant to CC in a dose of 150 mg for three cycles. Conception rate was 66% in 6month follow up period after LOD.

Conclusion: LOD is a safe and cost effective procedure. A single treatment results in uni-follicular ovulation. No need of continuous monitoring as seen with hormonal treatment. No fear of multiple births and ovarian hyper stimulation. Correction of hormonal levels prevents miscarriages. LOD increase the sensitivity to gonadotrophins. And it is as effective as gonadotrophins in PCOS.

Keywords: Polycystic ovary syndrome, Laparoscopic ovarian drilling, Clomiphene citrate resistance.

INTRODUCTION

The problem of polycystic ovarian disease/syndrome (PCOD/PCOS) has been the subject of research studies over the past six decades. The 2003 Rotterdam consensus on diagnostic criteria for PCOS concluded that it is a syndrome of ovarian dysfunction with clinical and biochemical hyperandrogenism and polycystic ovarian morphology as its cardinal features. According to the European Society of Human Reproduction and Embryology and American Society of Reproductive Medicine (ESHRE/ASRM) criteria, different phenotypes of polycystic ovarian syndrome patients can be distinguished including both anovulatory and ovulatory women¹.

The major clinical manifestations are menstrual irregularities, signs of androgen excess, and obesity². Anovulation is a common problem in women with polycystic ovarian disease. Clomiphene citrate (CC) is accepted as the first-line treatment of choice for infertile women with polycystic ovarian disease, but 25% of the patients do not respond to CC, and remain anovulatory despite increasing doses³. Human menopausal gonadotrophins, follicle stimulating hormone, or combination of

gonadotrophin-releasing hormone agonist and gonadotrophins may be used as a second-line treatment.

However, the patients with polycystic ovarian disease treated with these hormones tend to develop a multifollicle response, with the associated risks of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancies. Polycystic ovaries may raise serum luteinizing hormone and androgen levels that can lower the rates of ovulation, fertilization, and pregnancy⁴.

Laparoscopic ovarian drilling with diathermy has been reported to be a successful method of ovulation induction for those women who do not respond to clomiphene citrate, human menopausal gonadotrophins, follicle stimulating hormone, or combination of gonadotrophin releasing hormone agonist, and gonadotrophins⁵.

Pregnancy rates of 27–73% have been reported in the literature. An improved responsiveness to clomiphene citrate or gonadotrophin may be found after surgery⁶. By the end of first year 82% had normal menses, 71.6% ovulated spontaneously 56% were pregnant. At 18 month 66% were pregnant and 78% at the end of two years. Unlike ovulation stimulation regimens, there is no increase in risk of multiple pregnancy or ovarian hyperstimulation after LOD. Pregnancies are most likely to occur within 6 months of surgery⁷.

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Bayram et al in a randomized controlled trial (RCT) have recently compared the effectiveness of an electrocautery strategy vs. ovulation induction using recombinant follicle stimulating hormone in CC-resistant patients with PCOS concluding that both strategies were similarly effective in terms of ongoing pregnancy rate but the former strategy was related to a lower risk of multiple pregnancy⁸.

Although Clomiphene citrate is the first line treatment of choice for infertile women with polycystic ovarian syndrome, a significant number of patients are resistant to this treatment. Laparoscopic ovarian drilling is more suitable in our setup. The rationale behind this study is that for the reason of low cost, reduced side effects like hyperstimulation syndrome and the ease of monitoring of the therapy of infertile women with polycystic ovaries, laparoscopic ovarian drilling with diathermy should be considered to be a preferred choice for the infertile women with history of failed response to clomiphene treatment as compared to the use of gonadotrophins.

MATERIAL AND METHODS

This case series study was carried out in the Department of Obstetrics and Gynaecology, Nishtar Hospital, Multan from January 2014 to December 2014. A total of 100 patients with clomiphene citrate resistant polycystic ovarian syndrome. Data was entered and analyzed using computer programme SPSS 10. Descriptive statistics were applied to calculate mean and standard deviation for age. Frequency and percentage for women who became pregnant post treatment was calculated. Stratification by type of infertility, age of patient was undertaken to control for the effect of these variables and difference between patients evaluated statistically using Chi Square test.

Table 4: Outcomes of treatment with LOD (n=100)

Outcome	n	Age distribution (years)			Infertility distribution	
		<20	20-30	31-35	Prim	Second
Conception rate	66(66%)	20	43	03	51	15
No conception	34(34%)	09	12	13	21	13

DISCUSSION

The Polycystic Ovarian Syndrome (PCOS) remains an incompletely understood entity that appears with regularity in the practice of most gynaecologists. The Rotterdam 2004 Consensus Workshop (Revised 2003) proposed that PCOS is a syndrome of ovarian dysfunction, and recommended that two of the following criteria should be present to establish the diagnosis: 1) chronic oligo or anovulation for more than 6 months 2) clinical and/or biochemical evidence of hyperandrogenism, and 3) polycystic ovaries in

RESULTS

Total 5327 patients visited Gynae OPD during one year study period. Out of these 258 were diagnosed to have PCOS. Majority of patients were in age group 20-30 year's i.e., 55.03%. 29.45% were in age group < 20 years and 15.50% were in age group 31-35. Oligomenorrhea were the most common presenting feature i.e., in 89.14% of cases. Hirsutism was observed in 77.13% of cases and acne in 40.31% of cases of PCOS. Out of 258 cases of PCOS, 72.09% of cases were having primary infertility and 27.90% were having secondary infertility. 258 selected patients were given CC in dose of 150mg for 5 days for three cycles. Out of 258 cases of, 108 were resistant to CC in a dose of 150 mg for three cycles and 100 cases who fulfilled inclusion and exclusion criteria were selected for LOD. Conception rate was 66% in 6month follow up period and 34% of patients did not conceive.

Table 1: Age distribution (n=100)

Age (years)	n	%age
<20	29	29
20-30	55	55
31-35	16	16

Table 2: Presenting complaints (n=100)

Clinical features	n	%age
Oligomenoeerhea	89	89
Hirsutism	77	77
Acne	40	40

Table-3: Infertility status (n=100)

Type of infertility	n	%age
Primary	72	72
Secondary	28	28.9

ultrasound. Other disorders that mimic PCOS phenotype should be excluded.

As the presenting symptoms of this group of patients is often infertility due to chronic anovulation, restoration of ovulatory function assumes paramount importance. For all those patients of PCOS who are found to be having a poor response to Clomiphene Citrate, the choice of treatment rests between medical ovulation induction using higher doses, higher stimulants like gonadotrophins or the use of laparoscopic surgical method. Potential advantages

of the surgical methods include multiple ovulatory cycles from a single treatment and elimination of the risk of Ovarian Hyperstimulation Syndrome (OHSS). Additionally, high cost and intensive monitoring associated with gonadotrophin therapy can be avoided. The objective of this study was to determine the frequency of pregnancy following laparoscopic ovarian drilling in our patients with clomiphene citrate resistant polycystic ovarian syndrome.

Table 2 is showing number of PCOS cases in six month study period. PCOS is one of the most common endocrine disorders of women in the reproductive age group, with a prevalence of 4-12%¹⁰. In various European studies, the prevalence of PCOS was 6.5-8%¹¹. Under the Rotterdam criteria, the prevalence was 11.9 ± 2.4%¹². Our study is showing a little higher frequency of PCOS (26.63%) in infertility cases but this is corresponding with study of Driscoll DA in which the incidence were estimated to be 11-26%¹³. In another study, of a total of 113 consecutive women recruited, 32(28.3%) were diagnosed as having PCOS¹⁴. Overall frequency was 4.84% in the present study.

Clomiphene citrate has been used as a first-line ovulation induction agent for over 40 years¹⁵. The majority of women who have infertility associated with chronic anovulation in this disorder ovulate in response to clomiphene citrate¹⁶. However, up to 30 percent remain anovulatory. Furthermore, of the roughly 70% who do ovulate in response to clomiphene citrate, only one-half will conceive.

The initial therapy for anovulation is clomiphene citrate (CC) but, unfortunately, ovulation is not achieved in almost 40% of PCOS. Various authors report on failure to ovulate at particular dose/cycles¹⁷. The anovulatory rate at a dose of 150 mg in the study of Branigan et al¹⁸ was 28% and 20% in Lobo's¹⁹ study. The present study showed a 41.86% anovulatory rate with 150mg/three cycles (Table 3) which is comparable with above mentioned studies. Other reported a rate as high as 72% anovulation with 100 mg cc in three cycles²⁰. In 1.10 patients who failed to conceive on clomiphene citrate (treatment started from minimum dose of 50 mg/day to 150 mg/day from day 2-6 of menstrual cycle⁷).

Table 4 is showing age distribution of PCOS cases. Majority of cases (55%) in our study were in age group 20-30 years. This is corresponding with a previous study in which 37.5% presented in age group 15-25 years, 50% were in age group 26-35 years. Only 12.5% patients presented in age group 36-44 years. In another study, the age group of the subjects varied between 20 and 38 years. Only 12.5% were more than 31 years of age. There were two subjects who were more than 35 years of age in the study group and both of them were 38 years old.

There was only one patient who was more than 35 years in the control group and she was also 38 years of age²⁰.

Table 5 is showing presenting features of patients with PCOS. Oligomenorrhea was the most common clinical finding in all subjects i.e. 89% and 77% were having hirsutism. Acne was found to be observed in 40% of cases. This is comparable with a study in which Hirsutism was the most common clinical finding in all subjects of the study group and 75% of the control group showed hirsutism of various grades. Amenorrhea was more common than oligomenorrhea occurrence of hirsutism of 85% in the present study is almost similar to that of Adams²¹.

Table 6 is indicating type of infertility in PCOS cases. Primary infertility was in 72% of cases and secondary infertility was in 28%. This in agreement with a study in which 72.8% cases were of primary infertility and secondary infertility was observed in 27.2% of cases⁷. In another study, eleven (68.75%) patients had primary infertility. Five (31.25%) patients presented with secondary infertility²¹.

Table 7 is illustrating outcome of LOD. In our study conception rate were 66% in six month study period. Which is in agreement with most of the previous studies²². After treatment and 6 months follow up, ovulation occurred in 14(87.5%) patients. Eleven (68.75%) women conceived pregnancy. In another International study between June 1996 and June 2003, there were 182 pregnancies in 153 PCOS patients who were treated with laparoscopic ovarian drilling²³.

CONCLUSION

LOD is a safe and cost effective procedure. A single treatment results in unifollicular ovulation. No need of continuous monitoring as seen with hormonal treatment. No fear of multiple births and ovarian hyper stimulation. Correction of hormonal levels prevents miscarriages.

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