

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

SYED MUHAMMAD ALI¹, SOBIA MAZHAR², SAJJAD MASOOD³

ABSTRACT

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

Methods: This study was carried out in the Department of Obstetrics and Gynaecology Multan Medical & Dental College, Multan from November 2012 to May 2013. One hundred eligible patients who suffer from anovulatory infertility and who failed to respond to the treatment with clomiphene citrate were enrolled from outpatient department.

Results: Overall frequency of PCOS was 4.84%. Majority of cases of PCOS were in age group 20-30 years. 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: 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.

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 major clinical manifestations are menstrual irregularities, signs of androgen excess, and obesity¹. 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 doses². Human menopausal gonadotropins, follicle stimulating hormone, or combination of gonadotropin-releasing hormone agonist and gonadotropins may be used as a second-line treatment.

However, the patients treated with these hormones tend to develop a multifollicle response, with the associated risks of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancies. 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

gonadotropins, follicle stimulating hormone, or combination of gonadotropin releasing hormone agonist, and gonadotropins³. Pregnancy rates of 27 – 73% have been reported in the literature. 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 surgery⁴.

The objective of this study was to determine the frequency of pregnancy following laparoscopic ovarian drilling in patients with clomiphene citrate resistant polycystic ovarian syndrome.

MATERIAL AND METHODS

This study was carried out in the Department of Obstetrics and Gynaecology Multan Medical & Dental College, Multan from November 2012 to May 2013. One hundred eligible patients who suffer from anovulatory infertility and who failed to respond to the treatment with clomiphene citrate were enrolled from outpatient department. Laparoscopy was performed via three ports of entry. A 10 mm laparoscope was inserted in the primary sub-umbilical trocar with two additional 5 mm trocars in the lower abdomen. A grasping forceps was used to hold the ovarian ligament for manipulation of the ovary; the diathermy needle was introduced via the other secondary port. Four to six holes was made in the ovarian capsule

¹Associate Professor, DG Khan Medical College,

²Associate Professor

³Senior Medical Officer smashmultan@yahoo.com (03216174488)
Correspondence to Dr. Sajjad Masood, House 80, Lane 4, Askaria Colony Sher Shah Road Multan Telephone No: 0333-8400603, 0616539875 Email: drsajjad131@yahoo.com

with a unipolar coagulation current at a power of 40 watts for 4 seconds. Then the pregnancy was recorded (defined by positive urine hCG and the presence of an intrauterine pregnancy verified by a vaginal ultrasound) during 6 months follow up without the use of any additional ovulatory agents. Data was entered and analyzed using computer programme SPSS 10.

RESULTS

Total 5327 patients visited Gynae OPD during one year study period i.e. from 22-2-2008 to 22-10-2008 and 1-2-2009 to 31-5-2009. Out of these 258 were diagnosed to have PCOS. Majority of patients were in age group 20-30 year's i.e. 55.03%. 29.4% were in age group <20 years and 15.5% were in age group 31-35. Oligomenorrhea were the most common presenting feature i.e., in 89.1%of cases. Hirsutism were observed in 77.1% of cases and acne in 40.3% 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 patient's 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: Number of clomiphene resistant cases (n=258)

Clomiphene resistance	n	%age
PCOS cases	258	-
Clomiphene resistant cases	108	41.86%

Out of 258 cases of PCOS, 41.86% were resistant to CC in a dose of 150 mg for three cycles. Among 108 CC resistant cases, 100 were selected for LOD. Majority of patients (55%) were in age group 20-30 years

Table 2: Distribution according to age (n=100)

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

Table 3: Distribution according to presenting complains (n=100)

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

Oligomenorrhea were the most common presenting feature i.e. in 89%of cases.

Table 4: Distribution according to infertility status(n=100)

Type of infertility	n	%age
Primary Infertility		
Secondary Infertility		

Out of 100 cases of PCOS, Majority of cases (72%) were having primary infertility.

Table 5: Outcomes of treatment with lod (n=100)

Outcome of the treatment	n	Distribution according to age in years			Distribution according to Infertility status	
		<20	20-30	31-35	Primary infertility	Secondary infertility
Conception rate	66 (66%)	20	43	3	51	15
No conception	34 (34%)	09	12	13	21	13

100 were selected for LOD. Conception rate was 66% in 6 month follow up period.

DISCUSSION

The Polycystic Ovarian Syndrome (PCOS) remains an incompletely understood entity that appears with regularity in the practice of most gynaecologists. 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 gonadotropin 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%. In various European studies, the prevalence of PCOS was 6.5-8%. Under the Rotterdam criteria, the prevalence was 11.9 ± 2.4%. 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 %. In another study, of a total of 113 consecutive

women recruited, 32(28.3%) were diagnosed as having PCOS. Overall frequency was 4.84% in the present study.

Clomiphene citrate has been used as a first-line ovulation induction agent for over 40 years¹⁰. The majority of women who have infertility associated with chronic anovulation in this disorder ovulate in response to clomiphene citrate¹¹. However, up to 30 percent remain anovulatory. Furthermore, of the roughly 70 percent 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/cycles¹². The anovulatory rate at a dose of 150mg in the study of Branigan et al¹³ was 28% and 20% in Lobo's¹⁴ study. The present study showed a 41.86% anovulatory rate with 150mg/three cycles (Table 3) which is comparable with above mentioned studies. Other¹⁵ reported a rate as high as 72% anovulation with 100mg cc in three cycles. 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 cycle

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, 50.0% 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 age.

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 Adams.

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 cases. In another study, eleven (68.75%)

patients had primary infertility. Five (31.25%) patients presented with secondary infertility.

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 studies. Armar & Lachelin reported pregnancy rate of 66%¹⁷, Abdel Gadir 48%, Gjönaess 66%, Naether et al 70%¹⁸, Li et al 54%. 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 drilling¹⁹.

CONCLUSION

It can be concluded that laparoscopic ovarian drilling of ovaries increases the chances of ovulation and conception. 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. Patients who fail to ovulate after laparoscopic ovarian drilling and clomiphene citrate can still be treated with gonadotrophins, before proceeding to the costly and burdensome procedure of in vitro fertilisation and embryo transfer.

REFERENCES

1. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril* 2004;81:19-25.
2. Tulandi T, Watkin K, Tan SL. Reproductive performance and three-dimensional ultrasound volume determination of polycystic ovaries following laparoscopic ovarian drilling. *Int J Fertil* 1997;42:436-40
3. Balen AH, Jacobs HS. A prospective study comparing unilateral and bilateral laparoscopic ovarian diathermy in women with polycystic ovarian syndrome. *Fertil Steril* 1994;62:921-5.
4. Zafar MF, Chye NGS. Ovarian Drilling for Clomiphene Citrate Resistant Polycystic Ovarian Disease *Ann King Edward Med Coll* 2001;7:88-9.
5. Azziz R, Woods KS, Reyna R, et al. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J Clin Endocrinol Metab* 2004;89:2745-9.
6. Asuncion M, Calvo RM, San Millan JL et al. A prospective study of the prevalence of the polycystic

- ovary syndrome in unselected Caucasian women from Spain. *J Clin Endocrinol Metab* 2000;85:2434-8
7. March WA, Moore VM, Kristyn J. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. *Human Reproduction* 2010;25:544-51
 8. Driscoll DA. Polycystic ovary syndrome in adolescence. *Ann New York Acad Sci* 2003;997:49-55
 9. Alvarez-Blasco F, Jose I, Botella-Carretero JI, San Millan JL, Hector F, Morreale E. Prevalence and Characteristics of the Polycystic Ovary Syndrome in Overweight and Obese Women. *Arch Intern Med*. 2006;166:2081-6
 10. Kafy S, Tulandi T. New advances in ovulation induction. *Curr Opin Obstet Gynecol* 2007;19:248-52.
 11. Amer SA, Li TC, Metwally M. Randomized controlled trial comparing laparoscopic ovarian diathermy with clomiphene citrate as a first-line method of ovulation induction in women with polycystic ovary syndrome. *Hum Reprod* 2009;24:219-25
 12. George SS, George K, Irwin C. Sequential treatment of metformin and CC in clomiphene resistant women with polycystic ovary syndrome - A randomized controlled trial. *Hum Reprod* 2003;18:299-304
 13. Branigan EF, Estes MA. Treatment of chronic anovulation resistant to clomiphene citrate (CC) by using oral contraceptive ovarian suppression followed by repeat CC treatment. *Fertil Steril* 1999;71:544-6.
 14. Lobo RA, Gysler M, March CM, Goebelsmann U, Mishell DR Jr. Clinical and laboratory predictors of clomiphene response. *Fertil Steril* 1982;37:168-74
 15. Gysler M, March CM, Mishell DR Jr, Bailey EJ. A decade's experience with an individualized clomiphene treatment regimen including its effect on the postcoital test. *Fertil Steril* 1982;37:161-7.
 16. Dasari P, Pranahita GK. The efficacy of metformin and clomiphene citrate combination compared with clomiphene citrate alone for ovulation induction in infertile patients with PCOS. *J Hum Reprod Sci* 2009;2:18-22
 17. Armar NA and Lachelin GC. Laparoscopic ovarian diathermy: an effective treatment for anti-oestrogen resistant anovulatory infertility in women with the polycystic ovary syndrome. *Br J Obstet Gynaecol* 1993;100:161-64.
 18. Naether OGJ, Baukloh V, Fischer R and Kowalczyk T (1994) Long-term follow-up in 206 infertility patients with polycystic ovarian syndrome after laparoscopic electrocautery of the ovarian surface. *Hum Reprod* 1994;9:2342-49.
 19. Al-Ojaimi EH. Pregnancy outcome after laparoscopic ovarian drilling in women with polycystic ovarian syndrome. *Saudi Med J* 2006;27:519-25.