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Original Research Article

Clinical outcome of unilateral versus bilateral laparoscopic ovarian drilling in clomiphene citrate resistant cases of polycystic ovarian syndrome: a comparative study

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ABSTRACT

Background: The aim of the current study is to compare the efficacy of laparoscopic unilateral ovarian drilling with bilateral ovarian drilling in clomiphene citrate resistant cases of polycystic ovarian syndrome in terms of clinical response, change in biochemical parameters, ovulation rate, pregnancy rate and miscarriage rate.

Methods: The study was conducted on 45 women with anovulatory infertility due to PCOS with clomiphene citrate resistance. By random selection, all patients were divided in two groups. In group 1, unilateral ovarian drilling was done and in group 2, bilateral ovarian drilling was done. A maximum of 5 drills were performed using insulated unipolar diathermy needle. Patients were followed up for one year and the clinical outcome in two groups were recorded and compared.

Results: Post ovarian drilling it was seen that no major differences were noted between the two groups in return of spontaneous menstruation at 6 weeks (65% vs 60%), overall ovulation rate (55% vs 65%) and pregnancy rate (45% vs 40%). The mean fall in serum LH, serum FSH and serum testosterone were also similar in the two groups.

Conclusions: Unilateral laparoscopic ovarian drilling had similar efficacy as bilateral laparoscopic ovarian drilling in terms of restoration of normal menstrual pattern, ovulation and achieving pregnancy. It is an effective alternative minimally invasive procedure for patients with resistant PCOS.

Keywords: Bilateral, Clomiphene citrate resistance, Laparoscopic ovarian drilling, PCOS, Unilateral

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders among females of reproductive age. It is the leading cause of infertility due to anovulation.¹ Clomiphene citrate is the standard first line drug for induction of ovulation in these patients. The ovulation rate with this drug is 80%.² However, 15-20% of women still remain anovulatory despite treatment with an incremental dose of clomiphene citrate.³

Furthermore, there is discrepancy between ovulation rate and conception rate. The miscarriage rate is also high.

Women who are resistant to clomiphene citrate can be treated with gonadotropins. However, these are high-priced option and require intensive monitoring which can be demanding both for the patient and the clinicians. Ovarian hyperstimulation, multiple pregnancy and high miscarriage rate remains the significant risk.^{4,5}

Laparoscopic ovarian drilling (LOD) was first introduced by Gjoannaess in 1984.⁶ Since then it has been used as an alternative minimally invasive procedure in patients who are refractory to conventional treatment. LOD does not lead to ovarian hyperstimulation and it even corrects the hormonal imbalance associated in PCOS patients. It is a

cost effective procedure which results in good ovulation rates with less monitoring and decreased incidence of multiple pregnancy.

This procedure is associated at times with ovarian damage and risk of adhesion formation.^{7,8} Hence the idea of laparoscopic ovarian drilling of one ovary rather than both the ovaries was first proposed by Ballen et al.⁹ Unilateral ovarian drilling has been shown to have similar benefits with minimal ovarian damage or the risk for tubo ovarian adhesions.

A prospective study was conducted to compare the clinical outcome of unilateral versus bilateral laparoscopic ovarian drilling in clomiphene citrate resistant cases of PCOS.

METHODS

The current prospective study was conducted in Deen Dayal Upadhyay Hospital, New Delhi from Dec 2013-June 2015. A total of 45 women presenting with anovulatory infertility were enrolled in the study. All the women were diagnosed as PCOS on basis of Rotterdam's 2003 criteria and were resistant to clomiphene citrate treatment.¹⁰

Clomiphene citrate resistance was defined as persistent anovulation in patients despite receiving maximum dose of 150 mg clomiphene citrate for 5 days starting from third day of menstrual cycle.^{1,3} All women had normal hysterosalpingography, serum prolactin levels and serum TSH levels. Their partners' semen analysis was normal. Women with any other cause of infertility were excluded from the study.

A written informed consent was taken from each woman. By simple random selection, all patients were divided in two groups. Group 1 had 23 patients and group 2 had 22 patients. In group 1, unilateral ovarian drilling was done and in group 2, bilateral ovarian drilling was done. During laparoscopy uterus and adnexa were inspected and bilateral chromopertubation performed to check tubal patency. In ovaries which were enlarged, thick, pearly white and showing signs of PCOS drilling was carried out. Unipolar current of 40 W was used, capsule penetrated to depth of 5mm to drill a maximum of five holes. Ovarian surface was then cooled by irrigation with normal saline to minimize adhesion formation.

Women were asked to keep a record of their menstrual cycle. They were asked to report on day one of their first menstruation. Serum LH, FSH and Testosterone was measured on day 2 and ovulation was assessed by serial ultrasonography.

Patients were followed up for one year. Menstrual cycle and ovulation was assessed at three month, six month and one year. Ovulation rate, pregnancy rate and miscarriage rate in two groups were recorded and compared.

Statistical analysis

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Nominal categorical data between the groups were compared using Chi-square test or Fisher's exact test as appropriate whereas continuous variables by using student's t test. $P < 0.05$ was considered as statistically significant.

RESULTS

Of the total 45 patients recruited for the study 3 patients in group 1 and 2 patients in group 2 were lost to follow up.

The patients were compared in terms of demographic variables, clinical and biochemical characteristics as shown in Table 1. The average age of patients in both the groups was found to be 27 years.

The duration of marriage in both the groups was same with a mean duration of 4 years. Majority of the patients had only elementary education. 65% of the patient in group 1 and 55% of the patient in group 2 were having irregular menstrual cycle and 35% in group 1 and 45% in group 2 were having oligomenorrhoea. Both groups were comparable. 50% of patients in group 1 and 65% in group 2 had their BMI >30 .

Table 1: Baseline characteristics of study group.

Characteristics	Unilateral/Bilateral		P Value
	Group 1	Group 2	
Age years	27 (25-28)	27 (25.25-28.75)	0.956
Married life years	4.0 (2.63-5.38)	4.0 (3.13-5.0)	0.511
Education status			
Elementary	60%	50%	0.425
High school	35%	50%	
Socio economic status			
Low	45%	40%	0.288
Upper middle	45%	60%	
Lower middle	10%	0%	
Menstrual cycle history			
Irregular	65%	55%	0.519
Oligomenorrhoea	35%	45%	
BMI			
<30	50%	35%	0.343
>30	50%	65%	
Preoperative S. LH (IU/ml)	8.44±4.07	9.60±4.54	0.156
Preoperative S. FSH (IU/ml)	7.18±2.71	6.87±0.90	0.465
Preoperative S. testosterone (pg/ml)	2.21±0.12	2.26±0.14	0.156

Preoperatively raised levels of serum LH was seen in both groups, 8.44 ± 4.07 IU/ml in group 1 and 9.60 ± 4.54 IU/ml in group 2. Serum FSH and serum testosterone level were also slightly raised. Serum FSH was found to be 7.18 ± 2.71 IU/ml in group 1 and 6.87 ± 0.90 IU/ml in group 2 and serum testosterone was found to be 2.12 ± 0.12 pg/ml in group 1 and 2.26 ± 0.14 pg/ml in group 2. After laparoscopic ovarian drilling, serum LH was found to be significantly decreased. Also, slight decrease was noted in serum FSH and serum testosterone levels.

Post operatively on day 2 of menstrual cycle serum LH level was found to be 6.01 ± 0.83 IU/ml in group 1 and 5.95 ± 0.64 IU/ml in group 2 (p value 0.525). Serum FSH and serum testosterone was found to be 5.86 ± 0.92 IU/ml and 2.12 ± 0.11 pg/ml in group 1 and 5.91 ± 0.94 IU/ml and 2.12 ± 0.11 pg/ml in group 2, respectively (p value 0.925 and 0.922)

The mean fall in serum FSH in group 1 is 1.33 ± 2.46 IU/ml and in group 2 is 0.97 ± 0.73 IU/ml, with p value 0.882. The mean fall in serum LH in group 1 is 2.43 ± 3.77 IU/ml and in group 2 is 3.65 ± 4.72 IU/ml, with p value 0.304. This data shows no significant statistical difference in two groups. The mean fall in serum testosterone in group 1 is 0.09 ± 0.04 and in group 2 is 0.14 ± 0.07 , which shows the fall in serum testosterone is slightly higher in group 2 (p value 0.010).

Table 2: Clinical outcome of laparoscopic ovarian drilling.

	Unilateral/Bilateral		P value
	Group 1	Group 2	
Menstrual cycle			
Regular	8 (40%)	8 (40%)	1.000
Oligomenorrhoea	3 (15%)	4 (20%)	0.727
Amenorrhoea	9 (45%)	8 (40%)	0.749
Ovulation rate			
Spontaneous	8 (40%)	8 (40%)	1.000
Induced	3 (15%)	5 (25%)	0.695
Pregnancy Rate	9 (45%)	8 (40%)	0.749
Miscarriage Rate	0 (0%)	2 (10%)	0.487

After laparoscopic ovarian drilling, 65% of women in group 1 and 60% of women in group 2 had spontaneous menstruation within 6 weeks. For remaining women tablet medroxy progesterone acetate 10 mg twice for 5 days was used to induce menstruation. Menstrual cycle pattern was studied over a year. In group 1, 40% women had regular menstrual cycle, 15% women had oligomenorrhoea and 45% had amenorrhoea. In group 2, 40% women had regular menstrual cycle, 20% women had oligomenorrhoea and 40% women had amenorrhoea. This data shows statistically no difference in two groups.

The overall ovulation rate in group 1 was 55% and 65% in group 2 out of which spontaneous ovulation was noted in 40% of women in both the groups. We have also found 45% women got pregnant in group 1 and 40%

women in group 2. Of the 17 women who got pregnant, 10 women became pregnant within first six months of ovarian drilling. 2 women in group 2 had miscarriage. Clinical outcome after ovarian drilling is summarised in Table 2.

Current study shows, no statistically significant difference after unilateral and bilateral ovarian drilling in overall clinical response, ovulation rate, change in biochemical parameters, pregnancy rate and miscarriage rate.

DISCUSSION

Treating infertile women with PCOS resistant to clomiphene citrate is a difficult task. Laparoscopic ovarian drilling is a very promising procedure for anovulatory women with PCOS resistant to clomiphene citrate. It destroys the excessive androgen producing ovarian tissue and restores back the normal hormonal milieu of the ovary. Periovarian adhesions and damage to ovarian tissue is a major potential side effect in these patients. In the past wedge resection of ovary for treatment of PCOS did show reduction in LH levels but with side effects.¹¹ With the advent of laparoscopy and ovarian drilling side effect of ovarian tissue damage has been reduced. Ballen et al suggested laparoscopic drilling of a single ovary instead of both to further minimise these complications.⁹ They demonstrated that unilateral ovarian drilling corrects abnormal ovarian feedback and leads to ovarian activity in both the ovaries.

Youssef et al evaluated 87 patients with ovulation failure as a result of PCOS who were randomly allocated to unilateral ovarian drilling (n=43) and bilateral ovarian drilling (n=44).¹² They found that ovulation, pregnancy and miscarriage rates were similar in both the groups as was the fall in serum LH levels.

Roy et al in evaluated the effect of unilateral versus bilateral ovarian drilling in 22 patients in each group.¹³ They compared ovulation and pregnancy rates and even evaluated tubo-ovarian adhesion rates during caesarean section or a second look laparoscopy. 72.7% of the patient had regular menstrual cycle with unilateral drilling and 81.8% of patient had regular cycle with bilateral drilling. There was no significant difference between two groups in ovulation and pregnancy rates and tuboovarian adhesions. Abdelhafeez et al also reported that unilateral ovarian drilling is as effective as bilateral ovarian drilling in women with PCOS.¹⁴

Sunj et al said that by using less thermal energy in volume adjusted unilateral ovarian drilling compared to bilateral ovarian drilling improved results can be obtained.¹⁵

Sourouzi et al, after performing LOD, have found significant decrease in serum levels of LH and testosterone that were similar in unilateral ovarian

drilling and bilateral ovarian drilling group.¹⁶ In the current study, we have compared unilateral versus bilateral laparoscopic ovarian drilling in patients with clomiphene resistant PCOS for one year.

After unilateral laparoscopic ovarian drilling 40% of women had spontaneous ovulation, 15% had induced ovulation and after bilateral ovarian drilling 40% of the women had spontaneous ovulation, 25% had induced ovulation. This was similar to study conducted by Roy KK who found 36.3% spontaneous, 27.2% induced ovulation in unilateral ovarian drilling and 45.5% spontaneous and 18.2% induced ovulation in bilateral ovarian drilling. They had followed women for a year. But less than Sorouzi which had 60% spontaneous and 24.4% induced ovulation in unilateral ovarian drilling and 64.4% spontaneous and 24.4% induced ovulation in bilateral ovarian drilling. They had followed women for 6 months.

LOD has been associated with reduction of basal serum LH levels, a finding in previous and current studies. High basal serum LH has been linked to clomiphene citrate resistance in women with PCOS. Reduction in basal serum LH was known to be a marker of good response to LOD. In current study, there was slightly more fall in serum LH levels (3.65 ± 4.72 IU/ml) after bilateral LOD as compared to (2.43 ± 3.77 IU/ml) fall after unilateral LOD. But this difference is statistically insignificant in both the groups.

In present study there was also decrease in basal serum testosterone levels which was slightly more after bilateral laparoscopic ovarian drilling (0.14 ± 0.07 pg/ml) as compared to (0.09 ± 0.04 pg/ml) after unilateral laparoscopic ovarian drilling.

The study suggests that unilateral laparoscopic ovarian drilling seems to be equally efficacious as bilateral ovarian drilling in restoration of normal menstrual pattern. Not only does laparoscopic ovarian drilling produce high ovulation rates, but it also corrects the endocrine abnormalities associated with the syndrome. Benefits of laparoscopic ovarian drilling include the eliminated risk of cycle monitoring and low risk of multiple pregnancies and hyperstimulation. Furthermore, some clomiphene citrate resistant women respond once again to clomiphene citrate after laparoscopic electrocautery.

Unilateral drilling and fewer numbers of punctures on ovary reduce the risk of periovarian adhesion and premature ovarian failure. The rate of periovarian adhesion is different in various studies. Greater the damage to ovarian tissue higher the risk of adhesion formation.^{16,17} For the impact of LOD on ovarian reserve API has conducted a systemic review in 2009 and concluded that no solid evidence of a diminished ovarian reserve or premature ovarian failure was associated with LOD over years and the risk is just theoretical.¹⁸

CONCLUSION

In conclusion, unilateral laparoscopic ovarian drilling had similar efficacy as bilateral laparoscopic ovarian drilling. It helps in return of normal menstrual cycle, ovulation and thus achieves pregnancy. It can be recommended as a first line of treatment in few selected cases of anovulatory infertility.

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