

PCOS - Induction of Ovulation by Laparoscopic Needle Puncture of Ovarian Follicles (LPOF)

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Summary

Twenty percent cases of PCOS are resistant to medical induction of ovulation. Laparoscopic needle puncture of ovarian follicles (LPOF) has been designed to induce ovulation in such cases. Fifty two cases of infertility who were diagnosed to have resistant polycystic ovary syndrome (PCOS) were recruited for laparoscopy guided needle puncture of ovarian follicles (LPOF). After treatment, 19 (50%) patients could develop the leading follicle of ≥ 18 mm, though only 16 (42.1%) showed an evidence of ovulation. Of 16 patients who ovulated, 14 (87.5%) had the leading follicle size of ≥ 18 mm whereas only 2 (12.5%) did not have large (≥ 18 mm) leading follicle. Ovulation was observed in 28.5% (6/21) patients who received CC 50mg, 57% (4/7) patients who received CC 100mg and 60% (6/10) patients who received CC 100mg & HMG. In 4 patients ovulation occurred within two months, while in 11 patients it was seen within 2-4 months. Three (19%) patients conceived within 6 months of follow up. However, much better results are reported by other workers using different operative techniques.

93.7% of ovulation occurred within 4 months of punctures. This supports the fact that effect of surgery is maximum within first 4-6 months.

Objective: to study the effect of LPOF on ovulation induction in resistant polycystic ovarian syndrome (PCOS)

Introduction

The polycystic ovary syndrome (PCOS) is one of the most common and complicated endocrine disorders as well as the commonest cause of anovulatory infertility. It has been realized that this condition of polycystic ovaries is not an ovarian disease alone but a disease associated with gross disturbance of lipid and carbohydrate metabolism.

Chronic anovulation is the major underlying problem that presents in a variety of clinical manifestations like irregular menstrual cycles, infertility, hyperandrogenemia and hyperinsulinemia. The association of 20% (Balen, 1998) of PCOS with resistance to the medical induction of ovulation has expanded the treatment approach with newer modalities.

Laparoscopic needle puncture of ovarian

follicles (LPOF) has been designed to induce ovulation and has the potential advantage of reduced risks of ovarian hyperstimulation, multiple gestation and miscarriage.

Materials & Methods

This study was done over a period of two years from October 1997 to September 1999. Fifty two cases of infertility who were diagnosed to have resistant polycystic ovary syndrome (PCOS) were recruited for laparoscopy guided needle puncture of ovarian follicle (LPOF).

1. Inclusion Criteria

Patients diagnosed to have resistant PCOS i.e. those who had no evidence of ovulation after treatment with either of the following:

- 1) Clomiphene citrate (CC) 100 mg daily from Day 5-10

- for at least 3 cycles.
- 2) Combined therapy with CC (100mg daily from D -D) and human menopausal gonadotropins (HMG) 75 IU intramuscularly from D - D for at least 3 cycles.

2. Exclusion Criteria

- 1) Other infertility factors such as cervical and tubal block, endometriosis, hyperprolactinemia, hypo or hyperthyroidism, genital tract anomaly, and male infertility.
- 2) Abnormal blood sugar levels (FBS > 105 mg/dl or 2 hour GII blood sugar value > 140mg/dl).
- 3) Abnormal testosterone levels (> 3 ng/dl).
- 4) Body mass index > 28 kg /m².

3. Pre-operative intervention:

- 1) The basal (day 2) hormonal profile (LH, FSH, E₂, T₃, T₄, and TSH) was done.
- 2) The transvaginal sonographic examination was performed to look for the presence of necklace pattern of follicles and hyperchogenic ovarian stroma. Also the maximum endometrial thickness and the leading follicular size of > 18mm obtained on day 11-14 during follicular imaging of the previous treatment cycles were noted.
- 3) Blood sugar levels were determined either by doing fasting blood sugar (FBS) or by doing glucose tolerance test (GII).

4. Procedure of I POE

All the patients primarily underwent diagnostic laparoscopy and chromopertubation (CT) followed by laparoscopy guided needle puncture of ovarian follicles. The ovarian ligament was held by the grasping forceps and the ovary was stabilized.

Now, 8-10 punctures, about 5mm deep were made over the surface of each ovary. The punctured ovarian sites were allowed to drain out androgen rich follicular fluid. The punctured ovaries were irrigated thoroughly with ringer lactate by using suction irrigation pump.

5. Post I POE follow up

- 1) On day - 2 of the menstrual cycle LH and FSH levels were done.
- 2) All patients had ovulation induction with clomiphene citrate 50mg (D -D).
- 3) The follicular growth monitoring was performed for number and size of follicles.
- 4) Inj human chorionic gonadotrophin (hCG) 5000 IU intramuscularly was administered once the leading follicle was of 18 mm in size.
- 5) Intrauterine insemination (IUI) was performed 24-48 hours later, around ovulation, which was confirmed by IVS.
- 6) If there was no conception, then the next cycle was also induced with either clomiphene citrate 50 or increased dose (100mg) depending on the response of previous treatment cycle or combined

therapy with human menopausal gonadotropin (HMG) 75-150 IU.

- 7) The ovulation induction along with IUI was done for at least 3 consecutive cycles and the patients were followed up for 6 months.

Observations and Analysis

The statistical analysis of the observations was done either by chi-square test or students paired t test. The p-value of < 0.05 was considered statistically significant. From the final analysis, 14 patients were excluded due to poor follow up. So, total number of cases studied was 38.

The incidence of clinical, ultrasonographic and endocrinological features (Table I).

Table I
The incidence of clinical, ultrasonographic and endocrinological features

Features (n=38)		No.	%
Intertility	Primary	34	89.5
	Secondary	4	10.5
Menstrual cycles	Regular	12	31.5
	Irregular	26	68.5
Hirsutism	Present	11	29
	Absent	27	71
Obesity (BMI>25 kg/m ²)	Present	14	37
	Absent	24	63
Necklace pattern	Present	28	73.7
	Absent	10	26.3
Hyperchogenic stroma	Present	17	44.7
	Absent	21	55.3
Testosterone (ng/dl)	Normal (< 1)	31	81.5
	Abnormal (> 1, < 3)	7	18.5
Luteinising hormone (mIU/ml)	Normal (< 10)	17	44.7
	Abnormal (> 10)	21	55.3
LH: FSH ratio	Normal (< 2)	16	42
	Abnormal (> 2)	22	58

Among 38 patients who underwent laparoscopic guided needle puncture of ovarian follicles, 34 (89.5%) presented with primary infertility and 4 (10.5%) with secondary infertility, which indicates that women with PCOS are infertile primarily. Amongst all patients, 12 (31.5%) had regular cycles and 26 (68.5%) had irregular cycles. Hirsutism was present in 11 (29%) women. In 14 (37%) patients obesity (BMI > 25 kg /m²) was present which was determined by measuring body mass index (BMI) in kg /m². Mean value of BMI was 23.29 kg /m² with a standard deviation of 2.51, with minimum BMI value 19.1kg /m² and maximum 28.2 kg /m².

On pre-treatment transvaginal ultrasonographic evaluation, it was seen that characteristic "necklace" pattern of ovarian follicles was present in 28 (73.7%) patients. Hyperechogenic ovarian stroma as an associated ultrasonographic finding was seen only in 17 (44.7%) patients.

The pre-treatment basal (on day 2-5) levels of serum LH, FSH and testosterone were noted. The LH value was abnormal (>10 mU/ml) in 21 patients (55.3%). The LH value varied from 1.7 to 60.6 mU/ml with a mean of 13.46 ± 12.16 mU/ml and FSH value varied from 1.8 to 15 mU/ml with a mean of 6.03 ± 2.62 mU/ml (Table 2). The pre-treatment LH:FSH ratio was abnormal (>2) in 22 (58%) patients. The mean value of LH:FSH ratio was 2.34 ± 1.61 with a range from 0.37 to 6.60. Testosterone was in the abnormal range of 1-3 ng/dl in 7 (18.5%) patients only (Table 1).

Status of leading follicle size – pre & post LPOF

Before treatment, none of the 38 patients had leading follicle of ≥ 18 mm and all these patients were found to have multiple small follicles. After treatment, 19 (50%) patients could develop the leading follicle of ≥ 18 mm while remaining 19 (50%) patients had no improvement in folliculogenesis. This observation is highly significant ($p=0.0000005$).

Effect of LPOF on ovulation

Before the LPOF, all the 38 patients were anovulatory. After the LPOF, 16 (42.1%) showed the evidence of ovulation, which is a significant ($p=0.000006$) finding whereas in 22 (57.9%) patients there were no signs of post-treatment ovulation even with clomphene induction.

Association of follicle size and the ovulation.

Among all 16 patients who ovulated, 14 (87.5%) had the leading follicle size of ≥ 18 mm whereas only 2 (12.5%) did not have large (> 18 mm) leading follicle. This was again highly significant ($p=0.00008$). While among 22 anovulatory patients, 17 (95.5%) continued to have no effective folliculogenesis and though 5 (4.5%) showed

adequate leading follicular size there was no ovulation even despite the administration of hCG injection (Table II).

Table II
Association of follicle size and the ovulation

Post Rx leading follicle (n=38)	Post Rx ovulation	
	Present (n=16)	Absent (n=22)
≥ 18 mm (n=19)	14 (87.5%)	5 (4.5%)
< 18 mm (n=19)	2 (12.5%)	17 (95.5%)

$p=0.00008$

Table III
Association between ovulation inducing drugs and ovulation

Post Rx therapy (n=38)	Post Rx ovulation	
	Present (n=16)	Absent (n=22)
CC50 (n=21)	6 (28.5%)	15 (71.5%)
CC100 (n=7)	4 (57%)	3 (43%)
CC+HMG (n=10)	6 (60%)	4 (40%)

For ovulation induction, twenty one (55%) patients received CC50 mg (D₁-D₇), 7 received CC100 mg (D₂-D₇), and 10 received CC100 mg (D₁-D₇) along with human menopausal gonadotropins (HMG) (75 IU (D₁-D₇)). Sixteen patients showed signs of ovulation. Ovulation was observed in 28.5% (6/21) patients with CC50, in 57% (4/7) with CC100 and 60% (6/10) with CC100 & HMG. While remaining 22 patients did not show any ovulatory response. This signifies that ovulation rate in patients who underwent LPOF is better with sequential CC100 & gonadotropin therapy (Table III).

Duration of ovulation induction and ovulation

On studying the association of duration of therapy and ovulation, it was seen that among all the 16 patients who showed signs of ovulation, 1 (2) after CC50, 1 after CC100, 1 after CC100 & HMG had ovulation within 2 months, 11 (4) with CC50, 3 with CC100, 4 with CC100 & HMG within 2-4 months and only 1 (after CC10 & HMG) showed signs of ovulation

Table IV
Duration of ovulation induction and ovulation

Post Rx duration (months)	Post Rx therapy & ovulation present (n=16)		
	CC50 (n=6)	CC100 (n=4)	CC+HMG (n=6)
< 2 (n=4)	2	1	1
> 2 to < 4 (n=11)	4	3	4
> 4 to < 6 (n=1)	-	-	1

Table V
Comparison of ovulation rates (OR) and pregnancy rates (PR) with various puncture techniques (%)

Authors	Procedure	OR	PR
Stein & Leventhal, 1935	Ovarian wedge resection	80	25
Goldzieher et al, 1981	Ovarian wedge resection	80	63
Gjonnaes, 1984	Ovarian electrocautery	92	80
Greenblatt & Casper, 1987	Ovarian electrocautery	83	66
Huber et al, 1988	Ovarian laser drilling	62	-
Daniell & Miller, 1989	Ovarian laser drilling	70	56
Lulandi & Look, 1998	Ovarian electrocautery	88	70
Current study	Ovarian needle puncture	42	19

within 4-6 months (Table IV).

Ovulation and Pregnancy rates

Out of 16 patients who responded to treatment by showing ovulation, only 3 (19%) conceived within 6 months of follow up whereas no conception was seen in remaining 13 (81%) patients.

Discussion

The mechanisms by which the needle punctures act are destruction of thick ovarian capsule and the draining out of androgen rich fluid from the ovary. This leads to the normal milieu of hormonal microenvironment which in turn will help in ovulation and regularisation of the menstrual cycles.

The observations of the present study demonstrate that clinical characteristics of PCOS coexist with the altered endocrinological status and the classical morphological transformation of this syndrome, which can be detected by ultrasound examination. On comparing the LH levels, LH:FSH ratio, and testosterone levels as diagnostic criteria in PCOS subjects, it is observed that the incidence of abnormal values ranges from 40-60% (Van et al, 1997, Fox & Corrison, 1991, Lourds & Neus, 1994). The characteristic sonographic picture of ovaries showing "necklace" pattern of microcysts, is observed in more than 70% and hyperechogenic stroma in 50-70% patients (Adams et al, 1986, Ardeans et al, 1991). These wide ranges of incidences are mainly explained by the subjective variation or varied settings of the ultrasound machine.

These discrepancies of the clinical, endocrinological, or ultrasonographical criteria suggest that none of them individually has the "gold standard" diagnostic value.

In cases in which ovulation was seen, 87.5% had leading follicle of 18 mm. This supports the view of

Dickey et al (1993) that if the leading follicle is > 18mm the ovulation rate is better. Gjonnaes (1984) found that 92% patients ovulated within 4 months of electrocautery. In the current study where simple needle punctures were performed, among all patients who showed evidence of ovulation, 93.7% ovulated within 4 months of punctures. This supports the fact that the effect of surgery is the maximum within first 4-6 months.

After cauterizing the ovary at 6-10 points Gjonnaes (1984) found that the ovulation rate was 92.3%, whereas it was 66.7% if less than 6 cautery punctures were made. In the current study, after making 8-10 simple needle punctures in each ovary the ovulation rate was 42%, suggesting that though the number of simple punctures was equal or less than that of cauterized points, the extent of stromal damage would have been far less, theoretically, giving low ovulation rates in this study.

On comparing the average ovulation rate in relation to different techniques by different authors as given in Table V, it is found that average ovulation rate after wedge resection is 80%, after biopsy 60%, after laser surgery 70% and after electrocautery 85%. Whereas in this study of simple needle puncture technique, it is only 42%. Similarly, the pregnancy rate is low in comparison to other techniques.

This indicates that results in terms of ovulation and pregnancy rates are less after simple needle puncture in comparison to other surgical methods suggesting that only drainage of androgen rich fluid and inadequate stromal destruction is not sufficient enough to induce ovulation in anovulatory PCOS patients.

Conclusion

The available results and circumstantial evidences suggest that LPOF improves the ovulation rate in otherwise ovulation induction resistant infertile women with PCOS. LPOF shows better response to

ovulation treatment. LPOF can be used as one of the surgical ovulation induction method and has a place in the management of the resistant cases of PCOS. But this treatment is much less successful than wedge resection, biopsy, laser drilling & electrocautery.

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