

LAPAROSCOPIC OVARIAN DRILLING IN CLOMIPHENE RESISTANT PCO PATIENTS: A PREFERRED METHOD OF TREATMENT

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ABSTRACT

Objective: To determine the efficacy of ovarian drilling in PCO patients who failed to achieve pregnancy with medical treatment.

Methods and Main Results: 75 patients with a diagnosis of PCO of whom 48(64%) were primary infertile and 27(36%) were secondary infertile were clomiphene resistant. The other methods like bromocriptin, gonadotropins, GnRH-a and metformin had been given to these patients for infertility treatment without benefit. After ovarian drilling, pregnancy was achieved in 41 patients (54.6%), 30(40%) in group I (primary infertile group) and 11(14.6%) in group II (secondary infertile group). During the operation adhesiolysis was necessary in 14(18.6%) and removal of endometriotic lesions was indicated in 5(6.6%) in both groups.

Conclusion: Ovarian drilling is an ideal technique in PCO patients with failure of medical treatment, considering the benefit of also performing other necessary surgical interventions.

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INTRODUCTION

PCO is the most common endocrine disorder in women of reproductive age affecting 5-10% of premenopausal women. Women with this syndrome may present with menstrual irregularities, chronic anovulation, infertility, obesity and hyperandrogenism, and insulin resistance and compensatory hyperinsulinemia are prominent features of PCOs and occur when there is oligo- or amenorrhea.¹

Clomiphene citrate (CC) is usually used as the first-line drug to induce ovulation in women with PCOs.

Successful ovulation is achieved in 70-80% of women and 40-50% will conceive (The ESHRE cap1 workshop,

1997). Gonadotropin treatment can be offered when these anovulatory women fail to respond to CC. The use of gonadotropin is more expensive and associated with a much higher risk of multiple pregnancy and developing ovarian hyperstimulation syndrome. Also, dexamethasone and / or diabetes drugs, such as metformin and troglitazon, have been used to treat these patients, although these produce lower pregnancy rates.^{6,7} Another alternative, surgical treatment by ovarian wedge resection⁸ although successful, is no longer in use, with its need for laparotomy and the accompanying potential for the development of pelvic adhesions.⁹

Laparoscopic ovarian electro-coagulation is an effective alternative to wedge resection¹⁰ with decreased risk of adhesion formation¹¹ and favorable ovulation and pregnancy rates and endocrine changes.^{10,11,14}

This article is designed to review the results of laparoscopic ovarian electrocautery treatment in two groups of PCO patients with primary and secondary in-

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fertility who have not responded to clomiphene and also HMG, GnRH-a, Bromocriptin and metformin therapy.

PATIENTS AND METHODS

75 Iranian women attending the infertility clinic of a Shiraz university based hospital, were recruited into the study if they fulfilled the following criteria; age of women <40 years, day 2 serum FSH<10 IU/lit, PCO diagnosed by transvaginal ultrasonography, >10 follicles of 2-10mm in diameter and increased density of ovarian stroma, and irregular cycles and anovulation as shown by basal body temperature chart while on clomiphene citrate 100mg daily for 5 days over three cycles. Bilateral patent fallopian tubes were confirmed in all women by hysterosalpingography, husbands of all had normal semen variables. If there was no response to CC 100mg daily, then the dosage was increased up to 150mg daily, and if there was still no response, human menopausal gonadotropin was used to stimulate ovulation, in addition to HCG between the 14th and 16th day. Failure of ovulation was confirmed by ultrasound scan and/or basal body temperature chart.

The other options like bromocriptin and GnRH-agonist and also metformin were also tried for them, and finally in cases of no response, the patients were selected for laparoscopic ovarian cauterization.

During these procedures, if there were other problems like adhesions and endometriotic lesions, adhesiolysis and electrocautery of the involved focuses were done. Post-operatively, patients were followed for spontaneous ovulation, confirmed by basal body temperature chart, regular menses and spontaneous pregnancies. All patients were divided into two groups; 48(38%) with primary infertility (group I), and 27(36%) with secondary infertility (group II).

The data were analysed with Student's t-test.

RESULTS

The clinical characteristics of the patients before laparoscopic ovarian cauterization are presented in Table I.

After laparoscopic ovarian cauterization, the patients were followed-up for spontaneous ovulation and pregnancy rate and changes in hormonal profile. Normal menstruation cyclicity (27-35 days) was observed in 70.6% (group I) and 68.75% in group II, which was not different statistically. The overall ovulation rate was 70.19% in group I and 51.7% in group II. Spontaneous pregnancy rate was 40% (30 patients) in group I and 14.6% (11 patients) in group II, and ultimate pregnancy rate in both groups was 54.6% (Table II).

Table III compares LH, FSH, Prolactin, DHEAS and testosterone levels of patients pre-operative and 10 days after surgery post-operatively; a marked reduction in the mean LH, FSH, T, DHEA-S levels was seen in patients.

As shown in Table IV, the abnormal findings during laparoscopy, including adhesions and endometriosis were corrected, and overall 14 patients out of 75 (18.6%) had adhesions, and 5 patients out of 75 (6.6%) had endometriosis (mild to moderate).

DISCUSSION

In 1930, before we had a good understanding of the hypothalamic-pituitary ovarian axis, before the radioimmunoassay concept, and before the presence of drugs for ovulation induction, Stein and Leventhal described the classic syndrome which bears their names.

Over the next 35 years, surgical treatment in the form of wedge resection was the accepted treatment of PCO.¹⁹

Some authorities have reported mechanical problems after wedge resection in the form of periovarian and

Table I: Description of clinical and biochemical characteristics of primary and secondary infertile patients.

	Group I	Group II
Age	24.58±6.1	29.1±2.71
Duration of infertility (months)	72.3±33.73	69.81±31.92
Menstrual pattern		
Amenorrhea	8%	10.87%
Oligomenorrhea	87.1%	86.15%
Hirsutism	80%	78.5%
Acne	70%	81%

Table II: Outcome measures for ovulation and pregnancy rates.

	Group I	Group II	Total
Ovulation rate	70.19%	51.7%	-
Pregnancy rate(n)	40% (30)	14.6%(11)	54.6%(41)

Table III: Comparison of serum hormone levels pre-operation and post-operation.

	Pre-op	Post-op
LH	16.32±8.8	6.38±6.9
FSH	7.01±3.22	3.25±1.23
PRL	138±58.5	98±72.5
DHEAS	212.96±167	85.06±78.29
LH/FSH	3.01±3.03	2.7±1.76

Table IV: Surgical corrections other than cauterization which were performed.

Group	Adhesiolysis	Endometriosis excision	Total
Group I (n=48)	6/48 (12.6%)	3/48(6.25%)	9(18.75%)
Group II (n=27)	8/27(29.6%)	2/27(7.40%)	10(37%)
Total patients n=75	14/75(18.6%)	5/75(6.6%)	—

peritubal adhesions, and have largely replaced wedge resection with cauterization by laparoscopy.

Bilateral ovarian destruction using laparoscopic ovarian electrocautery by diathermy has been replaced nowadays by wedge resection as a surgical modality.¹³

A report from other authors showed a dramatic fall in LH, FSH, DHEAS and T levels after cauterization of ovaries ($p < 0.001$).^{25,3}

Also a decrease in LH level has been reported in many other studies,^{12,13,22} and Balen et al.²⁴ reported those who responded to cautery had a significantly greater fall in serum LH levels than those who failed to respond. We also detected a significant fall in FSH and LH levels. Another study reports no significant change in FSH level;¹⁰ rather, an increase is found. Also post-operative decrease in DHEAS is reported (14-25)²² supporting our results.

After laparoscopic ovarian electrocautery, normal spontaneous menstrual cycles (27-35 days) were observed in 70.6% of our patients, similar to that reported by other authors^{10,12,17,21,22} and our achieved spontaneous pregnancy rates were 54.6% which is in agreement with the findings of other studies.^{10,22,5}

An ovulation rate of 70.19% and 51.7% in group I and II respectively and an overall pregnancy rate of 54.6% in both groups, in addition to other surgical corrections for patients like adhesiolysis in 18.6% and removing endometriotic foci in 6.6% showed that laparoscopic ovarian cauterization could be a preferred method in CC-resistant PCO patients considering that other necessary operative procedures will also be done.

REFERENCES

- Hung E, Ju Ng, Ming N, et al: Effects of metformin on ovulation rate, hormonal and metabolic profiles in women with CC resistance. *Human Repr* 16(8): 1625-1631, 2001.
- Berger MJ, Tamor ML, Potton WC: Gonadotropin levels and secretory patterns in patients with typical and atypical polycystic ovarian disease. *Fertil Steril* 26: 619-624, 1975.
- Tan SL, Farhi J, Homoburg R, Jacobs HS: Induction of ovulation in clomiphene resistant polycystic ovary syndrome with pulsatile GnRH. *Obstet Gynecol* 88: 221-226, 1996.
- Frank S, Adam J, Mason IT, Palson D: Ovulatory disorders in women with polycystic ovary syndrome. *Clin Obstet Gynecol* 12: 605-633, 1985.
- Alborzi S, Khodai R: Ovarian size and response to laparoscopic ovarian cauterization in PCO. *Int J Gyn/Ob (74)*: 269-274, 2001.
- Nester JE, Jakubowicz DJ, Ewans WS, Pasquali R: Effect of metformin on spontaneous and clomiphene induced ovulation in the polycystic ovary syndrome. *New Engl J Med* 338: 1876-1880, 1998.
- Trott EA, Plouffe JRL, Hansen K, Hines R, Brann DW, Mahesh UB: Ovulation induction in clomiphene anovulatory women with normal dehydroepiandrosterone sulfate levels, beneficial effects of the addition of dexamethasone during the follicular phase. *Fertil Steril* 66: 484-486, 1996.
- Stein IF, Leventhal HI: Amenorrhea associated with bilateral polycystic ovaries. *Am J Obstet Gynecol* 29: 181-191, 1935.
- Buttram VCJR, Vaquero C: Post ovarian wedge resection adhesive disease. *Fertil Steril* 26: 874-876, 1975.
- Gjonnaess H: Polycystic ovarian syndrome treated by ovarian electrocautery through the laparoscopy. *Fertil Steril* 41: 20-24, 1984.
- Naether OJ, Fisher R: Adhesion formation after laparoscopic electro-coagulation of the ovarian surface in polycystic ovary patients. *Fertil Steril* 60: 95-98, 1993.
- Gjonnaess H: Late endocrine effect of ovarian electrocautery in women with polycystic ovary syndrome. *Fertil Steril* 69: 697-701, 1998.
- Felemban A, Tan SL, Tulandi T: Laparoscopic treatment of polycystic ovaries with insulated needle cautery: a re-appraisal. *Fertil Steril* 23: 266-269, 2000.
- Gjonnaess H: Comparison of ovarian electrocautery and oral contraceptives in the treatment of hyperandrogenism in women with polycystic ovary syndrome. *Acta Obstet Gynecol Scand* 78: 530-533, 1999.
- Dodson MG: Transvaginal ultrasound. 1st ed, New York, Churchill Livingstone, p.111, 1991.
- Ardaens Y, Robert Y, Lemaitre L, Fossati P, Dewailly D:

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- Polycystic ovarian disease: contribution of vaginal endosonography and reassessment of ultrasonic diagnosis. *Fertil Steril* 55(6): 1062-1068, 1991.
17. Gjonnaess H, Norman N: Endocrine effects of ovarian electrocautery in patients with polycystic ovarian disease. *Br J Obstet Gynecol* 94: 779-783, 1987.
 18. Armar NA, Lachelin GCL: Laparoscopic ovarian diathermy: an effective treatment for anti-estrogen resistant anovulatory infertility in women with polycystic ovaries. *Br J Obstet Gynecol* 100: 161-164, 1993.
 19. Balen AH, Jacobs HS: Gonadotropin surge attenuating factor: a missing link in the control of LH secretion? *Clin Endocrinol (Oxf.)* 35: 399-402, 1991.
 20. Tuiandi T, Saleh A, Morris D, Jacobs HS, Payne NN, Tan SL: Effects of laparoscopic ovarian drilling on serum vascular endothelial growth factor and on insulin responses to the oral glucose tolerance test in women with polycystic ovary syndrome. *Fertil Steril* 24(3): 585-588, 2000.
 21. Li TC, Saravelos H, Chow MS, Chisabingo R, Cook ID: Factors affecting the outcome of laparoscopic ovarian drilling for polycystic ovarian syndrome in women with anovulatory infertility. *Br J Obstet Gynecol* 105: 338-344, 1998.
 22. Abdel Gadir A, Khatim MS, Alnaser HMI, Mowafi RS, Shaw RW: Ovarian electrocautery responders versus non-responders. *Gynecol Endocrinol* 7: 43-48, 1993.
 23. Kyei-Mensah AA, Lin Tan S, Zaidi J, Jacobs HS: Relationship of ovarian stromal volume to serum androgen concentrations in patients with polycystic ovary syndrome. *Hum Reprod* 13(6): 1437-1441, 1998.
 24. Balen AH, Jacobs HS: A prospective study comparing unilateral and bilateral laparoscopic ovarian diathermy in women with polycystic ovarian syndrome. *Fertil Steril* 62: 921-925, 1994.
 25. Van der Weiden RMF, Alberta AT, de Jong FH, Brandenburh H: Endocrine effects of laparoscopic ovarian electrocautery in patients with polycystic ovarian disease resistant to clomiphene citrate. *Eur J Obstet Gynecol Reprod Biol* 32: 157-162, 1989.