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FACTORS INFLUENCING THE OUTCOME OF LAPAROSCOPIC OVARIAN ELECTEROCAUTERIZATION IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Background/Objective: To evaluate factors which increase the chance of ovulation and pregnancy after laparoscopic ovarian electerocauterization (LEC) in Clomiphene Citrate (CC) resistant polycystic ovarian syndrome (PCOS) patients.

Methods: An experimental prospective study was carried out in the infertility division of a university teaching hospital. Two hundred and ninety-nine women with PCOS who were resistant to CC were enrolled in this study. LEC was performed over a four years period between 1996 till 1999. Serum concentration of luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL), testosterone (T), dehydroepiandesterone sulfate (DHEAS), were measured before and ten days after LEC. The ovulation and pregnancy rates were also determined over a period of one year of follow-up.

Results: The overall ovulation rate was 78.3% but cumulative pregnancy rate 12 months after LEC was 47.8%. Women who conceived following surgery had mainly a shorter duration of infertility, secondary infertility and higher pre-operational LH levels.

Conclusion: PCOS women with anovulatory infertility responded favorably to LEC (clinic & para clinic). Three main factors that affect the outcome of surgery are duration of infertility, type of infertility and amount of pre-operational LH levels.

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Key Words • Polycystic ovarian syndrome • laparoscopic ovarian cautery • factors affect outcome

Introduction

A common presentation of PCOS is anovulatory infertility, for which there are several treatment options.[1,2] The first line of treatment for this problem is clomiphene citrate (CC).[3] Women who are resistant to CC can be treated with gonadotropin or pulsatile LH-releasing hormone.[4]

However, due to complications arising from medical therapy, such as multiple pregnancy and ovarian hyperstimulation syndrome, an alternative mode of treatment is a surgical approach.[5] The oldest treatment for anovulatory infertility associated with PCOS is bilateral ovarian wedge resection, which has been replaced by LEC because of its effectiveness and low complication rate.[6,7] There are several studies that report increased ovulation, pregnancy rate and positive endocrine changes after LEC.[8-11] The pregnancy rate after laparoscopic ovarian drilling by diathermy or various forms of laser treatment, vary from 20%-88%.[12-14]

The reason for these variations in ovulation and pregnancy rate is unclear, but may be due

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to factors affecting the outcome of surgery. Studies investigating the factors that affect the success rate of LEC included small series of patients.[2] The aim of this study was to evaluate the ovulation, pregnancy and hormonal change after LEC in a large number of patients (299) and to determine factors that would improve the success rate of LEC.

Materials and Methods

Patients:

From 1996 to 1999, two hundred and ninety-nine CC-resistant PCOS patients (patients who failed to ovulate with 200-250mg of CC x 5 days for 3-4 months) without severe male and tubal factors underwent LEC by monopolar cautery for anovulatory infertility in the Endocrinology and Infertility Unit of Shiraz University of Medical Sciences.

Inclusion criteria were as follows: menstrual abnormality (amenorrhea, oligomenorrhea, polymenorrhea or irregular bleeding), presence of more than nine ovarian subcapsular follicles measuring between 3-8 mm in diameter, serum LH to FSH ratio (LH/FSH) of 2.5 or more in the early follicular phase or during amenorrhic period, obesity (BMI >25 kg/m2), hirsutism or acne and finally, infertility. Patients with three or more of the aforementioned symptom were enrolled in the study.

Vaginal sonography was performed for all patients and ovarian volume and cross-sectional area were calculated using these formula: Volume $= 0.5233 \times D1 \times D2 \times D3$, cross sectional area = length $\times$ width $\times \pi/4$. If ovarian volume was more than 8 cm^3 and cross-sectional area >10 cm^2, the patient was considered as PCOS type 1, while type 2 PCOS was regarded as ovarian volume equal or less than 8 cm^3 and cross-sectional area 10 cm^2 or less. Ultra-sound examination was performed using a 6.5 MHz sector real-time transducer (Medison 600, Korea).

Patients were followed up for spontaneous ovulation and pregnancy. Ovulation was confirmed by regular menstruation and spontaneous pregnancy in the first post-operation year. If spontaneous regular menstruation failed to occur in the first three post-operation months, CC was started. The length of follow up after surgery was one year.

Laboratory methods:

After clinical examination, patients referred to the research unit affiliated to Shiraz University of Medical Sciences underwent complete para clinical examination.

LH, FSH were checked by IRMA (immune radiometric assay) and DHEAS, T, PRL were measured by RIA (radio immune assay). Tests were performed using Spectria kits (Finland). Normal serum ranges in our laboratory were as follows:

LH: 2.3-16.1 mIU/ml
FSH: 2.1-9 mIU/ml
PRL: 80-500 mU/ml
T: 0.2-0.9 ng/ml
DHEAS: 35-430 μg/dl

Methods of surgery:

Surgical manipulation was performed under general anesthesia via the two-puncture technique. After assessment of the pelvic structure and tubal patency, and immobilization of the ovaries, an insulated needle electrode was held against the ovary surface and by applying gentle pressure, 8-12 holes were made in each ovary.

All women were discharged 4-6 hours after LEC without complication.

Statistical analysis:

Statistical analyses were conducted using paired t test, Chi-square test, Fisher's exact test, and one-way ANOVA.

Results

The mean ($\pm$SD) age of the patients was 24.99

Table 1. The clinical features of 299 PCOS women who had laparoscopic surgery for anovulatory infertility.

Parameter	Mean ± SD
Total	299
Age (Yrs)	24.99 ± 4.41
Type of infertility	
Primary infertility:	213 (71.2%)
Secondary infertility:	86 (28.8%)
Duration of infertility (Yrs)	4.87 ± 3.42
Obesity	161 (53.8%)
Acne-Hirsutism	213 (71.2%)
Galactorrhea	34 (11.4%)
Type of ovary	
Type 1	183 (61.2%)
Type 2	116 (38.8%)
Menstruation	
Oligomenorrhea	219 (73.2%)
Amenorrhea	28 (9.4%)
Polymenorrhea	11 (3.7%)
Irregular bleeding	41 (13.7%)
Duration of infertility (Yrs)	
≤3	129 (43.1%)
>3	170 (56.9%)
Age groups (Yrs)	
≤30	261 (87.3%)
>30	38 (12.7%)

* **Note:** Values are given as numbers (%)

± 4.41 years and the duration of infertility was 4.87 ± 3.42 years. Other clinical features of the patients are presented in Table 1.

The main outcome measures; ovulation and pregnancy were 78.3% and 47.8%, respectively.

Changes in the mean hormonal levels before and after surgery are summarized in Table 2. As shown, there are significant falls in the mean hormonal levels of testosterone and DHEAS after the procedure.

The mean hormonal differences before and after LEC were compared in two groups of PCOS women; with and without pregnancy. The mean FSH difference was significantly higher in women who became pregnant ($p = 0.03$). There were significant hormonal changes in testosterone and DHEAS levels in responder groups.

To evaluate the factors affecting the surgical outcome, patients were divided into 4 groups: patients with ovulation; patients without ovulation; patients with pregnancy and patients without pregnancy. The clinical and para clinical parameters and results are listed in Tables 3 and 4. As shown in these tables, the only three important factors affecting the outcome of LEC were pre-operative LH levels, and type and duration of infertility.

Discussion

The exact mechanism as to why LEC is effective is still unknown.[3] To this end, however, several mechanisms have been postulated including: decreased serum concentrations of androgens and estrone, increased pituitary sensitivity to gonadotropin releasing hormone stimulation, reduction of intra-ovarian androgens and inhibin, enhanced follicular development after LEC, and possibly a decrease in the vascular endothelial growth factor.[3,15-17] In our PCOS patients suspected of having hyperandrogenism, serum androgens

Table 2: Hormonal change before and after LEC and their statistical significance.

Parameter	Pre-treatment hormone*	Post-treatment hormone*	Hormone difference*	P value
LH **	13.43 ± 9.48	12.25 ± 7.22	1.17 ± 11.75	0.25
FSH **	6.64 ± 4.17	6.74 ± 6.51	-0.1 ± 7.3 a	0.87
T**	0.78 ± 0.33	0.59 ± 0.44	0.19 ± 0.54	0.002
DHEAS †	328.43 ± 189.34	150.91 ± 91.67	177.51 ± 176.61	0.0001
PRL ‡	254.68 ± 159.35	276.84 ± 149.19	-22.16 ± 209.94 a	0.27

*Values are means±SEM. **(mIU/ml), ***(ng/ml), †(μg/dl), ‡ (mU/ml)

a: (-) indicate increasing hormonal level after operation

(T. DHEAS) were found to be within normal range, a finding which is in keeping with Kovacs's report.[16] PCOS women, have low levels of sex hormone binding globulin (SHBG), accompanied by high T levels.[18] Normal androgens levels with clinical hyperandrogenism may have been due to the elevation of free testosterone[18] which was not measured during the course of this study.

The two hormones that changed significantly after LEC were T and DHEAS. These finding favorably compare with previous observations.[7,15,16] A post-operative, reduction of LH was reported by many authors,[3,7,15] but in our study no significant change was detected. This finding accords with that of a previous report.[16] Ovulation and pregnancy without changes in LH may be due to a decrease in the bioactive LH level. One report found an increase in FSH levels after LEC[7] but in the present study, this elevation was only found in responder groups, which is in accord with other studies.[15,16] Since androgens were decreased in both responders and non-responders and FSH was increased only in responders, we conclude that changes in levels of FSH after LEC is the most important factor in improving ovulation and pregnancy rate.

Ultimately, the total ovulation and pregnancy rates in our study were 78.3% and 47.8%, respectively. Similar findings have also been reported by previous researchers[10,12-14,16] while some have reported higher pregnancy and ovulation rates.[2,3,5,7,19] We found that three factors significantly and independently influence the outcome of LEC: the duration of infertility, the type of infertility, and pre-operation LH levels. The chance of ovulation and pregnancy were higher in patients with secondary infertility of three years or less and higher pre-operation LH levels. In the subgroup of PCOS women that ovulated after LEC the mean (± SD) LH was 13.86 ± 9.6 versus 11.47 ± 5.6 in non-ovulating patients (P= 0.03).

We found that the majority of patients that ovulated after surgery had pre-operation LH levels of 11.4 or more. Our findings concerning the important factors that affect the outcome of LEC (pre-operation LH levels and duration of infertility) are in accordance with Li TC et al.. However, they also found that the type of infertility had no effect on the surgical outcome.[2] A better response after LEC in patients with higher pre-operation LH level may be due to higher androgens levels in these women and since androgens decrease significantly after LEC, one expects a higher success rate after the procedure. A favorable response after LEC in patients with secondary infertility and in women with infertility of three years or less, is probably due to immunological problem or other unknown infertility factors. We also found that other criteria such as age, obesity, acne- hirsutism, ovary size, type of menstruation, galactorrhea, and amount of other pre-operation hormones other than LH have no significant effect on surgery outcome.

Results of LEC in our large number of patients (299) show that three major factors predicting surgical outcome were pre-operation LH levels, and type and duration of infertility. These results may assist clinicians to predict the success rate of LEC in CC resistant PCOS patients and select those with a better prognosis for this procedure.

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