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THE EFFECTIVENESS OF LAPAROSCOPIC ELECTROCAUTERY IN CLOMIPHENE CITRATE RESISTANT PATIENTS WITH POLYCYSTIC OVARY SYNDROME IN RELATION TO OVARIAN SIZE

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ABSTRACT

121 women with Polycystic Ovarian Syndrome and clomiphene citrate resistance underwent laparoscopic ovarian cautery. 63 patients were type I or typical PCOS with ovarian volume >8mL and 58 patients were type II PCOS with ovarian volume <8mL. Serum concentrations of Luteinizing Hormone (LH), Follicular Stimulating Hormone (FSH), Prolactin (PRL), Testosterone (T), and Dehydroepiandrosterone Sulfate (DHEAS) were checked before cautery and 10 days after operation. This prospective study showed that PCOS patients with large ovaries have higher LH levels than patients with normal size ovaries. LH and T levels decreased after laparoscopic ovarian cauterization only in type I. The overall ovulation rate was 91.5% in type I and 89.3% in type II. Pregnancy rate was 60.8% in type I and 66.7% in type II. There was no significant difference in ovulation and pregnancy rates between the two groups of PCOS ($p>0.05$). It therefore appears that the result of laparoscopic ovarian cauterization does not depend on ovary size in clomphene citrate resistant patients with PCOS.

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Keywords: PCOS, Clomphene citrate resistant, Ovarian electrocautery.

INTRODUCTION

The common clinical findings suggesting PCOS include oligomenorrhea, amenorrhea, hirsutism, obesity and infertility. Bilateral enlarged ovaries with a thickened cortex are the common anatomic findings of PCOS but 29-40% of patients have normal sized ovaries.[1] some authors believed that these groups of patients might include those with polycystic changes secondary to various adrenal disorders, those with elements of hyperthecosis, those with early stage PCOS with large ovaries, and possibly those with a previously unrecognized form of the oligomenorrheic androgen excess syndrome.[2]

Clomiphene citrate remains the drug of choice for ovulation induction in PCOS patients. However, even with the use of increasing doses of clomiphene citrate, 10-15% of women remain anovulatory.[3] For these patients gonadotropins with or without GnRH therapy may be successful[4] but despite intensive monitoring, which is demanding both for the patient and the clinic, hyperstimulation and multiple pregnancy remain the main risk factors. Alternatively, surgical treatment by ovarian wedge resection,[5] although successful in inducing ovulatory cycles, has largely been abandoned because of the need for laparotomy and potential risk of pelvic adhesions.[6,7]

Laparoscopic ovarian electrocoagulation may be an

effective alternative to wedge resection.[8,9] With this method the incidence of adhesion formation has decreased.[10] There are several studies that report ovulation, pregnancy rate and positive endocrine changes after laparoscopic ovarian cauterization,[11-15] but this article is the first study that is designed to review the result of laparoscopic ovarian electrocautery treatment in women with two types of PCOS, to compare patient response to ovulation induction treatment before and after laparoscopic ovarian electrocautery, and to identify patient characteristics that predict a favorable response to cauterization. We set out to assess hormonal changes, ovulation and pregnancy rates and the value of ovarian cautery in two groups of women in whom medical treatment had not succeeded.

PATIENTS AND METHODS

We used the following criteria for diagnosis of PCOS: chronic anovulation with amenorrhea or oligomenorrhea with LH:FSH ratio >2 or hyperandrogenism (clinical or biochemical). Vaginal ultrasound was performed for all of the patients and ovarian volume calculated from the formula for a prolate ellipsoid (volume=$0.5233\times D_1\times D_2\times D_3$ where D_1, D_2, and D_3 are the three maximal longitudinal, anteroposterior and transverse diameters). If ovarian volume was more than 8 mL the patient was considered as PCO type I and those with ovarian volume equal or lower than 8 mL were regarded as PCO type II. Ovarian volume was recorded as the mean value for both ovaries.[16] The ultrasound examination was performed using a 7.5 MHz sector real-time transducer (Ketetz Comison 310 A).

Between January 1994 and May 1997, 121 patients with PCOS from Shiraz University (Faghihi and Nemazi Hospital) [63 patients type I, 58 patients type II] underwent laparoscopic ovarian electrocautery. All of those patients have had infertility as the major symptom and failed to respond to clomiphene citrate at a maximum dose of 250 mg/day.

The clinical characteristics and hormonal profile of the patients were studied before and 10 days after ovarian cauterization in both groups of PCOS.

Hormone assay

Hormone assays were performed by routine methods in our laboratory, first preoperatively and then ten days after operation (Endocrinology Section, Nemazi Hospital). All of the hormones were checked in one session.

Serum Luteinizing Hormone (LH), Follicular Stimulating Hormone (FSH), Testosterone (T), Prolactin (PRL) and Dehydroepiandrosterone Sulfate (DHEAS) were measued by radioimmunoassay. 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], and DHEAS [35-430 μg/dL]. Tests were perfonned using Spectria Kit (Finland).

Statistical method

The changes in each subject's mean hormone level before and after surgery were used as summary measures of the effects of the ovarian cautery, and the significance of the changes were assessed by Student's t-test, paired t-test, and χ^2 as appropriate.

Method

Surgical manipulation was performed under general anesthesia with the use of the two-puncture technique. After assessment of pelvic structures and tubal patency, unipolar cautery forceps were held against the ovarian surface with gentle pressure until penetration of the ovarian suface and capsule was achieved. Approximately 8-12 cautery points were applied to each ovary. Except for the usual side effects associated with general anesthesia and laparoscopy, no untoward side effect from the ovarian electrocautery was noted.

All women were discharged 4-6 hr after operation. No complication was reported other than mild abdominal discomfort.

After laparoscopic ovarian electrocauterization, patients were followed up for spontaneous menstruation and ovulation. Ovulation was confirmed using a basal body temperature chart and report of regular menstruation. If spontaneous regular menstruation or spontaneous pregnancy didn't occur, clomiphene citrate was started. Length of follow up after operation was 12 to 24 months.

RESULTS

The clinical characteristics and hormonal profile of the patients before laparoscopic ovarian electrocautery are presented in Table I. The result of this comparison showed higher secondary infertility in type II patients than in type I, but higher serum LH levels in type I compared to type II patients. Other clinical characteristics and hormonal profile were similar in both groups.

After laparoscopic ovarian electrocautery, patients were followed up for spontaneous ovulation and menstruation. Normal menstrual regularity (27-35 days) was observed in 67.7% (40) of patients with type I and 64.2% (34) in type II. No significant difference was found. For patients who remained oligomenorrheic or amenorrheic after operation, within 3 months, clomiphene citrate (100 mg) was used. 14 patients of type I and 14 patients of type II had ovulation after receiving 100 mg/day clomiphene citrate. Overall ovulation rate in type I was 91.5% and in type II was 89.3% and pregnancy rate was 60.8% (31 of 53 patients) in type I PCO and 66.7% (28 of 44 patients) in type II PCO. These results didn't show any significant difference between the two types.

Figure 1 compares serum LH, FSH, PRL, DHEAS and T levels of responding patients preoperatively and 10 days after surgery.

After operation a marked reduction in mean testoster-

Table I. Comparison of clinical and biochemical characteristics of type I and II PCOD.

Characteristics	Type I	Type II	Significance
Age (Q)*	24.03+3.9	25.89+4.68	P= 0.19
(n) †	(63)	(58)	
Age (Q)*	30.13+3.9	30.74+4.8	‡NS
(n)†			
Duration of infertility (mo)*	68.8+34.97	66.52+38.13	‡NS
(n)†	(61)	(57)	
Type of infertility:			
Primary (n) †	85.2% (54)	60.3%(35)	
Secondary (n) †	14.3% (9)	39.7% (23)	P= 0.003
Menstrual patern			
Amenorrhea (n)†	11% (6)	16% (9)	‡NS
Oligomenorrhea (n)†	89% (49)	84% (46)	‡NS
Hirsutism (n) †	78% (43)	69% (38)	‡NS
Acne (n) †	82% (45)	62% (34)	‡NS
Galctorrhea (n) †	13% (7)	18% (10)	‡NS
Hormonal profile:			
LH (mIU/mL)* §	14.77±8.31	11.44±6.05	P= 0.028
(n)†	(53)	(45)	
FSH (mIU/mL)* §	6.43±4.09	6.55±3.66	‡ NS
(n)* †	(53)	(45)	
PRL (mU/mL)* §	322.36±234	310±264	‡NS
(n)* †	(47)	(41)	
DHEAS (mg/dL)* §	430.23±493	454±630	‡NS
(n)* †	(26)	(18)	
Testosterone (ng/mL)* §	1.17±0.75	0.93±0.652	‡NS
(n)* †	(29)	(29)	

*Values are means+SD

† n= Number of patients

‡Not significant

§Conversion factors to SI units for LH, FSH, 1.00; PRL, 1.00; DHEAS, 2.56; T, 3.48.

one levels (mean ±SEM, 1.18 ±8.9 to 0.49 ±0.21 ng/mL, $p<0.001$) and LH level (14.99±8.9 to 11.97 ± 6.1 miU/mL, $p=0.053$) was observed in type I patients.

Gonadotropins, PRL, DHEAS and T levels in type II had no significant statistical change after operation.

DISCUSSION

The clinical entity of PCOS and its cause is not well defined. A fundamental feature is infertility associated with oligomenorrhea or even amenorrhea with or without elevation of androgen or androgenization. Stein and Leventhal[5] could demonstrate that ovarian wedge resection induced ovulation in a high percentage of patients. Because the association of this operation with tuboperitoneal disease has been reported[6,7] the procedure has been abandoned. In 1984 Gjonnaess introduced the laparoscopic method of ovarian electrocautery and reported a high ovulation rate of 92% as well as a high pregnancy rate of 69%.[9] Although the mechanism of ovulation is uncertain in ovarian cauterization, an increasing number of studies have reported the effectiveness of this procedure.

Several potential mechanisms of action of laparoscopic ovarian electrocautery have been suggested. One of these theories suggests that withdrawal of a factor such as inhibin was responsible for the increase in FSH secretion and recruitment of a new cohort of follicles.[8,9,11,12] Another theory involves ovarian cautery which may primarily result in reduction of intraovarian androgen and then decrease serum androgen levels. Reduction of androgen levels may cause a decrease in LH levels.[11,12] The last theory illustrated that potential mechanisms of action of laparoscopic ovarian cauterization is restoration of normal production of the putative gonadotropin surge at-

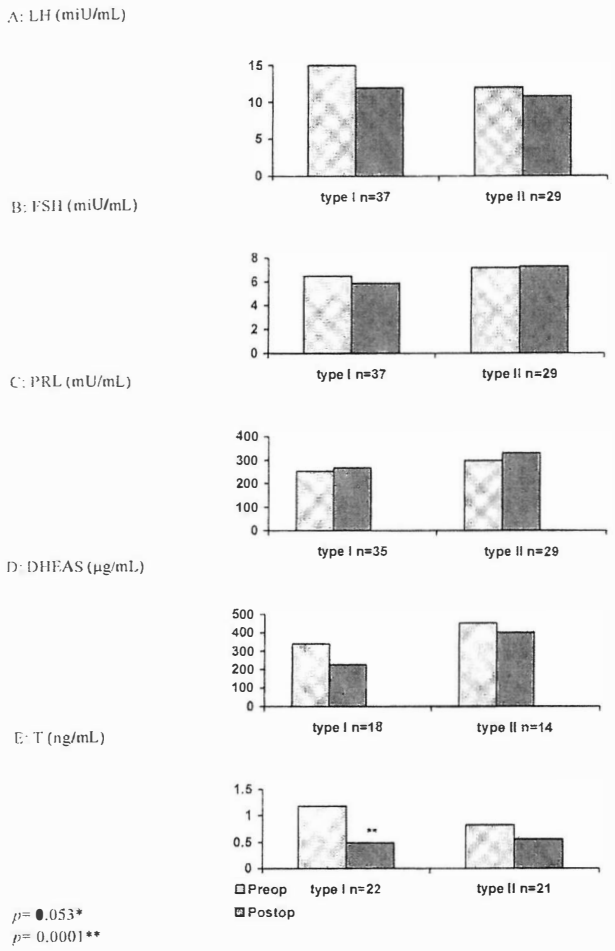

Fig. 1. Serum hormone levels before and after laparoscopic electrocoagulation of the ovarian surface in two types of PCOD. Conversion factors to SI units: LH, FSH, 1.00; PRL, 1.00; DHEAS, 2.56; T, 3.47.

tenuating factor from the ovary after cauterization of ovaries.[17] Fowler et al.[18] reported that this inhibitor appeared to have no effect on basal production of gonadotropins. In addition to above mentioned theories a theory describes that serum concentrations of vascular endothelial growth factor (VEGF) have been reported to be higher in PCOS patients, so it could be considered a factor affecting ovarian function. But no significant changes were reported in VEGF levels after restoration of ovarian function by cauterization.[19] Regardless of the affecting mechanisms, the effect of laparoscopic electric cauterization seems to be long lasting and only 1 to 2 percent of women will stop ovulation annually.[11]

In the present study our data demonstrated that laparoscopic ovarian cautery for type I patients is characterized by a dramatic fall in postoperative testosterone levels as well as decreased LH levels (smaller but significant). These hormonal changes can demonstrate why ovulation rates increase after operation. But there were no hormonal changes after laparoscopic ovarian cautery in type II patients although the ovulation rate was increased. So it is difficult to interpret these results. It may be due to a decreased bioactive LH level. Further studies might be of interest, both for understanding PCOS and for it's therapy.

On the basis of the result of the endocrine profile (Table I), LH levels in type I group was higher than type II. Berger et al.[2] achieved the same results. But ovulation and pregnancy rates were similar in both groups. Previous studies[13,14,15] showed the same ovulation and pregnancy rates among both groups regardless of ovarian size. Recent studies showed that PCOS patients with high basal serum LH concentration tend to respond poorly to gonadotropin stimulation with significantly lower rates of ovulation and pregnancy than women with normal LH levels.[20,21] The favorable effect of laparoscopic ovarian cauterization in women with high LH levels is also supported by other studies.[22,23]

It seems that the best treatment for clomiphene resistant PCO patients is laparoscopic ovarian electrocautery, due to the high ovulation and pregnancy rates achieved and few complications. But there is few data that indicate which patient is suitable for this procedure. Farhi et al.[23] showed that women with high serum LH levels respond favorably. Our results showed that ovarian size doesn't influence the result of ovarian cauterization. We were unable to identify any other clinical characteristics to contribute to an improved prediction of the response to laparoscopic ovarian electrocautery.

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