Multiple ovarian biopsy in the treatment of women with polycystic ovary syndrome (PCOS)

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Summary

Background: Ovarian electrocautery has been used with success in the treatment of PCOS women. However, unipolar coagulation carries the risk of serious injuries to pelvic organs. In an effort to avoid this potential risk, the efficacy of multiple ovarian biopsy was evaluated in our study.

Methods: Eleven PCOS patients were enrolled to the study. Four to eight biopsies were taken from both ovaries. The levels of LH, FSH, androgens and the reactivity of ACTH test were evaluated at standard intervals. The occurrence of ovulation was determined by ultrasound.

Results: Laparoscopy was followed by non-significant changes of endocrine parameters only. The ovulatory cycle was restored in only three women of the whole group.

Conclusions: Our study did not prove the efficacy of multiple ovarian biopsy in the treatment of PCOS women. The procedure caused only minor changes in endocrine parameters and rarely restored ovulation.

Key words: Polycystic ovary syndrome; Endocrine changes; Laparoscopy; ACTH test; Multiple biopsy.

Introduction

Surgical treatment of polycystic ovary syndrome (PCOS) has been shown to restore ovulation, normalize LH level, lower the LH/FSH ratio, lower the levels of androgens and enhance sensitivity to ovulation stimulation [1-2]. Various authors have described a variety of methods with different extent of surgical interventions on the ovaries. The method of ovarian electrocauterization is reported by most authors [2-6, 8-10]. However, the use of unipolar coagulation carries the risk of rare yet serious complications, especially injury to major blood vessels. Comparable ovulation rates and endocrine changes have been described using multiple ovarian biopsy. This method is not accompanied by the risk associated with the use of unipolar coagulation.

Our study was proposed to evaluate the effect of multiple ovarian biopsy in clomiphene-citrate resistant PCOS women. Hormone levels, ovulation rates and changes in ACTH test reactivity were monitored after the procedure.

Material and Methods

Subjects and methods

Eleven patients were prospectively included in our study. All women were Caucasians. The inclusion criteria were as follows: (1) an elevated LH/FSH ratio > 1.5, (2) elevated plasma levels of at least one androgen (testosterone > 2.7, nmol/L, or androstenedione > 6.0 nmol/L, or dehydroepiandrosterone > 10.5 nmol/L), (3) oligomenorrhea (menstrual period > 45 days) or amenorrhea, (4) typical appearance of the ovaries on ultrasound (dense center surrounded by a chain of at least 8 cysts < 10 mm in diameter), (5) exclusion of other endocrine disorders, (6) absence of medical or surgical treatment during the previous six months, and (7) anovulation during three cycles of treatment with 100 mg clomiphene-citrate confirmed by regular ultrasound measurements.

All subjects underwent a laparoscopic procedure after their informed written consent had been obtained. The procedure was performed during the early follicular phase of the menstrual cycle in all cases.

The plasma levels of LH, FSH, androstenedione, DHEA (dehydroepiandrosterone), DHEAS (dehydroepiandrosterone sulfate), testosterone, and SHBG (sex hormone-binding globulin) were measured at the following intervals: (1) prior to laparoscopy, (2) two days after the procedure, (3) during the first cycle, and (4) during the third cycle after the procedure. Provided spontaneous menstrual bleeding failed to occur by day 45 of the cycle, bleeding was induced by progesterone administration. The shortened ACTH test was performed before laparoscopy and during the first cycle after laparoscopy and the plasma levels of 17-hydroxyprogesterone were determined before ACTH stimulation and 30 and 60 minutes thereafter. All blood samples, except those obtained two days after the procedure, were taken between days 3 and 6 of the cycle. The blood samples were centrifuged and the serum was stored at –20°C until assayed.

Each patient had her height and weight taken and her body mass index (BMI) and waist-to-hip (WHR) ratio were calculated. Regular ultrasound measurements were performed during three cycles after the procedure to determine the occurrence of the ovulatory cycle.

Laparoscopy

Laparoscopy was performed under general anesthesia. Patients were placed in the Trendelenburg position and a 10 mm trocar placed subumbilically with two 5 mm trocars used on

Revised manuscript accepted for publication June 26, 2000

each side. Four to eight biopsies (according to the size of the ovary) were taken from each ovary using biopsy forceps. Each biopsy was about 4 mm in diameter and 4 to 8 mm in depth. Hemostasis was carefully induced and lavage with Ringer's solution was used to prevent postoperative adhesions.

Hormone assays

All steroids were determined by radioimmunoassay (RIA). Testosterone was determined by the method of Hampl *et al.* in a later modification and androstenedione by the method of Putz *et al.* [13-14]. Dehydroepiandrosterone and its sulfate were measured using commercial RIA kits from Immunotech (France). Both gonadotropins (LH and FSH) were determined by commercial RIA kits manufactured by Huma Lab (Slovakia). SHBG was determined using IRMA kits from Orion (Finland).

Statistical analysis

The following statistical tests were used for data processing: (1) two sample t-test, (2) paired t-test, (3) analysis of variance with repeated measures and grouping factor (ANOVA) followed by Sheffé's multiple comparison test.

The study was approved by the Local Ethics Committees of both institutions.

Results

Table 1 shows the endocrine parameters for the entire group of 11 women before laparoscopy and after the procedure. There was a decrease in the mean plasma levels of LH and in the LH/FSH ratio in all samples after the procedure. Nevertheless, these changes did not reach statistical significance at any of the intervals monitored. There was no significant change in the mean plasma levels of androstenedione, DHEA or T/SHBG ratio after the procedure.

A shortened ACTH test was performed before laparoscopy and during the first cycle thereafter. None of the subjects met the criteria for late-onset cortical adrenal hyperplasia before the procedure. Laparoscopy was not followed by a change in the mean levels of 17-hydroxyrpogesterone prior to ACTH stimulation or 30 and 60 minutes after the stimulation (Table 2). There was no difference in the mean increase in 17-hydroxyprogesterone between the ACTH tests performed before and after laparoscopy. The curves of 17-hydroxyprogesterone levels before and after the procedure were likewise not significantly different.

Regular ultrasound investigation demonstrated an ovulatory cycle after the procedure in three patients only. In one patient ovulation occurred during the third cycle, in another two patients during the second cycle after the procedure.

All women were discharged within two days following surgery. No postoperative complications were reported. All 11 women became pregnant within six months after the end of follow-up. Different protocols of ovarian stimulation were employed. Until pregnancy, none of the women complained of abdominal pain. None underwent a second-look laparoscopy.

Table 1. — *Mean plasma levels of luteinizing hormone (LH) (IU/L), dehydroepiandrosterone (DHEA) (nmol/L), androstenedione (A) (nmol/L) and mean value of ratio of luteinizing hormone (LH): follicle stimulating hormone (FSH) (IU/L), testosterone (T) (nmol/L): sex hormone-binding globulin (SHBG) (nmol/L) before laparoscopy and at an interval after the procedure (N=11).*

	Before LPS	Two days after LPS	1st cycle after LPS	3th cycle after LPS	P-value
LH	11.2±6.1	8.5±4.2	8.1±3.4	7.9±3.9	n.s.
LH/FSH	3.2±1.3	2.3±1.1	2.1±1.4	2.6±2.2	n.s.
A	6.5±2.8	6.4±2.6	6.4±3.1	7.5±4.2	n.s.
DHEA	23.2±15.4	17.6±12.9	26.9±22.8	23.5±12.1	n.s.
T/SHBG	0.08±0.05	0.06±0.03	0.08±0.03	0.08±0.04	n.s.

n.s. = non-significant.

Table 2. — *Mean plasma levels (nmol/L) and average increase in 17-hydroxyprogesterone during the ACTH test before laparoscopy and during the first cycle after the procedure (N=11).*

	Before LPS	1st cycle after LPS	P-value
Plasma level			
0 min.	2.56±0.6	2.93±0.9	n.s.
30 min.	4.9±1.4	5.32±2.2	n.s.
60 min.	5.43±3.5	5.38±2.1	n.s.
Mean increase			
30 min.	2.56±1.4	2.38±2.4	n.s.
60 min.	3.36±1.9	2.11±1.6	n.s.

n.s. = non-significant.

Discussion

Laparoscopic ovarian electrocautery was introduced in PCOS patients by Gjonnaess in 1984 [1]. The mechanism of the effect of surgical intervention in the treatment of PCOS is not known. Removal of a thickened tunica albuginea [15], destruction of ovarian stroma causing a decrease in androgen synthesis, the role of blood supply in the healing process increasing the delivery of gonadotropins [12] and, also, some intraovarian factors [16] have been proposed.

To date, a number of techniques with different extent of the intervention on the ovaries have been described. The most frequently reported technique is a modification of Gjonnaess" technique of unipolar cautery of the ovarian surface. Electrocautery is performed at four to ten sites on each ovary [3, 8, 10]. The ovulatory cycle occurs after the procedure in 81% to 92% of PCOS patients. Spontaneous ovulation usually develops within three to six weeks after the procedure. Most authors have demonstrated a transient rise in LH levels occurs within 24 hours after the procedure, to be followed by a significant fall in the levels [2, 5, 7, 10, 12]. Most studies report appreciable decreases in the mean levels of testosterone and androstenedione; some authors have also referred to changes in the levels of DHEA and DHEAS [5, 7, 8, 10].

The use of unipolar coagulation is associated with a serious risk of large vessel injury. As a result, the method of multiple biopsy was chosen to treat polycystic ovaries in our study. Good results using this technique have been described. Sumioki *et al.* performed 6-10 biopsies of capsular tissue in seven anovulatory PCOS patients [15].

He demonstrated restoration of ovulation in 85.7% of patients and significant decreases in testosterone, free testosterone and androstenedione after surgery. However, the biopsy forceps was equipped by unipolar coagulation in this study. Consequently, the effect of the intervention involved both removal of the ovarian capsule and monopolar electrocauterization. A large group of 23 infertile patients treated by multiple biopsy or single incision of the ovarian surface was presented by Campo [17]. An ovulation rate of 56% after the procedure was substantially lower compared to other techniques used [18]. The study failed to demonstrate a change in LH level; however, significant decreases in androstenedione and testosterone were shown in a group of 15 patients. In both studies, the endocrine parameters were assessed over a short interval, four days in one study and six weeks in the other one, after the procedure. Moreover, blood samples were obtained regardless of the interval from spontaneous or induced menstrual bleeding. Physiological variations of hormone production should be at least partially responsible for the endocrine changes established.

No significant changes in LH levels, LH/FSH ratio and androgens were demonstrated in our study after multiple ovarian biopsy. The unaltered parameters of adrenal steroidogenesis come as no surprise. The most important observation made in our study was that resumption of ovulation occurred in only three women of the entire group.

Conclusion

In our study we were unable to confirm the efficacy of multiple ovarian biopsy in the treatment of clomiphene-citrate resistant PCOS women. Ovulation was restored in a few cases and the procedure was followed by non-significant endocrine changes. Although we are well aware of the low number of participants, we were unable to continue the study protocol because of the pure response of patients. We conclude that the surgical procedure involving the ovarian cortex only is ineffective in the treatment of PCOS.

Acknowledgement

The study was supported by the Internal Grant Agency of the Ministry of Health of the Czech Republic (grant number 4847-3).

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