

# Impact Of Laparoscopic Ovarian Drilling On Hormonal Profile And Clinical Features In Women With Polycystic Ovary Syndrome

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## Abstract

**Objective:** To evaluate the impact of laparoscopic ovarian drilling on the hormonal profile and clinical features and its relation to spontaneous ovulation in women with polycystic ovary syndrome.

**Materials and Methods:** This was a prospective observational study including 104 women with polycystic ovary syndrome who underwent laparoscopic ovarian drilling (LOD). Hormonal assay and clinical features were assessed before and after LOD. Data were collected and compared.

**Results:** there was a highly significant decrease in the serum levels of LH (P-value  $\leq 0.001$ ), significant decrease in the serum levels androstenedione (P  $\leq 0.05$ ), and a highly significant elevation of serum prolactin (P-value  $\leq 0.001$ ) with no significant difference between pre-operative and post-operative serum levels of FSH and testosterone (P  $\leq 0.05$ ). There was a significant improvement of hirsutism, acne, regularity of the menstrual cycle (P  $< 0.05$ ) and resumption of spontaneous ovulation (P  $< 0.001$ ) following LOD. There was a significant difference between the ovulatory and anovulatory women following the operation regarding the serum level of androstenedione (P  $< 0.05$ ) and serum prolactin (P  $< 0.001$ ).

**Conclusion:** Although there was improvement in gonadotropin & androgen levels and clinical features of hyperandrogenemia. Anovulation following LOD may be due to hyperprolactinemia and/or elevated androstenedione, thus hormonal assay in anovulatory patients after ovarian drilling is recommended.

## INTRODUCTION

The polycystic ovary syndrome (PCOS) is associated with chronic anovulation and infertility. In most cases ovulation can be induced with clomiphene citrate (CC) which constitutes one of the first-line treatments for ovulation induction in these patients, as it is economical, has few adverse effects, and requires little monitoring<sup>1</sup>. But, approximately 25% of patients fail to ovulate and require alternative treatment<sup>2</sup>.

The second possible line of therapy after resistance to CC has been demonstrated in women with PCOS is exogenous gonadotropins. Human menopausal gonadotropins have been used but, have the risk of hyperstimulation and multifetal gestation<sup>3, 4</sup>.

In clomiphene-resistant PCOS women who are unable to

comply with the close monitoring necessary for gonadotrophin administration, laparoscopic ovarian drilling (LOD) is an acceptable alternative<sup>5</sup>. In a Cochrane Database Systematic Review article, there was no evidence of a difference in live birth rate and miscarriage rate in women with clomiphene-resistant PCOS undergoing LOD versus gonadotrophin treatment<sup>6</sup>.

The reported ovulation rate after LOD varies between 50% and 90%<sup>7</sup>, there is some disparity between hormonal improvement and ovulation rate following LOD<sup>8</sup>.

We performed this prospective observational study to evaluate the impact of laparoscopic ovarian drilling on the hormonal profile and clinical features and its relation to spontaneous ovulation in women with polycystic ovary syndrome.

## **MATERIALS AND METHODS**

### **Study design**

A prospective Observational study was designed taking 104 PCOS patients, admitted to the Department of Obstetrics and Gynecology, Menoufia University hospital, Egypt from May 2012 to July 2015.

The institutional review board approved the study protocol and an informed consent was obtained from all patients prior to commencing the study.

### **Sample size**

Based on the rate of spontaneous ovulation following LOD of 50-90% from the literature, we calculated the sample size at  $\alpha = 0.05$  and a study power of 90%. A total sample size of 90 patients was required after adding a percentage of 10% for possible drop out cases during the study.

### **Inclusion criteria**

(1)-PCOS was diagnosed according to the revised European Society of Human Reproduction and Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM) criteria of 2004 which were based on the Rotterdam criteria 9.

Clomiphene citrate resistance was defined as the absence of developing follicles after ovarian stimulation with 150 mg clomiphene citrate/day given for five days beginning with the 2nd day of the menstrual cycle. Patients were stimulated with clomiphene for a minimum of three and a maximum of six cycles 10.

(2)-A normal semen analysis.

(3)-A normal uterine cavity.

(4)- Bilateral tubal patency.

### **Exclusion criteria**

(1)-Semen abnormalities.

(2)-FSH >15 mIU/mL.

(3)-Contraindications for laparoscopy.

(4)- Medical disorders: diabetes mellitus and hypertension.

(5)- Endocrine disorders: hyperprolactinaemia (prolactin  $\geq$  22 ng/dl), thyroid disorders, cushing's syndrome and

acromegaly.

### **Clinical examination**

To measure the patient's weight, height, the presence of acne and/or hirsutism (according to the Ferriman-Gallway score > 8).

### **Hormonal assays**

Patients baseline blood samples were obtained before laparoscopic ovarian drilling (2–3 days after the commencement of spontaneous menstrual bleeding) to assess serum levels of LH, FSH, testosterone, androstenedione and prolactin.

The second blood sample was obtained in the early follicular phase (days 2-3) of the menstrual cycle after 3 months of the operation.

Radioimmunoassays were used to determine serum levels of LH (Autodelphia; Wallac Oy, Turku, Finland), FSH (Enzymun ES700; Böhringer Mannheim, Mannheim, Germany), testosterone (Immunotech, Westbrook, ME, USA), androstendione (Immunotech, Westbrook, ME, USA) and prolactin (Immunotech, Westbrook, ME, USA).

### **Normal values of hormonal levels**

FSH = 3–13 mIU/ml, LH = 1.5–12 mIU/ml,

Androstendione = 0.6-3 ng/ml, Testosterone= 0.2–0.9 ng/ml and Prolactin= 2-22 ng/ml.

### **Sonography**

Pelvic sonography (Acuson 128 XP 10, computed sonography system, Mountain View, California, USA) was carried out on day 12-16 for folliculometry before and after the operation. Ovulation is defined as the presence of at least one dominant follicle measuring  $\geq$  18 mm.

### **Surgical technique**

Laparoscopic ovarian drilling (LOD) was performed using three-puncture technique. The laparoscope was introduced through a subumbilical incision. After assessment of the pelvic structures and tubal patency, an insulated needle connected to a unipolar electrocautery with four to six cautery points 3–4 mm in diameter was created in each ovary with a current of 4 mA applied through the laparoscopic insulated needle.

### **Outcome measures**

The outcome of this study was to measure the degree of hormonal changes (LH, FSH, testosterone, androstenedione and prolactin) and clinical features of PCOS (menstrual regularity, spontaneous ovulation and features of hyperandrogenemia as hirsutism & acne) after 3 months following LOD.

### Statistical analysis

Data were collected, tabulated, statistically analyzed by computer using SPSS version 16 (SPSS Inc, Chicago, IL, USA). Quantitative data are expressed to measure the central tendency of data and diversion around the mean, mean (x) and standard deviation (SD). Qualitative data expressed in number and percentage.

All these tests were used as tests of significance at

- P value > 0.05 was considered statistically non significant.
- P value  $\leq$  0.05 was considered statistically significant.
- P value  $\leq$  0.001 was considered statistically highly significant.

[P value in bold in the tables is statistically significant]

## RESULTS

Table (1) displays the patient characteristics.

### Figure 1

Patient characteristics (n = 104)

Table (2) reveals the hormonal profile before and after laparoscopic ovarian drilling, there was a highly significant decrease in the serum levels of LH (P-value  $\leq$  0.001), significant decrease in the serum levels androstenedione (P  $\leq$  0.05), and a highly significant elevation of serum prolactin (P-value  $\leq$  0.001) with no significant difference between pre-operative and post-operative serum levels of FSH and testosterone (P  $\geq$  0.05).

### Figure 2

Hormonal profile before and after laparoscopic ovarian drilling

Table (3) shows the clinical features before and after laparoscopic ovarian drilling, there was a significant improvement of hirsutism, acne and regularity of the menstrual cycle (P < 0.05) as well as resumption of spontaneous ovulation (P < 0.001).

### Figure 3

Clinical features before and after laparoscopic ovarian drilling

Table (4) reveals the impact of laparoscopic ovarian drilling on hirsutism & acne in women with PCOS.

### Figure 4

The impact of laparoscopic ovarian drilling on hirsutism & acne in women with PCOS

Table (5) displays the comparison of study parameters in relation to resumption of spontaneous ovulation, there was a significant difference between the ovulatory and anovulatory women following LOD regarding the serum level of androstenedione (P < 0.05) and serum prolactin (P < 0.001).

### Figure 5

Comparison of study parameters in relation to resumption of spontaneous ovulation

## DISCUSSION

We confirm the previously reported endocrine changes shortly after LOD, including lowering of the serum concentrations of LH and androgens 5, 11. These endocrine changes seemed to last during the medium- and long-term follow-up periods 12.

In our study, women who remained anovulatory in spite of significant fall in LH and testosterone levels, prolactin was significantly elevated when measured 3 months after the operation. Gjonness et al 13 in their study on 17 women showed a transient hyperprolactinemia immediately after LOD, they believed that this phenomenon was due to operative stress. Hyperprolactinemia as a complication of operation, and/or anesthesia was previously described with the peak prolactin levels always occurring during surgery. Prolactin remained elevated in 62.5% when measured 6–10 weeks after operation 14, 15, 16.

In our study, postoperative androstenedione was higher among anovulatory women when compared to ovulatory women. In a previous trial, LH and androstenedione were accurate for predicting ovulation after LOD, reaching both a specificity and a positive predictive value of 100% 17.

Although chronic anovulation in women with PCOS is usually associated with menstrual irregularities 18, 50% of our patients had regular menses prior to LOD. This observation was confirmed in a previous study of 1741 women with PCOS in which 30% of patients had regular menses 19. The proportion of women with regular menstrual cycle increased significantly in our study from 50% to

92.3% following LOD. Many authors observed that LOD leads to restoration of regular menses in about 63-84% of patients 11, 20, 21.

In our study, LOD leads to improvement of hirsutism and acne in 64.7% and 50% in treated patients respectively. In a previous study, LOD produced short term improvement of hirsutism and acne in 33% and 52% respectively which is sustained for up to 9 years in 23% and 40% of cases respectively 22.

We conclude that after ovarian drilling, women who remained anovulatory in spite of decreased serum androgen levels and other hormonal profile improvement, may have an elevated prolactin &/or androstenedione levels. Hormonal assay in anovulatory patients after LOD is recommended.

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### Disclosure

We certify that no actual or potential conflicts of interest in relation to this article exist.

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