Effect of laparoscopic ovarian drilling on serum vascular endothelial growth factor and ovarian stromal blood flow in patients with polycystic ovarian syndrome

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Background Women with polycystic ovary syndrome have significant difference in their ovarian stromal blood flow indices when compared with women with normal ovaries.

Aim To determine the serum level of vascular endothelial growth factor (VEGF) and ovarian stromal blood flow changes in anovulatory women with polycystic ovarian syndrome before and after laparoscopic ovarian drilling (LOD).

Patients and methods This is a prospective, controlled study conducted at the Department of Obstetrics and Gynecology at Al Zahraa University Hospital. Thirty-eight women with polycystic ovarian syndrome (PCOS) according to Rotterdam Criteria, 2003, aged 25–40 years, BMI between 20 and 30 kg/m^2, having normal hysterosalpingography (HSG), resistant to clomifene citrate treatment, and partners having normal semen analysis according to WHO criteria were included. Thirty-eight women with polycystic ovarian syndrome resistant to clomifene citrate treatment and 18 healthy fertile women served as the control group. Ovarian Doppler and serum levels of VEGF, luteinizing hormone (LH), follicular stimulating hormone (FSH), and total testosterone were measured in the early follicular phase of PCOS (before LOD) and control cases, then PCOS women undergo LOD, then ovarian Doppler and serum levels of VEGF, LH, FSH, and total testosterone were measured in the early follicular phase within 3 months after LOD

Results After LOD, serum level of VEGF concentrations in women with PCOS significantly decrease in its level after LOD; LH decreased significantly from 11.1±1.4 mIU/ml before LOD to 5.8±0.8 mIU/ml after LOD. FSH increased significantly from 4.5±0.6 mIU/ml before LOD to 7±0.1 mIU/ml after LOD and total testosterone decreased significantly from 0.9±0.2 ng/ml before LOD to 0.5±0.1 ng/ml after LOD. Ovarian stromal blood flow velocity declined significantly after LOD in women with PCOS. There is significant increase in the resistance index, pulsatility index after LOD when compared with its value before LOD levels.

Conclusion LOD reduced serum levels of VEGF, in addition to ovarian blood flow indices, in women with PCOS. LOD is a good second choice to induce ovulation in patients with PCOS who are clomifene citrate resistant, as it improves ovulation in infertile anovulatory PCOS women.
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Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrinal disorder that occurs in more than 10% of women of reproductive age and is associated with increased prevalence of cardiovascular risk factors (i.e. insulin resistance, hypertension, and dyslipidemia), metabolic syndrome, and cardiovascular diseases [1].

Three international conferences have developed somewhat different but overlapping diagnostic criteria for adult women: the National Institutes of Health Conference Criteria (1990), the Rotterdam Consensus Criteria (2003) [2], and the Androgen Excess-PCOS Society consensus criteria (2006). The National Institutes of Health criteria included hyperandrogenism, chronic anovulation, and exclusion of other causes of these symptoms. The Rotterdam Criteria are the broadest and include the features of the other definitions. They allow PCOS to be diagnosed with a combination of chronic anovulation and polycystic ovary morphology without hyperandrogenism [2–4].

Blood flow to the ovaries was concluded to be influenced by local factors more than hormone levels in circulation. The ovarian artery blood flow resistance parameters in an ovulatory PCOS group were significantly higher as compared with the ovulatory group [5].

Ovarian angiogenesis is a tightly regulated process that needs a delicate balance of angiogenic factors, which is disrupted in women with PCOS. This altered angiogenesis may contribute to the ovarian features of PCOS such as abnormal follicular development, increase in the quantity of small follicles, and failure in the selection of the dominant follicle, with anovulation and cyst formation [6].

Doppler allows detection of the vascularization network within the ovarian stroma; vascular endothelial growth factor (VEGF) is a diffusible endothelial cell mitogen with potent angiogenic properties. Within the ovary, it is expressed in the theca cells, granulosa and lutein cells and the interstitial ovarian tissue [7].

VEGF expression in the ovary are increased in women with polycystic ovary (PCO) and PCOS [7].

Laparoscopic ovarian drilling (LOD) has evolved into a safe and effective surgical option for CC-resistant PCOS cases. It is as effective as gonadotropins in terms of clinical pregnancy rates and live birth rates with the obvious advantages of spontaneous mono-ovulation thereby minimizing the need for intensive monitoring and eliminating the risks of ovarian hyperstimulation syndrome and multiple pregnancies [8].

The aim of this study was to determine the serum level of VEGF and ovarian stromal blood flow changes (by using two-dimensional color Doppler ultrasonography) in anovulatory women with polycystic ovarian syndrome before and after LOD.

Patients and methods

This prospective, controlled study was carried out in the Department of Obstetrics and Gynecology, at Al Zahraa University Hospital in the period between September 2015 and September 2018. The study included 38 women with polycystic ovarian syndrome resistant to clomifene citrate treatment and 18 healthy fertile women as the control group attended the infertility outpatient clinic.

Inclusion criteria

(1) Age between 25 and 40 years with anovulatory infertility.
(2) BMI between 20 and 30 kg/m^2.
(3) Have normal hysterosalpingography (HSG).
(4) Partner had normal semen analysis according to WHO criteria.
(5) Female diagnosed PCOS according to the 2003 ESHRE/ASRM (Rotterdam, Biotech, china) criteria.
(6) The Rotterdam consensus expanded the diagnostic criteria to include at least two of the following three features: (a) oligomenorrhea, that is, cycle lasting longer than 35 days or anovulation, (b) clinical and/or biochemical signs of hyperandrogenism, (c) polycystic ovaries by sonographic features.
(7) Resistant to clomifene citrate treatment. Clomifene citrate resistance was defined as three consecutive cycles with clomifene citrate clomiphene citrate (CC) 150 mg daily for 5 days without ovulation.

Exclusion criteria

(1) Hyperprolactinemia.
(2) Women with infertility due to any factor other than anovulation (e.g. tubal or male factors).
(3) Women with a history of ovarian surgery or pathology detected by TVS, or any organic pelvic diseases at laparoscopy or diseases potentially affecting the ovarian environment and/or function (including endometriosis and leiomyoma.
(4) Women with a single ovary.

Ethical considerations

The study protocol was approved by the local Ethics Committee of Faculty of Medicine, Al Zahraa University. An informed consent was taken from all patients and their husbands before starting the study and every patient had the right to leave the study at any time.

Methods

The following was done:

(1) A full detailed history was taken from all patients.
(2) General examination.
(3) Abdominal examination.
(4) Local examination.
(5) Ultrasound: transvaginal ultrasound to exclude patients with ovarian masses or pelviabdominal masses

Hormonal profile

Serum levels of VEGF, luteinizing hormone (LH), follicular stimulating hormone (FSH), and total testosterone were measured in the early follicular phase (day 3 of spontaneous cycle in oligomenorrhea patients). In amenorrhea patients (after exclusion of pregnancy) they received progesterone (oral norethisterone acetate 10 mg daily for 5 days) to induce withdrawal bleeding and hormonal profile was measured in day 3 of this withdrawal bleeding.

Assay of VEGF was done by using a Quantikine VEGF ELISA kit.

Doppler study before laparoscopic ovarian drilling

Transvaginal 2D color Doppler probe using a SonoAce Medison X4 ultrasound machine (Samsung Medison, Korea) with a 3.5 MHz sector transducer for transabdominal and 7.5 MHz sector transducer for TVS. The patients were placed at lithotomy position after they had evacuated their urinary bladder and on the same days of the hormonal assay, baseline 2D TVS was used to examine the uterus for any abnormality and measuring the uterine size and endometrial thickness and then to identify PCO criteria in both ovaries and ovarian volume was measured using the formula (length×width×height×0.523), which is calculated automatically by the software of the ultrasound machine. Then Doppler ultrasound scanning was performed to assess the ovarian stromal blood flow. By Doppler flow, imaging signals were searched for ovarian stroma away from the ovarian surface and away from the wall of the follicles. By placing the Doppler gate over the ovarian stroma, areas of maximum intensity, representing the greatest Doppler frequency shifts, were visualized, and then selected for pulsed Doppler examination; pulsatility index (PI) and resistance index (RI) were calculated in each selected Doppler wave.

Laparoscopic ovarian drilling

LOD was performed under general anesthesia using the three-puncture technique (one puncture 10 mm at the umbilicus and the other two punctures 5 mm at both the iliac fossa) in the early follicular phase (after stoppage of menstrual or withdrawal bleeding). After exclusion of any pelvic pathology, the ovaries were evaluated for polycystic ovary criteria (bilateral ovarian enlargement with smooth glistening surface unbroken by the usual wrinkles and thick, smooth, whitish capsule). Methylene blue test was done for all patients to examine the tubal patency and bilateral tubal patency was mandatory before ovarian drilling. A specially designed monopolar electrocautery probe was used to penetrate the ovarian capsule at four points (regardless of the size of the ovary). Monopolar coagulating current at a 40 W power setting was used. The needle was pushed through the ovarian capsule to about 4 mm depth into the ovarian tissue and electricity was activated for 4 s. The ovary was then cooled using a 200 ml crystalloid solution before releasing the ligament.

Follow-up of the patient

(1) Hormonal assay (VEGF, FSH, LH, and total testosterone) was performed after LOD in the early follicular phase. On day 3 of the first natural menstrual cycle (which occurs within 3 months after LOD) or progestin-induced cycle (after exclusion of pregnancy(.
(2) Blood flow assessment (PI–RI) was performed in the early follicular phase, on day 3 of the first natural menstrual cycle (which occurs within 3 months after LOD) or progestin-induced cycle (after exclusion of pregnancy). Ovulation was assessed after LOD by serial transvaginal ultrasound until visualization of preovulatory follicle of at least 18 m in diameter.

Ovulation was confirmed by seeing the follicle collapse on subsequent transvaginal ultrasound, appearance of fluid in the cul-de-sac. Patients who did not ovulate after drilling as evidenced by poor or no follicular growth by serial transvaginal ultrasound folliculometry.

Analytical statistics

Statistical tests used in this study were conducted, using Student's *t*-test, χ^2-test, Fisher's exact test, paired sample *t*-test. *P* is significant if less than 0.05 at a confidence interval of 95% (Figs 1–10).

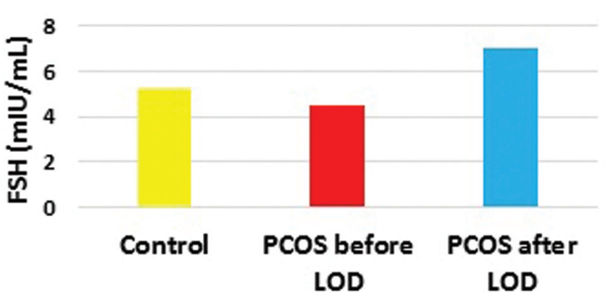
Results

Table 1 shows the mean age of PCOS women as 27.4 years, mean BMI was 25.3. No significant differences were found in age and BMI between PCOS and control groups.

Table 2 shows that eight (21.1%) cases had hirsutism, 22 (58%) had oligomenorrhea, 16 (42%) had secondary amenorrhea, 23 (61%) cases had primary infertility, 15 (39%) cases had secondary infertility. Mean infertility duration was 3.1 years.

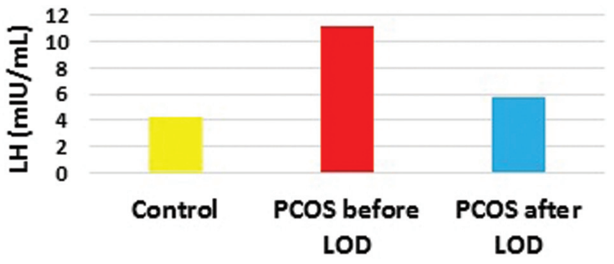
Table 3 shows that the PCOS group showed significantly higher level of LH, LH/FSH ratio, total testosterone, VEGF, and significantly lower FSH, when compared with the control group.

Figure 1



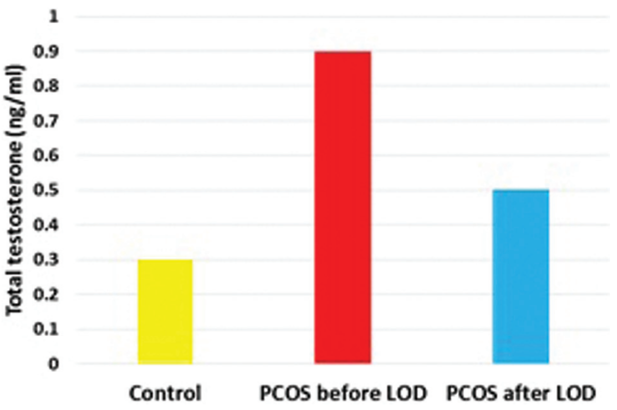
FSH level in the controll group, PCOS before and after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome.

Figure 2



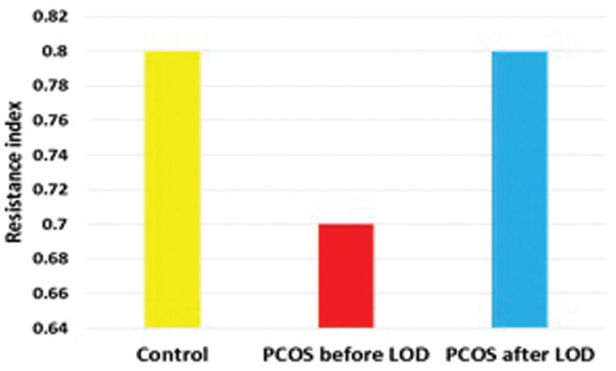
LH level in the control, PCOS before and after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome.

Figure 4



Total testosterone level in the control, PCOS before and after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome.

Figure 6

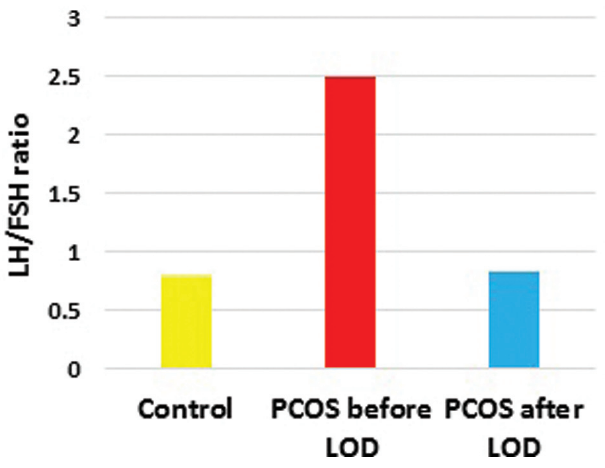


RI level in the control, PCOS before and after LOD. LOD, laparoscopic ovarian drilling; RI, resistance index; PCOS, polycystic ovarian syndrome.

Table 4 shows that the PCOS group showed significantly larger ovarian volume, significantly lower RI, PI when compared with the control group.

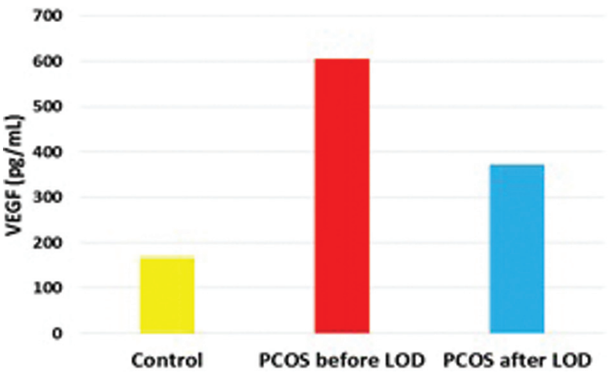
The PCOS group after LOD showed a significant decrease in the level of LH, LH/FSH ratio, total

Figure 3



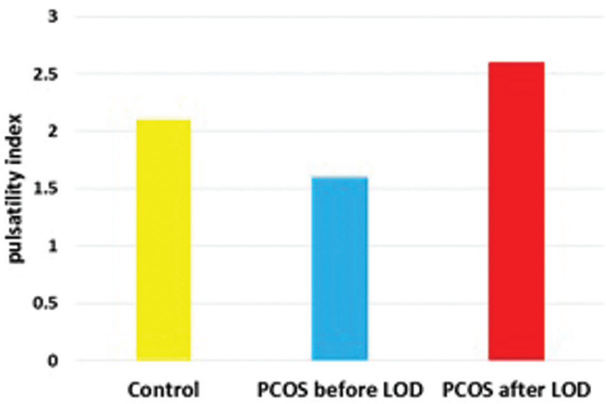
LH/FSH level in the control, PCOS before and after LOD. FSH, follicular stimulating hormone; LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome.

Figure 5



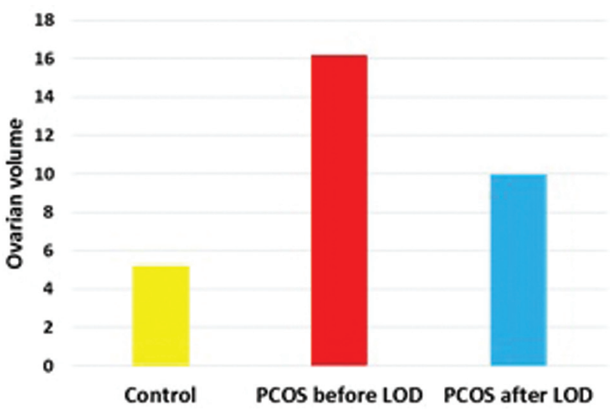
VEGF level in the control, PCOS before and after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome; VEGF, vascular endothelial growth factor.

Figure 7



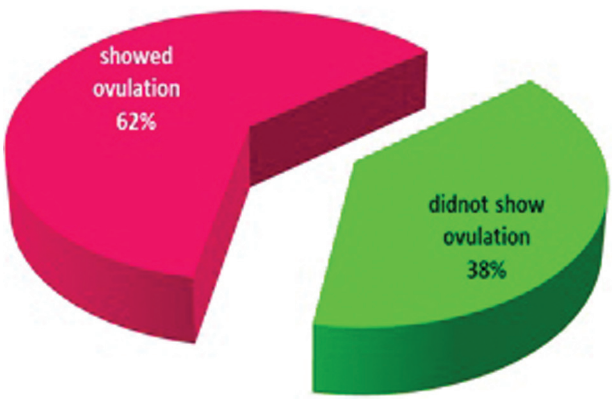
PI level in the control, PCOS before and after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome; PI, pulsatility index.

Figure 8



Ovarian volume in the control, PCOS before and after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome.

Figure 10



Ovulation in PCOS women after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome.

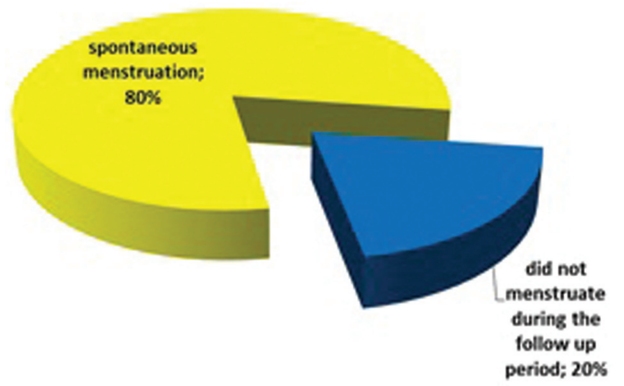
testosterone, VEGF; significant increase in the level of FSH when compared with before LOD levels (Table 5).

The PCOS group after LOD showed a significant decrease in the size of ovarian volume; significant increase in RI, PI when compared with before LOD levels (Table 6).

Discussion

In this study, we investigated various clinical and biochemical factors that may predict the outcome of LOD. Age, BMI, duration of infertility, menstrual cycle pattern, type of infertility, hirsutism, and ovarian volume were comparable. In this study the mean age of PCOS women was 27.4 years and mean BMI was 25 kg/m^2; the mean BMI in the control group was 24.2±1.1 kg/m^2. No significant differences were found in age and BMI between PCOS and control group (P=0.117^T). In agreement with our study, Moramezi *et al.* [9] found nonsignificant difference in BMI between the studied groups. In contrast to our study, Younesi *et al.* [10] found that BMI in PCOS was 28.1

Figure 9



Menstruation in PCOS women after LOD. LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome.

Table 1 Comparison of age and BMI between all studied groups

	Control (N=18) (mean±SD)	PCOS (N=38) (mean±SD)	P
Age (years)	27.4±4.8	27.4±3.7	0.996^T
BMI (kg/m^2)	24.2±1.1	25.3±1.9	0.117^T

T, Student *t*-test. PCOS, polycystic ovarian syndrome.

Table 2 Clinical data in all studied PCOS cases

	PCOS (N=38)
Hirsutism [*N* (%)]	8 (21)
Menstrual pattern [*N* (%)]	
Oligomenorrhea	22 (58)
Secondary amenorrhea	16 (42)
Type of infertility [*N* (%)]	
Primary	23 (61)
Secondary	15 (39)
Duration of infertility (mean±SD) (years)	3.1±0.9

PCOS, polycystic ovarian syndrome.

Table 3 Comparison of laboratory data between cases before laparoscopic ovarian drilling and control group

	Control (N=18) (mean±SD)	PCOS (N=38) (mean±SD)	P
FSH (mIU/ml)	5.2±1.1	4.5±0.6	0.002^T
LH (mIU/ml)	4.2±1.3	11.1±1.4	$<$0.001^T
LH/FSH ratio	0.8±0.1	2.5±0.4	$<$0.001^T
Total testosterone (ng/ml)	0.3±0.1	0.9±0.2	$<$0.001^T
VEGF (pg/ml)	167.9±47.8	605.3±93.8	$<$0.001^T

T, Student's *t*-test; FSH, follicular stimulating hormone; LH, luteinizing hormone; PCOS, polycystic ovarian syndrome; VEGF, vascular endothelial growth factor.

Table 4 Comparison of radiologic data between cases before laparoscopic ovarian drilling and control groups

	Control (*N*=18) (mean±SD)	PCOS (*N*=38) (mean±SD)	*P*
Resistance index	0.8±0.1	0.7±0.1	$<0.001^T$
Pulsatility index	2.1±0.6	1.6±0.5	0.001^T
Ovarian volume (cm^3)	5.2±0.6	16.2±3.3	$<0.001^T$

T, Student *t*-test. PCOS, polycystic ovarian syndrome.

Table 5 Comparison of laboratory data before and after laparoscopic ovarian drilling in PCOS group

	Before LOD (*N*=38) (mean ±SD)	After LOD (*N*=38) (mean ±SD)	*P*
FSH (mIU/ml)	4.5±0.6	7±0.1	$<0.001^{PT}$
LH (mIU/ml)	11.1±1.4	5.8±0.8	$<0.001^{PT}$
LH/FSH ratio	2.5±0.4	0.82±0.4	$<0.001^{PT}$
Total testosterone (ng/ml)	0.9±0.2	0.5±0.1	$<0.001^{PT}$
VEGF (pg/ml)	605.3±93.8	371.9±85.8	$<0.001^{PT}$

FSH, follicular stimulating hormone, LH, luteinizing hormone; LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome; PT, paired sample *t*-test; VEGF, vascular endothelial growth factor.

Table 6 Comparison of radiologic data before and after laparoscopic ovarian drilling in PCOS group

	Before LOD (*N*=38) (mean±SD)	After LOD (*N*=38) (mean ±SD)	*P*
Resistance index	0.7±0.1	0.8±0.1	$<0.001^{PT}$
Pulsatility index	1.6±0.5	2.6±0.3	$<0.001^{PT}$
Ovarian volume (cm^3)	16.2±3.3	10±1.7	$<0.001^{PT}$

LOD, laparoscopic ovarian drilling; PCOS, polycystic ovarian syndrome; PT, paired sample *t*-test.

±4.6 kg/m^2; it was significantly higher than normal women (BMI was 24.3±3.8 kg/m^2). In our study, the mean infertility duration was 3.1 years. This agrees with Amer *et al.* [11] who showed that ovulation and pregnancy rates are significantly decreased in patients with increasing duration of infertility (>3 years). As regards the ovarian volume in our study, there is significant decrease in ovarian volume in the PCOS group after LOD. It decreases from 16.2±3.3 cm^3 before LOD to 10±1.7 cm^3 after LOD, $P<0.001^T$. This agrees with Gad Al-Rab *et al.* [12] who found a significant reduction in ovarian volume from 18.9±1.7 cm^3 before LOD to 10.5±1.8 cm^3 after LOD. In consistence with our results, Elmashad [13] showed significant reduction of ovarian volume in PCOS women in response to LOD from 13.8±2.1 before LOD to 7.4±2.9 after LOD. In contrary to our study [14], it has been found that ovarian volume did not significantly affect after LOD.

The prevalence of hirsutism among PCO women in this study was 21%. This agrees with the study done by Sridhar and Susmitha [15], who found that 20% of PCOS women had hirsutism. In our study the LH; FSH; LH/FSH ratio: PCOS group showed significantly higher level of LH, LH/FSH ratio (before LOD) than normal fertile women. In this study the mean LH before LOD 11.1±1.4 mIU/ml decreased to 5.8±0.8 mIU/ml after LOD, FSH was 4.5 ±0.6 mIU/ml before LOD and significantly increased to 7±0.1 mIU/ml after LOD; the LH/FSH ratio was 2.5±0.4 mIU/ml before LOD that decreased to 0.82 ±0.4 mIU/ml after LOD. Our results showed significant decrease in the level of LH, LH/FSH ratio before and after LOD and significant increase in the level of FSH after LOD compared with its level before LOD ($P<0.001^T$).

The result of our study showed that total testosterone 0.9±0.2 ng/ml was decreased to 0.5±0.1 ng/ml; our results showed significant decrease in total testosterone level, after LOD compared with its level before LOD, $P<0.001^T$. This agrees with Ismail *et al.* [14] who found that LH decreased significantly from 13.1±1.9 before LOD to 6±0.6 after LOD and FSH; it increased significantly from 6.16±0.34 before LOD to 7.6±0.8 after LOD.

Total testosterone decreased significantly from 1.04 ±0.23 to 0.51±0.2 after LOD. This also agrees with the study done by Paramu [16] who found a significant decrease in LH, and LH: FSH ratio before and after LOD. There is significant decrease in serum testosterone before and after LOD. In contrast to our study in one point in which he found that no significant change in the levels of FSH before and after LOD. This also agrees with the study done by Elnaggar *et al.* [17], in Zagazig University Hospital carried out on 50 patients suffering from polycystic ovarian disease. They noticed that there was a significant decrease in serum LH levels from 14.84 ±4.37 before drilling to 6.06±1.52 after drilling. There was a significant decrease in LH-to-FSH ratio from 2.31±0.77 before drilling to 0.95±0.23 after drilling, but there was insignificant change in serum FSH levels from 6.59±1.08 before drilling to 6.43±0.91 after drilling, which is in contrast to our results. Our results show significant increase in the level of FSH after LOD. The difference may be due to that they had conducted their studies on different age groups, different patient number and different patient criteria as hyperprolactinemia is not excluded from the study. In agreement with our study, the study done by Samy *et al.* [18] observed that serum LH, LH/FSH ratio, and testosterone were significantly higher in women with PCOS (before LOD) in comparison to with women with normal ovaries, LH, LH/FSH ratio, and testosterone significantly decrease in PCOS patients after LOD.

In consistence with our study, El Behery *et al.* [19] found that the serum levels of LH and the LH/FSH ratio were significantly higher in the PCOS group before LOD than in the control group. After LOD in the PCOS group, there was a significant reduction both in the serum levels of LH and in the LH/FSH ratio.

They also found that serum testosterone significantly decreases after LOD. Contrary to our results, the change in serum FSH was not significant. Our results show a significant increase in the level of FSH after LOD.

As regards VEGF in this study it was significantly elevated in the PCOS group (before LOD) compared with the control group as this agrees with the study by Peitsidis and Agrawalb [7]. They found that the serum level of VEGF was significantly elevated in PCOS women than normal women. In our study serum level of VEGF concentrations in women with PCOS significantly decrease in its level after LOD, $P<0.001^{T}$. The reduction in LH and testosterone resulting from LOD may explain the reduction of VEGF after LOD. These reductions in VEGF levels may be the cause of increased Doppler indices suggesting corrected stromal blood flow, which may reduce ovarian hyperstimulation syndrome.

In consistence with our study [19], they founded that the serum levels of VEGF was significantly higher in the PCOS group before LOD than in the control group, after LOD. There was a significant reduction in the serum levels of VEGF. In a study done by Samy *et al.* [18] that was performed at Shams University Maternity Hospital on 40 clomifene citrate-resistant PCOS infertile patients and 22 healthy fertile women. A blood sample was taken from each patient before LOD. A second sample was taken on day 3 of the first postoperative cycle after LOD. In agreement with our study, they found that the level of serum VEGF concentrations in women with PCOS was significantly higher than in women with normal ovaries, in disagreement with our study. They found no significant change in serum VEGF level in PCOS women pre-LOD and post-LOD. Our results show significant reduction in serum levels of VEGF after LOD. In agreement with this study, the study done by Amin *et al.* [20] conclude that VEGF and IGF-1 levels are higher in women with PCOS than in healthy women. LOD reduced VEGF, as well as LH and testosterone and also ovarian blood flow velocities in PCOS.

Contrary to our study, the study done by Tulandi *et al.* [21] did not find significant difference in serum VEGF levels before and after LOD. This difference may be because they applied the electric current for only 2 s (4 s in our study). This study has reported a significant positive correlation between VEGF with LH and LH/FSH and significant negative correlation between VEGF with FSH after LOD. As regards Doppler study, the results of this study demonstrated that ovarian stromal blood flow velocity declined significantly after LOD in women with PCOS. In our study there is significant increase in the RI, PI after LOD when compared with its value before LOD levels. RI significantly increase from 0.7 ±0.1 before LOD to 0.8±0.1 after LOD PI significantly increased from 1.6±0.5 before LOD to 2.6±0.3 after LOD, $P<0.001^{T}$.

This agrees with the study done by Ismail *et al.* [14] at Zagazig University which included 59 infertile women with PCOS who undergo Doppler study before and after LOD. It has been found that PI significantly increased from 2.02±0.56 before LOD to 2.98±0.5 after LOD. RI it significantly increased from 0.75±0.06 before LOD to 0.86±0.05 after LOD. The results obtained from a study done by Safdarian *et al.* [22] also found that PI significantly increased from 2.01±0.64 before LOD to 2.89±0.57 after LOD. As regards RI, it significantly increased from 0.76±0.11 before LOD to 0.84±0.08 after LOD.

In agreement to our study, a study done by Gad Al-Rab *et al.* [12] carried out in Minia University Hospital applied on 30 clomifene citrate-resistant women with PCOS undergoing LOD and 30 fertile women with normal ovaries concluded that serum VEGF and ovarian blood flow indices were higher in women with PCOS than in normal women. LOD reduced serum levels of VEGF, in addition to ovarian blood flow indices, in women with PCOS, the only difference from our study was that they used 3D Doppler and we used 2D Doppler US.

In consistence with our study, a study done by Kamal *et al.* [23] included 80 patients with CC-resistant PCOS undergoing LOD. Pre-LOD and post-LOD ovarian reserve parameters (AMH, ovarian volume, and ovarian stromal blood flow by 3D Doppler US) showed a significant reduction in ovarian stromal blood flow indices. In contrast to our study, the study done by Vizer *et al.* [24] reported an increased intraovarian blood flow after the procedure. The size of the studied group (10 patients) does not allow its results to be conclusive and such correlation would require further study. In our study, the follow-up of patients after LOD revealed: that 80% of cases showed spontaneous menstruation, 20% of cases did not menstruate during the follow-up period.

Sridhar and Susmitha [15] showed 87% of the patients had their menses; around 10% were still with amenorrhea. They did not follow hormonal profile after LOD and also did not record ovulation rate within the menstruating group. The percentage of occurrence of menstruation was higher than that of our study and that may be due to the fact that patients included in the study has high LH level; the mean was 26.2±3.95 mlU/ml, which is higher than the mean LH level in our study which was11.1±1.4.

This may be also due to the different technique of laparoscopy used; the diathermy probe was inserted to around 1 cm deep and 50 Hz current was applied for 2 s at 4–8 points into each ovary. In our study; the needle was pushed through the ovarian capsule for about 4 mm depth into the ovarian tissue and electricity was activated for 4 s, current at a 40 W power setting was used. As regards ovulation in our study, 65% showed ovulation as evidenced by folliculometry (leading mean follicular diameter>18 mm followed by seeing follicle collapse on subsequent transvaginal ultrasound, appearance of fluid in the cul-de-sac(. However, 35% did not show ovulation.

The ovulation rate in this study is close to the study done by Amer *et al.* [25]; 30 women with clomifene-resistant PCOS were included in the study. All women underwent LOD, ovulation occurred in 67%. In a study done by Ismail *et al.* [14], 70% cases showed ovulation and 30% did not show ovulation and that is close to our results [26]; 61% of the patients achieved spontaneous ovulation after LOD; this value is less than reported in our study. In our study 35% of PCOS women fail to respond to LOD (fail to ovulate). It may be due to the amount of electric current which is not sufficient to produce an effect in those patients, as we did not determine the amount of thermal energy according to the ovarian volume or size but the amount of thermal energy was fixed in all patients regardless of the ovarian size. Another possible explanation may be an inherent resistance of the ovary to the effects of drilling.

Conclusion

(1) LOD reduced serum levels of VEGF, in addition to ovarian blood flow indices, in women with PCOS.
(2) LOD is a good second choice to induce ovulation in patients with PCOS who are clomifene citrate resistant, as it improve chances of ovulation in infertile and ovulatory PCOS women.

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Conflicts of interest

There are no conflicts of interest.

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