Transvaginal needle versus laparoscopic ovarian drilling in drug-resistant polycystic ovary syndrome: a randomized, controlled study

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Objective
The aim of this study was to evaluate the outcome of ovarian needle drilling using transvaginal ultrasound guidance as an alternative to the traditional laparoscopic electrosurgical drilling for patients with polycystic ovary syndrome (PCOS).

Background
Ovarian drilling has been established as a treatment for drug-resistant PCOS.

Patients and methods
The study comprised 84 patients with PCOS who are resistant to ovulation induction using clomiphene citrate. The patients were randomly divided into two groups; in the first group of 42 patients ovarian needle drilling was done using transvaginal ultrasound guidance, whereas in the other group of 42 patients laparoscopic electrosurgery ovarian drilling was done.

Results
No significant differences were found between the two groups with regard to age, parity, BMI, and ultrasound finding of PCOS. The duration of ultrasound-guided transvaginal ovarian drilling was 15.59 ± 2.83 min, whereas it was 38.45 ± 5.46 min for laparoscopic drilling, with a statistically significant difference between the two groups. There were significant improvements after intervention in both groups without differences regarding resumption of regular menstruation, improvement of hyperandrogenic symptoms such as acne and hirsutism, occurrence of ovulation, and pregnancy. As regards hormonal profiles, serum luteinizing hormone, and luteinizing hormone/follicle stimulating hormone levels, AQ5 but not in the follicle stimulating hormone were found to be markedly decreased after intervention in both groups.

Conclusion
The results of this study have shown that the outcome of a simple rapid technique such as ultrasound-guided transvaginal ovarian drilling was comparable to the standard laparoscopic monopolar drilling in resumption of regular menstruation, improvement of hyperandrogenic symptoms, occurrence of ovulation and pregnancy in patients with PCOS resistant to ovulation induction using clomiphene citrate without all the risks expected from the later.

Keywords:
drug resistant, laparoscopic, needle drilling, transvaginal, ultrasound

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Introduction

Polycystic ovary syndrome (PCOS) is a common disorder that affects women in the childbearing period [1]. Chronic anovulation, hyperandrogenism, and oligomenorrhea/amenorrhea are its main cornerstone [2]. Clomiphene citrate is the drug of choice as first line for induction of ovulation among those peoples; gonadotrophins are considered the next step for clomiphene citrate-resistant infertile women. After failure of medical induction of ovulation, ovarian drilling has been established for drug-resistant PCOS [3]. Ovarian drilling can be done by electrocautery [4], laser [5], and ovarian hydrocoagulation [6]. Laparoscopic ovarian drilling (LOD) is costly, requires hospital treatment and general anesthesia and the risk of intraoperative and postoperative adhesions cannot be ignored [7]. The mechanism of action of ultrasound-guided ovarian drilling is thought to be similar to that of LOD [8]. A significant reduction in androgen levels in the serum has been observed [9]. Spontaneous ovulation in consecutive cycles occurred in 23% of cases and successful ovulation was obtained by clomiphene citrate in 77% of cases; in addition, the hazards of ovulation induction can be completely avoided [10].

Patients and methods

Randomized, controlled study comprised 84 patients with PCOS resistant to medical induction of ovulation using clomiphene citrate among those attending the outpatient clinic at Menoufia University Hospital and a private clinic in the period from 2015 to 2016 after giving informed written consent.

Sample size calculation: it was assumed that the ovulation rate after LOD to be 80% [11] and the ovulation rate after ultrasound-guided transvaginal ovarian needle drilling (UTND) was assumed to be 49% [8]. Accordingly, at a study power of 80% (with $\alpha = 0.05$), the required total sample size for the previous assumptions is 84 women.

Diagnosis of PCOS was based on the 2003 Rotterdam criteria [2]. All women had patent fallopian tubes by hysterosalpingography, normal serum prolactin, and thyroid-stimulating hormone and their partners had normal semen analysis according to the WHO criteria. Clomiphene citrate resistance in this study means women were previously treated with 100 mg daily for 5 days starting from the third day of the cycle for 2–3 cycles with persistent anovulation or ovulation with very thin endometrium, of less than 5 mm, at the time of human chorionic gonadotropin administration. Randomization was done according to a trial sequence determined by a computer-generated number list that was developed by a statistician. The trial sequence was hidden into opaque sequenced envelopes with each envelope containing an assignment for a single patient. Patient allocation was through a nurse picking up. The study was not blinded because the clinicians as well as the patients were aware of the treatment group.

There were 89 patients included in the study; 44 performed UTND (two cases lost to follow-up) and 45 performed LOD (three cases lost to follow-up) ending in 42 patients analyzed in each group.

Group 1 (UTND): The vagina and the perineum were prepared with an antiseptic solution after placement in dorsal lithotomy position and after performing transvaginal ultrasound to scan the pelvis. The UTND was performed, under heavy sedation with propofol, using a 16 G, 35-cm long, sharp needle (the same used in ovum pickup in in-vitro fertilization). Each ovary was punctured from three to six punctures through a single cortical entry according to the size of the ovaries. Transvaginal ultrasound scanning to rule out any complications of the procedure was done to all cases before discharge. The total duration of the procedure and the duration of postoperative hospital stay were recorded, and intraoperative or postoperative complications were reported.

Group 2 (LOD): A three-puncture laparoscopy was performed under general anesthesia. Four punctures using a monopolar electrosurgical probe with a coagulating current of 40 W were made in each ovary depending on its size, each measuring 4 mm in diameter and 5–7 mm in depth. Each ovary was cooled by saline solution irrigation. The duration of the procedure was recorded, and intraoperative or postoperative complications were reported.

Follow-up

All patients in both groups had serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and serum total testosterone levels measured on day 3 of the next menses after the procedure. Transvaginal ultrasound was done to all patients for the mean follicular diameter and endometrial thickness on days 10, 12, and 14 of the cycle after taking 100 mg/day of clomiphene citrate for 5 days starting from the third day of the next cycle and for six consecutive cycles or until pregnancy occurred.

Serum progesterone (ng/ml) was measured midluteal by radioimmunoassay. Ovulation was considered when serum progesterone was more than 5 ng/ml. The follow-up continued for 6 months after the procedure. All patients who showed ovulation were advised about timed intercourse. Serum pregnancy test was performed for the diagnosis of pregnancy.

Statistical analysis

Results were analyzed by SPSS, version 20 (SPSS Inc., Chicago, Illinois, USA). Two types of statistics were done: descriptive such as %, mean, and SD, or analytical such as Student's *t*-test (it is a single test used to indicate the presence of any significant difference between two groups for a normally distributed quantitative variable), χ^2-Test (used to compare between two groups or more regarding one qualitative variable), McNemar's test (used to compare between preresults and postresults of one qualitative variable), Paired *t*-test (it is a single test used to collectively indicate the presence of any significant difference between different time sequences for a normally distributed quantitative variable) and *P* value (it is considered significant if ≤0.05 and highly significant if ≤0.01).

Results

The study comprised 84 patients divided randomly into two groups each group comprising 42 clomiphene citrate-resistant PCOS.

As regards patient characteristics (age, parity, BMI, hormonal profiles, clinical manifestations, and PCOS

picture by ultrasound), no significant differences were found between the two groups (Table 1).

There was resumption of regular menstruation, improvement of hyperandrogenic symptoms such as acne and hirsutism, occurrence of ovulation and pregnancy after intervention in the two groups without difference. Hormonal changes after UTND and LOD showed a significant decrease in serum LH and LH/FSH ratio but not in the serum FSH or serum total testosterone (Table 2 and Fig. 1). The duration of UTND was 15.59 ± 2.83 min, whereas it was 38.45 ± 5.46 min for laparoscopic drilling. The duration of postoperative hospital stay was also markedly shorter after UTND (Fig. 2). One case of mild pelvic collection after UTND resolved spontaneously after 1 weak.

Discussion

After failure of medical induction of ovulation using clomiphene citrate, ovarian drilling has been established for drug-resistant PCOS [3]. Several methods of laparoscopic treatment have been studied especially electrocautery and laser treatment. The first technique is most commonly being used as the required equipment is available in most hospitals [12]. Laparoscopic cauterization followed by clomiphene citrate has been considered the treatment of choice for women with clomiphene citrate-resistant PCOS [13]. Whatever the mechanism of action, the hormone status is corrected, bilateral ovarian activity is restored even following unilateral diathermy and pituitary became sensitive to gonadotropin-releasing hormone [14]. The mechanism of action is unknown but may be related to endocrine changes that result from the procedure. A significant reduction in androgen (testosterone and androstenedione) levels in the serum has been observed [15]. From this study, the transvaginal ultrasound-guided needle drilling can act at the ovarian levels to induce the ovulation. The outcome of this simple technique (multiple puncture of the ovarian

Table 1 Characteristics of patients in the two groups

	UTND (*n*=42)	LOD (*n*=42)	*t*-Test	*P*
Age (years)	27.14±3.32	27.38±3.58	0.31	0.753
BMI (kg/m^2)	30.35±3.32	27.38±3.58	0.95	0.343
Parity				
Nullipara	54	44	χ^2=1.91	0.59
Primipara	24	26		
Multipara	22	28		
Menstrual cycle irregularities (%)	76.2	71.4	χ^2=0.24	0.620
Hyperandrogenism (%)	33.3	35.7	χ^2=0.05	0.818
PCO on US (%)	71.4	71.4	-	-
Serum FSH (mIu/ml)	4.98±1.0	5.10±0.87	0.60	0.549
Serum LH (mIU/ml)	13.55±3.35	12.76±2.52	1.22	0.225
Serum LH/FSH ratio	1.63±0.45	1.62±0.41	0.04	0.961

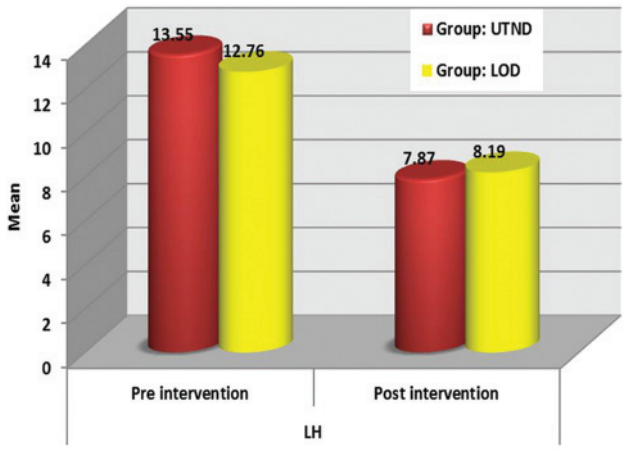
FSH, follicle-stimulating hormone; LH, luteinizing hormone; LOD, laparoscopic ovarian drilling; PCO, polycystic ovary; US, ultrasound; UTND, ultrasound-guided transvaginal ovarian needle drilling.

Table 2 Outcome after needle and laparoscopic ovarian drilling

	UTND (*n*=42)	LOD (*n*=42)	*t*-Test	*P*
Regular menstruation (%)	66.7	66.7	-	-
Acne/hirsutism (%)	19	21.4	χ^2=0.07	0.786
Ovulation next cycle (%)	57	59	χ^2=0.05	0.824
Pregnancy in 6 months (%)	31	35.7	χ^2=0.21	0.643
Serum FSH (mIU/ml)	5.15±1.03	5.34±0.89	0.87	0.384
Serum LH (mIU/ml)	7.87±1.72	8.19±2.20	0.73	0.642
Serum LH/FSH ratio	2.72±0.84	2.42±0.46	2.01	0.048
Serum T (nmol/ml)	1.12±0.10	1.09±0.10	1.43	0.155

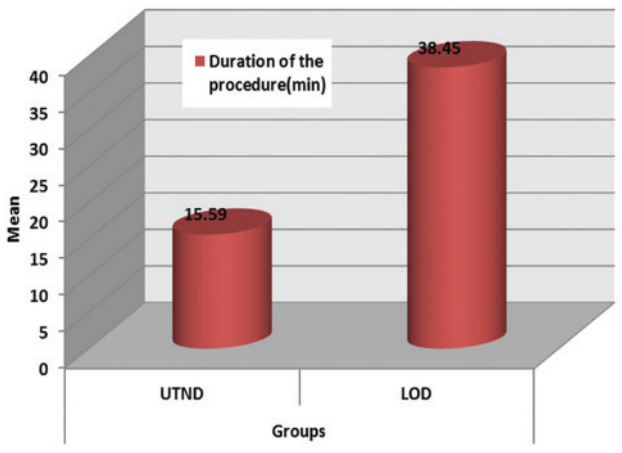
FSH, follicle-stimulating hormone; LH, luteinizing hormone; LOD, laparoscopic ovarian drilling; UTND, ultrasound-guided transvaginal ovarian needle drilling.

Figure 1



Distribution of the studied groups regarding luteinizing hormone (preintervention and postintervention).

Figure 2



Procedure duration of the studied groups.

stroma by a sharp needle) was comparable to the standard monopolar drilling (diathermy coagulation of ovarian stroma at different points) without all the risks expected from the later. The results of both methods of ovarian drilling were similar with regard to the resumption of regular menstruation, improvement of acne and hirsutism, occurrence of ovulation and pregnancy. The duration of the procedure was markedly shorter in UTND. Also in agreement with previous studies using UTND only [8] or ultrasonographic guided ovarian stroma hydrocoagulation using hot saline [6] or transvaginal ultrasound-guided ovarian interstitial laser treatment [16] for hormonal changes; we found a significant decrease in LH and LH/FSH levels but not in FSH levels. Unfortunately, in this study there was no significant decrease in serum total testosterone level after intervention in both groups that may be explained as an elevation in the free level by direct radioimmunoassay is considered most sensitive than elevation in the total level of testosterone because elevated insulin levels and elevated androgen levels both act to inhibit hepatic production of sex hormone-binding globulin [17]. The free androgen index (concurrent measurement of sex hormone-binding globulin and total testosterone levels) offers a practical alternative to the measurement of free testosterone levels in the assessment of patients with PCOS; however, some patients with hirsutism have normal levels of free testosterone. Therefore, the value of measuring free testosterone levels or the free androgen index in the diagnosis and assessment of clinical hyperandrogenism needs to be questioned [18]. There was one case of postintervention mild pelvic collection resolved after 1 weak with antibiotics and anti-inflammatory drugs. After UTND, the patients needed markedly lower doses of analgesics and were discharged within a markedly shorter period of time than after LOD. Difficulty in fixing the ovaries during drilling have been noticed sometimes and are overcome easily by slightly raising the shoulders of the patients especially with the heavy weight of the polycystic ovaries, gentle lower abdominal wall pressure aided by assistant's hands and sometimes mild induction of ovulation to increase the size of ovaries was needed to help in getting the ovaries accessible.

UTND can be implied for current clinical practice and future research as this simple technique can be used as a first-line office procedure for the induction of ovulation in clomiphene citrate-resistant PCOS [8]. In addition, the hazards of ovulation induction as ovarian hyperstimulation syndrome can be avoided or minimized. UTND may decrease the risk of ovarian hyperstimulation syndrome if done before controlled ovarian hyperstimulation in patients with PCOS to improve in-vitro fertilization) outcomes [10] It may also improve pregnancy outcomes in patients with PCOS as well as LOD [19].

Conclusion

We think that UTND fulfills the criteria of the ideal office procedure because it is safe and can be undertaken in a short period of time with minimal coast compared with the conventional LOD.

Limitations of study

In the present study, follow up of the patients after the procedure continued for only 6 months; however, a longer duration of follow-up is required to verify its long-term effects. Also, some patients were lost and excluded in the period of follow-up.

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Conflicts of interest

There are no conflicts of interest.

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