Middle East Fertility Society Journal (2013) **18**, 202–207

Middle East Fertility Society

Middle East Fertility Society Journal

www.mefsjournal.org
www.sciencedirect.com

ORIGINAL ARTICLE

Metformin versus laparoscopic unilateral ovarian drilling in clomiphene resistant women with polycystic ovary syndrome

Ibrahim Abd Elgafor el sharkwy *

Department of Obstetric and Gynecology, Faculty of Medicine, Zagazig University, Egypt

Received 31 May 2012; accepted 25 December 2012
Available online 14 June 2013

KEYWORDS

Metformin;
Unilateral drilling;
Clomiphene resistant;
Polycystic ovary

Abstract *Objectives:* To compare the hormonal-metabolic profiles and reproductive outcomes between women receiving metformin and women undergoing unilateral ovarian drilling in clomiphene citrate(CC) resistant patients with polycystic ovary syndrome (PCOS)

Design: Non randomized controlled trial.

Setting: Obstetrics and Gynecology department, Faculty of medicine, Zagazig University, Egypt.

Methods: A total of 120 patients were divided into group 1(n = 58) who received metformin therapy and group 2 (n = 62) who underwent unilateral ovarian drilling. Hormonal-metabolic profiles changes after treatment were reported and reproductive outcomes were compared between both groups.

Main outcome: FSH and LH were reduced significantly in unilateral drilling group ($P = < 0.001$and 0.001), while there was significant improvement in testosterone level , fasting insulin, fasting glucose to insulin ratio and homeostasis model assessment index in metformin therapy group. Pregnancy and ovulation rates were higher after unilateral drilling with significant difference ($P = 0.048$ and 0.004). No significant difference in early miscarriage rate between both groups ($P = 0.51$).

Conclusion: Unilateral LOD was associated with greater ovulation and pregnancy rates than metformin in women with PCOS who did not conceive with CC.

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women in the child bearing period with an incidence of 5–10% (1,2). Insulin resistance and hyperinsulinemia are common in PCOS (3). Insulin resistance with resulting hyperinsulinemia directly stimulates ovarian androgen production, increases LH release in PCOS and stimulates

* Tel.: +20 1224363595.
E-mail address: IbrahimSharkwy@yahoo.com.

Peer review under responsibility of Middle East Fertility Society.

Production and hosting by Elsevier

1110-5690 © 2013 Production and hosting by Elsevier B.V. on behalf of Middle East Fertility Society.
http://dx.doi.org/10.1016/j.mefs.2012.12.008

steroidogenesis (4). First line of treatment of PCOS is usually clomiphene citrate, since it is known to result in higher ovulation and pregnancy (5,6). Metformin an oral biguanide was seen to be effective in achieving ovulation and improving the clinical and biochemical features of PCOS (7). Meta-analysis recommended that metformin must be the first choice for anovulatory women with PCOS (8). Laparoscopic ovarian drilling is a one day surgery that has been established as an effective second line method of ovulation induction in clomiphene citrate (CC) resistant PCOS patients with high ovulation (80%) and pregnancy rate (60–80%) (9). Unilateral ovarian drilling was first introduced by Ballen et al. (10) who demonstrated that unilateral diathermy leads to bilateral ovarian activity. Other study showed no evidence of a difference in ovulation rate and clinical pregnancy rate between unilateral and bilateral drilling of the ovaries (11). The aim of this study was to compare hormonal levels, metabolic effects and reproductive outcomes between metformin treatment and laparoscopic unilateral ovarian drilling.

2. Patients and methods

This study was conducted from February 2010 to March 2012 on 124 patients with anovulatory infertility resistant to clomiphene citrate (CC) who presented to the Infertility Clinic of Department of Obstetrics and Gynecology of Zagzig University. All patients gave informed consent to the study, which had been approved by local ethics committee. PCOS was diagnosed on basis of the revised Rotterdam 2003 criteria (12). The presence of 2 out of 3 criteria (oligo and/or anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovary) was recommended as diagnostic of PCOS. Clomiphene citrate resistance was defined as the failure to achieve adequate follicular maturation after three consecutive induction cycles with CC at 150 mg /day for 5 days (13). Exclusion criteria included patients with other causes of infertility like male factor, tubal factors and endocrinal factors also patients who received medications or other regimens of ovulation induction before the study. At the start of study complete history, physical examination, basal level of FSH, LH and testosterone hormones were registered and metabolic assessment included the evaluation of fasting glucose (FG) and fasting insulin (FI), fasting glucose to fasting insulin ratio (FG/FI) and homeostasis model assessment index (HOMA) (14). Then our patients had been divided into two groups, without randomization as some patients were worried about laparoscopy and others could not tolerate the financial burden of laparoscopy, the first group received 850 mg of metformin twice daily, the second group underwent unilateral ovarian drilling through the three punctures technique under general anesthesia, after production of pneumoperitoneum using a verrus needle, a 10 mm video laparoscope was inserted infraumbilically, followed by the lateral insertion of a 5 mm ancillary trocar in each iliac fossa. The ovarian ligament of one ovary was held by babcock forceps and four drills were performed, then the ovary was cooled by irrigating with normal saline solution and 500 ml of this solution left in the pelvis at the end of procedure. Three months later all the previous investigations were repeated and all participants registered their bleeding periods in a calendar and folliculometry was performed and number of pregnancies and miscarriages were noted till the end of 6 months. Clinical pregnancy; defined as sonographically visualized intra-uterine gestational sac with pulsating fetal pole. Miscarriage was defined as the spontaneous loss of a pregnancy before the end of the 20th week.

The primary outcome was ovulation rate. The secondary outcomes were clinical pregnancy and first trimester (13 weeks) miscarriage rates.

The sample size was calculated according to the ovulation rate as a primary outcome in this study. In previous report (15), LOD was associated with an average ovulation rate of 55% (range, 30–90%). On the assumption that a 25% difference in the ovulation rate with metformin would be clinically relevant, we needed 62 patients in each arm to demonstrate this difference to have statistical significance with a type I error probability (α) of 0.05, a type II error (β) of 0.2, and a power of 80%. Data were analyzed using SPSS version 10 (SPSS, Chicago, IL, USA) and are expressed as mean ± SD and/or percentages. Comparisons between measures (Mean + SD) were done using Student's t-test for unpaired data, while comparisons between measures (Mean + SD) in paired data were done by paired t test. The χ^2 test was used for comparisons of ovulation, pregnancy, and miscarriage rates. $P \leqslant 0.05$ was considered statistically significant.

3. Results

At the start of the study, 124 patients were assigned to the metformin group ($n = 62$) and the unilateral LOD ($n = 62$), only four patients lost to follow up in the metformin group. The baseline characteristics of women in both groups are shown in (Table 1) they were found comparable in terms of age, period of infertility, body mass index (BMI), cycle pattern, hormonal and metabolic profile. Three months after treatment the metformin group showed a significant improvement of cycle regularity ($P = <0.001$) and a significant decrease in testosterone level ($P = <0.001$), fasting insulin level ($P = <0.001$) and HOMA index ($P = <0.001$), while FG/FI ratio showed a significant increase ($P = 0.029$), the decrease in FSH, LH and FG levels had not reached significance. On the other hand the unilateral ovarian drilling group showed a significant improvement of cycle regularity ($P = <0.001$) and a significant reduction in FSH and LH levels ($P = <0.001$ and 0.001), no significant changes were found in other studied variables (Table 2). We compared the clinical and biochemical response between the metformin group and the unilateral ovarian drilling group 3 months after treatment (Table 3). Both groups showed a comparable slight decrease in BMI ($P = 0.076$) and FG ($P = 0.397$), mean decrease in serum concentration of FSH and LH was more in the unilateral drilling group than the metformin group but the difference was not statistically significant, mean decrease in serum concentration of testosterone, FI and HOMA index was more in the metformin group compared with the unilateral drilling group with statistically significant difference, consequently an improvement of FG/FI ratio was more in the metformin group with statistically significant difference. Reproductive outcomes had been compared between the two groups after 6 months (Table 4). The difference in clinical outcome in terms of regular cycle between two groups was not statistically significant ($P = 0.87$). Pregnancy and ovulation rates were significantly higher in the unilateral drilling group ($P = 0.048$ and 0.004).

Table 1 Basal characteristics of the studied population.

		Metformin group N (58)	Unilateral drilling group N (62)	*P*-value
AGE (year)	Mean ± (SD)	23.7 (1.8)	24.1 (2.1)	0.43
BMI (kg/m2)	Mean ± (SD)	31.6 (3.2)	32.2 (4.5)	0.56
Period of infertility (year)	Mean ± (SD)	3.5 (0.9)	3.9 (1.1)	0.13
Menstrual history				
Amenorrhea	Number (%)	20 (34.5)	24 (38.7)	0.73
Oligomenorrhea	Number (%)	38 (65.5)	38 (61.3)	0.85
Hormonal-metabolic profile				
FSH	Mean ± (SD)	5.23 (1.2)	5.9 (1.5)	0.062
LH	Mean ± (SD)	10.89 (3.7)	10.36 (2.9)	0.54
Testosterone	Mean ± (SD)	4.81 (1.2)	4.65 (1.15)	0.59
FG	Mean ± (SD)	85.6 (7.6)	88.4 (8.1)	0.17
FI	Mean ± (SD)	12.7 (3.4)	13.1 (4.1)	0.68
FG/FI ratio	Mean ± (SD)	6.4 (1.8)	6.7 (2.1)	0.55
HOMA	Mean ± (SD)	2.72 (0.37)	2.85 (0.61)	0.48

BMI, body mass index.

Table 2 Before and after metformin and unilateral drilling.

	Metformin group N. (58)		*P*-value	Unilateral drilling group N. (62)		*P*-value
	Before	After[1]		Before	After[2]	
BMI (kg/m^2) mean ± (SD)	31.6 (3.2)	30.48 (3.7)	0.56	32.2 (4.5)	32.15 (4.7)	0.96
Menstrual history						
Regular N. (%)	0 (0)	30 (51.7)	< 0.001*	0 (0)	34 (54.8)	< 0.001*
Amenorrhea N. (%)	20 (34.5)	12 (20.7)		24 (38.7)	10 (16.1)	
Oligomenorrhea N. (%)	38 (65.5)	16 (27.6)		38 (61.3)	18 (29.1)	
Hormonal profile						
FSH mean ± (SD)	5.23 (1.2)	4.96 (1.9)	0.43	5.9 (1.5)	4.3 (1.28)	< 0.001 *
LH mean ± (SD)	10.89 (3.7)	9.45 (4.2)	0.17	10.36 (2.9)	7.42 (3.8)	0.001*
Testosterone mean ± (SD)	4.81 (1.2)	3.59 (1.1)	< 0.001*	4.65 (1.15)	4.11 (1.2)	0.074
FG mean ± (SD)	85.6 (7.6)	82.4 (6.8)	0.096	88.4 (8.1)	86.3 (7.6)	0.295
FI mean ± (SD)	12.7 (3.4)	8.9 (2.6)	< 0.001*	13.1 (4.1)	11.4 (3.9)	0.099
FG/FI ratio mean ± (SD)	6.4 (1.8)	9.45 (2.7)	0.029*	6.7 (2.1)	7.52 (2.8)	0.196
HOMA mean ± (SD)	2.72 (0.37)	1.89 (0.45)	< 0.001*	2.85 (0.61)	2.59 (0.47)	0.062

* $P < 0.05$.
[1] Number 50 after therapy, as 8 patients got pregnant in first 3 months.
[2] Number 47 after therapy, as 15 patients got pregnant in first 3 months.

Table 3 The change in different parameters after intervention in both metformin and unilateral drilling.

	Metformin Mean ± (SD)	Unilateral drilling Mean ± (SD)	*P*-value
BMI (kg/m^2)	0.22 (0.1)	0.18 (0.07)	0.076
Hormonal-metabolic profile			
FSH	0.27 (0.1)	1.6 (1.2)	0.019*
LH	1.49 (0.6)	3.19 (1.6)	0.024*
Testosterone	1.3 (0.65)	0.54 (0.26)	0.021*
FG	2.3 (0.82)	2.1 (1.03)	0.397
FI	3.8 (1.1)	1.26 (0.15)	0.002*
FG/FI ratio	3.15 (1.2)	0.65 (0.3)	0.002*
HOMA	0.85 (0.13)	0.53 (0.12)	< 0.001*

* $P < 0.05$.

Table 4 Reproductive outcome.

		Metformin group N (58)	Unilateral drilling group N (62)	*P*-value	OR (95% CI)
Menstrual history					
Regularity	N. (%)	30 (51.7)	34 (54.8)	0.87	0.88 (0.4–1.93)
Reproductive outcome					
Ovulation rate[1]	N. (%)	140/290 (48.3)	226/334 (67.7)	0.048*	0.44 (0.2–0.99)
Pregnancy rate[2]	N. (%)	16 (27.6)	34 (54.8)	0.004*	0.31 (0.14–0.72)
Miscarriage rate[3]	N. (%)	3 (18.7)	8 (23.5)	0.51	0.6 (0.18–1.97)

* $P < 0.05$.
[1] Calculated as the number of ovulatory cycles divided by the number of cycles.
[2] Calculated as the number of clinical pregnancies divided by the number of patients.
[3] Calculated as the number of first-trimester spontaneous miscarriage divided by the number of clinical pregnancies.

There was no significant difference in miscarriage rate between both groups ($P = 0.51$).

4. Discussion

In the present study, ovulation and pregnancy rates in patients managed by unilateral LOD (67.7% and 54.8%, respectively) are in agreement with other studies that have reported rates of 30–90% and 13–88%, respectively, depending on the follow-up period (15,27,38). This variation regarding the reproductive outcomes is mostly due to the heterogeneity of the samples studied and the different techniques used.

Ovulation and pregnancy rates were better in the unilateral drilling group compared with metformin that could be interpreted by the great reduction of luteinizing hormone that is seen with LOD, which has an important role in restoring normal intraovarian paracrine signaling and reducing local androgen production (36). These results are consistent with other study (16), but two other studies (17,18) disagree with the present results, in the first study (17), no significant difference was found in the ovulation or pregnancy rates between patients who received metformin or LOD; however, the second study reported a higher pregnancy rate in the metformin group (18).

In the present study there was no significant difference in the first trimester miscarriage rate between both groups. These results are consistent with those of Hamed et al. (16), in contrast to those of Palomba et al. (18) who reported significantly lower miscarriage rates with metformin compared with LOD. However, our study was not adequately powered to detect such a difference, and this needs further studies with a larger sample size, additional data, and a long-term follow-up period is required to evaluate the effects of these two methods of treatment in patients with PCOS who are resistant to CC.

In this study, after 3 months of metformin treatment there was no significant decrease in BMI, this in agreement with previous studies (19–21), while others (22–24) observed a significant reduction in BMI with metformin. Variations in study groups in pretreatment BMI, metformin dose, concomitant life-style changes and patient adherence to treatment may account for these differences. With metformin there was a non-significant decline in the serum concentration of FSH and LH hormones, other studies reported variable changes in the serum concentration of FSH either decreased (25) or increased (26) but serum concentration of LH decreased in these studies. Different hormone responses may be related to duration of treatment. Another explanation may be they are related to the hypothalamic pituitary response to the insulin sensitizing medications and/or the intrinsic ovarian metabolic changes.

This study showed that, PCOS patients benefit from metformin treatment with regard to hyperandrogenism. Metformin possibly exerts this effect through increasing sex hormone binding globulins (SHBG), modulation of adrenal androgen production, or decreasing intra ovarian androgen production (27). Also a significant reduction in FI, and improvement of FG/FI ratio, that could be explained by the metabolic actions of metformin were seen. It inhibits hepatic glucose output and improves the peripheral insulin sensitivity with an increase in glucose utilization by skeletal muscles (7), the decrease in testosterone and FI in addition to improved FG/FI ratio are consistent with those reported by Palomba et al. (28) also Trolle et al. (27) who studied the effect of metformin treatment on obese and non obese women in a randomized, double-blind, placebo controlled cross-over trial concluded that metformin therapy significantly reduced testosterone and improved insulin resistance in obese women, while Tans et al. (26) had revealed that, metformin improved parameters of insulin resistance and hyperandrogenemia in PCOS women irrespective of pretreatment insulin resistance. Our findings are in contrast to Aruna et al. (29) who found no changes were noticed in the total testosterone, FI, and FG/FI ratio; these different results can be attributed to criteria of their patient selection.

Ovarian electrocautery is a well accepted intervention for ovulation induction in clomiphene citrate resistant PCOS women (30). However there is a continuing concern about the adverse effects of laparoscopic ovarian drilling (LOD) particularly on periovarian adhesion formation and premature ovarian failure (31). The greater the amount of damage to the surface of the ovary the greater the risk of periovarian adhesions (32) also the large number of punctures have made the risk greater for premature ovarian failure (2). Recent study demonstrated that unilateral laparoscopic drilling is effective as bilateral ovarian diathermy in normalization of ovarian function in CC resistant women with PCOS (33), and in inducing ovulation and achieving pregnancy (32). So in this study unilateral ovarian drilling had been chosen as treatment in CC resistant women with PCOS.

In agreement with other reports (34,35) unilateral drilling in the current study showed a significant decrease in the levels of LH that could be explained by the reduction of ovarian theca

cell mass and consequently androgen production. Converting this androgen to an estrogen corrects disturbances of the ovarian–pituitary feedback, resulting in a decrease of luteinizing hormone pulse amplitude (36).

Reduction of FSH in the present study is consistent with the decrease in FSH level after unilateral LOD (34) and bilateral LOD (37,38). No other studies were found to compare between metformin and unilateral drilling.

In conclusion, both metformin and unilateral ovarian drilling are effective in treatment of women with PCOS and clomiphene resistance. But unilateral LOD is associated with greater ovulation and pregnancy rates, and with using it as a substitute for bilateral LOD good reproductive outcomes are gained and many potential adverse effects could be avoided. The current study had some limitations because it was non randomized so our findings cannot be considered conclusive and further randomized large sample studies are required to evaluate results of this study.

References

(1) Matalliotakis I, Kourtis A, Koukoura O, Panidis D. Polycystic ovary syndrome: etiology and pathogenesis. Arch Gynecol Obstet. 2006;274(4):187–97.

(2) Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Consensus on infertility treatment related to polycystic ovary syndrome. Hum Reprod 2008;23:462–77.

(3) Ehrmann DA, Kasza K, Azziz R, Legro RS, Ghazzi MN. Effect of race and family history of type 2 diabetes on metabolic status of women with polycystic ovary syndrome. J Clin Endocrinol Metab 2005;90:66–71.

(4) Dunaif A. Current concepts in the polycystic ovary syndrome. Annu Rev Med 2001;52:401–19.

(5) Legro RS, Barnhart HX, Schlaff WD, Carr BR, Diamond MP, Carson SA, et al. Cooperative multicenter reproductive medicine network: clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. N Engl J Med 2007;356:551–66.

(6) Moll E, Bossuyt PM, Korevaar JC, Lambalk CB, van der Veen F. Effect of clomifene citrate plus metformin and clomifene citrate plus placebo on induction of ovulation in women with newly diagnosed polycystic ovary syndrome: randomised double blind clinical trial. BMJ 2006;332:1485.

(7) Norman RJ. Editorial: metformin – comparison with other therapies in ovulation induction in polycystic ovary syndrome. J Clin Endocrinol Metab 2004;89(10):4797–800.

(8) Lord JM, Flight IHK, Norman RJ. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. BMJ 2003;327:951–3.

(9) Farquhar C, Lilford R, Marjoribanks J, Vanderkerckhove P. Laparoscopic drilling by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome. Cochrane Database Syst Rev 2005:3, CD001122.

(10) Balen AH, Jacobs HS. A prospective study comparing unilateral and bilateral laparoscopic ovarian diathermy in women with the polycystic ovary syndrome. Fertil Steril 1994;62:921–5.

(11) Mizyen AL. Unilateral versus bilateral LOD in infertile women with PCOS. Abstract of 16th Annual Meeting of ESHRE 2000:262.

(12) Fauser B, Tarlatzis B, Chang J, Azziz R. Rotterdam the, ESHRE/ASRM-sponsored PCOS consensus workshop group Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004;19:41–7.

(13) Brown J, Farquhar C, Beck J, Boothroyd C, Hughes E. Clomiphene and anti-oestrogens for ovulation induction in PCOS. **Cochrane Database Syst Rev** 2009;4. Article ID CD002249.

(14) Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment. Diabetologia 1985;28:412–9.

(15) Seow KM, Juan CC, Hwang JL, Ho LT. Laparoscopic surgery in polycystic ovary syndrome: reproductive and metabolic effects. Semin Reprod Med 2008;26(1):101–10.

(16) Hamed HO, Hasan AF, Ahmed OG, Ahmed MA. Metformin versus laparoscopic ovarian drilling in clomiphene- and insulin-resistant women with polycystic ovary syndrome. Int J Gynecol Obstet 2010;108:143–7.

(17) Malkawi HY, Qublan HS, Hamaideh AH. Medical vs. surgical treatment for clomiphene citrate-resistant women with polycystic ovary syndrome. J Obstet Gynaecol 2003;23:289–93.

(18) Palomba S, Orio Jr F, Nardo LG, Falbo A. Metformin administration versus laparoscopic ovarian diathermy in clomiphene citrate-resistant women with polycystic ovary syndrome a prospective parallel randomized double-blind placebo controlled-trial. J Clin Endocrinol Metab 2004;89(10):4797–800.

(19) Fleming R, Hopkinson ZE, Wallace AM, Greer IA, Sattar N. Ovarian function and metabolic factors in women with oligomenorrhea treated with metformin in a randomized double blind placebo-controlled trial. J Clin Endocrinol Metab 2002;87:569–74.

(20) Tan S, Hahn S, Benson S, Dietz T, Lahner H, Moeller LC, et al. Metformin improves polycystic ovary syndrome symptoms irrespective of pre-treatment insulin resistance. Eur J Endocrinol 2007;157:669–76.

(21) Trolle B, Flyvbjerg A, Kesmodel U, Lauszus FF. Efficacy of metformin in obese and non-obese women with polycystic ovary syndrome: a randomized, double-blinded, placebo-controlled cross-over trial. Hum Reprod 2007;22:2967–73.

(22) Moghetti P, Castello R, Negri C, Tosi F, Perrone F, Caputo M, et al. Metformin effects on clinical features, endocrine and metabolic profiles, and insulin sensitivity in polycystic ovary syndrome: a randomized, double-blind, placebo-controlled 6-month trial, followed by open, long-term clinical evaluation. J Clin Endocrinol Metab 2000;85:139–46.

(23) Bridger T, MacDonald S, Baltzer F, Rodd C. Randomized placebo-controlled trial of metformin for adolescents with polycystic ovary syndrome. Arch Pediatr Adolesc Med 2006;160:241–6.

(24) Lord J, Thomas R, Fox B, Acharya U, Wilkin T. The effect of metformin on fat distribution and the metabolic syndrome in women with polycystic ovary syndrome-a randomised, double-blind, placebo-controlled trial. BJOG 2006;113:817–24.

(25) Ramzy MA, Al-Inany H, Aboulmaaty Z, El-Kateb Z, Abdel Badie M. The use of metformin in overweight and lean infertile patients with polycystic ovarian syndrome: a randomized controlled trial. Middle East Fertil Soc J 2003;8:193–208.

(26) Neena C. Efficacy of sequential treatment of metformin and clomiphene citrate in clomiphene resistant women with polycystic ovary syndrome. J Obstet Gynecol India 2007;57:69–72.

(27) Pirwany IR, Tulandi T. Laparoscopic treatment of polycystic ovaries: is it time to relinquish the procedure? Fertil Steril 2003;80(2):241–51.

(28) Palomba S, Falbo A, Russo T, Orio F, Tolino A, Zullo F. Systemic and local effects of metformin administration in patients with polycystic ovary syndrome: (PCOS) relationship to the ovulatory response. Hum Reprod 2010;25:1005–13.

(29) Aruna J, Mittal S, Kumar S, Misra R, Dadhwal V, Vimala N. Metformin therapy in women with polycystic ovary syndrome. Int J Gynecol Obstet 2004;87:237–41.

(30) Rajashekar L, Krishna D, Patil M. Polycystic ovaries and infertility: our experience. J Hum Reprod Sci 2008;1:65–72.

(31) Fraquhar C, Lilford RJ, Marjoribanks J, Vandekerkhove P. Laparoscopic drilling by diathermy or laser for ovulation

induction of anovulatory polycystic ovary syndrome. **Cochrane Database Syst Rev** 2008;4, CD00122:Pub3.

(32) Naether OGJ, Fischer R, Weise HC. Laparoscopic electrocoagulation of the ovarian surface in infertile patients with polycystic ovarian disease. Fertil Steril 1993;60:88–94.

(33) Lemieux S, Lewis GF, Ben-Chetrit A, Steiner G, Greenblatt EM. Correction of hyperandrogenemia by laparoscopic ovarian cautery in women with polycystic ovarian syndrome is not accompanied by improved insulin sensitivity or lipid–lipoprotein levels. J Clin Endocrinol Metab 1999;84:4278–82.

(34) Roy K, Baruah J, Moda N, Kumar S. Evaluation of unilateral versus bilateral ovarian drilling in clomiphene citrate resistant cases of polycystic ovarian syndrome. Arch Gynecol Obstet 2009;280:573–8.

(35) Youssef H, Atallah MM. Unilateral ovarian drilling in polycystic ovarian syndrome: a prospective randomized study. Reprod Biomed Online 2007;15(4):457–62.

(36) Farquhar CM. The role of ovarian surgery in polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol 2004;18(5):789–802.

(37) Ashrafinia M, Hosseini R, Moini A, Eslami B, Asgari Z. Comparison of metformin treatment and laparoscopic ovarian diathermy in patients with polycystic ovary syndrome. Int J Gynecol Obstet 2009;107:236–9.

(38) Api M, Gorgen H, Cetin A. Laparoscopic ovarian drilling in polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol 2005;119:76–81.