Laparoscopic ovarian drilling: An alternative but not the ultimate in the management of polycystic ovary syndrome

Abstract
Since its introduction in 1984, laparoscopic ovarian drilling has evolved into a safe and effective surgical treatment for anovulatory, infertile women with polycystic ovary syndrome (PCOS), unresponsive to clomiphene citrate. It is as effective as gonadotropins in terms of pregnancy and live birth rates, but without the risks of ovarian hyperstimulation syndrome and multiple pregnancies. It improves ovarian responsiveness to successive ovulation induction agents. Its favorable reproductive and endocrinal effects are sustained long. Despite its advantages, its use in unselected cases of PCOS or for non-fertility indications is not prudent owing to the potential risks of iatrogenic adhesions and ovarian insufficiency.

Key words: Clomiphene citrate resistance, laparoscopic ovarian drilling, polycystic ovary syndrome

INTRODUCTION
Polycystic ovary syndrome (PCOS), a common endocrine disorder affecting women in the reproductive age group, is a predominant cause of anovulatory infertility\(^1\) with a prevalence rate of 17-20% (Rotterdam diagnostic criteria).\(^2\,^3\) Clomiphene citrate (CC), a selective estrogen receptor modulator, still remains the first line of treatment for ovulation induction (OI) in PCOS patients.\(^4\,^8\) CC-resistance refers to the failure to ovulate with 150 mg of CC for at least 3 cycles, while CC-failure is defined as failure to conceive with CC despite successful regular ovulation for 6-9 cycles.\(^8\) Since its inception in 1984, 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 (OHSS) and multiple pregnancies.\(^4\,^9\,^11\) However, there are concerns regarding the long-term effects on ovarian function, especially iatrogenic adhesions and decreased ovarian reserve (DOR), which may potentially jeopardize future fertility. Hence, this procedure should be employed rationally in selected CC-resistant cases for the sole purpose of correction of anovulatory infertility.

The aim of this review is to evaluate and summarize the current body of literature regarding the role of LOD in management of PCOS entailing its different pre, intra and postoperative aspects.

MATERIALS AND METHODS
A systematic search of Medline, PubMed, the Cochrane Library, the National Guideline Clearinghouse, and the Health Technology Assessment Database was performed from January 1, 1984 to December 31, 2013 using key...
words “PCOS,” “laparoscopic ovarian surgery,” “LOD,” “laparoscopic ovarian diathermy,” “laparoscopic ablative therapy” and “laparoscopic ovarian electrocautery.” Relevant evidence was identified and assessed for quality and suitability for inclusion in the following order — Systematic reviews, meta-analyses, guidelines, randomized controlled trials (RCTs), prospective cohort studies, observational studies, nonsystematic reviews, and case series.

Mechanism of action
The exact mechanism is yet to be elucidated. The most plausible one is the destruction of ovarian follicles and stroma resulting in a decrease in androgen and inhibit levels and a secondary rise in follicle-stimulating hormone (FSH) levels. Production of inflammatory growth factors like insulin-like growth factor-1, in response to thermal injury, further potentiates the actions of FSH on folliculogenesis, while increased blood flow to the ovary provoked by surgery, facilitates increased delivery of gonadotropins.

Indications
The main indication for LOD is CC-resistant PCOS as a second-line therapy for anovulatory infertile PCOS cases; specifically, as an alternative to gonadotropins. Royal College of Obstetricians and Gynecologists, American College of Obstetricians and Gynecologists, Society of Obstetricians and Gynecologists, Canada and the recent PCOS consensus working group recommend its use in highly selected cases, particularly in those with hypersecretion of luteinizing hormone (LH), normal body mass index, those needing laparoscopic assessment of the pelvis or who live too far away from the hospital for the intensive monitoring required during gonadotropin therapy. Despite its theoretical advantages, LOD is not superior to CC, neither as a first-line therapy for OI nor for CC-failure or prior to in vitro fertilization (IVF). A recent Cochrane systematic review of 9 RCTs and 16 trials concluded that there was no evidence of a significant difference in rates of clinical pregnancy (39.7 vs. 40.5%) or live birth (34 vs. 38%) in women with clomiphene-resistant PCOS undergoing LOD compared to other medical treatments. This implies that LOD is a valid, but not the sole option for CC-resistant PCOS. The evidence for improvement in biochemical hyperandrogenism translating into comparable improvement in clinical hyperandrogenism is not clear; hence LOD should not be offered for non-fertility indications like amelioration of acne or hirsutism or for regularization of menstrual cycles.

Surgical technique
Standardization of the surgical techniques is lacking. Reproductive outcomes are comparable with laser and diathermy. Electrocautery, using an insulated unipolar needle electrode with a non-insulated distal end measuring 1-2 cm, is the most commonly used method, although few authors have reported similar ovulation and pregnancy rates with bipolar energy. The number of punctures is empirically chosen depending on the ovarian size. In the original procedure, 3-8 diathermy punctures (each of 3 mm diameter and 2-4 mm depth) per ovary were applied, using power setting of 200-300 W for 2-4 s. Most surgeons perform four punctures per ovary, each for 4 s at 40 W (rule of 4), delivering 640 J of energy per ovary (the lowest effective dose recommended). Nevertheless, clinical response is dose-dependent, with higher ovulation and pregnancy rates observed by increasing dose of thermal energy up to 600 J/ovary, irrespective of ovarian volume. Conversely, adjusting thermal dose based on ovarian volume (60 J/cc) has better reproductive outcomes with similar postoperative adhesion rates than fixed dose of 600 J/ovary. Despite lack of convincing evidence and significant reduction in operative time, most gynecologists still perform bilateral over unilateral drilling.

Different modifications of the classic needle electrode technique such as laparoscopic ovarian multi-needle intervention, LOD using a monopolar hook electrode, LOD using the harmonic scalpel and office microlaparoscopic ovarian drilling are proposed. Various transcervical methods such as transvaginal hydrolaparoscopy and transvaginal sonography-guided ovarian interstitial laser treatment are also developed. However, larger prospective studies are needed to validate the use, safety, efficacy and long-term effects of these alternate techniques.

Predictors of success
On an average, 20-30% of anovulatory PCOS women fail to respond to LOD; possibly due to inadequate destruction of ovarian stroma or inherent resistance of the ovaries. The rationality of increasing the number of punctures or thermal energy applied to improve response at the expense of increased risks of adhesions and premature ovarian failure (POF) is yet to be proved. Several prognostic factors are evaluated to predict successful outcomes, knowledge of which may be useful in judicious patient selection thus avoiding unnecessary surgery. Some of these appear to play a consistent role like preoperative LH concentrations and duration of infertility. However, impact of other factors such as obesity, insulin resistance, metabolic syndrome and hyperandrogenism on LOD outcomes is still disputable.

Reproductive outcomes and endocrinal changes after laparoscopic ovarian drilling
The clinical and endocrine response to LOD is governed by a dose-response relationship. Four punctures per ovary
using a power setting of 30 W applied for 5 s/puncture (i.e., 600 J/ovary) are sufficient to produce optimal response (67% spontaneous ovulation and conception rates). Reducing the thermal energy (<300 J/ovary) and/or number of punctures (2/ovary) reduces the chances of spontaneous ovulation and conception, while higher thermal doses (>1000 J/ovary) and/or number of punctures (≥7/ovary) causes extensive tissue destruction without additional improvement in outcomes. Table 2 depicts the spontaneous ovulation and pregnancy rates after various techniques of LOD, which have varied from 30-90% to 13-88% respectively, within 1-year of the procedure. LOD alone is usually effective in <50% of women. In such cases, addition of CC and recombinant FSH (rFSH) may be considered after 3 and 6 months respectively. LOD also improves the sensitivity of the ovaries towards subsequent CC and FSH, especially in those who are less hyperandrogenic and less insulin-resistant.

The overall miscarriage rate varies from 0% to 36.5%. Significant reduction of miscarriage rates after LOD were observed by Amer et al (reduced from 54% to 17%). However, Cochrane systematic review did not find any significant differences in the abortion rates between LOD and other medical treatments (7.3% vs. 6.6%).

The improved reproductive outcomes stem from an favorable intra-ovarian and systemic endocrinial milieu after LOD — Decreased plasma LH and in its pulsations, increased FSH, decreased LH:FSH ratio, a temporary fall in inhibin B, increased sex hormone binding globulin and a constant fall in androgens, free androgen index and Ferriman-Gallwey score. Moreover, these beneficial reproductive and endocrinal effects are observed to chronically persist.

Improvement in hormonal profiles does not translate into a comparable improvement in insulin sensitivity or reduction in risk of gestational diabetes mellitus (GDM). Although patients with metabolic syndrome should not be precluded from LOD, adjuvant therapy with insulin sensitizers should be considered. Few studies have demonstrated no impact on metabolic parameters. Although, lower ovulation and pregnancy rates are reported in obese PCOS compared to lean counterparts, one prospective study contradicts this. Hence, obesity should not be considered as a contraindication, although anesthetic and surgical risks are increased in obese women. However, impact of LOD in PCOS associated with obesity, IR or metabolic syndrome needs further research for clarification.

Complications

One of the main shortcomings of LOD is iatrogenic adhesions due to bleeding from the ovarian surface or premature contact between the ovary and the bowel after cauterization. Adhesion rates ranged from 0 to 100%, involving higher risks with laser, probably owing to lesser thermal penetration (2-4 mm) by the cone-shaped lesions of laser drilling compared with cylinder-shaped lesions (8 mm) of monopolar electrocaugulation. Most studies reported mild to moderate adhesions which do not seem to affect pregnancy rates after LOD. Adhesion prevention strategies like liberal peritoneal lavage, application of adhesion barriers like Interceed and performance of adhesiolyis at early second-look laparoscopy are not effective in preventing

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**Table 1: Predictors of success of LOD**

| Publication, year | Number of cases (n) | Evaluation criteria | Unfavourable prognostic factors |
|-------------------|---------------------|---------------------|---------------------------------|
| Gjonnaess, 1994   | 252                 | Ovulation           | High BMI, low SHBG, associated tubal factor, endometriosis, oligoosperma |
| Li et al., 1998   | 118                 | Pregnancy           | Infertility >3 years, LH <10 IU/L, laser drilling |
| Kriplani et al., 2001 | 66                 | Pregnancy           | Associated tubal or male factors, LH <10 IU/L, infertility >3 years |
| Al Ojaimi, 2003   | 181                 | Pregnancy           | BMI <30 kg/m², age >30 years, basal LH <10 IU/L, obesity, high TGs, TC and LDL-C, low SHBG, high fasting insulin, low insulin sensitivity |
| Duleba et al., 2003 | 33                 | Pregnancy           | Older age, obesity, insulin resistance, adhesions |
| Stegmann et al., 2003 | 86                 | Ovulation and pregnancy | BMI ≥35 kg/m², FAI ≥15, serum T ≥4.5 nmol/L, basal LH <10 IU/L, duration of infertility >3 years |
| Amer et al., 2004  | 200                 | Ovulation and pregnancy | Menarche at <13 years, LH:FSH <2, fasting glucose <4.5 mmol/L |
| van Wely et al., 2005 | 83                 | Ovulation           | Age >35 years, basal FSH >10 IU/L |
| Palomba et al., 2006 | 60                 | Ovulation and pregnancy | Basal serum AMH >7.7 ng/mL |
| Amer et al., 2009  | 29                  | Ovulation           | LH <12.1 IU/L, androstenedione <3.26 ng/ml |
| Ott et al., 2009   | 100                 | Ovulation           | BMI ≥25 kg/m², age >30 years, duration of infertility >3.5 years |
| Baghdadi et al., 2012 (collaborative meta-analysis) | 1784 from 14 articles | Ovulation and pregnancy | High LH:FSH ratio |
| Kaur et al., 2013  | 73                  | Pregnancy           | |

AMH: Anti-Mullerian hormone, BMI: Body mass index, FAI: Free androgen index, FSH: Follicle-stimulating hormone, LDL-C: Low-density lipoprotein cholesterol, LH: Luteinizing hormone, SHBG: Sex hormone binding globulin, T: Testosterone, TC: Total cholesterol, TGs: Triglycerides, LOD: Laparoscopic ovarian drilling.
de novo adhesions or in improving pregnancy rates.\[29\] Ovary should be raised before application of energy and saline washed after the procedure to decrease the temperature thereby reducing the risk of injury.\[56\]

Another potential risk is POF, especially if the ovarian blood supply is damaged inadvertently or if large number of punctures are made, leading to excessive destruction of ovarian follicular pool or production of anti-ovarian antibodies.\[4\] Only one isolated case of ovarian atrophy following high-energy drilling (eight coagulation points at 400 W for 5 s) is reported.\[88\] When applied correctly, it does not appear to compromise the ovarian reserve. A prospective comparative study found that the extent of ovarian tissue damage was limited, ranging from 0.4% after four to 1% after eight coagulation punctures, each of 40 W for 5 s.\[89\] In fact, changes in ovarian reserve markers can be interpreted as normalization of ovarian function rather than a reduction of ovarian reserve.\[73,90\] Coagulation should not be done within 8-10 mm of the ovarian hilum.\[86,88\] Unilateral drilling,\[33,73\] use of the harmonic scalpel,\[37\] use of bipolar energy or <5 perforations with monopolar energy\[15\] are associated with lesser risk of adhesions and DOR but with equivalent reproductive outcomes.

**Alternative strategies in clomiphene citrate-resistant polycystic ovary syndrome and comparison of efficacy with laparoscopic ovarian drilling**

A comparison of the efficacy between LOD and other drugs for OI in CC-resistant PCOS is demonstrated in Table 3. LOD is equally efficacious to rFSH in terms of ovulation, pregnancy and live birth rates.\[34,91,92,100,101\]

### Table 2: Reproductive outcomes after LOD in PCOS patients

| Publication with year | Number of cases | Drilling technique | Ovulation rates (%) | Pregnancy rates (%) |
|-----------------------|-----------------|--------------------|---------------------|---------------------|
| Gjönnass, 1984\[27\] | 62 | EC | 92 | 69 |
| Daniell and Miller, 1989\[28\] | 85 | Laser | 71 | 56 |
| Merchant, 1996\[29\] | 74 | EC (low-watt bipolar) | 87 | 57 |
| Grzechocinska et al., 2000\[30\] | 22 | EC | 90.9 | 63.6 |
| Fellingham et al., 2000\[31\] | 112 | EC | 73.2 | 58 |
| Fernandez et al., 2001\[32\] | 13 | THL with bipolar | 46 | 23 |
| Kriplani et al., 2001\[33\] | 70 | EC | 81.8 | 54.5 |
| Amer et al., 2002\[34\] | 110 | EC/argon laser | 67 | 61 |
| Takeuchi et al., 2002\[35\] | 34 | Harmonic scalpel laser versus ND:Yag laser | 94 for both | 77 versus 60 |
| Amer et al., 2003\[36\] | 30 | EC with 4/3/2/1 puncture/ovary | 67/44/33/33 | 67/56/17/0 |
| Malkawi et al., 2003\[37\] | 97 | EC | 83.5 | 59.8 |
| Stegmann et al., 2003\[38\] | 86 | EC | 66 | 50 |
| Al Ojaimi, 2003\[39\] | 181 | EC | 70.1 | 32.5 |
| Amer et al., 2004\[40\] | 200 | EC | 57 | 50 |
| Bayram et al., 2004\[41\] | 83 | EC with bipolar | 70 | 37 |
| Cleemane et al., 2004\[42\] | 57 | EC | ND | 61 |
| Fernandez et al., 2004\[43\] | 80 | THL with bipolar | 91 | 39.7 |
| Apri et al., 2005\[44\] | 45 | EC | 93.3 | 64.4 |
| Kucuk and Kilic-Okman, 2005\[45\] | 83 | EC | 77 | 54 |
| van Wely et al., 2005\[46\] | 135 | EC with bipolar | 67.5 | 49 |
| Mariano et al., 2006\[47\] | 60 | EC (LOD vs. MLOD) | 74.85 (72 vs. 77.7) | 19.4 versus 20 |
| Palomba et al., 2006\[48\] | 60 | EC | 57.1 | 13.0 |
| Sharma et al., 2006\[49\] | 20 | EC (unipolar vs. bipolar) | 60 versus 80 | 60 versus 80 |
| Godnik and Jovovic, 2007\[50\] | 45 | Laparoscopic electroincision | 87 | 61 |
| Kato et al., 2007\[51\] | 32 | EC | 76.1 | 53.1 |
| Amer et al., 2009\[52\] | 33 | EC | 64 | 23 |
| Ott et al., 2009\[53\] | 100 | Monopolar EC and hook electrode | 71 | 60.6 |
| Abu Hashim et al., 2010\[54\] | 132 | EC | 69.3 | 17.5 |
| Zhu et al., 2010\[55\] | 80 | TVS-guided OILT | 5/15/75/80 | 5/10/45/40 |
| (1/2/3/4-5 punctures/ovary) | | | | |
| Abu Hashim et al., 2011\[56\] | 144 | EC | 68.2 | 17 |
| Kong et al., 2011\[57\] | 89 | EC | 61 | 55 |
| Ott et al., 2011\[58\] | 38 | Monopolar hook electrode | 75.8 | 80.6 |
| Poujade et al., 2011\[59\] | 74 | THL with bipolar | ND | 27 |
| Zakeriah et al., 2011\[60\] | 108 | EC (adjusted dose vs. fixed dose) | 81.8 versus 62.2 | 51.7 versus 36.8 |
| Nasr et al., 2012\[61\] | 60 | EC versus harmonic scalpel | 89 versus 92.9 | 50 versus 57 |
| Kaur et al., 2013\[62\] | 100 | EC | ND | 47.3 |
| el Sharkawy et al., 2013\[63\] | 62 | Unilateral LOD | 67.7 | 54.8 |

LOD: Laparoscopic ovarian drilling, PCOS: Polycystic ovary syndrome, EC: Electrocauterization, LOD: Laparoscopic ovarian drilling, MLOD: Microlaparoscopic ovarian drilling, OILT: Ovarian interstitial laser treatment, PCOS: Polycystic ovary syndrome, THL: Transvaginal hydrolaparoscopy, TVS: Transvaginal sonography, ND: Not determined
Although cumulative conception rates at 6 months are lower with LOD than gonadotropin, they even-out after 12 months.\[21\] However, 2 RCTs found that the adjuvant therapy with CC or gonadotropins was required to achieve equivalent pregnancy and live birth rates in patients remaining anovulatory 8-12 weeks after LOD or those who subsequently became anovulatory.\[62,93\]

Trials comparing metformin with LOD in CC-resistant PCOS have shown variable results.\[61,78,94\] with some favoring LOD plus CC and the live-birth rates than LOD

**Table 3: Comparison of efficacy between LOD and other medical treatments in CC-resistant PCOS**

| Publication with year, study design | Treatment compared | Number of cases | Results |
|-------------------------------------|--------------------|-----------------|---------|
| Farquhar et al., 2012\[20\] Cochrane database systematic review | LOD versus medical drugs for OI | 9 trials (n = 1210) reported on live birth rate per couple | Comparable live birth, clinical pregnancy and miscarriage rates with LOD and other medical OI agents Similar live births when compared with CC plus tamoxifen, gonadotrophins, AI or CC Significantly fewer live births following LOD compared with CC plus metformin Similar ovulation and pregnancy rates when compared to CC plus metformin, CC plus tamoxifen, AI or rosiglitazone plus CC Lower rate of multiple pregnancies by LOD compared with trials using gonadotrophins |
| Bayram et al., 2004\[82\] randomized controlled | LOD versus uFSH/rFSH | 168 | Similar cumulative pregnancy rate and miscarriage rate between LOD and FSH respectively Lower rates of cumulative ongoing pregnancy with LOD alone but becomes comparable after addition of CC and rFSH Lower rates of multiple pregnancies after LOD |
| Kaya et al., 2005\[4\] randomized prospective Ghafarnegad et al., 2010\[52\] randomized | LOMNI versus rFSH | 35 | Similar cumulative pregnancy rates but lower cost in LOMNI group |
| Mehrabian and Eessaei, 2012\[32\] randomized controlled | LOD versus HMG | 104 | Lower pregnancy rates in LOD group but becomes comparable after addition of CC and rFSH |
| Malkawi et al., 2003\[81\] prospective comparative | Metformin versus LOD | 161 | No difference in menstrual cyclicity, ovulation or clinical pregnancy rates but higher live birth rates in the metformin group |
| Hamed et al., 2010\[94\] randomized | LOD versus metformin | 110 | More regular cycles, higher rates of ovulation and pregnancy in LOD group but better amelioration of insulin resistance in the metformin group |
| Palomba et al., 2004\[7\] randomized double blind placebo controlled | Metformin versus LOD | 121 | Similar ovulation rates but higher pregnancy and live birth rates and lower miscarriage rates after metformin than LOD |
| Palomba et al., 2005\[95\] randomized double blind placebo controlled | Metformin plus CC versus LOD plus CC Metformin versus unilateral LOD | 28, 120 | Similar ovulation, pregnancy, abortion and the live-birth rates Higher ovulation and pregnancy rates in unilateral LOD group but better attenuation of insulin resistance in the metformin group |
| Palomba et al., 2010\[8\] randomized controlled | CC plus metformin versus LOD CC plus metformin versus LOD | 50, 282 | Similar miscarriage rates Similar pregnancy and live-birth rates per cycle but lower ovulation rate per cycle in LOD group Similar ovulation and pregnancy rates per cycle |
| Abu Hashim et al., 2011\[94\] randomized prospective | Letrozole versus LOD | 260 | Similar ovulation and pregnancy rates |
| Abu Hashim et al., 2010\[97\] randomized prospective | Letrozole versus LOD | 140 | Higher ovulation rate in the letrozole group but similar rates of pregnancy and live birth |
| Abdellah, 2011\[95\] randomized | LOD versus tamoxifen plus CC | 150 | Similar ovulation, pregnancy and live birth rates |
| Zakherah et al., 2010\[98\] randomized prospective | Rosiglitazone plus CC versus unilateral LOD plus CC | 43 | Similar ovulation rate and pregnancy rate |

AI: Aromatase inhibitors, CC: Clomiphene-citrate, HMG: Human menopausal gonadotropin, GnRH: Gonadotropin-releasing hormone, LOD: Laparoscopic ovarian drilling, rFSH: Recombinant follicle-stimulating hormone, uFSH: Urinary follicle-stimulating hormone, PCOS: Polycystic ovary syndrome, OI: Ovulation induction, LOMNI: Laparoscopic ovarian multi-needle intervention.
Laparoscopic ovarian drilling in clomiphene citrate-failure and as first-line therapy in polycystic ovary syndrome

Role of LOD in CC-failure or as first-line therapy in PCOS remains largely undetermined. Only one RCT, comparing the efficacy of LOD versus continuation of CC up to six further cycles in 176 CC-failure PCOS patients, observed similar improvement in cycle length, pregnancy, miscarriage and live birth rates. When compared to CC as first-line therapy in PCOS, one comparative study found higher ovulation (90.9% vs. 68%) and pregnancy (63.6% vs. 28%) rates in the LOD group while an RCT found no difference at 12 months. Interestingly, when offered to women after CC-resistance/failure, LOD achieved a pregnancy rate 2 times higher than that resulting from LOD as a first-line therapy (55% vs. 27%). This possibly suggests that LOD may be more effective in CC-resistant PCOS women than in women without previous knowledge of their response to CC. Currently, LOD is not recommended for CC-failure PCOS or as first-line therapy due to lack of its superiority over CC.

Pregnancy outcomes after laparoscopic ovarian drilling

Multiple pregnancy rate varies from 0% to 10%, but is significantly lower than gonadotropins, thus making LOD an attractive option for CC-resistant PCOS. No difference in the incidence of OHSS and miscarriage rates is seen between LOD and other medical treatments. LOD does not seem to improve risk of GDM, and higher incidence of GDM and pregnancy-induced hypertension have been reported after LOD.

Cost-effectiveness

Laparoscopic ovarian drilling is more cost-effective than gonadotropins as single-treatment results in several mono-ovulatory cycles thus allowing multiple attempts at conception whereas one course of gonadotropin therapy yields a single ovulatory cycle with the inherent need for intensive monitoring. The higher incidence of multiple pregnancies incurs extra costs in those who conceive with FSH.

What next after laparoscopic ovarian drilling failure?

Laparoscopic ovarian drilling failure is defined as failure to ovulate within 6-8 weeks, recurrence of anovulatory status after an initial response or failure to conceive despite regular ovulation for 12 months. Since LOD improves responsiveness of the polycystic ovaries to subsequent OI agents, reintroduction of drug treatments (first CC and then gonadotrophins) and possibly IVF can be considered in those do not spontaneously become pregnant within 6 months after LOD once ovulation has been re-established or after 3 months when ovulation has not been detected.

Re-drilling — should it be done?

The effectiveness of a second LOD, that is re-drilling in women with PCOS was investigated in a retrospective study comprising of 20 women who had undergone LOD 1-6 years prior. Overall, ovulation and pregnancy rates were 60% and 53%, respectively, with better outcomes in LOD-sensitive than LOD-resistant cases (83 and 67% vs. 25 and 29%, respectively). However, there are concerns of adhesions and DOR, precluding the feasibility of a RCT to address this issue. Until then, repeated application of LOD should not be encouraged.

CONCLUSION

Laparoscopic ovarian drilling is currently recommended as a safe, efficacious and cost-effective alternative to gonadotropins for OI in infertile, anovulatory, CC-resistant PCOS women without the risks of OHSS or multiple gestation. Monopolar diathermy is the most widely used technique, although no technique is superior. Restoration of regular ovulation and menstruation as well as reduction in androgen and LH levels persist long-term. The evidence on the improvement of insulin sensitivity, lipid and lipoprotein disturbances, acne and hirsutism, are not clear; hence it should not be used for such non-fertility indications. Although iatrogenic adhesion formation and DOR are potential complications, they are of little clinical significance and can be minimized by limiting the number of punctures and energy applied. A detailed knowledge of the clinical and hormonal profile of the patients may be useful in a careful selection of cases likely to respond to LOD. Since LOD improves ovarian responsiveness to CC and gonadotropins, these may be considered after LOD failure instead of repeat LOD, before proceeding to the last resort that is, IVF. Despite its advantages, LOD is neither the first-line therapy in PCOS nor the treatment of choice in CC-resistant PCOS owing to the advent of a multitude of safe and efficacious oral alternatives and wider
acceptance of relatively safe low-dose step-up regimen of gonadotropin therapy. Rather, it should be reserved to well-chosen anovulatory CC-resistant PCOS cases — Those with young age, raised LH levels, exaggerated response to gonadotropins, noncompliance or nonfeasibility with frequent, intensive monitoring or needing laparoscopic assessment of the pelvis. Importantly, reproductive specialists should remember that it is only an alternative, not the ultimate in management of PCOS.

REFERENCES

1. Overbeek A, Lambalk CB. Phenotypic and pharmacogenetic aspects of ovulation induction in WHO II anovulatory women. Gynecol Endocrinol 2009;25:22-34.
2. March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010;25:544-51.
3. Yildiz BO, Bozdag G, Yapici Z, Esinler I, Yarali H. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. Hum Reprod 2012;27:3067-73.
4. Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Consensus on infertility treatment related to polycystic ovary syndrome. Fertil Steril 2008;90:505-22.
5. Brown J, Farquhar C, Beck J, Boothroyd C, Hughes E. Clomiphene and anti-oestrogens for ovulation induction in PCOS. Cochrane Database Syst Rev 2009;7:CD002249.
6. Abu Hashim H. Clomiphene citrate alternatives for the initial management of polycystic ovary syndrome: An evidence-based approach. Arch Gynecol Obstet 2012;285:1737-45.
7. Bouchard P. Treatment of infertility in women with polycystic ovary syndrome. Ann Endocrinol (Paris) 2010;71:225-7.
8. Vause TD, Cheung AP, Sierra S, Claman P, Graham J, Guillemijn JA, et al. Ovulation induction in polycystic ovary syndrome: No 242, May 2010. Int J Gynaecol Obstet 2010;111:95-100.
9. Amer SA. Laparoscopic ovarian surgery for polycystic ovarian syndrome. In: Dunlop W, Ledger WL, editors. Recent Advances in Obstetrics and Gynaecology. 24th ed. London: Royal Society of Medicine Press Ltd.; 2009. p. 227-3.
10. Flyckt RL, Goldberg JM. Laparoscopic ovarian drilling for clomiphene-resistant polycystic ovary syndrome. Semin Reprod Med 2011;29:138-46.
11. Abu Hashim H, Al-Imany H, De Voc M, Tournaye H. Three decades of Gijnnaes's laparoscopic ovarian drilling for treatment of PCOS: what do we know? An evidence-based approach. Arch Gynecol Obstet 2013;288:409-22.
12. Felemban A, Tan SL, Tulandi T. Laparoscopic treatment of polycystic ovaries with insulated needle cautery: A reappraisal. Fertil Steril 2000;73:266-9.
13. Kato M, Kikuchi I, Shimanihi K, Kobori H, Aida T, Kitade M, et al. Efficacy of laparoscopic ovarian drilling for polycystic ovary syndrome resistant to clomiphene citrate. J Obstet Gynaecol Res 2007;33:174-80.
14. Seow KM, Juan CC, Hwang JI, Ho LT. Laparoscopic surgery in polycystic ovary syndrome: Reproductive and metabolic effects. Semin Reprod Med 2008;26:101-10.
15. Fernandez H, Morin-Surruca M, Torre A, Faivre E, Deffieux X, Gervaise A. Ovarian drilling for surgical treatment of polycystic ovarian syndrome: A comprehensive review. Reprod Biomed Online 2011;22:556-68.
16. Royal College of Obstetricians and Gynaecologists (RCOG). Long-term consequences of polycystic ovary syndrome. (Green-top Guideline; No. 33). London, (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2007. p. 1-11.
drilling for polycystic ovary syndrome using harmonic scalpel. J Diabetes Metab 2012;56:008.

38. Salah TM. Office microlaparoscopic ovarian drilling (OMLOD) versus conventional laparoscopic ovarian drilling (LOD) for women with polycystic ovary syndrome. Arch Gynecol Obstet 2013;287:361-7.

39. Marianowski P, Kaminski P, Wielgos M, Szymusik I. The changes of hormonal serum levels and ovulation/pregnancy rates after ovarian electrocautery in microlaparoscopy and laparoscopy in patients with PCOS. Neuro Endocrinol Lett 2006;27:214-8.

40. Poujade O, Gervaise A, Fairey E, Deffieux X, Fernandez H. Surgical management of infertility due to polycystic ovarian syndrome after failure of medical management. Eur J Obstet Gynecol Reprod Biol 2011;158:242-7.

41. Fernandez H, Alby JD, Gervaise A, de Tayrac R, Frydman R. Operative transvaginal hyaluraprosphy for treatment of polycystic ovary syndrome: A new minimally invasive surgery. Fertil Steril 2001;75:607-11.

42. Fernandez H, Watrelot A, Alby JD, Kadoch J, Gervaise A, deTayrac R, et al. Fertility after ovarian drilling by transvaginal fertiloscopy for treatment of polycystic ovary syndrome. J Am Assoc Gynecol Laparosc 2004;11:374-8.

43. Zhu W, Fu Z, Chen X, Li X, Tang Z, Zhou Y, et al. Transvaginal ultrasound-guided ovarian interstitial laser treatment in anovulatory women with polycystic ovary syndrome: A randomized clinical trial on the effect of laser dose used on the outcome. Fertil Steril 2010;94:268-75.

44. Ferraretti AP, Giannaroli L, Magli MC, Jammalone E, Feliciani E, Fortini D. Transvaginal ovarian drilling: A new surgical treatment for improving the clinical outcome of assisted reproductive technologies in patients with polycystic ovary syndrome. Fertil Steril 2001;76:812-6.

45. Stegmann BJ, Craig HR, Bay RC, Coonrod DV, Brady MJ, Garbaciak JA Jr. Characteristics predictive of response to ovarian diathermy in women with polycystic ovary syndrome. Am J Obstet Gynecol 2003;188:1171-3.

46. Al Ojaimi EH. Laparoscopic ovarian drilling for polycystic ovary syndrome in clomiphene citrate-resistant women with anovulatory infertility. Bahrain Med Bull 2003;2:1-14.

47. van Wely M, Bayram N, van der Veen F, Bossuyt PM. Predictors for treatment failure after laparoscopic electrocauterization of the ovaries in women with clomiphene citrate resistant polycystic ovary syndrome. Hum Reprod 2005;20:900-5.

48. Amer SA, Li TC, Ledger WL. Ovulation induction using laparoscopic ovarian drilling in women with polycystic ovarian syndrome: Predictors of success. Hum Reprod 2004;19:1719-24.

49. Baghjadi LR, Abu Hashim H, Amer SA, Palomba S, Falbo A, Al-Ojaimi E, et al. Impact of obesity on reproductive outcomes after ovarian ablative therapy in PCOS: A collaborative meta-analysis. Reprod Biomed Online 2012;25:227-41.

50. Gjønnaess H. Ovarian electrocautery in the treatment of women with polycystic ovary syndrome (PCOS). Factors affecting the results. Acta Obest Gynecol Scand 1994;73:407-12.

51. Li TC, Saravelos H, Chow MS, Chisabingo R, Cooke ID. Factors affecting the outcome of laparoscopic ovarian drilling for polycystic ovarian syndrome in women with anovulatory infertility. Br J Obstet Gynaecol 1998;105:338-44.

52. Kriplani A, Manchanda R, Agarwal N, Nayar B. Laparoscopic ovarian drilling in clomiphene citrate-resistant women with polycystic ovary syndrome. J Am Assoc Gynecol Laparosc 2001;8:511-8.

53. Ott J, Wirth S, Nouri K, Kurz C, Mayerhofer K, Huber JC, et al. Luteinizing hormone and androstendione are independent predictors of ovulation after laparoscopic ovarian drilling: A retrospective cohort study. Reprod Biol Endocrinol 2009;7:153.

54. Amer SA, Li TC, Ledger WL. The value of measuring anti-Mullerian hormone in women with anovulatory polycystic ovary syndrome undergoing laparoscopic ovarian diathermy. Hum Reprod 2009;24:2769-70.

55. Palomba S, Falbo A, Orio F Jr, Russo T, Sbano F, D’Alessandro P, et al. Efficacy of laparoscopic ovarian diathermy in clomiphene citrate-resistant women with polycystic ovary syndrome: Relationships with chronological and ovarian age. Gynecol Endocrinol 2006;22:329-35.

56. Kaur M, Pranesh G, Mittal M, Gahan A, Deepika K, Sashikala T, et al. Outcome of laparoscopic ovarian drilling in patients of clomiphene resistant polycystic ovary syndrome in a tertiary care center. Int J Infertil Fetal Med 2013;4:39-44.

57. Duleba AJ, Banaszewska B, Spaczynski RZ, Pawelczyk LK. Success of laparoscopic ovarian wedge resection is related to obesity, lipid profile, and insulin levels. Fertil Steril 2003;79:1008-14.

58. Daniell JF, Miller W. Polycystic ovaries treated by laparoscopic laser vaporization. Fertil Steril 1989;51:232-6.

59. Merchant RN. Treatment of polycystic ovary disease with laparoscopic low-watt bipolar electrocauterization of the ovaries. J Am Assoc Gynecol Laparosc 1996;3:503-8.

60. Grzecchinska B, Fracki S, Marianowski L. Results of clomiphene citrate ovarian stimulation versus laparoscopic electrocauterization of the ovaries in infertile women with polycystic ovary syndrome. Gynecol Endocrinol 2004;18:138-43.

61. API M, Görgen H, Cetin A. Laparoscopic ovarian drilling in polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol 2005;119:76-81.

62. Bayram N, van Wely M, Kajaik EM, Bossuyt PM, van der Veen F. Using an electrocautery strategy or recombinant follicle stimulating hormone to induce ovulation in polycystic ovary syndrome: Randomised controlled trial. BMJ 2004;328:192.

63. Cleemann L, Lauthus FF, Trolle B. Laparoscopic ovarian drilling as first line of treatment in infertile women with polycystic ovary syndrome. Gynecol Endocrinol 2004;18:138-43.

64. Ame SA, Li TC, Ledger WL. Ovulation induction using laparoscopic ovarian drilling in women with polycystic ovarian syndrome: A randomized controlled trial. J Obstet Gynaecol Res 2011;37:169-77.

65. Kong GW, Cheung LP, Lok H. Effects of laparoscopic ovarian drilling in treating infertile anovulatory polycystic ovary syndrome patients with and without metabolic syndrome. Hong Kong Med J 2011;17:5-10.

66. el Sharkwa IA. Metformin versus laparoscopic unilateral ovarian drilling in clomiphene-resistant women with polycystic ovary syndrome: A randomized controlled trial. Arch Gynecol Obstet 2010;282:567-71.

67. Abu Hashim H, El Lakany N, Sherrif L. Combined metformin and clomiphene citrate versus laparoscopic ovarian drilling for ovulation induction in clomiphene-resistant women with polycystic ovary syndrome: A randomized controlled trial. J Obstet Gynaecol Ont 2013;37:169-77.

68. Abu Hashim H, Mashaly AM, Badawy A. Letrozole versus laparoscopic ovarian diathermy for ovulation induction in clomiphene-resistant women with polycystic ovary syndrome: A randomized controlled trial. Arch Gynecol Obstet 2010;282:567-71.

69. Abu Hashim H, El Shakry I. Metformin versus laparoscopic unilateral ovarian drilling in clomiphene resistant women with polycystic ovary syndrome. Middle East Fertili Soc J 2013;18:202-7.

70. Soliman EM, Attia AM, Elebrashi AN, Younis AS, Salit ME. Laparoscopic ovarian electrocautery improves ovarian response to gonadotropins in clomiphene citrate resistant patients with polycystic ovary syndrome. Middle East Fertili Soc J 2005;1:120-5.

71. Abu Hashim H, El-Shafei M, Badawy A, Wafa A, Zaglod H. Does laparoscopic ovarian diathermy change clomiphene-resistant PCOS into clomiphene-sensitive? Arch Gynecol Obstet 2011;284:503-7.

72. Kandil M, Selim M. Hormonal and sonographic assessment of ovarian reserve before and after laparoscopic ovarian drilling in polycystic ovary syndrome. BJOG 2005;112:1427-30.

73. Amer SA, Banu Z, Li TC, Cooke ID. Long-term follow-up of patients with polycystic ovary syndrome after laparoscopic ovarian drilling: Endocrine and ultrasonographic outcomes. Hum Reprod 2002;17:2851-7.

74. Gjønnaess H. Late endocrine effects of ovarian electrocautery in women with polycystic ovary syndrome. Fertil Steril 1999;69:697-701.

75. Mohiuddin S, Bestellink D, Farquhar C. Long-term follow up of women with laparoscopic ovarian diathermy for women with
clomiphene-resistant polycystic ovarian syndrome. Aust N Z J Obstet Gynaecol 2007;47:508-11.

77. Nahuis MJ, Kose N, Bayram N, van Dessel HJ, Braat DD, Hamilton CJ, et al. Long-term outcomes in women with polycystic ovary syndrome initially randomized to receive laparoscopic electrocautery of the ovaries or ovulation induction with gonadotrophins. Hum Reprod 2011;26:1899-904.

78. Palomba S, Orrio F Jr, Nardo LG, Falbo A, Russo T, Corea D, et al. 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;89:4801-9.

79. Tulandi T, Saleh A, Morris D, Jacobs HS, Payne NN, Tan SL. Effects of laparoscopic ovarian drilling on serum vascular endothelial growth factor and on insulin responses to the oral glucose tolerance test in women with polycystic ovary syndrome. Fertil Steril 2000;74:585-8.

80. 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;84:4279-82.

81. Tiitinen A, Tenhunen A, Seppälä M. Ovarian electrocauterization causes LH-regulated but not insulin-regulated endocrine changes. Clin Endocrinol (Oxf) 1993;39:181-4.

82. Gürgün T, Urman B, Aksu T, Yarali H, Develioglu O, Kinsirci HA. The effect of short-interval laparoscopic lysis of adhesions on pregnancy rates following Nd:YAG laser photocoagulation of polycystic ovaries. Obstet Gynecol 1992;80:45-7.

83. Naether OG, Fischer R. Adhesion formation after laparoscopic electrocautery of the ovarian surface in polycystic ovary patients. Fertil Steril 1993;60:95-8.

84. Greenblatt EM, Casper RF. Adhesion formation after laparoscopic ovarian cautery for polycystic ovarian syndrome: Lack of correlation with pregnancy rate. Fertil Steril 1993;60:766-70.

85. Saravelos H, Li TC. Post-operative adhesions after laparoscopic electrosurgical treatment for polycystic ovarian syndrome with the application of Intercede to one ovary: A prospective randomized controlled study. Hum Reprod 1996;11:992-7.

86. Mercorio F, Mercorio A, Di Spiezo Sardo A, Barba GV, Pellicano M, Nappi C. Evaluation of ovarian adhesion formation after laparoscopic ovarian drilling by second-look minilaparoscopy. Fertil Steril 2008;89:1229-33.

87. Naether OG. Significant reduction of adnexal adhesions following laparoscopic electrocautery of the ovarian surface (LEOS) by lavage and artificial ascites. Gynaecol Endosc 1995;4:17-19.

88. Dabirrahmani H. Complications of laparoscopic ovarian cauterization. Fertil Steril 1989;52:878-9.

89. El-Sheikhah A, Aboulghar M, Read R, El-Hendawy E. The extent of ovarian damage produced by ovarian cauterisation in the human. J Obstet Gynaecol 2004;24:664-6.

90. Api M. Is ovarian reserve diminished after laparoscopic ovarian drilling? Gynecol Endocrinol 2009;25:159-65.

91. Farquhar CM, Williamson K, Gudeck G, Johnson NP, Garland J, Sadler L. A randomized controlled trial of laparoscopic ovarian diathermy versus gonadotropin therapy for women with clomiphene citrate-resistant polycystic ovary syndrome. Fertil Steril 2002;78:404-11.

92. Ghaflamegad M, Arjmand N, Khazaiepour Z. Pregnancy rate of gonadotrophin therapy and laparoscopic ovarian electrodessication in polycystic ovary syndrome resistant to clomiphene citrate: A comparative study. Tehran Univ Med J 2010;67:712-7.

93. Mehrabian F, Eissaie F. The laparoscopic ovarian electrocautery versus gonadotropin therapy in infertile women with clomiphene citrate-resistant polycystic ovary syndrome; a randomized controlled trial. J Pak Med Assoc 2012;62:542-4.

94. 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 Gynaecol Obstet 2010;108:143-7.

95. Palomba S, Orrio F Jr, Falbo A, Russo T, Caterina G, Manguso F, et al. Metformin administration and laparoscopic ovarian drilling improve ovarian response to clomiphene citrate (CC) in oligo-ovulatory CC-resistant women with polycystic ovary syndrome. Clin Endocrinol (Oxf) 2005;63:631-5.

96. Palomba S, Falbo A, Battista L, Russo T, Venturella R, Tolino A, et al. Laparoscopic ovarian diathermy vs clomiphene citrate plus metformin as second-line strategy for infertile anovulatory patients with polycystic ovary syndrome: A randomized controlled trial. Am J Obstet Gynecol 2010;202:577.e1-8.

97. Abdellah MS. Reproductive outcome after letrozole versus laparoscopic ovarian drilling for clomiphene-resistant polycystic ovary syndrome. Int J Gynaecol Obstet 2011;113:218-21.

98. Zakherah MS, Nasr A, EIs Saman AM, Shaaban OM, Shahin AY. Clomiphene citrate plus tamoxifen versus laparoscopic ovarian drilling in women with clomiphene-resistant polycystic ovary syndrome. Int J Gynaecol Obstet 2010;108:240-3.

99. Roy KK, Baruah J, Sharma A, Sharma JB, Kumar S, Kachava G, et al. A prospective randomized trial comparing the clinical and endocrinological outcome with rosiglitazone versus laparoscopic ovarian drilling in patients with polycystic ovarian disease resistant to ovulation induction with clomiphene citrate. Arch Gynecol Obstet 2010;281:939-44.

100. van Wely M, Bayram N, van der Veen F, Bossuyt PM. An economic comparison of a laparoscopic electrocautery strategy and ovulation induction with recombinant FSH in women with clomiphene citrate-resistant polycystic ovary syndrome. Hum Reprod 2004;19:1741-5.

101. Malikwi HY, Qublan HS. Laparoscopic ovarian drilling in the treatment of polycystic ovary syndrome: How many punctures per ovary are needed to improve the reproductive outcome? J Obstet Gynaecol Res 2005;31:115-9.

102. Saleh AM, Khalil HS. Review of nonsurgical and surgical treatment and the role of insulin-sensitizing agents in the management of infertile women with polycystic ovary syndrome. Acta Obstet Gynecol Scand 2004;83:614-21.

103. Palomba S, Falbo A, Zullo F. Management strategies for ovulation induction in women with polycystic ovary syndrome and the role of insulin-sensitizing agents in the management of polycystic ovaries. Obstet Gynecol Scand 2004;83:614-21.

104. Al-Ojaimi EH. Pregnancy outcomes after laparoscopic ovarian drilling in women with polycystic ovarian syndrome. Saudi Med J 2006;27:519-25.

105. Farquhar CM, Williamson K, Brown PM, Garland J. An economic evaluation of laparoscopic ovarian diathermy versus gonadotrophin therapy for women with clomiphene citrate resistant polycystic ovary syndrome. Hum Reprod 2004;19:1110-5.

106. Nahuis MJ, Oude Lohuis E, Kose N, Bayram N, Hompes P, Oosterhuis GJ, et al. Long-term follow-up of laparoscopic electrocautery of the ovaries versus ovulation induction with recombinant FSH in clomiphene citrate-resistant women with polycystic ovary syndrome: An economic evaluation. Hum Reprod 2012;27:3577-82.

107. Amer SA, Li TC, Cooke ID. Repeated laparoscopic ovarian diathermy is effective in women with anovulatory infertility due to polycystic ovary syndrome. Fertil Steril 2003;79:1211-5.