

Marlin Fuad Mubarak · Suruchi Arora ·
Roger Williams

Laparoscopic ovarian drilling for women with anovulatory polycystic ovarian syndrome: a district general hospital experience

Received: 3 October 2005 / Accepted: 29 December 2005 / Published online: 28 February 2006
© Springer-Verlag Berlin / Heidelberg 2006

Abstract This is a retrospective study involving 100 anovulatory women with polycystic ovarian syndrome (PCOS) who had laparoscopic ovarian drilling (LOD) between January 1995 and May 2002 at the Royal Berkshire Hospital, Reading, a large district general hospital (DGH). The aim was to evaluate the efficacy of LOD in the treatment of women with anovulatory PCOS in a DGH setting. We also looked at the factors predicting the clinical outcome to be able to counsel the patients pre-operatively. The study showed that the spontaneous pregnancy rate after LOD was 32.46%. A further 28.5% conceived after induction of ovulation with clomiphene citrate (CC) or purified follicular stimulating hormone (Metrodin HP), with a cumulative pregnancy rate of 74%. We did not find a significant difference in the luteinising hormone to follicular stimulating hormone (LH:FSH) ratio of greater than 2.5, LH level of greater than 10 IU/l, body mass index (BMI), age or duration of infertility between the group of women who conceived and those who failed to conceive, in response to LOD.

Keywords Clomiphene citrate · LOD ·
Ovulation induction · PCOS

Introduction

Polycystic ovarian syndrome (PCOS) was first described by Stein and Leventhal in 1935. It is a heterogeneous disorder that involves various clinical and biochemical disorders as well the polycystic appearance of the ovaries on ultrasound. Classical features of anovulation, hyperandrogenism and obesity are variably expressed.

One of the endocrine disorders associated with PCOS is anovulatory infertility. Clomiphene citrate (CC) is the first choice of treatment for subfertile anovulatory women with

PCOS and has a cumulative conception rate of 67.3% [1]. Adverse effects of CC include multiple pregnancy, with twins in 9% and triplets in less than 1% of the treated women [2]. This carries an increased risk of fetal and maternal morbidity and mortality as well as having financial implications for the family and the National Health Service.

The issue arises of what to do in women who do not conceive in response to CC. Current evidence suggests that laparoscopic ovarian drilling (LOD) is effective in inducing ovulation in women with anovulatory PCOS who fail to conceive in response to CC [3, 4]. LOD has been shown to be as effective as gonadotrophins in these women [2, 5, 6]. In most studies, the pregnancy rate after LOD has been reported to be in the region of 50%, with a cumulative pregnancy rate of 54–70% over a 12-month period [4, 7].

Laparoscopic ovarian drilling has the advantage of being a one-step treatment. It does not require intensive ultrasound monitoring as there is lower incidence of multiple pregnancy and no risk of ovarian hyperstimulation [8]. On the other hand, gonadotrophins are expensive, stressful and time-consuming, requiring intensive monitoring [2]. Even if spontaneous ovulation does not result from LOD, there is an increase in ovarian sensitivity to subsequent CC and gonadotrophins [2, 9]. Furthermore, LOD appears to normalise ovarian function and morphology in women with PCOS with long-lasting effects, ranging between 72 months and 9 years [10, 11].

Surgery does carry its own risks. One concern is adhesion formation following LOD. This was found to be of less clinical significance following LOD than following wedge resection of the ovary [8, 11].

An additional concern is the theoretical risk of premature ovarian failure, but this has yet to be established.

The response of women with PCOS to LOD is believed to depend on their pre-treatment characteristics, women with high basal LH concentration having a better clinical and endocrine response [8]. Our aim was to see if the published results of success after LOD for anovulatory PCOS are reproducible in a district general hospital (DGH) setting and to assess the factors affecting the pregnancy rate.

M. F. Mubarak (✉) · S. Arora · R. Williams
Department of Obstetrics and Gynaecology,
Royal Berkshire Hospital,
Reading, UK
e-mail: MMAF14@aol.com

Materials and methods

Royal Berkshire Hospital, Reading, is a large DGH hospital with a designated fertility clinic supported by a consultant gynaecologist with a special interest in fertility, a fertility nurse specialist and a gynaecology ultrasound specialist.

All women with anovulatory PCOS who had LOD between September 1996 and May 2002 were identified from theatre records and their data were retrieved from their hospital notes.

This amounted to a study of 100 women. A diagnosis of PCOS was based on the following criteria:

1. Anovulatory infertility
2. Hyperandrogenism (clinical and/or biochemical)
3. Polycystic ovaries on ultrasound, with exclusion of other aetiologies

The presence of any two of the above was considered diagnostic for PCOS. The diagnostic criteria for PCOS in our study are in agreement with the revised 2003 Rotterdam ESHRE criteria [12].

Patients were selected for LOD if they were unresponsive to CC (defined as anovulation in response to 100 mg of CC) or failed to conceive despite successful ovulation, in the absence of other contributing factors to their subfertility.

Laparoscopic ovarian drilling was performed using a Valleylab Force 2 Electrosurgical Unit at a setting of 35 W; cutting blend 1. Six punctures were made in each ovary. The current was applied for 5 s per puncture, giving a total thermal energy of 150 J (30×5) per puncture. The surface of the ovary was intermittently cooled with Hartmann's solution. The same experienced consultant gynaecologist performed this procedure on all 100 women in the study.

Follow-up data for 12–24 months were available. Out of the 100 women in the study, 23 were excluded from the analysis. Fifteen women out of the 23 had to be excluded due to bilateral tubal obstruction or severe male factor infertility, the LOD having been performed only to facilitate in vitro fertilisation (IVF). The other 8 women were lost to follow-up immediately after the procedure.

Women with endometriosis not affecting the patency of their tubes were included in the study.

The data were computerised and analysed using Microsoft Excel. Analysis was performed on 77 women. The Chi-squared test for unrelated data was used for statistical analysis. A two-sided value of $p < 0.05$ was chosen as the level of significance.

Results

The characteristics of all 77 women included in the analysis are shown in Table 1.

During laparoscopy, 9 women were found to have endometriosis, which was treated with laser ablation. Three women were found to have endometriomata, which were excised laparoscopically. Another 11 women were found to have adhesions that were released at the

Table 1 Characteristics of women who had laparoscopic ovarian drilling (LOD). BMI body mass index, LH luteinising hormone, FSH follicle stimulating hormone, USS ultrasound scan, PCOS polycystic ovarian syndrome

Characteristics	Results
Age	27.98 [3.91] (20–35)
BMI	27.98 [5.9] (18.6–38)
Duration of infertility (months)	21.6 [19.2] (8–96)
LH:FSH ratio	2.34 [1.33] (0.3–7.7)
Plasma LH	11.81 [6.44] (1.7–25.9)
Infertility	
Primary	60 (77.9)
Secondary	17 (22)
USS characteristic of PCOS	75 (97.4)
Menstrual cycle pattern	
Oligomenorrhoea	89 (85.8)
Amenorrhoea	11 (14.2)

Values are given as n (%) and mean [SD] (range)

time of laparoscopy. There was one dermoid cyst that required laparotomy.

In our series, 98.7% ($n=76$) of the women had evidence of PCO on ultrasound. Also, 55.1% women had LH levels elevated to more than 10 IU/l. BMI of more than 29 was found in 41% of the women. They were all encouraged to lose weight and referred to the dietician for advice.

Following LOD, 25 women (32.46%) conceived spontaneously. A further 22 women (28.5%) conceived after medical stimulation of the ovaries with CC (16 women) or purified FSH (6 women). Six women in our study achieved 2 pregnancies. One woman had 3 pregnancies with 2 of them ending in miscarriage. The total pregnancy rate was 61%, with a cumulative pregnancy rate of 74% (57 pregnancies in 47 women). There were 8 spontaneous miscarriages (14%) out of the total 57 pregnancies achieved.

As shown in Table 2, we did not find any statistically significant difference between the characteristics of women who had LOD and conceived either spontaneously or after further induction of ovulation and those who failed to conceive when we looked at the age, BMI, duration of subfertility, serum LH levels and LH:FSH ratio.

Table 2 Characteristics of women who had LOD and conceived (group A) and women who failed to conceive (group B). NS not significant

Characteristics	Group A	Group B	p
Age	28.18 (20–35)	27.62 (21–35)	NS
BMI	28.5 (20–30)	27.42 (18.6–37.9)	NS
Duration of infertility	22.3 (20–38)	20.5 (6–60)	NS
Serum LH	11.86 (1.7–25.9)	11.74 (13–25.9)	NS
LH:FSH ratio	2.45 (0.3–7.7)	2.2 (0.5–4.6)	NS

Values are given as mean (range)

Discussion

Although this is a retrospective study originating from 1995, the criteria that were used by the fertility clinic of the Royal Berkshire Hospital for establishing the diagnosis of PCOS fulfil the ESHRE 2003 criteria [12].

We have used pregnancy rate as a measure of successful outcome as this is what matters to the couple. In particular, failure to achieve a pregnancy means that the next step in their treatment is IVF.

Our results are similar to those reported in the literature, which varied from 20 to 88%, with an average of 55% [13]. We had a total pregnancy rate of 61% with a cumulative rate of 74%. No multiple pregnancies, side effects or complications were reported in our study.

Looking at the characteristics of the women who conceived in response to LOD either spontaneously or after further induction of ovulation, we did not find their serum LH level, LH:FSH ratio, age, duration of subfertility or BMI to be different from those who failed to conceive, even after LOD. Hence, these factors are not predictors of treatment outcome. This is important information for the pre-operative counselling of the couple. These results correlate with previously published studies [3, 4].

Al-Ojman [3], in a large study, concluded that there is a positive correlation between the outcome of surgery and obesity. This challenges the hypothesis that LOD in obese women results in a poor response, whilst a high level of LH is associated with a better response [7, 14]. In a recent study that used a multivariable prediction model with prospective data collection, it was found that the LH:FSH ratio has the most predictive variable for ovarian response after LOD [15].

These differences may be explained by the difference in entry criteria used in the different studies. Also, varied diagnostic criteria for PCOS may have altered the results.

The prevalence of early pregnancy loss is increased in women with PCOS to as high as 44% [16], with the rate remaining high after medical induction of ovulation. In our study, the miscarriage rate was 14%, which is similar to the previously quoted figures. This is also comparable to the incidence of miscarriages in spontaneous pregnancies. It has been suggested that hypersecretion of LH results in reproductive dysfunction, which, in turn, results in the reduction in embryo survival [17]. The reduced miscarriage rate in the LOD-treated women may be explained by decreased LH levels after the procedure [13].

In conclusion, we believe that using the revised 2003 Rotterdam ESHRE criteria for the diagnosis of PCOS and using LOD as a treatment option for women who are resistant to CC might help to evaluate the different management protocols for PCOS and identify the factors that may influence the outcome of these treatments.

References

1. Kousta E, White DM, Franks S (1997) Modern use of clomiphene citrate in induction of ovulation. *Hum Reprod Update* 3:359–365
2. Farquhar C, Vandekerckhove P, Liford R (2000) Laparoscopic ‘drilling’ by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome. *Cochrane Database Syst Rev Issue 2:CD001122*
3. Al-Ojaimi EH (2004) Endocrine changes after laparoscopic ovarian drilling in clomiphene citrate-resistant women with polycystic ovary syndrome. *Saudi Med J* 25:1032–1039
4. Cleemann L, Lauszus FF, Trolle B (2004) Laparoscopic ovarian drilling as first line for treatment in infertile women with polycystic ovary syndrome. *Gynecol Endocrinol* 18:138–143
5. Muenstermann U, Kleinstein J (2000) Long-term GnRH analogue treatment is equivalent to laparoscopic laser diathermy in polycystic ovarian syndrome patients with severe ovarian dysfunction. *Hum Reprod* 15:2526–2530
6. Saleh AM, Khalil HS (2004) Review of nonsurgical and surgical treatment and the role of sensitizing agents in the management of infertile women with polycystic ovary syndrome. *Acta Obstet Gynecol Scand* 83:614–621
7. Li TC, Saravelos H, Chow MS, Chisabingo R, Cooke ID (1998) Factors affecting the outcome of laparoscopic ovarian drilling for polycystic ovarian syndrome in women with anovulatory infertility. *Br J Obstet Gynaecol* 105:338–344
8. Balen AH (2004) Ovulation induction. *Curr Obstet Gynaecol* 14:261–268
9. Bayram N, Van Wely M, Kaaijak EM, Bossuyt PM, Van der Veen F (2004) Using an electrocautery strategy or recombinant follicle stimulating hormone to induce ovulation in polycystic ovary syndrome: randomised controlled trial. *BMJ* 328:192–195
10. Amer SAK, Gopalan V, Li TC, Ledger WL, Cooke ID (2002) Long-term follow-up of patients with polycystic ovary syndrome after laparoscopic ovarian drilling: clinical outcome. *Hum Reprod* 17:2035–2042
11. Naether OG, Fischer R (1993) Adhesion formation after laparoscopic electrocoagulation of the ovarian surface in polycystic ovary patients. *Fertil Steril* 60:95–98
12. Rotterdam ESHRE/ASRM-sponsored PCOS Consensus Workshop Group (2003) Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Hum Reprod* 19:41–47
13. Donesky BW, Adashi EY (1995) Surgically induced ovulation in the polycystic ovary syndrome: wedge resection revisited in the age of laparoscopy. *Fertil Steril* 63:439–443
14. Amer SA, Li TC, Ledger WL (2004) Ovulation induction using laparoscopic ovarian drilling in women with polycystic ovarian syndrome: predictor of success. *Hum Reprod* 19:1719–1724
15. Van Wely M, Bayram N, Van der Veen F, Bossuyt PM (2005) Predictors for treatment failure after laparoscopic electrocautery of the ovaries in women with clomiphene citrate resistant polycystic ovary syndrome. *Hum Reprod* 20:900–905
16. Glueck CJ, Wang P, Fontaine RN (1999) Plasminogen activator inhibitor activity: independent risk factor for the high miscarriage rate during pregnancy in women with polycystic ovarian syndrome. *Metabolism* 48:1589–1595
17. Regan L, Owen EJ, Jacobs HS (1990) Hypersecretion of luteinising hormone, infertility and miscarriage. *Lancet* 336:1141–1144