L/S ovarian surgery in PCOS

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History

- Surgical approaches with PCOS date back to the 1930s, when bilateral ovarian wedge resection was found to result in restoration of regular menses and pregnancy.

History

• Bilateral ovarian wedge resection...
• Effective in producing ovulatory cycles in previously anovulatory women, but fell out of favor due to;
  – postoperative adhesion formation and,
  – the introduction of ovulation-inducing medications such as clomiphene citrate.
Then comes...

Ovarian Drilling...
Indication

• Clomiphene citrate resistance
• Patients undergoing laparoscopy for tubal patency
• Poor response to any ovulation inducing agents whether CC or Gonadotropins
Literature

The literature now contains reports of over 1000 women in whom partial ovarian resection or ablation was done via a laparoscopic approach in the hope of restoring some ovulatory function.
Success

• Pregnancy has occurred in approximately 55 percent of women undergoing this procedure, a figure that compares favorably with conception rates after three to six cycles of gonadotropin therapy.

• Randomized controlled trials suggest that ovarian diathermy (electrocautery), when compared to gonadotropin therapy, results in similar success rates, but lower multiple gestation rates.

Farquhar C, Lilford RJ, Marjoribanks J, Vandekerckhove P. Laparoscopic "drilling" by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome. Cochrane Database Syst Rev. 2005
Endocrinology after L/S

- After LOD, serum androstenedione, LH, testosterone and inhibin

- Serum FSH

- The net effect is normalization of some of the endocrine abnormalities associated with the polycystic ovary syndrome.

Mechanism

• The mechanism by which controlled partial destruction of the ovary results in follicle development and ovulation is unknown.

• While the hormonal changes probably contribute, it is not clear that they are the sole mechanism for restoration of ovulation.
Mechanism

• The wedge resection technique mainly destroys stromal (androgen-producing) elements; however, other procedures, such as ultrasound-guided transvaginal aspiration of the follicles, appear to produce similar results while having a minimal effect on the stroma.

Mechanism

• The most plausible mechanism involves a sudden drop in intraovarian androgens (and perhaps estrogens) that results in increased FSH secretion and an intrafollicular environment...
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Number of Patients</th>
<th>LH</th>
<th>FSH</th>
<th>Testosterone</th>
<th>Fasting Insulin</th>
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<td>58</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>ND</td>
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</table>

ND, no data; NS, no significant changes observed; ↓, significant decrease observed; ↑, significant increase observed.
Techniques

• Wedge resection via L/T
• L/S techniques
  – Multiple punch biopsies, Electrocautery (diathermy), Laser
• Transvaginal
  – Fertiloscopic approach, US guided laser approach

Donesky BW et al. Surgically induced ovulation in the polycystic ovary syndrome: wedge resection revisited in the age of laparoscopy. Fertil Steril. 1995
Techniques

• Each method shares a common goal of creating focal areas of damage in the ovarian cortex and stroma.

• The most extensively studied procedure has been that of electrocautery, which is used to create thermal damage and necrosis of the "excess" ovarian stroma.
Unipolar Needle Electrode

• Most popular method
• Most of the authors prefer the unipolar needle electrode because of the easy set-up and the wide availability of the equipment needed.
Unipolar Needle Electrode

- Unipolar needle electrode that is insulated 1-3 mm in diameter and 4 mm in depth
- 4 – 6 punctures of each ovary can produce substantial thermal damage to the stromal compartment
- Punctures from the end of the ovary nearest the uterus and from the side of the ovary. (...keeps the surface damage away from the fallopian tube as much as possible.)
Laser

• With the development of laparoscopic laser delivery systems, it was inevitable that this modality would also be applied.

• Similar to that of electrocautery, as the ovarian cortex over follicles is vaporized.

• Since lasers focus their energy more precisely than electrocautery, less peripheral thermal damage is inflicted → IN THEORY...

Laser

• Although the literature suggests that laser cautery is as effective as electrocautery, the laser is becoming less popular in PCOS.

• The reasons seem to center on concerns about the amount of ovarian surface damage and the potential for adhesion formation after laser treatment.
Electrocautery is superior WHY?

• Less cost, easy application
• Achieve higher ovulation and pregnancy rates
• Less surface injury than CO2 laser therefore less adhesions (Keckstein et al, 1989)
• Effects of electrocautery may last longer than effect of laser (Shaleh and Khalil, 2004)
Cumulative rates 12 months after LOD

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Spontaneous ovulation</th>
<th>Pregnancy rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrocoagulation</td>
<td>82.7 %</td>
<td>64.8 %</td>
</tr>
<tr>
<td>Laser vaporization</td>
<td>77.5 %</td>
<td>54.5 %</td>
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</table>

Shaleh and Khalil, 2004
Transvaginal Hydrolaparoscopy

• To perform ovarian drilling resulting in an even less invasive procedure...

• Of 15 women who underwent a second-look laparoscopy, 11 women were found to be free of adhesions.


Schematic diagram of fertiloscopy. The hysteroscope is placed through the transvaginal introducer and the pelvis is filled with fluid. The intrauterine catheter is for chromotubation.

Abstract

**Objective and design** This was a prospective controlled study to compare the beneficial effects of office microlaparoscopic ovarian drilling (OMLOD) under augmented local anesthesia, as a new modality treatment option, compared to those following ovarian drilling with the conventional traditional 10-mm laparoscope (laparoscopic ovarian drilling, LOD) under general anesthesia.

**Methods** The study included 60 anovulatory women with polycystic ovary syndrome (PCOS) who underwent OMLOD (study group) and 60 anovulatory PCOS women, in whom conventional LOD using 10-mm laparoscope under general anesthesia was performed (comparison group). Transvaginal ultrasound scan and blood sampling to measure the serum concentrations of LH, FSH, testosterone and androstenedione were performed before and after the procedure. Intraoperative and postoperative pain scores in candidate women were evaluated during the office microlaparoscopic procedure, in addition to the number of candidates who needed extra analgesia.

**Results** Women undergoing OMLOD showed good intraoperative and postoperative pain scores. The number of patients discharged within 2 h after the office procedure was significantly higher, without the need for postoperative analgesia in most patients. The LH:FSH ratio, mean serum concentrations of LH and testosterone and free androgen index decreased significantly after both OMLOD and LOD.

The mean ovarian volume decreased significantly ($P < 0.05$) 1 year after both OMLOD and LOD. There were no significant differences in those results after both procedures.

**Conclusion** Intra- and postoperatively augmented local anesthesia allows outpatient bilateral ovarian drilling by microlaparoscopy without general anesthesia. The high pregnancy rate, the simplicity of the method and the faster discharge time offer a new option for patients with PCOS who are resistant to clomiphene citrate. Moreover, ovarian drilling could be performed simultaneously during the routine diagnostic microlaparoscopy and integrated into the fertility workup of these patients.

Keywords: Endocrine effects · Office microlaparoscopic ovarian drilling · Long-term follow-up · Polycystic ovary syndrome · Polycystic ovaries

Office microlaparoscopic ovarian drilling (OMLOD) versus conventional laparoscopic ovarian drilling (LOD) for women with polycystic ovary syndrome

Imaduldin M. Salah
The microlaparoscopic instruments, and the setup for the office microlaparoscopy under augmented local anesthesia

The microlaparoscopic image of the pelvis before the ovarian drilling procedure, which is apparently similar to the 10-mm laparoscopic view; b the microlaparoscopic ovarian drilling and c the microlaparoscopic image after the microlaparoscopic ovarian drilling (OMLOD) procedure
Puncture? Energy?

• The number of punctures is only one of several variables which determines the amount of electrical energy delivered to the ovary...

• The amount of energy (J) used is: power (w) x duration (sec) x No. of punctures

• Dabirashrafi (1989) → 400w x 5 sec x 8 hole → 16,000O joule → OVARIAN ATROPHY...
The Sheffield Prospective Dose Finding Study

- 30 women divided into ten groups, each group with 3 women
- Dose in each group to be determined by the response of previous group
- Energy utilized for each puncture is standardized (150 J/puncture)

Amer, Li & Cooke, 2003
Conception rates after LOD
Sheffield Prospective Study

Pregnancy

0% 10% 20% 30% 40% 50% 60% 70% 80%

17%
56%
67%

600 j/ovary
Energy...

- Rockett of London diathermy needle
- Needle 8 mm long, 2 mm diameter
- Monopolar coagulation
  - 30 W
  - 4 holes
  - 5 seconds
  - 600 joule
Patient selection

• Retrospective; 200 patients with anovulatory infertility due to PCOS who underwent LOD between 1990 and 2002; Multiple logistic regression analysis ...

LH and Pregnancy rates in LOD

Pregnancy rate

LH (IU/L)
Free Androgen Index and the outcome of LOD

P < 0.01

P < 0.001
BMI and the outcome of LOD

- **<29**
  - Ovulation
  - Pregnancy

- **29-34**
  - Ovulation
  - Pregnancy

- **>34**
  - Ovulation
  - Pregnancy

- \( P < 0.01 \)
- \( P < 0.05 \)
With proper patient selection, the pregnancy rate after LOD is up to 80%.

Is repeat surgery effective?

Prev responders: 83%
Prev non-responders: 25%
Overall: 60%

Ovulation rates

Is repeat surgery effective?

CONCLUSION(S):
Repeat LOD is highly effective in women who previously responded to the first procedure.

## New trends

<table>
<thead>
<tr>
<th>LOD (n=29)</th>
<th>AMH &lt; 7.7</th>
<th>AMH ≥ 7.7</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovulation</td>
<td>95%</td>
<td>60%</td>
<td>0.036</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>63%</td>
<td>30%</td>
<td>0.095</td>
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</table>

Amer, Human Reproduction 2009
First line treatment

<table>
<thead>
<tr>
<th></th>
<th>LOD group (n=33)</th>
<th>Clomiphene group (n=32)</th>
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<tbody>
<tr>
<td>Ovulation</td>
<td>64%</td>
<td>76%</td>
</tr>
<tr>
<td>Conception after first treatment</td>
<td>27%</td>
<td>44%</td>
</tr>
<tr>
<td>Conception after second treatment (at 12m)</td>
<td>53%</td>
<td>63%</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Live Birth</td>
<td>46%</td>
<td>56%</td>
</tr>
</tbody>
</table>

Amer, Human Reproduction 2009
Complications

• Most women who had the procedure were found to have adhesions when a second-look laparoscopy was performed later, although the adhesions did not appear to cause problems relating to conception.


Complications

- There is one report of unilateral ovarian atrophy after laparoscopic ovarian electrocautery.

Complications

- An epidemiologic study demonstrated earlier menopause in women who underwent ovarian reductive surgery of any type.
- The women having the earliest menopause (nearly 10 years earlier than in normal women) were those who had undergone bilateral ovarian wedge resection before age 30.

But...

- The long-term follow-up study by Dahlgren et al. showed that menopause occurred later in PCOS women who underwent ovarian wedge resection compared with non-PCOS women.

Complications

• One study reported a decrease in anti-müllerian hormone (AMH) in women who underwent ovarian drilling. While potentially providing a way to assess adequacy of treatment, this finding underscores the fact that these are destructive procedures that result in the loss of oocytes.

Elmashad AI. Impact of laparoscopic ovarian drilling on anti-Müllerian hormone levels and ovarian stromal blood flow using three-dimensional power Doppler in women with anovulatory polycystic ovary syndrome. Fertil Steril 2011; 95:2342
1. LOS can achieve unifollicular ovulation with no risk of OHSS or high-order multiples.

2. Intensive monitoring of follicular development is not required after LOS.

3. LOS is an alternative to gonadotrophin therapy for CC-resistant anovulatory PCOS.

4. The treatment is best suited to those for whom frequent ultrasound monitoring is impractical.

5. LOS is a single treatment using existing equipment.

6. The risks of surgery are minimal and include the risk of laparoscopy, adhesion formation and destruction of normal ovarian tissue. Minimal damage should be caused to the ovaries. Irrigation with an adhesion barrier may be useful, but there is no evidence of efficacy from prospective studies. Surgery should be performed by appropriately trained personnel.

7. LOS should not be offered for non-fertility indications
Thank you...

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### Comparison between laparoscopic ovulation induction and gonadotropin ovulation induction

<table>
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<tr>
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<th>Laparoscopy</th>
<th>Gonadotropin Administration</th>
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<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td>- Pregnancy rates comparable to gonadotropins</td>
<td>- High probability of successful ovulation induction</td>
</tr>
<tr>
<td></td>
<td>- No additional procedures required</td>
<td>- Conception rates comparable to laparoscopy</td>
</tr>
<tr>
<td></td>
<td>- Minimal monitoring required</td>
<td>- No known risk of adhesive damage</td>
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<tr>
<td></td>
<td>- One treatment produces multiple ovulatory cycles</td>
<td></td>
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<tr>
<td></td>
<td>- Usually produces monovulatory cycles</td>
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<tr>
<td></td>
<td>- No increased risk of ovarian hyperstimulation</td>
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<td></td>
<td>- No expensive medications required</td>
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<tr>
<td><strong>Disadvantages</strong></td>
<td>- Initial surgery not entirely risk-free</td>
<td>- High cost</td>
</tr>
<tr>
<td></td>
<td>- Adhesions</td>
<td>- Intensive monitoring required</td>
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<tr>
<td></td>
<td>- Ovarian atrophy</td>
<td>- One ovulatory event per cycle</td>
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<td></td>
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<td>- Increased risk of multiple gestations</td>
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<tr>
<td></td>
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<td>- Increased risk of ovarian hyperstimulation</td>
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</table>
LOD vs Medical Treatment

• systematic review of 25 randomized trials evaluating laparoscopic ovarian drilling (with or without medical induction of ovulation) in 2,481 women with subfertility and clomiphene-resistant polycystic ovary syndrome (PCOS)

Laparoscopic drilling by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome (Review)

Farquhar C, Brown J, Marjoribanks J
LOD vs Medical Treatment

– medical treatments in control groups included
  • gonadotropins (8 trials)
  • metformin (2 trials)
  • clomiphene citrate (2 trials)
  • clomiphene citrate plus metformin (3 trials)
  • clomiphene citrate plus tamoxifen (2 trials)
  • clomiphene citrate plus rosiglitazone (1 trial)
  • aromatase inhibitors (2 trials)
LOD vs Medical Treatment

– comparing laparoscopic ovarian drilling to medical treatment

• no significant differences in
  – live birth rate (odds ratio 0.86, 95% CI 0.74-1, p = 0.056) in analysis of 8 trials with 1,034 patients
  – miscarriage rate (odds ratio 1.1, 95% CI 0.74-1.61) in analysis of 15 trials with 1,592 women
  – pregnancy rate (defined as gestational sac seen on ultrasound) per woman randomized (odds ratio 0.94, 95% CI 0.78-1.14) in analysis of 18 trials with 1,930 women

• drilling associated with lower multiple pregnancy rate per ongoing pregnancy (odds ratio 0.21, 95% CI 0.08-0.58) in analysis of 12 trials with 1,129 patients
Life style modification

First line treatment CC

CC fail to result pregnancy

Second line

Gonadotrophins

Multipl pregnancy intense monitoring

CC and Gonadotrophin cumulative
Live birth rate: 72%

Laparoscopic ovarian surgery

LOD alone 50% pregnancy

If failed-----ovulation induction again

If failed-----Third line treatment IVF