

Laparoscopic Ovarian Drilling versus Medical Treatment in Management of Clomiphene Citrate Polycystic Ovarian Syndrome

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Abstract

Polycystic ovarian syndrome (PCOS) has remained an enigma since it was first described as a clinical entity by Stein and Leventhal in 1935. The treatment of this condition has evolved through ovarian wedge resection at laparotomy, induction of ovulation with clomiphene citrate (CC) to laparoscopic ovarian drilling or other chemotherapeutic agents when CC treatment has failed. Evidence shows that laparoscopic ovarian drilling (LOD) reverses all the abnormalities associated with PCOS especially in those with CC treatment failure. The same could be said for these chemotherapeutic agents (metformin, gonadotropin-releasing hormone analogues (GnRHa), or follicle stimulating hormone (FSH) alone or in combination with CC). The seeming comparative advantage of LOD is in its one off therapy, sustained reversal of the pathology, high ovulation and pregnancy rates, cost safety reduced risk of multiple pregnancy and acceptability by patients.

Keywords: Laparoscopic drilling, laser, diathermy, polycystic ovarian syndrome, polycystic ovaries hyperandrogenemia, insulin resistance,

AIMS/OBJECTIVES

The aim of this review is to highlight the efficacy and safety of laparoscopic ovarian drilling in the management of clomiphene resistant polycystic ovarian syndrome. The effectiveness, safety and controversies of laparoscopic ovarian drilling is compared to the different chemotherapeutic agents used in treatments for clomiphene resistant PCOS.

MATERIALS AND METHODS

A literature search was conducted with Google search engine, Highwire press and PubMed. Laparoscopic ovarian drilling, polycystic ovarian syndrome, clomiphene citrate, metformin, GnRHa with polycystic ovaries were entered as search words.

Articles were selected for review from all the citations produced from the search. These were selected based on predetermined criteria as stated below.

1. Year of publication not exceeding 15 years ago.
2. Randomized controlled trials and systematic reviews were favored and other studies of high power addressing the criteria for comparison.

3. Method of patient selection to involve only those with polycystic ovarian syndrome (WHO Type II).
4. Laparoscopic ovarian drilling done for clomiphene resistant polycystic ovaries was compared with any further medical treatment with metformin, CC, FSH or GnRHa.

These articles were reviewed for the following considerations.

1. Technique, operative care and time for laparoscopic ovarian drilling.
2. Operative and postoperative complication/morbidity.
3. Length of hospital stay and time to normal activity.
4. Safety cost and effectiveness.
5. Quality-of-life analysis.

DIAGNOSIS OF PCOS/PATIENT SELECTION FOR LOD

The diagnosis of polycystic ovarian syndrome is by clinical and ancillary investigations revealing the presence of 1) Irregular menstrual cycles and anovulation with onset at puberty. (Note that 25 percent of women who have PCOS have regular menstrual cycles), elevated total and free

testosterone levels (hyperandrogenemia) and the presence of polycystic ovaries as recognized at the ESHRE/ASRM consensus meeting in Rotterdam in 2003. A refined definition of the PCOS also was agreed and this encompasses a description of the morphology of the polycystic ovary. It was agreed that the criteria fulfilling sufficient specificity and sensitivity to define the polycystic ovary (PCO) are the presence of 12 or more follicles measuring 2 to 9 mm in diameter and increased ovarian volume ($>10 \text{ cm}^3$). If there is a follicle greater than 10 mm in diameter, the scan should be repeated at a time of ovarian quiescence to calculate volume and area.^{1,2} Patients presenting with this description are termed to be clomiphene citrate resistant if they fail to ovulate after 3 to 4 cycles of treatment with CC. Some of these patients are offered LOD while others are offered other chemotherapeutic agents such as gonadotrophins, metformin, GnRHa to overcome the problem of anovulation and infertility in the CC resistant women.²⁻⁵

EVOLUTION OF LOD

Ovarian wedge resection was the mode of treatment for women with PCOS prior to the '70s when CC was introduced as an ovulation induction agent. Physicians thought that it was the increased ovarian size that resulted in the anovulation and infertility and so wedge resection was considered appropriate. This was a major breakthrough as it resulted in about 80% ovulation and 50% conception rates. However, many of the women later reverted back to the anovulatory state and the development of postoperative pelvic adhesions was thought to be the cause of the low pregnancy rates.² With the advent of CC, which had the advantage of cost and low monitoring, and high ovulation and pregnancy rates, a group of women was identified that failed to ovulate with CC. Laparoscopic ovarian drilling was introduced in the '90s as another surgical method of ovulation induction with the aim of minimising the pelvic adhesions caused by open surgery. This has met with certain degree of success with respect to restoring ovulation and fertility with reduction in chances of pelvic adhesion.

OPERATIVE CARE AND TECHNIQUE OF THE LOD

Preoperative Preparation

Patient is screened for medical diseases through the history, physical examinations and ancillary investigations, and usually for infertility if present. Patient will undergo an overnight fast prior to surgery. An indwelling urinary catheter

is retained in the bladder in the theater and anesthesia administered.

ANESTHESIA

An intravenous access is secured with maintenance of water and electrolyte balance.

General anesthesia with endotracheal intubation and close monitoring is recommended.

Patient Position

Patient should be in steep Trendelenburg's and Lithotomy position.⁵

Position of Surgical Team

The surgeon stands to the left of the patient with camera man on his right. Monitor should be placed opposite the surgeon to maintain co-axial alignment. One assistant should stand between the patient's legs to do uterine manipulation if required and the instrument trolley should be towards the left leg of the patient with a scrubbed assistant.

Port Positions and Ovarian Drilling

The patient is cleaned, painted with antiseptic lotion and draped. The light cable, insufflation tube, electrosurgical cautery wires, suction irrigation tube and Veress needle should be checked. Focusing and white balancing of the telescope is done, then pneumoperitoneum is created by Veress needle using the inferior crease of the umbilicus. Once pneumoperitoneum has been created then 10 mm or 5 mm port is introduced into the abdominal cavity through the inferior crease of the umbilicus for a 5 mm or 10 mm telescope. Another 5 mm port is introduced into the abdominal cavity under vision through the left iliac fossae and a diagnostic laparoscopy with chromotubation for tubal patency done. Thereafter, an atraumatic grasper is used to hold the utero-ovarian ligament to stabilize the ovary to perform the ovarian drilling.^{2,4} Laparoscopic treatment options include multiple ovarian punch biopsy, ovarian electrocauterization and laser vaporization or photo-coagulation, harmonic scapel.^{5,6} About 4 to 5 holes drilled into each ovary is adequate^{2-4,7,9} and are relatively easy to perform with the procedure lasting about 30 minutes in experienced hands. These options of drilling into the ovary have similar success rate in inducing ovulation and achieving pregnancy.⁸

Operative and Postoperative Complications

The procedure is devoid of major complications, and yield satisfactory ovulation and conception rates. However, adhesion formation is a potential complication following such procedures.^{4,5} Other potential complications include premature ovarian failure in the future.³ The procedure usually done as a day case and patient need not be admitted. Postoperative pain is relieved with mild analgesics such as paracetamol for 2 to 3 days. Other potential risks is that of anesthesia which is beyond the scope of this review.

Safety and Cost-effectiveness

The procedure does not add to more cost or risk from anesthesia for a patient having diagnostic laparoscopy for evaluation of infertility. Successful pregnancy from treatment with LOD will of course treat the patients infertility fulfilling the desire of the patient. LOD is more effective than or equivalent to metformin, GnRHa, or FSH in resolving anovulation and pregnancy.^{3,9-11} Systematic review has shown that there is no difference in ongoing pregnancy, births and miscarriages between LOD and FSH but LOD has reduced risk of multiple pregnancy.¹² FSH and to lower extent CC have the added risk of causing ovarian hyperstimulation syndrome (OHSS),⁴ which is a potentially fatal condition. Furthermore, GnRHa is expensive and could cause distressing pseudomenopausal symptoms and which may require add back hormone therapy for the treatment to continue.⁴ The cumulative cost of treatment with FSH over LOD was found to be higher in a randomized trials and one systematic review.¹³⁻¹⁵ This may be similar with other chemotherapeutic agents that have higher risks of multiple gestation. In a study, the median time to pregnancy after LOD was 135 days and LOD alone resolves infertility within 4 to 6 months in 50 to 60% of couples. The researchers were advocating a strategy of diagnostic laparoscopy and LOD as the first line of treatment of infertility in women with PCOS as this will shorten the time to pregnancy for many women, reduce the need for medical ovulation induction and enable diagnosis of those women with anatomic infertility, who can achieve pregnancy only by *in vitro* fertilization treatment.¹⁶

There is however, a risk of periovarian adhesions and premature ovarian failure in the future. Studies to determine ovarian reserve and possibility of future premature ovarian failure are few and equivocal. There were statistically significant differences between Day 3 FSH, inhibin B levels, ovarian volume and antral follicle count before and after LOD in some of the reports. Although, the after LOD values

were found to be lower than the before LOD values by means of ovarian reserve markers, the after values stayed higher than normal when compared with normal women without PCOS.^{17,18} Even though the fear for ovarian reserve and premature ovarian failure is not unfounded with LOD, hormone replacement therapy could be used if need be. Some studies have tried to identify makers for positive response to LOD to include high levels of Luteinizing hormones and androstendione, short period of infertility (< 3 years) and absence of pre-existing tubal disease and advocate their use to identify patients who will respond well to LOD.^{19,20}

Quality-of-life Analysis

LOD promotes a better quality-of-life when used in women especially amongst those who have not conceived following treatment. A study on women's health-related quality-of-life (HRQoL) on 168 CC-resistant women with PCOS that were randomly assigned to receive either laparoscopic electrocautery of the ovaries followed by CC or recombinant FSH (rFSH) if anovulation persisted. Overall, HRQoL was not affected in both groups. In women still under treatment, rFSH was slightly more burdensome for women's HRQoL than electrocautery.²¹

Future prospects of LOD:

With increasing evidence that LOD is more effective with less cost, and as techniques to reduce periovarian adhesions improves, more practitioners will begin to consider it ahead of chemotherapeutic agents in treatment of CC-resistant PCOS.

CONCLUSION

LOD has obvious comparative advantages to competitive chemotherapeutic agents. Reduction in overall cost of treatment and risk of multiple gestation implies that it may be the treatment of choice in women with CC-resistant PCOS.

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