Ovarian Drilling in Polycystic Ovary Syndrome Patients

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Polycystic ovary syndrome (PCOS) is the leading cause of anovulatory infertility. Many pharmacological strategies have been applied for the induction of ovulation with a non-negligible rate of severe complications such as ovarian hyperstimulation syndrome and multiple pregnancies. Ovarian drilling (OD) is adopted as a second-line treatment, to be performed in case of medical therapy. Laparoscopic ovarian drilling (LOD), the contemporary version of ovarian wedge resection, is considered effective for gonadotropins in terms of live birth rates, but without the risks of iatrogenic complications in gonadotropin therapy. Its endocrinal effects are longer lasting and, after the accomplishment of this procedure, ovarian responsiveness to successive ovulation induction agents is enhanced. Traditional LOD, however, is burdened by the potential risks of iatrogenic adhesions and decreased ovarian reserve and, therefore, should only be considered in selected cases. To overcome these limits, novel tailored and mini-invasive approaches, which are still waiting for wide acceptance, have been introduced.

Keywords: polycystic ovary syndrome ; infertility ; ovarian drilling ; laparoscopy

1. Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrinopathy, characterized by oligoanovulation, hyperandrogenism, and an abnormal ovarian morphology characterized by multiple small subcapsular follicular ‘cysts’ [1][2].

PCOS is the leading cause of anovulatory infertility, accounting for nearly 80% of all cases [3]. Many therapeutic strategies have been applied for inducing ovulation in these patients: clomiphene citrate (CC) is considered a convenient and economic choice; however, 15% to 40% of patients are CC-resistant and deserve to be treated with gonadotropins or other medical ovulation-induction agents. These medications are not always successful, can be time-consuming, and can cause adverse events such as multiple pregnancies or require cycle cancellation due to an excessive response. Ovarian drilling (OD) is a second-line treatment to be considered in case of medical therapy failure. OD results in an overall spontaneous ovulation rate of 30–90% and final pregnancy rates of 13–88% [4]. Over the years, different OD techniques have been described in the literature. Most of them are intended to overcome some negative aspects of the traditional laparoscopic approach such as the risk of adhesion development, ovarian reserve damage, and abdominal wall trauma while maintaining comparable reproductive outcomes.

2. Laparoscopic Ovarian Drilling

In 1935, Stein and Leventhal reported the first successful treatment of infertile PCOS women through laparotomic “wedge resection” procedure [5]. Regardless of these promising results, the surgical approach was outdone by pharmacological treatment due to the high risk of pelvic adhesions following surgery. The surgical treatment of CC-resistant PCOS cases improved remarkably with the introduction of a minimally invasive approach: laparoscopic ovarian drilling (LOD) [6]. The exact mechanism by which small perforations using heat or a laser result in follicular growth and ovulation is yet to be elucidated and it is not known whether a prevalent action is exerted through a direct effect on the ovary or through a systemic endocrine mechanism. The most plausible mechanism is that the thermal destruction of ovarian follicles and a part of the ovarian androgen-producing stroma results in the reduction in local and serum androgens, re-establishing an intrafollicular environment more convenient for normal follicular maturation and ovulation and a secondary rise in follicle-stimulating hormone (FSH) levels. In addition, the release of a cascade of local growth factors such as insulin-like growth factors interacting with FSH, following a surgery-mediated increase in ovarian blood in response to thermal injury, has been suggested to allow follicular growth and subsequent ovulation [7]. Further possible mechanisms are the decrease in anti-Müllerian hormone (AMH) concentrations and the production of “holes” in the very thick cortical wall of the polycystic ovary [8]. The efficacy of ovarian drilling is widely variable in the literature: in a comprehensive review, ovarian drilling is deemed to restore fertility in 20–64% of women with PCOS previously suffering from anovulatory infertility who did not respond to CC treatment; 70% of pregnancies occurred in the first 6 postoperative months [9]. The surgical approach has some advantages in comparison to medical treatment [10][11][12][13]: no significant differences were found with respect to live birth rate and miscarriage between LOD and gonadotropins or other medical treatment in women resistant to CC, with the advantage of spontaneous mono-ovulation without the need for intensive monitoring in order to minimize the risks of multiple pregnancies or OHSS. For a similar success rate, LOD might be indicated as a second-line therapy instead of gonadotrophins to avoid gonadotropin-related adverse events (**Table 1**).

Table 1. Ovarian drilling: key factors to success.

• Patient should be carefully selected considering that obesity (BMI > 25), low basal luteinizing hormone (LH) (<10 IU/L), duration of infertility > 3 years, marked biochemical hyperandrogenism (free androgen index—FAI > 15) and high basal anti-müllerian hormone AMH (>7.7 ng/mL) are predictors of poor response.
2. The most accredited strategy consists of performing four punctures bilaterally, for a depth of 3–4 m, each for 4 s at 40 W (rule of 4) delivering 640 J of energy per ovary.
3. Mini laparoscopy with a 5.0 mm laparoscope and ancillary ports of 3 mm under regional anesthesia could be employed to ensure a faster recovery and better cosmetic results.
4. Before the application of energy, the ovary should be carefully lifted away from the intestine and ureters.
5. Peritoneal cavity and ovaries should be cooled using up to 1000 mL of isotonic solution to heat lesions and reduce the risk of post-operative adhesion formation.

Although no differences in pregnancy rate were reported even when LOD was compared to CC treatment as first-line therapy [14], there is insufficient evidence to support the use of LOD as first-line therapy except if laparoscopy is indicated for another reason (e.g., a diagnostic evaluation for tubal patency). Beyond the reduced risk of OHSS and multiple pregnancies, further advantages of LOD over medical treatment should be considered:

(a) Even if the effect of ovarian diathermy is not permanent and should, therefore, be reserved for infertile women, the positive reproductive outcome seems to last for several years in many women with the advantage of repeated spontaneous ovulation and further pregnancies as opposed to multiple rounds of ovulation induction [15].

(b) The increased responsiveness of the ovary to CC or gonadotropin medical therapy after LOD failure can be of invaluable help before proceeding to assisted reproductive therapy [16], mainly in vitro fertilization (IVF), which is considered an effective treatment option in anovulatory PCOS patients who do not become pregnant with ovarian drilling [17]. The stimulation in PCOS women is typically more difficult than healthy women and often experience a higher cycle cancellation rate when compared with normo-responders. The incidence of OHSS has been reported to be statistically significantly lower among patients with antecedent surgical treatment [18].

(c) LOD is considerably less expensive than ovulation induction with gonadotropins: a single treatment results in several mono-ovulatory cycles, whereas one course of gonadotropin therapy yields a single ovulatory cycle with an inherent cost for intensive monitoring. The higher incidence of multiple pregnancies incurs extra costs in those who conceive with gonadotrophins [19][20].

Finally, the aforementioned lower cycle cancellation rates in patients later submitted to IVF as well as the reduced incidence of OHSS contribute to lessening indirect costs.

3. Alternative Options to Traditional Surgical Ovarian Drilling

Unilateral ovarian drilling (ULOD) has been proposed as a modification of the standard LOD methodology with encouraging results [21]. ULOD induces activity in both ovaries and minimizes procedure time; the lack of significant differences in terms of clinical and biochemical response, ovulation rate, and pregnancy rate if compared with conventional bilateral LOD (BLOD) let us consider this technique suitable for CC-resistant PCOS [22][23][24]. At the moment, due to the paucity of available studies, it is uncertain if the equivalent reproductive outcome is associated with a lower risk of post-operative adhesions and ovarian reserve damage [25] and, therefore, more studies are warranted before this technique overtakes the traditional one. However, in case of ULOD, the right ovary should be the selected site because the left ovary seems more prone to the development of post-LOD adhesion if compared with the right one [26]. An interesting alternative that was recently introduced [27] involves the adjustment of energy applied according to the preoperative ovarian volume following the formula described by Sunj et al. [28]. The thermally adjusted ULOD, compared to the fixed-dose BLOD, has been tested only in a single RCT: dose-adjusted ULOD applied to the larger ovary has comparable ovulation and pregnancy rates to fixed-dose BLOD at 3-month follow-up periods, with a decrease in its effectiveness after 6 months [25]. As a consequence, it is still doubtful if the adjusted diathermy is able to ameliorate androgen control and enhance follicular growth, resulting in better reproductive outcomes compared with the fixed dose [29].

The mini-invasive theory has been largely applied to the ovarian drilling procedure. Over the years, laparoscopic surgical procedures have shown refinements in an attempt to reduce abdominal wall trauma, postoperative pain, and hernia formation and to improve cosmesis by decreasing the number of ports or reducing the port size with a shift from larger (10 mm) to a smaller endoscope; additional goals are the possibility of performing ovarian drilling as an outpatient procedure without the need for general anesthesia with comparable results to the more invasive procedure [30].

The feasibility and efficacy of mini-laparoscopy with a 5.0 mm laparoscope and ancillary ports of 3 mm under local anesthesia and conscious sedation have been successfully reported [31]. Beneficial effects in terms of pregnancy rate and faster discharge time (<2 h) render office micro-laparoscopic ovarian drilling (OMLOD) a new modality treatment option to be performed in an outpatient setting, under local anesthesia, with a very low pain score [32]. In conformity with the concept of mini-invasiveness, vaginal access has been proposed as a possible route for ovarian drilling.

Transvaginal hydrolaparoscopy (THL) under general anesthesia using bipolar electrosurgery was first reported by Fernandez et al. as a new approach for ovarian drilling in women with PCOS [33]. Further advances in THL have now allowed ovarian drilling to be performed by the transvaginal route in a day surgery regimen [34]. At present, THL could be considered as an outpatient tool useful to perform in the same time diagnostic infertility investigation and minimal operative procedures with a low complication and failure rate: in a retrospective cohort study of 2288 procedures, of which 374 were ovarian drilling, failure to access the pouch of Douglas occurred in 23 patients (1%). The complication rate was 0.74%, due to bowel perforations (n = 13) and bleeding (n = 4) requiring laparoscopy. All bowel perforations were treated conservatively, with 6 days of antibiotics, and no further complications occurred [35]. The efficacy of transvaginal hydrolaparoscopic ovarian drilling (THLOD) in terms of ovulation and pregnancy rates in PCOS patients was reported in several studies with comparable results to those of laparoscopy [34][36][37][38]. THLOD has a lower risk of adhesions than LOD (44). This finding was ascribed both to the instillation of saline solution into the peritoneal cavity rather than the irritative action of pneumoperitoneum and the shorter duration of the procedure [39].

Noteworthily, in a case–control study on 123 women with clomiphene-resistant PCOS, the same authors evaluated the effects of THLOD on ovarian volume, power Doppler flow indices and serum AMH levels. A significant reduction was achieved in these parameters as compared to the preoperative values [28]. In addition, THLOD, as already suggested by Ferraretti et al. [17], due to the recovery of ovary sensitivity to gonadotrophins after ovarian drilling, could be considered as an effective low invasive and low-cost method for improvement in ovarian response in PCOS poor responding patients admitted to IVF treatment [40].

In recent years, there have been reports on the role of ultrasound-guided transvaginal ovarian needle drilling (UTND) as a novel surgical method used to induce ovulation for women with clomiphene-resistant PCOS in an outpatient setting. The idea of needle drilling came to mind through the observation of successful spontaneous ovarian ovulatory performance in patients with PCOS after previous follicular aspiration for IVF treatment. A long sharp needle (35 cm—16 gauge) connected to a continuous manual vacuum pressure is used to puncture each ovary from different angles to aspirate all visible small follicles, under the guidance of the ultrasound [41]. Aspiration of follicular fluid through UTND reduces intraovarian and serum androgen and LH levels, rapidly restoring feedback to the hypothalamus and pituitary. It is likely that the removal of other factors, such as inhibin and other intraovarian substances, may also be involved. Preliminary data suggest that UTND is a safe technique and the outcome with regard to the ovulatory and pregnancy rate is comparable to the standard bipolar drilling without the potential risks of thermal damage [42]. With conscious sedation, this procedure is well-tolerated by the patient and can be repeated in case of failed ovulation or recurrent anovulatory states.

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