About IJMA [last updated October, 1st, 2021]

✓ International Journal of Medical Arts is the Official Journal of the Damietta Faculty of Medicine, Al-Azhar University, Egypt
✓ It is an International, Open Access, Double-blind, Peer-reviewed Journal
✓ Published four times a year
✓ The First Issue was published in July 2019
✓ Published under the following license: Creative Commons Attribution-ShareAlike 4.0 International Public License (CC BY-SA 4.0). It had updated from the Creative Commons license [CC BY] in volume 2, Issue 4, October 2020.
✓ The Egyptian Knowledge Bank hosts the web site of IJMA
✓ The Egyptian Knowledge Bank supports IJMA
✓ IJMA follows the regulations of the International Committee of Medical Journal Editors
✓ IJMA is indexed in the “Directory of Open Access Journals” [15 January 2021].
✓ IJMA is indexed in J-Gate [29-6-2021]
✓ IJMA is a member of the International Society of Managing and Technical Editors
✓ IJMA introduced to the search engine [BASE] through DOAJ
Effects of Different Methods of Laparoscopic Ovarian Drilling and its Outcome in Patients with Polycystic Ovary Syndrome

Mona Ebrahim Hamoda [1], Alaa Eldin Mahmoud Megahed [2], Abd Elraouf Mohammad Oun [2]

1 Department of Obstetrics and Gynecology, Meniat-El-Nasr Central Hospital, Ministry of Health, Egypt
2 Department of Obstetrics and Gynecology, Damietta Faculty of Medicine, Al-Azhar University, Egypt

Corresponding author: Mona Ebrahim Hamoda
Email: monaebrahemhamouda@gmail.com

Submission date: June 16, 2021; Acceptance date: November 6, 2021

ABSTRACT

Background: Polycystic ovary syndrome [PCOS] is an important and common etiology for anovulatory infertility. Clomiphene citrate [CC] is the first line of treatment. One fourth of females are resistant to CC. Laparoscopic ovarian drilling [LOD] has developed manage CC-resistant cases. However, no consensus was established on the ideal drilling method.

Aim of the work: This study aimed to evaluate the efficacy of different LOD methods for anovulatory infertility in CC-resistant PCOS patients.

Patients and Methods: The study participants [200] were assigned randomly to one of four equal groups. Group [I] treated by unilateral cutting LOD. Group [II] treated by unilateral electro-coagulative LOD. Group [III] treated by bilateral cutting LOD. Group [IV] treated by bilateral electro-coagulative LOD. All participants were submitted to history taking, clinical examination, laboratory investigation, antral follicular count [AFC], and transvaginal ultrasound. After LOD, follow up included regularity of menstrual cycle, ovulation, and hormonal assay [at six months after ovarian drilling]. Also, ovulation, pregnancy and miscarriage rates were documented.

Results: The study groups showed no significant difference regarding patient characteristics [e.g., body mass index, infertility duration and menstrual cycle history], and hormonal profile before and after LOD. The spontaneous ovulation rate was 40%, 42.0%, 46.0% and 40.0% in groups I, II, III and IV, respectively. The pregnancy rate was 32.0%, 38.0%, 44.0% and 42.0% in groups I, II, III and IV, respectively. In all groups, hormonal profile and AFC showed significant improvement after LOD compared with corresponding pre-LOD values. However, levels of FSH are significantly non-significant.

Conclusion: Different techniques of LOD are equally effective and safe [e.g., unilateral ovarian drilling is as effective and safe as bilateral drilling, regardless of the drilling method [coagulative or cutting] with comparable ovulation, pregnancy and miscarriage rates.

Keywords: Laparoscopic Ovarian Drilling; Polycystic Ovary; Syndrome; LH; FSH

This is an open-access article registered under the Creative Commons, ShareAlike 4.0 International license [CC BY-SA 4.0] [https://creativecommons.org/licenses/by-sa/4.0/legalcode.

INTRODUCTION

Female infertility is diagnosed if there is a failure of pregnancy after 12 months of regular unguarded intercourse \(^\text{[1]}\). The main causes include, but not limited to, gonadal dysgenesis, reduced ovarian reserve, polycystic ovarian syndrome \([\text{PCOS}]\), hyperprolactinemia and chronic anovulation. About 25-30\% of infertile females had ovulatory dysfunction. Thus, there is a rising demand for different treatment modalities for this condition \(^\text{[2]}\).

PCOS is considered the most common cause of anovulatory infertility \(^\text{[3]}\). Clomiphene citrate \([\text{CC}]\), a selective estrogen receptor modulator, is used for stimulation of ovulation. It is the first line of treatment for PCOS \(^\text{[4]}\). The ovulatory rate with CC is 70-80\%; however, the pregnancy rate is only 20-40\%. The cumulative conception rates with incremental doses are 50\%, 45\%, and 33\% with 50 mg, 100 mg, and 150 mg at 3 months and 62\%, 66\%, and 38\% at 6 months, respectively \(^\text{[5]}\). CC resistance is confirmed upon ovulation failure after reaching a maximum dose of 150 mg per day for five consecutive days starting on the menstrual cycle third day \(^\text{[6]}\).

Laparoscopic ovarian drilling \([\text{LOD}]\) has developed in 1980s and considered a safe and successful option for CC-resistant PCOS. Clinically, pregnancy and live birth rates are like gonadotropins. However, LOD is advantageous by mono-ovulation and reduction of the necessity of intensive monitoring. The risk of ovarian hyperstimulation syndrome \([\text{OHSS}]\) and multiple pregnancies are eliminated in LOD \(^\text{[7]}\).

Unilateral LOD \([\text{ULOD}]\) proposed to be a useful treatment for infertile PCOS females with CC-resistance. In LOD, surgeons can tailor the applied energy applied to the single ovary, based on its preoperative volume. The usual used energy is 60 j/cc \(^\text{[8]}\). Compared to bilateral LOD in CC-resistant 96 females, the unilateral LOD produced a significant higher ovulation rate in the first postoperative cycle \(73 \text{ vs. } 49\%; \text{ p} = 0.014\). At 6 months, the increase of cumulative ovulation rate in unilateral LOD was marginally significant than bilateral LOD \(82 \text{ vs. } 64\%; \text{ P} = 0.050\). This was achieved with lower energy used in unilateral group \(^\text{[9]}\).

Another trial reported significant reduction of serum anti-Mullerian hormone \([\text{AMH}]\) after LOD in both uni- and bilateral groups. The reduction was higher among the bilateral than unilateral group in the first follow-up month and continued till the end of follow up period at the end of the 6-month of follow-up \(^\text{[10]}\).

LOD has several advantages over gonadotrophin ovarian stimulation therapy. These included avoidance of OHSS, multiple pregnancies, cost reduction, and removed the need for intensive monitoring \(^\text{[11]}\). Furthermore, one LOD produced many physiological ovulatory cycles and repeated gestations without the need for second intervention or repeated courses of drug therapy. Moreover, there is an evidence of long-term benefits of LOD on the reproductive and endocrinological aspects \(^\text{[12]}\).

However, LOD is not without complications. A potential complication is the formation of iatrogenic adhesions due to the early contact between the drilled ovary and surrounding bowel or due to bleeding ovary after cauteterization \(^\text{[13]}\). Additionally, there is a high risk with laser, due to lesser thermal penetration \([2-4 \text{ mm}]\) or cone-shaped, lesions of laser drilling \(^\text{[14]}\).

AIM OF THE WORK

This study aimed to evaluate the efficacy of different methods of laparoscopic ovarian drilling in treatment of an ovulatory infertility in CC-resistant PCOS and its outcome.

PATIENTS AND METHODS

Study design

This is a prospective clinical study. Women suffering from polycystic ovary syndrome \([\text{PCOS}]\), with failed medical treatment, were participating in the study. They were selected from the outpatient clinic of Department of Obstetrics and Gynecology \([\text{Damietta Faculty of Medicine, Al-Azhar University hospital}]\). The study duration extended from the first of January 2019 to the last of October 2019.

Women who fulfilled the following inclusion criteria were included. 1) Infertile patients with age ranged from 20-35 years; 2) Body mass index \([\text{BMI}]\) between 20 and 30 Kg/m\(^2\); 3) Normal husband’s semen analysis; and 4) Patient suffered from PCOs only. On the opposite side, the exclusion criteria were: 1) Age below 20 or above 35 years; 2) Other causes of infertility, such as bilateral tubal block, moderate or severe endometriosis, and thyroid diseases.

The study participants were divided randomly, through closed envelope method, into four equal groups. Group \([\text{I}]\) included women treated by unilateral cutting laparoscopic ovarian drilling. The second group \([\text{II}]\) included women treated by unilateral electro-coagulative laparoscopic ovarian drilling. The third group \([\text{III}]\) incorporated women treated by bilateral cutting laparoscopic ovarian drilling. Finally, the fourth group \([\text{IV}]\) contained women treated by bilateral electro-coagulative laparoscopic ovarian drilling.

After selection, counseling, consent attainment, all participants were submitted to full history taking, complete physical examination, routine, and special laboratory investigation that included blood grouping, random blood
sugar, urine analysis, follicle stimulating hormone, luteinizing hormone, testosterone, anti-Mullerian hormone, and antral follicular count [AFC].

For laboratory investigations, the anti-Mullerian hormone [AMH] was measured by the method described by Kumar et al. [19], FSH determined by the technique described in Arslan et al. [18], LH determined according to Pauerstein et al. [17], and testosterone hormone [LH] measurements [19].

All women underwent ultrasound scan using a Voluson 730 Pro machine [GE, Milan, Italy] with a multifrequency volume endovaginal probe, to assess the bilateral AFC. Technically, once the ovary was recognized, we scrolled through the ovary in two planes [vertical and transverse] by the transducer. Each antral follicle was recognized and measured until the whole ovary had been analyzed. Antral follicle size was calculated as described by Deb et al. [19].

Laparoscopic ovarian drilling: Laparoscopy [Karl Storz gmbh of Tuttlingen, Germany] was performed under general anesthesia. We used a 10 mm laparoscope and a unipolar needle electrode with a coagulating current set at 40 W power. Pelvic organs were inspected, and injection of methylene-blue dye was completed for the tubal assessment. The ovary was lifted and sited away from any nearby structures. We performed surgery on the ovary in two planes [vertical and transverse] by the transducer. Each antral follicle was recognized and measured until the whole ovary had been analyzed. Antral follicle size was calculated as described by Deb et al. [19].

Follow up evaluation: regularity of menstrual cycle, ovulation, and hormonal assay were assessed at six months after ovarian drilling. Additionally, ovulation rate, pregnancy rate and miscarriage rate were documented.

Ethical considerations: Study protocol was submitted for approval by Institution Research Board [IRB] of Damietta Faculty of Medicine, Al-Azhar University [IRB approval number: 00012367-19-01-003]. Administration consent had been signed by the hospital authorities. We explained the study protocol for each participant and her consent for participation had been obtained. Confidentiality and privacy were respected in all levels of the study. The collected data used exclusively for the research purpose.

Statistical analysis: The collected data were organized, tabulated, and analysed using SPSS version 20 [IBM®SPSS® Inc, Chicago, USA]. Qualitative data expressed in frequency and percentage distributions. Quantitative, normally distributed data expressed in mean and standard deviation [SD]. For comparison between two groups, a simple Analysis of Variance [ANOVA] test was carried out and multiple comparisons between two groups was achieved using the "Post Hoc LSD". Qualitative data were compared by Chi square or Mann-Whitney test when appropriate. For all tests, p value <0.05 was considered significant.

RESULTS

Patient’s age, body mass index [BMI], infertility duration, age of menarche and cycle history were comparable between studied cases with no significant differences [Table 1].

Before laparoscopic ovarian drilling, the mean level of LH, FSH, testosterone, AMH and AFC showed non-significant difference between groups. A similar statistical situation was observed after ovarian drilling [Table 2].

In the present study, ovulation rate, pregnancy rate and miscarriage rate were comparable between study groups without statistically significant differences. Spontaneous ovulation rate was 40%, 42.0%, 46.0% and 40.0% in groups I, II, III and IV, respectively. Additionally, induced ovulation rate was 14%, 18%, 18% and 16.0% in groups I, II, III and IV, respectively. The pregnancy rate was 32.0%, 38.0%, 44.0% and 42.0% in groups I, II, III and IV, respectively. Miscarriage was reported in none, one, one and two patients in groups I, II, III and IV, respectively [Table 3].

In all groups, there were significant changes in the hormonal levels of LH, testosterone, AMH and antral follicle count after treatment when compared with their corresponding pre-intervention values. However, levels of FSH are significantly non-significant [Table 4].

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
<th>Test</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>28.48±2.23</td>
<td>27.52±2.5</td>
<td>28.52±3.32</td>
<td>28.24±2.44</td>
<td>0.76</td>
<td>0.52</td>
</tr>
<tr>
<td>BMI [Kg/m²]</td>
<td>27.55±1.45</td>
<td>27.86±1.47</td>
<td>27.94±1.33</td>
<td>27.64±1.43</td>
<td>0.42</td>
<td>0.74</td>
</tr>
<tr>
<td>Infertility duration [years]</td>
<td>3.16±1.14</td>
<td>3.72±1.36</td>
<td>2.96±1.14</td>
<td>3.32±1.25</td>
<td>0.46</td>
<td>0.71</td>
</tr>
<tr>
<td>Menarche [years]</td>
<td>12.32±1.46</td>
<td>12.28±1.45</td>
<td>11.88±1.48</td>
<td>12.16±1.48</td>
<td>1.72</td>
<td>0.17</td>
</tr>
<tr>
<td>Cycle history</td>
<td>Menorrhagia</td>
<td>10 [20.0%]</td>
<td>13 [26.0%]</td>
<td>12 [24.0%]</td>
<td>13 [26.0%]</td>
<td>1.24</td>
</tr>
<tr>
<td></td>
<td>Oligomenorrhagia</td>
<td>40 [80.0%]</td>
<td>37 [74%]</td>
<td>38 [76.0%]</td>
<td>37 [74.0%]</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

This work aimed to assess the efficacy of different methods of LOD in treatment of anovulatory infertility in PCOS. Patient’s characteristics were comparable between study groups. Majority of patients were overweight [BMI in all groups was around 27 kg/m²]. Ismail et al. [20] reported that, patient age, body mass index [BMI], infertility duration, pattern of menstrual cycle and type of infertility did not differ significantly between study groups. Additionally, Lebbi et al. [21] reported that 77% of them were presented with high BMI with a mean value of 27.8 kg/m². On the other side, Abu Hashim et al. [22] reported that obesity represented one of the predictors of poor outcome of LOD in PCOS.

In all study groups, LH decreased significantly after laparoscopic ovarian drilling than values before drilling [11.45±0.58, 11.65±0.69, 11.38±0.41, and 11.53±0.53 IU/L in groups I, II, III, and IV respectively, before drilling, versus 6.61±0.61, 6.81±0.59, 6.62±0.64, and 6.79±0.55 in group I,
II, III and IV, respectively after drilling]. Testosterone showed similar change. These results agree with Abdelhafiez et al. [23] and Zahiri Sorouri et al. [4] who reported a significant decrease in serum levels of LH and testosterone in women after LOD. Laul et al. [24] reported that LOD has been associated with a significant decrease of basal serum LH levels. Basal LH reduction was already known to be an indicator of good response to LOD. Also, they reported a reduction in basal serum testosterone.

On the other side, Elmashad [25] reported insignificant reduction of FSH after LOD, while testosterone significantly decreased. The reduction agrees with the current results. However, the insignificant reduction contradicts to current results. This could be explained by possible damage to the ovarian parenchyma after bipolar electrocoagulation during laparoscopy.

In the current work, AMH significantly decreased after drilling in all groups when compared to values before drilling. The difference between study groups was statistically non-significant before or after drilling. Al-Assadi et al. [26] reported a significant reduction in the AMH level after LOD. This was explained by the reduction in the number of AFC caused by thermal destruction to the ovarian tissue. Additionally, Amer et al. [27] showed significant reduction of AMH from 6.1 ng/ml before drilling to 4.7 ng/ml, one week after drilling and remains at the same level. They included PCOS patients who underwent bilateral diathermy LOD. Kandi and Salim [23] examined AMH level after treatment by CC, uni- and bilateral LOD and showed significant reduction of ovarian reserve only after bilateral LOD.

On the other side, Amer et al. [29] conclude that laparoscopic ovarian puncture does not change AMH serum level in women with PCOS. This was ascribed to the inappropriate drilling of the ovary.

Interestingly, Mohamed et al. [30] reported a significant decrease of serum AMH after ovarian cystectomy. This indicates that any ovarian surgical trauma is associated with follicular loss and consequent decrease of AMH synthesis.

LOD mechanism of action is the damage of the androgen-producing ovarian stroma, leading to a reduction in the circulating androgens and estrone [E1] due to reduced peripheral androgen aromatization. This E1 reduction leads to decreased positive LH-feedback and reduced FSH-negative feedback at the pituitary gland level. So, LH decreases and FSH increases resulting in follicular development. Local and systemic actions may induce ovulation in these patients [4].

Another theory is the production of non-steroidal factors due to ovarian injury resulting in restoration of the normal ovarian-pituitary relationship. The last theory is that injury to the ovarian tissue results in production of certain growth factors, which increase the sensitivity of the ovary to the circulating gonadotrophins resulting in normal follicular growth [31].

Chang et al. [32] and Farzadi et al. conclude that, LOD had normalized ovarian function which is a crucial issue in the follicular recruitment and maturation. Therefore, LOD has no negative effect on ovarian supply.

Rezk et al. [10] reported a marked increase in AFC at 6-months after ULOD than BLOD. This may refer to the inadequate follicle destruction in the dose-adjusted ULOD, thereby explaining the lower rates of ovulation and pregnancy at the 6-month follow-up in this trial.

In the current work, Ovulation, pregnancy, and miscarriage rates were comparable between groups regardless method of drilling. The lowest ovulation rate was 54% [group I] and the highest was 64% [group III]. The lowest pregnancy rate was 32% [group I] and the highest was 44% in group III. Miscarriage rate did not exceed 4%. Roy et al. [34] assessed the effect of unilateral versus bilateral LOD in 22 females. They reported no significant differences between two groups in terms of clinical and biochemical data, ovulation and gestational rates, and postoperative adhesions. They advocated ULOD than BLOD as a suitable management option in CC-resistant infertile females with PCOS, as it had similar response with reduced adhesions. Youssef and Atallah [35] evaluated 87 patients with ovulation failure due to PCOS who were categorized for ULOD [n=43] or BLOD [n=44]. Ovulation, pregnancy, and miscarriage rates were comparable between groups.

Most recently, Turgut et al. [36] reported a pregnancy rate of 54.1% and 34.2% for unilateral and bilateral LOD respectively after one year of follow up. However, the difference was statistically non-significant [P = 0.083]. The high pregnancy rate was observed in the first 6 months after LOD [70.0% in unilateral and 69.2% in the bilateral groups]. They finally concluded that, ULOD is preferable than BLOD in CC-resistant PCOS females, especially with large ovarian volume. This attributed to high rate of pregnancy with lower side effects.

In a recent review, Seow et al. [27] reported 30-90% ovulation rate and 13-88% final gestational rate. They explained LOD effects by thermal effects, leading to morphological and biochemical changes [e.g., artificial holes formation in the thick ovarian cortex, loosening of cortical wall, ovarian follicle destruction, reduced cells of the theca and/or granulosa layers, damage of ovarian stroma, and subsequent acute inflammatory reactions with initiation of immune response]. All these changes are associated with
decreased levels of androgens, apoptosis of pre-antral follicles to atresia, re-starting of normal follicular recruitment, development, and maturation, and lastly, the normalization of the "hypothalamus–pituitary–ovary" axis and spontaneous ovulation.

A recent meta-analysis by Zhang et al. [38] concluded that, unilateral LOD seems to be suitable alternative for bilateral LOD in CC-resistant PCOS, although more studies involving long-term assessment of reproductive efficacy and varying forms of LOD are warranted.

CONCLUSION

In conclusion, unilateral ovarian drilling is as effective as bilateral drilling, regardless of the technique [coagulative or cutting] with comparable ovulation, pregnancy and miscarriage rates.

Financial and Non-financial Relationships and Activities of Interest

None

REFERENCES


