

Risk of adhesions formation following microsurgical monopolar laparoscopic ovarian drilling: a comparative study

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Abstract The objective of the study was to determine the prevalence, extent, and location of adhesion formation following microsurgical monopolar laparoscopic ovarian drilling (LOD) among fertile and infertile women with clomiphene-resistant polycystic ovaries (PCO). The design was a longitudinal cohort follow-up study. The study was performed at the endoscopic unit of a tertiary university center. Three hundred and forty-seven patients with PCO were scheduled for LOD as a treatment option for clomiphene-resistant anovulation. Microsurgical monopolar LOD was performed in all cases. Two hundred and forty-six patients without possible additional predisposing factor for postoperative adhesion formation were followed up. To assess the sole effect of LOD on adhesion formation, only 51 eligible patients were classified into two groups; Group A comprised 22 women who conceived within 6 months following LOD and subjected to cesarean section, while group B included 29 women who failed to conceive over the same period of time and subjected to second-look laparoscopy. The main outcome measure was an evaluation of the prevalence, side, site, and severity of pelvic adhesions following microsurgical monopolar LOD. In total, adhesions were diagnosed in 40 cases (78.4%). Adhesions were diagnosed in 15 cases (68.1%) and 25 cases (86.2%) in groups A and B, respectively, without a statistically significant difference ($p=0.21$). Periovarian adhesions were diagnosed in 47/51 (92%) of cases in both groups. In 29 (56.8%) cases in both groups, adhesions were diagnosed on both sides (right and left adnexae) divided as

eight (36.3%) and 21 (72.4%) in groups A and B, respectively, with a statistically significant difference ($p=0.01$). The documented high prevalence of adhesions among infertile as well as women who conceived following LOD is an added evidence to the established risk of post-LOD adhesion formation. Following microsurgical principles would minimize the risk of these adhesions except periovarian adhesions. There is a bad need for studies on more refinement of LOD to make it as less adhesiogenic procedure as possible.

Keyword Laparoscopy · Ovarian drilling · Cesarean section · Adhesions

Introduction

Polycystic ovarian disease (PCO) is currently considered as possibly the most frequent cause of female infertility [1]. Despite being variable according to age and population, the prevalence of PCOS has been reported in 37.3% among women with self-reported oligomenorrhea and/or hirsutism [2]. In modern practice, the only allowed surgical method of ovulation induction for women with clomiphene citrate-resistant polycystic ovarian syndrome (PCOS) is laparoscopic ovarian drilling (LOD). Drilling aims to destroy a part of the ovarian stroma, which may help correct endocrine abnormalities and trigger ovulation. LOD has been evaluated in well-designed trials and may be an alternative to gonadotropins (GTs) [2]. A systematic review of four randomized controlled trials found no significant differences between LOD after 6–12 months follow-up and three to six cycles of ovulation induction with GTs in cumulative pregnancy rate (OR 1.42; 95% CI 0.84 to 2.42) or miscarriage rate (OR 0.61; 95% CI 0.17 to 2.16) in

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women with clomiphene citrate-resistant PCOS [3]. There was insufficient evidence to support any one surgical technique over another relating to adhesion formation, e.g., laser, monopolar, or bipolar diathermy [3]. For a long time, reasonable ovulation rates between 53% and 92% have been reported following LOD [4, 5]. Evidence-based advantages of LOD of PCO include minimal risk of ovarian hyperstimulation syndrome [6] and less cost if compared to GTs with comparable ovulation and pregnancy rates. Reduced multiple pregnancy rates is a clear superiority point of LOD over GTs [7–9]. In recent years, due to the previously mentioned advantages, the practice of LOD is increasing worldwide to the extent that it became one of the most commonly performed fertility-enhancing laparoscopic operation in many centers, particularly in the developing countries. Many surgeons are underestimating the possible risks of LOD, which include all the risks associated with laparoscopic surgery, as well as the potential for pelvic adhesions [3] and the very rare possibility of ovarian atrophy. Studies on postdrilling adhesions mainly focus on second-look laparoscopy for infertile women [10–12]. Frequent cases of pregnancy following LOD make a false sense of safety of LOD as regard remote sequelae, including adhesion formation. Many respectable societies interested in reproductive surgery recommend construction of unbiased studies to evaluate the best laparoscopic tool for drilling as well as adhesions formation risk following LOD [13]. This study was designed to determine the prevalence, extent, and location of adhesion formation following microsurgical monopolar LOD among fertile and infertile women with clomiphene-resistant PCO.

Materials and methods

This longitudinal cohort follow-up study was conducted between November 2004 and October 2007 at the Endoscopy Unit of the Woman's Health University Center, Assiut University, Assiut, Egypt, and comprised 347 PCO patients scheduled for LOD as a treatment option for clomiphene resistance on maximal dosing (150 mg daily for 5 days, starting on day 2) [14]. The diagnosis of PCOS was based on the clinical and biochemical evidence of androgen excess and PCO picture on transvaginal ultrasonography following the Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group sonographic description [15]. The study was approved by the Institutional Review Board of the Faculty of Medicine. All patients gave a clear written consent to participate in this study. Preoperative thorough history taking and careful general and abdominal examinations were done in all cases. Other factors of infertility were within normal including semen analysis, hysterosalpingography, normal serum prolactin, and thyroid hormones.

Patients with evidence of general or local abdominal contraindications to laparoscopy were excluded from this study (four cases) due to previous intestinal resection anastomosis in two cases, extensive abdominal incisions in one case, and congestive heart failure in one case. Additional exclusion criteria were a history of pelvic surgery (16 patients); occurrence of intraoperative complications (three cases), i.e., unusual ovarian surface or ovarian ligament bleedings necessitating excessive diathermy hemostasis or suturing; postoperative pelvic infection or hematoma as diagnosed by transvaginal ultrasonography (one case); or non-use of prophylactic antibiotics (two cases). Moreover, 75 cases were excluded from the study, as the intraoperative panoramic screening revealed concurrent pelvic adhesions (33 cases), typical or atypical endometriosis (21 cases), small simple ovarian cysts (nine cases), and paraovarian or paratubal cysts (12 cases). The remaining 246 cases were subjected to bilateral LOD, utilizing standard triple puncture technique only done by the authors mainly the first one. All surgeons were instructed to strictly follow microsurgical principles [16] in the form of minimizing tissue trauma particularly surface ovarian burn induced by the secondary coagulation, drilling of the antimesenteric surface only, firing the electrode after surface penetration using fine needles only for 5 s, with a current at a 30-W power setting to make a puncture that was approximately 4 mm in diameter and 6–8 mm deep, meticulous hemostasis, proper suction–irrigation of the pelvis, and leaving 500–1,000 cc of lactated ringer's solution intraperitoneally at the end of the procedure. The numbers of drills was tailored according to the ovarian size, with a range of four to six drills per ovary. All operations were done in nearly the same manner. Preoperatively, all patients received prophylactic antibiotics and were discharged within few hours after the procedure.

All cases were followed up for at least 6 months, with monitoring of regularity of the cycles, occurrence of ovulation, and ultimately pregnancy. Ovulation monitoring started the subsequent cycle following LOD. Follicular development was monitored using transvaginal ultrasonography from day 10 of the cycle. Human chorionic gonadotropin at dose of 5,000 IU was used to trigger ovulation when at least one follicle exceeding 18 mm was noted. Occurrence of ovulation was proved by either sonographic detection of corpus luteum or estimation of high luteal phase luteinizing hormone (LH). If ovulation was not achieved, ovulation stimulation was started on the D2 with clomiphene citrate 100 mg/day of the subsequent cycle. Pregnant cases were offered the usual low-risk antenatal care till delivery (extended follow-up period). If there was an indication for cesarean section (group A, 22 cases), the uterus was exteriorated after closure of the uterine incision. Meticulous comments on adnexal adhe-

sions were guided by the AFS Classification [17]. On the other hand, infertile patients for 6 months were counseled for a second-look laparoscopy provided normal or reasonable other factors of infertility. If the patient accepted, she was subjected to a second-look laparoscopy (group B, 29 patients), where the pelvis was meticulously evaluated for any evidence of adhesions as in group A. In both groups, adhesions were evaluated for the side (right or left), site (periovarian, tuboovarian, peritubal, Douglas, adnexouterine, adnexolateral pelvic wall), and extent (mild, moderate, and severe). Microsurgical adhesiolysis was performed. Data were collected and analyzed with SPSS version 11 (SPSS, Chicago, IL, USA) and expressed as mean±standard deviation (SD). Statistical methods were applied, including descriptive statistics (frequency, percentage, mean, and SD) and tests of significance (the incidence and grade of adhesions in both groups were compared by χ^2 statistics or Fisher's exact test, as appropriate). A p value <0.05 was considered statistically significant.

Results

This study comprised 347 cases with PCO planned for LOD. To assess the sole effect of LOD on adhesion formation, only 51 eligible cases were subjected to either cesarean section or second-look laparoscopy. Figure 1 demonstrates the flowchart of cases throughout the study. Demographic data of those 51 cases are shown in Table 1. Operative details in both groups are shown in Table 2. Regularity of menstrual cycles was regained in 45/67 (67%)

and 65/99 (65.5%) in groups A and B, respectively ($p=0.5$). Sonographically documented ovulation supported by elevated luteal phase serum progesterone was achieved in 44/67 (65.6%) and 41/99 (41.4%) cases in both groups, respectively ($p=0.002$). However, proved ovulation rose to 62/99 (62.6%) in group B just on 100 mg clomiphene citrate therapy started from day 2 of the subsequent cycle without statistically significant difference if compared to group A ($p=0.7$).

Those patients who did not conceive within 6 months underwent second-look conventional laparoscopy with the notable findings of a high percentage of postoperative adhesions. We succeeded to perform it in only 29 (29%) out of 99 infertile cases utilizing conventional laparoscopy. In total, in both groups, adhesions were diagnosed in 40 (78.4%) cases and 15 (68.1%) and 25 (86.2%) cases in groups A and B, respectively, without a statistically significant difference ($p=0.21$). In 29 (56.8%) cases in both groups, adhesions were diagnosed on both sides (right and left adnexae) divided as eight (36.3%) and 21 (72.4%) in groups A and B, respectively, with a statistically significant difference ($p=0.01$). Detailed demonstration of adhesion formation in both groups is shown in Table 3 strictly following the AFS classification. We reported important adhesion sites that are not included in AFS classification, which are Douglas pouch adhesions (two cases), tuboovarian adhesions (14 cases), and adnexouterine adhesions (four cases) in both groups. Collectively, periovarian adhesions were diagnosed in 47/51 (92%) of cases in both groups. No information was obtained from patients that delivered vaginally or were lost to follow-up. In group

Fig. 1 Flowchart of the study population

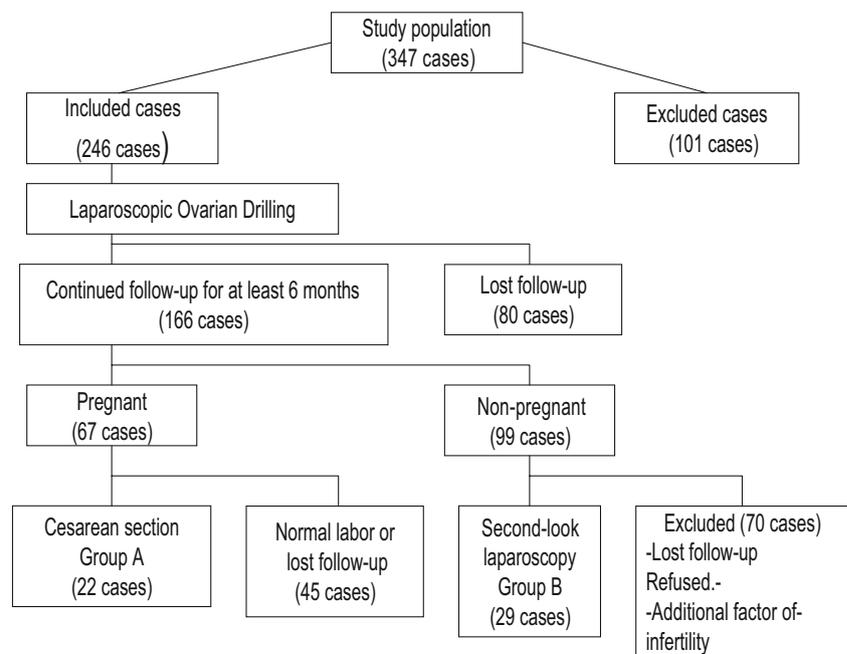


Table 1 Demographic data of the studied patients

	Group A (22 cases)	Group B (29 cases)	Significance <i>p</i> value
Age [years] [means±SD] (range)	26.36±2.19 (19–31)	27.64±4.21 (22–32)	NS
Parity	0.7±3.0 (0–2)	0.4±1.0 (0–1)	NS
BMI (kg/m ²) (range)	26.1±5.0 (17–40)	27.3±4.5 (18–39)	NS
Infertility			
Period (years) [means±SD] (range)	4.27±1.35 (1–8)	5.09±2.40	NS
Primary, <i>n</i> (%)	19 (86.4%)	23 (79%)	NS
Secondary, <i>n</i> (%)	3 (13.6%)	6 (21%)	NS
Menstrual cycle pattern			
Regular, <i>n</i> (%)	3 (13.6%)	3 (10.5%)	NS
Oligomenorrhea, <i>n</i> (%)	16 (72.8%)	22 (75.8%)	NS
Amenorrhea, <i>n</i> (%)	3 (13.6%)	4 (13.7%)	NS
LH/FSH ratio (range)	2.2 (0.6–3.2)	2.3 (0.6–3.5)	NS
Interval from primary LOD (months) [means±SD] (range)	16.50±10.11 (11–22)	5.40±5.63 (6–14)	0.001

B, after microsurgical lysis of two cases with Douglas pouch fine adhesions, pregnancy was achieved within 3 months.

Discussion

LOD of PCO is a continuous dilemma that requires more studies. One of the advantages of LOD over gonadotropin therapy (GT) is concomitant diagnosis and treatment of any associated lesions that may attribute to the patient's problem of infertility. This is clear in this study where associated fertility-jeopardizing problems were diagnosed in 75 (21.6%) out of 347 PCO patients who were excluded. Moreover, a diagnostic hysteroscopy can be easily performed at the end of the procedure to evaluate the endometrial cavity in selected cases. Lastly, it is evident that LOD is more cost effective than GTs, which represents a valuable advantage particularly in developing countries with limited resources, where GT therapy is more expensive and is not covered by most of the health insurance systems. However, LOD has virtually been abandoned by

reproductive endocrinologist as medical therapy for PCO has improved. Postoperative adhesion formation is a potential complication in up to 85% of patients [18]. Moreover, there are ongoing concerns about long-term effects of LOD on ovarian function [19]. Ovarian reserve assessed by hormonal levels and ultrasonography seems to be lower in the LOD than in the PCOS group without LOD in a recent study [20]. This risk of damaged ovarian reserve could be minimized if LOD is restricted to patients with high preoperative LH level, as demonstrated in a retrospective cohort study [21]. The influence of LOD on age of menopause onset is unclear [22].

In this study, 22 women who conceived within 6 months following LOD and subjected to cesarean section were included to test the pattern of adhesions among those women who get pregnant following LOD. Lack of correlation of adhesions to pregnancy rate was previously reported [10]. Occurrence of pregnancy is not a guarantee that LOD is a safe procedure if adhesion formation is concerned. It is well known that adhesions do not always affect fertility. Since the ovaries are paired organs, the doubled probability of pregnancy would dilute the effect of

Table 2 Distribution of adhesions among both groups according to AFS classification

Adhesions	Right adnexa			Left adnexa		
	Group A (22 cases)	Group B (29 cases)	Total (51 cases)	Group A (22 cases)	Group B (29 cases)	Total (51 cases)
None	8 (36.3%)	7 (24%)	15 (29.4%)	13 (59%)	8 (27.5%)	21 (41%)
Filmy						
Periovarian	8 (36.3%)	10 (34.4%)	18 (35.2%)	7 (31.8%)	10 (34.4%)	17 (33.3%)
Peritubal	1 (4.5%)	1 (3.4%)	2 (3.9%)	1 (4.5%)	2 (6.8%)	3 (5.8%)
Douglas pouch	0	1 (3.4%)	1 (1.9%)	0	1 (3.4%)	1 (1.9%)
Tuboovarian	0	1 (3.4%)	1 (1.9%)	0	1 (3.4%)	1 (1.9%)
Dense						
Periovarian	6	3	9	1 (4.5%)	2 (6.8%)	3 (5.8%)
Peritubal	0	2 (6.8%)	2 (3.9%)	0	1 (3.4%)	1 (1.9%)
Tuboovarian or adnexouterine	0	3 (10.3%)	3 (5.8%)	0	4 (13.7)	4 (7.8%)

Table 3 Prevalence of postdrilling adhesions in this study versus some published studies

Authors	Year	Sample size	Adhesions/second look (%)	Remarks
Weise et al. [27]	1991	39	7/26 (26.9%)	–
Gurgan et al. [28]	1991	7	6/7 (85.7%)	–
Dabirashrafi et al. [29]	1991	31	2/12 (16.6%)	Mild to moderate
Naether and Fischer [30]	1993	199	12/62 (19%)	The incidence reduced to 16.6% with the use of abdominal lavage
Naether et al. [31]	1993	133	7/26 (26.9%)	–
Greenblatt and Casper [11]	1993	8	8/8 (100%)	7/8 (87.5%) got pregnant
Saravelos and Li [32]	1996	21	7/21 (33%)	Unilateral: 3/21 (14%) Bilateral: 4/21 (19%)
Felmban et al. [33]	2000	112	4/15 (26.6%)	Periovarian adhesions
Mercorio et al. [24]	2007	90	54/90 (60%)	Unilateral: 25/54 (46.3%) Bilateral: 29/54 (53.7%)
Current study	2008	347	40/51 (78.4%)	Unilateral: 11 (27.5%) Bilateral: 29 (56.8%) Periovarian: 47/51 (92%)

adhesions on reproductive performance. Unilaterality of adhesions is another factor supported by some studies, which demonstrated that adhesion formation was more on the left side than the right side [23]. Moreover, most of adhesions seen in group A were filmy and periovarian, except one case of peritubal dense adhesions. Contrarily, in group B, peritubal, tuboovarian, or adnexouterine dense adhesions were reported, which would explain pregnancy failure in this group.

In group A, pregnancy might have occurred due to the site and consistency of these adhesions and the unilaterality of adhesions in five cases, which gives a chance for pregnancy from the other side provided that there is good ovulation. Thus, thin periovarian adhesions are the least adhesions that would affect fertility. Periovarian adhesions would seriously jeopardize fertility whenever the whole ovary is entirely entrapped to the extent that ovulation process is hindered. This concept is supported by a pilot study [10], where periovarian adhesions of variable severity were diagnosed in 100% of cases at second-look laparoscopy. However, the authors reported seven of eight women (87.5%) spontaneously conceived eight singleton pregnancies without any further therapy.

Second-look laparoscopy is a difficult decision for many patients who are already psychologically depressed due to prolonged period of infertility. This is clear in this study, where second-look laparoscopy was performed in only 29 (29%) out of 99 infertile cases utilizing conventional laparoscopy. To increase acceptability of patients to this procedure, we would suggest inclusion of minilaparoscopy (endoscopes ranging from 2 to 5 mm in diameter) during preoperative counseling, as it could be easily done under local infiltration as an office procedure. In a recent study utilizing minilaparoscopic second-look laparoscopy [23], only six patients (6.2%) decided to withdraw from a study,

including 96 cases, and did not undergo the second-look procedure. Despite being in its infancy, microlaparoscopy (endoscopes of <2 mm in diameter) is a promising outpatient procedure that could be performed under local anesthesia with mild sedation [24]. Based on these data, it is recommended to incorporate second-look microlaparoscopy in the counseling of patients planned for LOD in the near future to increase acceptability for second look if pregnancy could not be achieved despite proper ovulation.

In this study, we reported important adhesion sites that are not included in the AFS classification [17], particularly Douglas pouch adhesions (two cases), tuboovarian adhesions (14 cases), and adnexouterine adhesions (four cases). It is not clear whether the adhesions found were significant from a fertility standpoint, as the grading system does not address them. Nevertheless, after microsurgical lysis of the two cases with Douglas pouch fine adhesions in group B, pregnancy was achieved within 3 months. This can be explained by possible interference of this type of adhesions with ovum pick up. Moreover, tuboovarian or ovarian fossa adhesions have no place in the AFS classification. Likewise, adnexouterine or adnexopelvic wall adhesions are reported under the heading of other findings but are not included in the classification. Collectively, these sites represented 20 (50%) out of 40 cases of adhesions in our study without finding a suitable score based on the AFS classification. Data presented in this study are very preliminary and call for more extensive studies. A more detailed classification has been published by the Adhesion Scoring Group [25], which was proposed to be a more comprehensive scoring system based on evaluation of 23 individual locations in the abdominal cavity for severity and extent of total area or length. However, it seems to be complicated and again missing important items like adnexouterine or tuboovarian adhesions as well as ovarian

fossa adhesions. In this study, we did not follow it as we did not find any further published studies testing it in contrast to the AFS classification.

Postdrilling adhesion formation may occur in 30% to 100% of patients undergoing LOD [22], which represents a real limiting factor for LOD. Table 3 summarizes the results of this study versus examples of the published studies [10, 23, 26–32] on postdrilling adhesions. It is clear that the idea of evaluating postdrilling adhesions by second look is not new. Despite this plethora of publications, recent recommendations of fertility-interested societies call for more well-designed unbiased studies on adhesion formation following LOD [13]. If compared to other studies, it is evident that the rate of adhesions in our population is relatively high. However, in only 8% of cases, adhesions were diagnosed between the ovary and the adjacent organs. This positive finding of LOD highlights the importance of following microsurgical principles during reconstructive adnexal laparoscopic surgery. Most of the published studies focus on ovulation and pregnancy rates following LOD [9] rather than evaluating the safety of this invasive procedure that destroys the intact surface epithelium of the ovary to have an access to the stroma. This study was designed to be specific, informative, and practical, that is why any contributing factor that would predispose to adhesion formation (101 cases, 29.1%) was excluded. This point is missing in many published studies on LOD [11, 12]. A well-designed recent study [23] focused on demonstrating preferential spread of adhesions more on the left side and attributed this pattern to endometriosis, but did not stress on the type of adhesions common after LOD. Since this study is interested in evaluating the technique of microsurgical monopolar LOD per se, 22 women who conceived within 6 months following LOD and subjected to cesarean section cases were quoted. It is important to know the distribution of adhesions among cases of group A to highlight the type of adhesions that would poorly affect fertility. The reported high prevalence of periovarian adhesions in this study (92%) is a great evidence that LOD is an invasive procedure that destroys the intact ovarian surface epithelium. Even if microsurgical principles are followed, an inevitable inherent high incidence of periovarian adhesions would be anticipated due to the monopolar electrode firing on direct contact with the ovarian surface with subsequent secondary coagulation. An important issue in this study is to evaluate the prevalence of adhesions among patients in a developing country set up.

Nevertheless, limitations of this study are many. Both strict inclusion criteria and high numbers lost to follow-up weaken the collected data. An attempt was made to draw conclusions from the comparisons with two thirds of one group excluded from consideration. These 51 women with adhesions have suitable follow-up out of a total of 246 for a

21% known outcome figure (low sample size). It would be hard, therefore, to generalize to the entire group from such a sample other than to say that adhesions are common. Lastly, comparisons were made between groups with a dissimilar endpoint.

For a long time, it has been suggested that LOD is advised only when hormonal therapy failed or if the patient is at high risk of hyperstimulation or multiple pregnancy [26]. The unequivocal high rate of adhesion formation following LOD shown in a recent study suggested the importance of undertaking complete and comprehensive medical therapy before proceeding with surgical treatment [23]. In our study, despite that we were restricted to microsurgical principles, our data are also alarming against LOD. More research should be seriously constructed to focus on different techniques that would make LOD as valuable as possible without the nightmare of adhesion formation, for example, evaluating bipolar fine-needle drilling approach as compared to bipolar hydrolaparoscopic approach [33]. In conclusion, the documented high prevalence of adhesions among infertile as well as women who conceived following LOD is an adding evidence to the established risk of post-LOD adhesion formation. Following microsurgical principles would minimize the risk of these adhesions except periovarian adhesions. There is a bad need for studies on more refinement of LOD to make it as less adhesiogenic procedure as possible.

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