

## A Modified Technique of Laparoscopic Ovarian Drilling for Polycystic Ovary Syndrome Using Harmonic Scalpel

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### Abstract

**Objective:** To review our experience with a modified technique of laparoscopic ovarian drilling (LOD) using harmonic scalpel as a new energy modality and to compare its effect with electrocautery in managing Clomiphene resistant polycystic ovary syndrome as regard to ovulation rate, pregnancy rate, hormonal profile and ultrasonographic changes that reflect ovarian reserve and reproductive outcome.

**Patients and methods:** Sixty patients presented by infertility due to PCOS were randomly allocated into two equal groups. Group I was subjected to laparoscopic ovarian drilling using electrocautery and Group II were subjected to laparoscopic ovarian drilling using harmonic scalpel. All patients were assessed twice (before the induction procedure and three months later, if pregnancy did not occur). Patients were assessed clinically (to determine menstrual regularity and body mass index), sonographically (to measure ovarian volume and antral follicle count at time of ovarian quiescence) and laboratory (to measure basal serum LH, FSH, LH/FSH ratio, total testosterone and estradiol). Also a 2<sup>nd</sup> look laparoscopy was performed in those patients who failed to conceive within six months of the initial laparoscopic procedure to assess the presence of adhesion and its type.

**Results:** Laparoscopic ovarian drilling using harmonic scalpel improved menstrual pattern, ovulation rate, pregnancy rate, hormonal profile similar to electrocautery without a significant difference. However it was associated significantly with a minimal effect on ovarian volume, antral follicle count and post operative adhesion.

**Conclusions:** We consider our LOD technique using harmonic scalpel as a new energy modality in managing Clomiphene resistant polycystic ovary syndrome practicable with less extensive destruction of the ovarian capsule and thereby of the ovarian reserve and with minimal incidence of post operative adhesion.

### Introduction

Polycystic ovary syndrome is the most common cause of anovulatory infertility affecting between 4% and 6% of women of reproductive age. Bilateral ovarian wedge resection, proposed by Stein et al. [1] was the only treatment available for this syndrome. However, as ovulation inducing medical agents became available, the medical induction of ovulation became the dominant form of treatment [2]. Clomiphene citrate (c.c) was used for a long time as a first line of treatment. However, 15-20% of women remain anovulatory despite receiving incremental dose of CC. Furthermore, there was a discrepancy between the ovulation and conception rates. Gonadotropin therapy is usually the next step following failure with clomiphene [3]. However Setji et al. [4] stated that because of the peculiarly high sensitivity of polycystic ovaries to gonadotropin stimulation it was plagued by an unacceptable rate of multiple pregnancies and ovarian hyperstimulation syndrome. An alternative to the medical approach is surgical treatment. The most widely used surgical treatment is laparoscopic ovarian drilling.

Cleemann et al. [5] stated that Laparoscopic ovarian drilling (LOD) can resolve infertility within 4-6 months in 50-60% of couples. So a strategy with LOD in women with PCOS will shorten the time to pregnancy, reduce the need for medical ovulation induction and enable diagnosis of those women with anatomic infertility who can achieve pregnancy only by IVF treatment.

The rapid acceptance of laparoscopic surgery in gynecology has brought a re-evaluation of the types of energy currently used for cutting and coagulation during these procedures. Electro surgery has undergone significant improvements with respect to safety and delivery, but there was still considerable concern with regard to unintentional tissue damage [6]. The ultrasonically activated

scalpel (UAS) and laparoscopic coagulation shears (LCS) use high-frequency ultrasound energy and can be tried as a substitute for electro surgery. The ultrasonically activated scalpel consists of a piezoelectric transducer that is housed in a hand piece and causes a blade tip to vibrate longitudinally at an ultrasonic level (55,500 times per second) and excursion over a distance of 50-100  $\mu$ m. The thermal spread of the ultrasonically activated scalpel is about 0.05mm, compared with 0.35 mm for that produced by electrocautery [7].

### Aim of the Study

To review our experience with a modified technique of laparoscopic ovarian drilling (LOD) using harmonic scalpel as a new energy modality in managing Clomiphene resistant polycystic ovary syndrome.

To compare its effect with electrocautery as regard to ovulation rate, pregnancy rate, hormonal profile and ultrasonographic changes that reflect ovarian reserve and reproductive outcome.

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To compare post operative adhesion formation of harmonic scalpel and electrocautery.

## Patient and Methods

60 patients presented by Clomiphene resistant PCOS were selected from those patients attending our infertility clinic, department of Obstetrics and Gynecology, Al-Azhar University hospitals in Assiut during the period from 2009 to 2010.

The diagnosis of patients depended on the Rotterdam European Society of Human Reproduction/American Society for Reproductive Medicine Sponsored PCOS Consensus Workshop Group that convened in 2003 and required the existence of two of the following three criteria to make the diagnosis of PCOS: oligo-ovulation/anovulation, clinical or biochemical signs of hyperandrogenism and Polycystic ovaries by ultrasound.

All patients were assessed clinically (to determine menstrual pattern and body mass index), sonographically (to measure ovarian volume and antral follicle count at time of ovarian quiescence) and laboratory (to measure day 3 to 5 serum LH, FSH, LH/FSH ratio, total testosterone and estradiol). Serum concentration of E<sub>2</sub>, FSH and LH were measured by chemiluminescent immuno-assay provided by Diagnostic products, and interpretation of assays was performed according to manufacturer recommendations [8]. In oligomenorrheic patients and at random in amenorrheic ones as long as pregnancy was ruled out by pregnancy test and/or ultrasonography. All patients were assessed twice one before the induction procedure and the other is three months after, if pregnancy did not occur.

Patients were randomly allocated into two equal groups:

Group (I) was subjected to laparoscopic ovarian drilling using electrocautery.

Group (II) was subjected to laparoscopic ovarian drilling using harmonic scalpel.

Laparoscopic procedures were performed in the follicular phase of natural or induced cycle via three ports of entry after insufflation of the peritoneal cavity by electronic high-flow pneumoperitoneum insufflator with CO<sub>2</sub> gas.

**In group I:** The drilling was performed using an insulated unipolar electrocautery needle electrode. The uninsulated part of the needle was 8 mm long and its diameter was <1 mm. The needle was inserted into the ovarian surface as close to perpendicularly as possible. A short duration of a cutting current of 100 Watt was used to aid the entry of the needle. The whole length of the needle was inserted into the ovary and was activated for 2-3 seconds with 40 Watt of coagulating current at each point.

**In group II:** Harmonic scalpel (ETHICONE ULTRACISSION, Germany) was used as a substitute for electro cautery. We used the only active (vibrating) blade of laparoscopic coagulation shear (LCS) which has a tip of about 1 mm and a length of about 1 cm. After activation of the blade, the ovaries were drilled using the whole length of the active blade.

In both groups a total of 6 punctures per ovary were created, tubal patency and mobility were confirmed by flushing of the tubes with methylene blue. Women with a blocked tube or tubes were excluded from this study.

After drilling, the ovary was allowed to cool in a pole of saline to prevent excessive heat trauma. The abdominal cavity was then rinsed

with 500-1000 cc of sterile saline to remove blood and coagulated tissue and minimizes post operative adhesion.

All patients were followed up for 6 months to evaluate the changes in menstrual pattern, hormonal profile, ultrasonographic finding, ovulation rate and pregnancy rate as well as assessment of post laparoscopic adhesion by 2<sup>nd</sup> look laparoscopy if pregnancy did not occur within six months of the initial procedure.

The statistical analysis was performed with the use of commercial software programs (SPSS for Windows, version 9). The Student's *t*-test for independent samples was used to compare baseline differences. Chi-square or Fisher exact tests were used as appropriate for categorical variables. A *p* value of less than 0.05 was considered statistically significant.

## Results

The baseline clinical hormonal and ultrasonographic characteristics of both groups are shown in table 1.

Follow up and Outcomes:

56 patients had been followed up for six months, four patients were lost during follow up, two from each group, and they had been excluded from the rest of statistics.

(A) Post induction menstrual pattern:

Both groups were associated with significantly higher percentage of regular cycles (92.85 % for each), however there were no statistically significant differences between both groups (*p*>0.05) (Table 2).

(B) Post induction Hormonal profile:

There was a significant reduction in the mean levels of LH, LH/FSH ratio and Testosterone in both group (*p*<0.05). On the other hand there were no significant changes of the mean levels of FSH and E<sub>2</sub> in any group (*p*>0.05) (Table 3).

(C) Post-induction ultrasonographic characteristics:

There was a reduction in both ovarian volume and antral follicle

Variable	Group (I) (n=30)	Group (II) (n=30)
<b>Clinical characteristics:</b>		
Age (years) Mean ± SD	24.95 ± 2.4	24.8 ± 3.1
Duration of infertility (years) Mean ± SD	5.4 ± 2.4	6.2 ± 2.4
<b>Menstrual pattern [No. (%)]</b>		
• Oligomenorrhea	20 (66.7%)	21 (70.0%)
• 2ry amenorrhea	9 (30%)	8 (26.6%)
• Polymenorrhea	1 (3.6%)	1 (3.4%)
BMI (Kg/m <sup>2</sup> ) Mean ± SD	28.7 ± 3.86	29.1 ± 4.7
<b>Hormonal profile (Mean ± SD)</b>		
• LH (IU/L)	13.1 ± 2.11	12.8 ± 1.88
• FSH (IU/L)	5.69 ± 0.93	5.3 ± 0.93
• LH: FSH ratio	2.36 ± 0.54	2.49 ± 0.57
• Total testosterone. (ng/ml)	0.96 ± 0.16	0.96 ± 0.14
• Serum E <sub>2</sub> (pg/ml)	75.77 ± 6.13	77.9 ± 5.24
<b>Ultrasonographic characteristics (Mean ± SD)</b>		
• Ovarian volume (cm <sup>3</sup> )	11.66 ± 2.17	12.5 ± 1.66
• Antral follicle count (AFC)	16.1 ± 2	16. ± 2.3

There were no statistically significant differences between both groups (*P*>0.05)

**Table 1:** Clinical, hormonal and ultrasonographic characteristics of the studied groups.

Menstrual pattern	Pre-induction (n=30)	Post-induction (n=28)	P- Value
Group(I)			
Normal cycle	0 (0%)	26(92.8%)	<0.01
Oligomenorrhea	20 (66.7%)	2 (7.15%)	
2ry amenorrhea	9 (30%)	0 (0%)	
Polymenorrhea	1 (3.6%)	0 (0%)	
Group(II)			
Normal cycle	0 (0%)	26(92.8%)	<0.01
Oligomenorrhea	21(70.0%)	2 (7.15%)	
2ry amenorrhea	8 (26.6%)	0 (0%)	
Polymenorrhea	1 (3.4%)	0 (0%)	

Values are given as (No. (%))  
Group I and group II; p>0.05

**Table 2:** Menstrual pattern before and after ovarian drilling.

Hormone	Pre-induction (n=30)	Post-induction (n=28)	P- Value
Group(I) : Electrocautery			
LH (IU/L)	13.1 ± 2.1	8.23 ± 1.1	<0.05
FSH (IU/L)	5.69 ± 0.93	6.0 ± 1.0	>0.05
LH/FSH ratio	2.36 ± 0.54	1.4 ± 0.3	<0.05
Testosterone (ng/ml)	0.69 ± 0.16	0.622 ± 0.11	<0.05
Estradiol (pg/ml)	75.77 ± 6.13	75.47 ± 5.2	>0.05
Group(II): Harmonic scalpel			
LH (IU/L)	12.8 ± 1.9	7.76 ± 1.1	<0.05
FSH (IU/L)	5.3 ± 0.94	5.32 ± 1.1	>0.05
LH/FSH ratio	2.49 ± 0.57	1.48 ± 0.4	<0.05
Testosterone (ng/ml)	0.69 ± 0.14	0.68 ± 0.11	<0.05
Estradiol (pg/ml)	77.9 ± 5.24	76.02 ± 4.4	>0.05

Values are given as mean ± SD  
Group I and group II; p>0.05

**Table 3:** Pre-induction and post-induction hormonal levels of both groups.

count (AFC) after each method of induction; however the reduction was statistically insignificant in harmonic scalpel group, (P>0.05), while it was statistically significant in electrocautery group (P<0.001) (Table 4).

#### (D) Ovulation and pregnancy rates:

In spite of that harmonic scalpel group is apparently associated with a higher ovulation and pregnancy rates, however the difference between both groups was statistically insignificant (P>0.05) (Table 5).

#### (E) Assessment of post operative adhesion formation:

Second look laparoscopy was carried out for those patients who failed to conceive after six months of the initial laparoscopic induction procedure. The total number of cases who didn't get pregnant in group I and II is 26 patients. Six cases failed to undergo second look laparoscopy due to drop out and were excluded from the statistical analysis. The number of patients who underwent 2<sup>nd</sup> look laparoscopy was twenty patients (eleven patients from group I and nine patients from group II). Also there was an opportunity to evaluate pelvic adhesion in four patients who delivered by cesarean section in our department (two patients from each group). Assessment of post LOD adhesion formation, According to American Fertility Society (AFS) classification of adnexal adhesions 1988, showed that the incidence and type of post LOD adhesion of the harmonic scalpel group was significantly lesser than that produced by electrocautery (Table 6).

## Discussion

Clomiphene citrate is considered to be the first Line of treatment

of infertile women with PCOS, the ovulation rate with this drug is 80-85%. However, 15-20% of women remain anovulatory despite receiving incremental dose of CC; furthermore, conception rate is only 40-50% this discrepancy between ovulation and conception rates is attributed mainly to the anti-estrogenic effects of Clomiphene at the level of the endometrium and cervical mucus [3]. For Clomiphene citrate resistant patients, gonadotropin therapy was usually offered. However this treatment is expensive, time consuming and requires intensive monitoring because of its association with ovarian hyper stimulation syndrome (OHSS) and polyfollicular growth that increases the incidence of multiple pregnancies [2,9].

Surgical treatment of PCOS was renewed by adoption of minimally invasive laparoscopic surgery. Various laparoscopic techniques have been described with the use of different energy modalities aiming to improve the success rate and decrease the post operative adhesion [9]. The new energy modality that use ultrasonic energy in performing cutting or coagulation of tissue during laparoscopic or open surgery have been tested before in general surgery and its advantages in safety and delivery have been proved, however evaluation of this type of energy in treating infertile women with PCOS through performing laparoscopic ovarian drilling did not evaluated until now. So this study was conducted to evaluate the results of laparoscopic ovarian drilling using harmonic scalpel in infertility patients with PCOS as regard to ovulation rate, pregnancy rate, hormonal profile and ultrasonographic changes that reflect the ovarian reserve and reproductive outcome.

In the present study regular menstruation after ovarian drilling was established in 92.8% of patients in both groups. Comparison of the menstrual pattern before and after surgery showed that, oligomenorrhea dropped from 66.7% and 70% to 7.2% for both groups, and 2ry amenorrhea dropped from 30% and 26.6% to 0.0% in electrocautery and harmonic scalpel groups respectively. These results are comparable with that of [9] where regular menstrual pattern was established in 94% and 88% and oligomenorrhea dropped to 6% and 12% in electrocautery and harmonic scalpel groups respectively. The present study is also comparable to Api et al. [10] where regular

Variable	Pre induction	Post induction	P Value
Group(I)			
Ovarian volume (cm <sup>3</sup> )	11.66 ± 2.17	10 ± 1.9	<0.001
Antral follicle count	16.1 ± 2.02	14.14 ± 1.76	<0.001
Group(II)			
Ovarian volume (cm <sup>3</sup> )	12.5 ± 1.66	11.3 ± 1.1	>0.05
Antral follicle count	16 ± 2.3	15.4 ± 1.89	>0.05

Values are given as Mean ± SD.  
Group (I) and group (II); p<0.05

**Table 4:** Pre and post induction Ultrasonographic characteristics of both groups.

Variable	Group (I) (n=28)	Group (II) (n=28)	P value
Ovulation (No. %).	25 (89%)	26 (92.9%)	p>0.05
Pregnancy (No. %).	14 (50%)	16 (57%)	

**Table 5:** Post induction ovulation and pregnancy rates of both groups.

Type of adhesion	Electrocautery (n=13)	Harmonic scalpel (n=11)	P value
None	10 (76.9%)	10 (90.9%)	<0.01
Minimal	2 (15.4%)	1 (9.1%)	
Mild	1 (7.9%)	0 (0%)	
Total adhesion	3 (23.1%)	1 (9.1%)	

Values are given as (No. (%))

**Table 6:** Incidence and type of post laparoscopic drilling adnexal adhesion.

menstrual pattern was established in 93.3%. However Felemban et al. [3] reported regular menstrual pattern of 80.4% and oligomenorrhea of 19.6% after electrocautery. This difference may be attributed to different criteria used for diagnosis of PCOS or different study size.

In the present study both groups were associated with a statistically significant reduction in the mean levels of serum LH, LH/FSH ratio and total testosterone ( $p > 0.05$ ). However there was no statistically significant difference between both types of energy used. These results are in agreement with that of Felemban et al. [3], Takeuchi et al. [9]; Kovacs et al. [11]; Cleeman et al. [5]; Api et al. [10]; Kucuk et al. [12] and Kandil et al. [8]. In the present study we could not find any significant change in the mean levels of estradiol and FSH after induction in both groups. These results are in agreement with Felemban et al. [3]; Takeuchi et al. [9] and Kucuk et al. [12]. On contrary to our finding Api et al. [10] reported a significant rise of FSH level after laparoscopic ovarian drilling with electrocautery.

The present study showed no significant reduction in ovarian volume or antral follicle count in harmonic scalpel group. On the other hand the reduction in ovarian volume and antral follicle count was statistically significant in electrocautery group where ovarian volume decreased from  $11.6 \pm 2.17$  to  $10 \pm 1.9$  ( $P < 0.001$ ) and the antral follicle count decreased from  $16.1 \pm 2$  to  $14.1 \pm 1.7$  ( $P < 0.001$ ). These findings are comparable to the results obtained by Kandil et al. [8]. This reduction of ovarian reserve can be attributed to the lateral thermal damage of ovarian tissue occurred by electrocautery where single drilling resulted in 0.4 mL destruction of ovarian tissue, so an average of 3.2 ml of ovarian volume were destroyed when 8 drillings in both ovaries were done. In the present study we didn't find any significant reduction in ovarian volume or antral follicle count after ovarian drilling using harmonic scalpel, This is attributed to the minimal lateral thermal damage to ovarian Tissue (0.05 ml) which is approximately 1/8 of damage that obtained by electrocautery. However until now our study is the second study after Takeuchi et al. [9], which evaluate the use of harmonic scalpel in LOD, as regard to hormonal change, ovulation and pregnancy rates as Takeuchi et al. [9] and in addition it evaluate ultrasonographic changes which reflects ovarian reserve, so further studies should be conducted to evaluate the effect of this technique on this issue.

In the present study ovulation rate was 92.9% and 89% in harmonic scalpel and electrocautery groups respectively. There was no statistically significant difference between both groups; this result is comparable to that of Takeuchi et al. [9] where ovulation rate was 94% in both groups. In the present study the pregnancy rates were 57% and 50% for harmonic scalpel and electrocautery groups respectively. The difference between the two groups was statistically insignificant. Many studies reported different ovulation and pregnancy rates after different laparoscopic techniques and are shown in table 7. The differences among these variable studies may be attributed to different laparoscopic techniques, different periods of follow up or the use of medical ovulation induction agents as cc after electrocautery. Takeuchi et al. [9] reported pregnancy rate of 53% and 50% after harmonic scalpel and electrocautery ovarian drilling respectively which is in accordance with the present study.

In the present study assessment of post laparoscopic adhesion after each type of energy was determined according to the classification of American Fertility Society (1988).

The incidence of adhesion formation was 9.1 % (minimal and confined to the ovarian surface) for harmonic scalpel group and 23%

Reference	Technique	% ovulation	% pregnancy
Huber et al. [13]	Laser	41.7	23
Daniell and Miller [14]	Laser	83.8	66.7
Utsunomiyat et al. [15]	Biopsy	93.8	50
Gadir et al. [16]	Cauterization	26.5	43.8
Tasaka et al. [17]	Cauterization	91	36
Gurgan et al. [18]	Cauterization	71	57
Kovacs et al. [19]	Cauterization	70	20
Pellicer and Remohi [20]	Cauterization	67	52.6
Ostrzenski [21]	Laser	92	92
Armar and Lachelln [22]	Cauterization	86	66
Gjonnaess [23]	Cauterization	92	84
Takeuchi et al. [9]	Harmonic scalpel	94	53
	cauterization	94	50

**Table 7:** Ovulation and pregnancy rates after different laparoscopic treatment of PCOS (Takeuchi et al. [9]).

References	Technique	% of adhesion
Portuondo et al. [24]	Ovarian biopsy	0
Grochmal [25]	ND: YAG laser	3
Lyles et al. [26]	Cauterization/ND:YAGlaser	100
Daniell and Miller [14]	CO <sub>2</sub> KTP laser	0
	CO <sub>2</sub> laser	43
Keckstein [27]	ND: YAG laser	0
	Cauterization	86
Gurgan et al. [18]	ND: YAG laser	80
	Cauterization	35
Naether et al. [28]	Cauterization	85
Gurgan et al. [29]	ND: YAG laser	19
Naether and Fischer [30]	Cauterization	0
Dabirashrafi et al. [31]	Cauterization	0

**Table 8:** Second look laparoscopy following different surgical treatments of PCOS.

(minimal and mild adhesion) for electrocautery group. The incidence and type of adhesion after using harmonic scalped were significantly lesser than electrocautery ( $P < 0.5$ ). Many studies assessed adhesion formation following LOD by electrocautery or laser but very few studies assed the incidence of pelvic adhesion following the use of harmonic scalpel in gynecological surgery, so further studies should be directed to evaluate this issue (Table 8).

## Conclusions and Recommendations

We consider our LOD technique using harmonic scalpel as a new energy modality in managing Clomiphene resistant polycystic ovary syndrome a practicable minimally invasive procedure with less extensive destruction of the ovarian capsule. It results in regular menstrual pattern with ovulation and pregnancy rates comparable to electrocautery, with minimal effect on ovarian volume and antral follicle count which affect ovarian reserve. It has also a minimal incidence of post operative adhesion.

We recommend application of our modified technique of LOD that used harmonic scalpel instead of traditional technique that used electrocautery in managing clomiphene resistant polycystic ovary syndrome.

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