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EVALUATION OF OVARIAN RESERVE AFTER LAPAROSCOPIC OVARIAN DRILLING IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Background: Polycystic Ovary Syndrome (PCOS) is a widespread endocrine disorder that affects 4-8 percent of women during reproductive age. Infertility affects 40 percent of women with (PCOS). About 90-95% of women in infertility clinics have polycystic ovarian syndrome due to lack of ovulation. Ovarian perforation by laparoscopy is the second line after medicinal treatment. **Objective of the research:** to evaluate the effect of Laparoscopic Ovarian Drilling on ovarian reserve in patients with polycystic ovarian syndrome before and after LOD measured by the levels of anti-Mullerian hormone in the blood (AMH**)**, FSH hormone on a specific day from the onset of menstruation, ovarian volume and (AFC) antral follicle count. **Patients and methods:** This study was conducted on 60 PCOS patients resistant to clomiphene citrate therapy who underwent LOD ovarian perforation at Tishreen University Hospital. The syndrome was diagnosed on the basis of the Rotterdam criterion and ovarian diseases detected by transvaginal ultrasound were excluded from the study. **Results:** there was a significant negative correlation between age and the difference in the level of AMH in the blood before and after LOD. There is no statistically significant relationship between obesity or clinical hyperandrogenism (hirsutism and / or acne vulgaris) and any differences between pre-and post-LOD values of ultrasound or biochemical markers of ovarian reserve. The presence of menopause was significantly associated with a higher difference between the AFC before and after LOD of the ovaries. Anti-Mullerian hormone, AFC and ovarian size decreased significantly after LOD ($P < 0.001$) ،while FSH hormone increased significantly from the onset of menstruation after LOD ($P < 0.001$). **Conclusion:** It can be concluded that LOD for PCO women causes a pronounced deficiency of AMH, and a pronounced increase of FSH with the onset of menstruation. The size of the AFC and ovaries also decreases significantly.

KEYWORDS: PCO: Polycystic Ovary Syndrome, **LOD**: Transabdominal Laparoscopic Ovarian Drilling, **AMH**: Anti-Mullerian hormone, **FSH** hormone, **AFC:** antral follicle count.

INTRODUCTION

Polycystic ovary syndrome is associated with menopause, hirsutism and polycystic ovarian hyperplasia. The diagnosis of polycystic ovary syndrome was based on the recommendations of the National Institutes of Health. The European Society of Human Reproduction and the American Society of Reproductive Medicine (ASRM) proposed new criteria for the diagnosis of polycystic ovary syndrome at a combined meeting in 2003.[1] The Rotterdam Consensus Group reviewed the criteria for the diagnosis of PCOS: two important criteria for the diagnosis of PCOS: anovulation, clinical and biochemical hyperandrogenic syndrome and other cases of the syndrome (congenital adrenal hyperplasia, androgen-secreting tumors and Cushing's syndrome) and / or polycystic hyperandrogenism (polycystic ovary syndrome).[2]

Although the initial defect of the PCO is not specific, the treatment is aimed at restoring ovulation cycles to achieve pregnancy, Stein and Leventhal (1935) [3] found that the first known treatment for patients with PCO syndrome was ovarian wedge resection, which was frequently performed but nowadays stopped or reduced due to surgical adhesions.[4]

Either surgical treatment of laparoscopic ovarian drilling (LOD) may prevent or reduce the need for gonadotropins or may enhance their use.[5,6,7]

LOD causes trauma and less postoperative adhesion. But it can harm ovarian tissue and lead to a reduction in ovarian reserve due to the amount of coagulated tissue during the procedures and the associated widening of the size of the holes.

The ovarian reserve relates to the size, number and efficiency of ovulum. The ovarian reserve is the reproductive capacity of the ovary in which multiple follicles appear.[8] The ovarian reserve and the ability of women to have children are diminishing due to aging (Hansen et al. 2008).[9] Evaluation of the Anti-Mullerian hormone (AMH) whose levels in serum can be used as an indicator of ovarian reserve.[10] AMH hormone levels in the blood increase during //bleeding// of menstrual cycle and during the full cycle there are slight changes to prevent cycles // intra cycles // [11]

PATIENTS AND METHODS

The study involved all patients attending the outpatient clinic of Obstetrics and gynecology at Tishreen University Hospital, Lattakia, from the first of January 2022 to the first of January 2023.

A prospective observational analytical Study of patients who underwent laparoscopic ovarian drilling and who did not respond to medicinal treatment.

This study involved patients of reproductive age (19-35) with polycystic ovary syndrome (PCOS) according to Rotterdam criteria, who were resistant to treatment with Clomiphene Citrate.

The sample size was calculated using OpenEpi version 2.3.1. Data from a previous related study revealed that the average number of antral follicles was 16.1 ± 1.5 before ovarian drilling and 15.1 ± 1.9 after ovarian drilling , which is a statistically significant difference (p = 0.007). The minimum sample size of 38 cases was provided by calculation according to these values. Because it is preferable to increase the number from 20 to 30 to increase the credibility and accuracy, the study and research continued until we reached 60 patients who completed the entire research but who did not drop out of the study and follow-up.

The inclusion criteria include: a patient of reproductive age (19 – 39 years old) diagnosed as PCOS according to Rotterdam criteria, hyperandrogenism and the presence of> 10 follicles, ultrasound examination with a diameter of 2-9 mm in each ovary. Clomiphene Citrate resistant to interaction with up to 150 mg / day of Clomiphene Citrate has failed for at least three cycles.

The exclusion criteria include: age less than 19 and older than 39 years. Pre-existing endocrine diseases such as diabetes mellitus, hyperprolactinemia, hypothyroidism. Previous cesarean section or any previous abdominal surgery. Body mass index BMI > 40 kg / m^2.

We explained all the previous procedures to the patients who participated in the study. Written consent (informed consent) was taken from all patients and informed that they had the right to refuse or withdraw.

All patients had the following: full medical history (obstetrics and gynecology). Body mass index BMI kg / m^2, general examination (including vital signs). Examination of the abdomen. Gynecological examination.

Steps

Transvaginal ultrasound was performed on the second day of the cycle before laparoscopic ovarian drilling. Polycystic ovarian syndrome was diagnosed on the basis of Rotterdam criteria; with at least two of these findings: oligomenorrhea or amenorrhea, 8 or less menstruation at the last 12 months. Clinical symptoms of hyperandrogenism and / or biochemical symptoms exclude cases of hyperandrogenism (congenital hyperplasia, androgen-secreting tumor and Cushing's syndromes).[12]

Blood samples were taken for all patients participating in the study to assess AMH and FSH on the second and third days of the menstrual cycle.

Transvaginal ultrasound: the ultrasound examination was performed in the second cycle with a 7.5 MHz transvaginal test under full magnification of the ovaries. The second dimension has been identified. The vaginal probe was rotated to 90 degrees to obtain the third dimension, after determining the longer ovarian axis. Ultrasound views: an enlarged or regular ovary with a size of more than 10 follicles (diameter from 2 to 9 mm) and a dense stroma with several subcortical follicles.

Laparoscopic Ovarian Drilling was performed under general anesthesia. A 10 mm diagnostic laparoscope, along with a maneuvering (movement) probe with the second 5 mm hole, placed above the pubis in the median line, was used to assess the pelvis after confirming the presence of bilateral polycystic ovaries and the opening of the proboscis examined with Methylene Cyanosis. Each ovary is moved by grasping its ligament with 5 mm traumatic grasping forceps passing through a 5 mm suprapubic trocar, and each ovary is pierced four times with a diameter of 4 mm.

After surgery, ovarian size and AFC were assessed by transvaginal ultrasound with evaluation of gonads and gonadotropin releasing hormone, FSH and AMH.

Transvaginal ultrasound with hormonal assessment of HCG, FSH and AMH was performed on the second day of menstruation after LOD. If menstruation does not

occur after six weeks of LOD, a Progesterone Challenge test should be performed to induce pull bleeding, ovarian size and AFC have been evaluated by vaginal ultrasound with evaluation of gonadotropin releasing hormone, FSH and AMH.

Current statistical method: the Microsoft Excel 2010 and Windows 15.0 packages for Statistical Social Sciences (SPSS) were used for statistical analytical research. The domain, mean, standard deviations (where they are parametric), range and median (where they are not parametric) must be expressed continuously. A number and binary ratios or categorical data were presented. Repeated measurements in the same group will be compared using bidirectional ANOVA (variance analysis), the Wilcoxon classification test (for continuous nonparametric variables) and The Chi-squared and McNemar test (categorical variables). The significance level is set at 0.05.

RESULTS

Table 1: Demographic data of the sample.

	Range	Mean ±SD
Age (years)	18-38	26±3.14
BMI (kg\m^2)	19.5-36.8	28.62±4.17

All the women included had menstrual irregularities, in the form of oligomenorrhea in 44 (73.33%) and amenorrhea in 16 (26.66%). Of the 60 included patients, 44 (73.33%) had clinical manifestations of hyperandrogenism, in the form of hirsutism 25 (41.66%) and acne vulgaris 35 (58.33%) (Table 2).

Measurements of the ovaries before and after LOD by ultrasound and the AFC before and after LOD in order to study the ovarian reserve and the effect of drilling in Tables (3,5). Changes in the concentrations of AMH & FSH hormones th serum before and after perforation is also useful to know the reserve of the ovaries in Tables (4, 6).

Table 2: Characteristics of the menstrual cycle and clinical features of hyperandrogenism.

		Number	Percentage %
Irregular menstrual cycle	Oligomenorrhea	44	73.33%
	Amenorrhe	16	26.66%
Clinical Hyperandrogenism	Hirsutism	25	41.66%
	Acne Vulgaris	25	58.33%

Table 3: Pre-LOD ultrasound signs of ovarian reserve in the included women.

	Range	Mean±SD
Size of right ovary (cm ^{3})	9.5-14.8	12.12±1.62
Size of left ovary (cm^3)	9.4-14.21	11.89±1.58
AFC right ovary	12-19	14.53±1.89
AFC left ovary	11-18	14.29±1.72

Table 4: Pre-LOD biochemical markers of ovarian reserve in the included women.

	Range	Mean± SD
FSH (mIU/ml)	3.5-8.8	5.68±1.62
AMH(ng/ml)	5.4-15.21	11.89±1.98

A significant decrease in the size of the ovary and AFC was found in both sides when the post-LOD values were compared with the pre-LOD values (Table 5).

The level of FSH and AMH in the blood decreased significantly when comparing post-LOD values with pre-LOD values (Table 6).

There was a significant negative correlation between age and differences between pre-LOD and post-Lod. There was a non-significant correlation between age and BMI and other differences between the acoustic signs before and after LOD or biochemical signs of ovarian reserve (Table 7).

Table 5: Double differences between the signs of ultrasound before and after LOD in the ovarian reserve in the included women.

	Before LOD		After LOD		P
	Range	Mean±SD	Range	Mean±SD	P
Size of right ovary	9.5-14.8	12.12±1.62	6-11.2	8.65±1.54	P<0.01
Size of left ovary	9.4-14.21	11.89±1.58	6-11.1	8.21±1.33	P<0.01
AFC right ovary	12-19	14.53±1.89	6-12	8.12±1.75	P<0.01
AFC left ovary	11-18	14.29±1.72	6-12	8.1±1.43	P<0.01

Figure 1: The size of ovaries before and after drilling

Figure 2: AFC changes before and after LOD.

Table 6: Double differences between biochemical markers before and after perforation of ovarian reserve.

	Before LOD		After LOD		P
	Range	Mean±SD	Range	Mean±SD	
FSH (mIU/ml)	3.5-8.8	5.68±1.62	4-12.5	8.91±2.65	P<0.01
AMH (ng/ml)	5.4-15.21	11.89±1.89	2.3-10.9	4.82±2.45	P<0.01

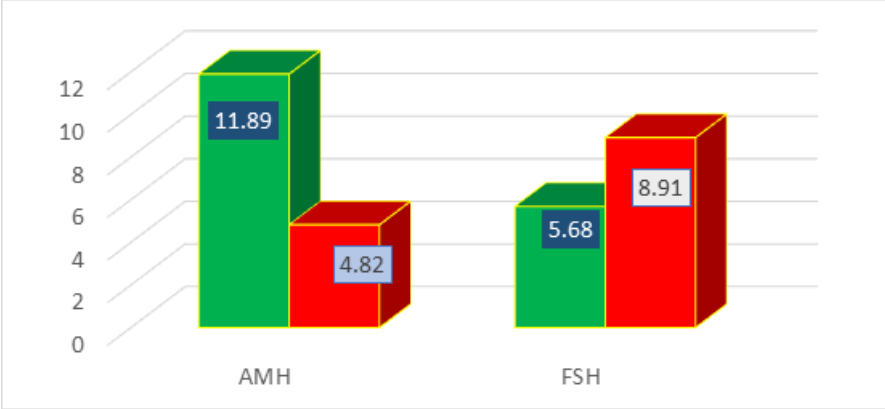

Figure 3: concentration changes of hormones AMH & FSH before and after LOD.

Table 7: Shows the correlation of IVF ovarian reserve variables with the demographic variables of the patient.

Variables	Correlation variables	Pearson	P value
The difference between the size of right ovary before and after drilling	Age	N	P>0.05
	BMI	N	P>0.05
The difference between the size of left ovary before and after drilling	Age	N	P>0.05
	BMI	N	P>0.05
The difference between AFC of the right ovary before and after drilling	Age	S	P>0.05
	BMI	N	P>0.05
The difference between AFC of the left ovary before and after drilling	Age	S	P>0.05
	BMI	N	P>0.05
The difference between FSH value before and after drilling	Age	N	P>0.05
	BMI	N	P>0.05
The difference between AMH value before and after drilling	Age	HS	P<0.01
	BMI	N	P>0.05

Table 8: Correlation of differences between Echographic and biochemical markers of ovarian reserve before and after LOD, with age, BMI and amenorrhea.

Variables	Correlation variables	Kendall's tau-b	P value
The difference between the size of right ovary before and after drilling	Obesity	N	P>0.05
	Amenorrhea	N	P>0.05
	Clinical Hyperandrogenism	N	P>0.05
The difference between the size of right ovary before and after drilling	Obesity	N	P>0.05
	Amenorrhea	N	P>0.05
	Clinical Hyperandrogenism	N	P>0.05
The difference between AFC of the right ovary before and after drilling	Obesity	N	P>0.05
	Amenorrhea	HS	P<0.01
	Clinical Hyperandrogenism	N	P>0.05
The difference between AFC of the left ovary before and after drilling	Obesity	N	P>0.05
	Amenorrhea	HS	P<0.01
	Clinical Hyperandrogenism	N	P>0.05
The difference between FSH value before and after drilling	Obesity	N	P>0.05
	Amenorrhea	N	P>0.05
	Clinical Hyperandrogenism	N	P>0.05
The difference between AMH value before and after drilling	Obesity	N	P>0.05
	Amenorrhea	N	P>0.05
	Clinical Hyperandrogenism	N	P>0.05

There was no significant association between obesity, clinical hyperandrogenism (hirsutism and / or acne vulgaris) and any of the differences between pre-and post-LOD values of ultrasound or biochemical markers of ovarian reserve. The presence of amenorrhea was significantly associated with a higher difference between the AFC before and after LOD of the right ovary (Table 8).

DISCUSSION

In the current study, the effect of laparoscopic ovarian drilling on ovarian reserve was examined in patients with

polycystic ovary syndrome and was also assessed by the size of the ovary, the number of antral follicles by transvaginal ultrasound, follicle-stimulating hormone in blood and Anti-Mullerian hormone levels before and after laparoscopic ovarian drilling on the second day of the menstrual cycle.

Weerakiet et al., 2007 showed that the ovarian reserve assessed by hormonal levels and ultrasound imaging, appears to be lower in LOD compared to the PCOS group. Women with PCOS with and without LOD had a significantly larger ovarian reserve than their age counterparts with normal ovulation[13] This is consistent with what we found in our study.

Kandil & Selim, 2005 reported that the number of antral follicles and the size of the assembled ovary showed significant decrease after bilateral drilling 16.5 follicles 1.3 versus 14.9 follicles 2.1; and 11.5 follicles 1.0 versus 10.3 follicles 1. 1 / mm3;. We concluded that a decreased ovarian reserve may occur after bilateral ovarian perforation, but not after Clomiphene Citrate induction of ovulation or unilateral drilling, and this is consistent with what we found in our study as well (14) and then Kandil et al., 2018 also confirmed this fact that although LOD is simple, safe and less invasive, it effects on the ovarian reserve. Multiple studies are warranted to confirm its efficacy as a second-line therapy in patients with CC resistance in PCOS patients[15] which we also recommended.

Kamal et al., 2018 showed a very significant decrease in AMH serum (p <.001) after LOD with a significant decrease in the indicators of OV, AFC and the blood supply (VI, FI and VFI) of the right and left ovaries (p <.05). LOD significantly reduced ovarian reserve (AMH, OV and AFC) and ovarian lymphocytic blood flow indices (VI, FI and VFI) with no noticeable correlation between AMH levels and Doppler indices. Which is also consistent with our study.

Meanwhile Farzadi et al., 2012 had a different opinion assessing serum levels of Anti-Mullerian hormone, Testosterone, Luteinizing hormone (LH) and the number of antral follicles before laparoscopic surgery and during a Week, 3 and 6 months after surgery.

Summery

Laparoscopic ovarian drilling did not change Anti-mullerian hormone, Testosterone and Luteinizing hormone levels in women with PCOS and therefore has no negative effects on the ovarian reserve.[16] In contrast to our study. The results of the current study are consistent with the Amer and Ledger (2009) study that examined the importance of measuring Anti-Mullerian hormone in women with LAB. The average plasma concentrations of AMH before treatment were 6.1 (1.0-21.0) and 5.7 (1.3-9.5) ng / mL in women with LOD and Clomiphene Citrate treatment respectively. Compared with unresponsive women [9.0 (6.1-17.1) ng / mL], the preoperative AMH hormone [5.6 (1.0-21.0) ng / mL] was also marginally lower in women who ovulated after LOD (number = 24). From characteristic curve tests, AMH was a useful indicator of the absence of ovulation after LODs with an area of less than 0.804 (P = 0.025). They found that the amount of pre-treatment AMH seemed to be a good indicator of LOD reactions in the ovary. The decrease in the AMH hormone to 65% of pre-LOD levels may result in small follicles that are the source of the AMH hormone. If this is correct, then the decrease in the AMH hormone is due to LOD. It can lead to an increase in follicular response from the beginning of the menstrual cycle to the generalization of FSH on the second day, which makes it easier for the dominant follicle to increase growth and selection. Literally, the postoperative decrease in the AMH hormone can be the result of atresia of many small molecules as part of the normal growth of the follicle that leads to ovulation. If that is real, it may be due to the ovulation according to LOD rather than the cause of the observed decrease in the AMH hormone. The hypothesis that decreased AMH hormone is the cause of ovulation was supported by the finding that the level of FSH on the second day after menstruation didn't elevate after LOD, which indicates that on the second day after the onset of menstruation, ovulation increased the sensitivity of the follicles to the FSH hormone.

CONCLUSION

It can be concluded the consequences that occur in women after polycystic ovary syndrome : the Anti-Mullerian hormone is significantly reduced. FSH on the second day of the onset of menstruation increases significantly. The size of the antral and ovarian follicle AFC decreases significantly.

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