Effects of Laparoscopic Ovarian Drilling on Restoration of Menstrual Cycles, Hormonal Profiles and Pregnancy Rate in Women with Polycystic Ovary Syndrome

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Abstract

One of the major cause of an ovulatory infertility is polycystic ovary syndrome with a multifactorial etiology. Laparoscopic ovarian drilling (LOD) is regarded as the method of choice for inducing ovulation in those not responding to oral ovulation induction with PCOS.

A prospective study was carried out for assessment of effects of LOD on menstruation, serum levels of hormones, and reproductive outcome including ovulation and pregnancy rate.

A total of 169 patients with an ovulatory infertility underwent LOD over a period of about two years. All patients assessed three times for clinical characteristics and serum hormone levels LH, FSH, testosterone, SHBG, prolactin and AMH. FAI and LH/FSH ratio calculated, first before the procedure, second within one week after and the last one after three months with the ovulation and pregnancy outcome follow up until six month.

The prevalence of irregular menstrual pattern was 89.3%, significantly ($P< 0.001$) decreased to 19.5% after the procedure with improvement of hirsutism, acne and scalp hair loss, there was a highly significant decrease in the serum levels of LH, testosterone, AMH, FAI and LH/FSH ratio ($P < 0.001$) and a highly significant elevation of serum SHBG and prolactin post-operatively, resumption of spontaneous ovulation of 56.2%, and the pregnancy rate of all the study group was 26%. In conclusion, LOD regarded as a method for improvement of the hormones, restoration of menstruation and increasing ovulation and pregnancy rate.

Keywords: *PCOS: Polycystic ovary syndrome; LOD: Laparoscopic ovarian drilling,*

Introduction

PCOS is defined as one of the most common female endocrinopathy affecting reproductive aged women around the world and a major cause of anovulatory infertility[1]. Has been defined using various criteria including menstrual irregularity, hyperandrogenism, and polycystic ovary morphology[2].Until recently no universaly accepted clinical definition existed for this condition[3]. The prevalence of PCOS, like that of any other complex multifactorial disorder, depends on which criteria are used for definition. Affecting 6-21%of reproductive aged women,depending on population studied and diagnostic criteria applied[4]. Gonadotrophin abnormalities in PCOS include LH hypersecretion due to increased LH pulse amplitude in 30-90% of women with PCOS[5]. FSH levels tend to be normal or reduced compared to regularly ovulating women, resulting in an increased LH/FSH ratio[6]. Laparoscopic ovarian drilling was first described by Gjonnaess in 1984[7]as an alternative to ovarian wedge resection to treat PCOS, to destroy the tissues that produce androgen and decrease conversion of androgens to estrogens peripherally. Specifically, serum levels of androgens and LH fall and level of FSH have been demonstrated to increase after LOD[8].These changes in hormones thought to convert the adverse androgen dominant intra follicular environment to estrogenic and

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normal ovarian pituitary feedback mechanism[9]. The aim of this study was to define the effectiveness of LOD on menstrual cycle regulation, normalization of the hormones after the surgery and the rate of ovulation and pregnancy in an ovulatory infertility PCOS patients who failed to respond to medical treatment.

Patients and Method

This was a prospective, cross sectional study carried out on 169 women confirmed to have PCOS based on Rotterdam criteria[10](at least two of the following criteria were present: oligo-anovulation, clinical or biochemical hyperandrogenism, and polycystic ovaries on ultrasonography who were clomiphene-resistant (failed to ovulate after maximum dose of clomophine for 3-6 cycles), allocated to undergo LOD, attending outpatient fertility clinic in Maternity Teaching Hospital, public maternity hospital in Erbil, Iraq. Patients were recruited from September, 2016 to November, 2018. All women enrolled were informed about the study with informed consent and they were subjected to detailed history and examination.

The age of the included subjects was between 20-39 years with no male or tubal factor infertility. Those with other etiologies of hyperandrogenism, AMH<4 ng/ml and FSH >12.5 mIU/ml wre excluded from the study.

Blood analyses were conducted three times first at the second to fourth day of the cycle without ovulation induction before, second within one week and the third one three months after the procedure for serum hormones including LH, FSH, total testosterone, SHBG, prolactin and AMH. Serum hormone levels were measured by Elecsys machine (Roche Diagnostics, Hitachi, Switzerland) which was used for determination of human LH, FSH, total testosterone, prolactin and SHBG levels. AMH was measured by Enzyme linked immunosorbent assay (ELISA) kit. LOD performed for both ovaries by or in the presence of the first author, using mono polar diathermy at 40 watts making 4 punctures in both ovaries for 4 seconds each, with follow up for ovulation and pregnancy rate up to 6 months

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 22). Numerical variables were summarized as means and standard deviations. Categorical variables were presented in form of frequencies and percentages. Paired t test was used to compare the means before and after laparoscopy. McNemar test was used to compare the percentages before and after the laparoscopy. A p value of ≤ 0.05 was considered statistically significant.

Results

The study included 169 infertile women with polycystic ovary syndrome (PCOS) not responding to medical treatment under went LOD we didn't observe any intraoperative or postoperative complications. The mean age$\pm$SD of the women was 29.63$\pm$4.5 years, ranging from 20 to 39 years, and the median was 29 years as presented in Table 1 which shows that the largest proportion (45.6%) of the sample lies in the age group 25-29 years. The duration of infertility of 65.7% of the sample was five or more years. The majority of the women(76.9%) had primary infertility. Regarding the menstrual pattern, it was irregular in 89.3% of the sample (mostly as oligomenorrhea) and more than half (59.2%) of the women were obese.

It is evident in Table 2 that the prevalence of the medical conditions mentioned in the table had significantly decreased after LOD except for acanthosis negricans (p=0.238). It is worth to mention that the prevalence of irregular menstrual pattern was 89.3% before laparoscopy, which significantly(p<0.001) decreased after laparoscopy to 19.5%.

Table 3 shows that the means of the following hormone had significantly (p<0.001) increased after one week of laparoscopy: LH, FSH, SHBG and prolactin, while there was a significant decrease in the means of the following: testosterone(p<0.001), AMH(p<0.001), FAI(p<0.001), and LH/FSH ratio (p=0.005). The same pattern can be observed after three months except for the LH where it is evident that its mean decreased to 7.17(p<0.001).Table 4 shows a significant decrease in the means of the following hormones three months after laparoscopy compared with the means of one week after laparoscopy: LH(p<0.001), testosterone (p=0.001), AMH(p<0.001), FAI (p<0.001), and LH/FSH ratio(p<0.001), while there was significant increase in the following means: FSH (p=0.001), SHBG(p<0.001), and prolactin (p=0.029).Finally, results showed that the ovulation rate was 56.2%, and the total pregnancy rate within six months was 26%.

Table 1. Basic characteristics of the study sample**.**

	No.	(%)	Mean	(+ SD)
Age (years)				
20-24	19	(11.2)		
25-29	77	(45.6)		
30-34	42	(24.9)		
35-39	31	(18.3)	29.63	(+4.5)
Duration of infertility (years)				
< 5	58	(34.3)		
≥ 5	111	(65.7)	5.6	(+2.28)
Type of infertility				
Primary	130	(76.9)		
Secondary	39	(23.1)		
Menstrual pattern				
Regular	18	(10.7)		
Irregular	151	(89.3)		
Pattern of irregular menstruation (n = 151)				
Oligomenorrhea	125	(74.0)		
Amenorrhea	26	(15.4)		
BMI (Kg / m2)				
< 25	17	(10.1)		
25-29	52	(30.8)		
≥ 30	100	(59.2)	30.02	(+4.00)
Total	169	(100.0)		

Table 2. Prevalence of some clinical features before and after the LOD

	Before N = 169		**After N = 169**		**p**
Medical conditions	No.	(%)	No.	(%)	
Irregular menstrual pattern	151	(89.3)	33	(19.5)	< 0.001
Hirsute	126	(74.6)	97	(57.4)	< 0.001
Acne	86	(50.9)	21	(12.4)	< 0.001
Acanthosis negricans	36	(21.3)	30	(17.8)	0.238
Greasy skin	116	(68.6)	27	(16.0)	< 0.001
Scalp hair loss	70	(41.4)	49	(29.0)	0.001

Table 3. Means of the hormones, before, one week, and three months after LOD

	Before		A week after			Three months after		
	Mean	(+SD)	Mean	(+SD)	P*	Mean	(+SD)	P**
LH	10.13	(+3.24)	11.44	(+3.20)	< 0.001	7.17	(+1.85)	< 0.001
FSH	4.58	(+1.13)	5.53	(+1.05)	< 0.001	5.88	(+1.25)	< 0.001
T	0.85	(+0.53)	0.65	(+0.37)	< 0.001	0.46	(+0.30)	< 0.001
SHBG	20.25	(+8.74)	28.50	(+13.76)	< 0.001	38.09	(+17.01)	< 0.001
AMH	7.45	(+1.74)	5.89	(+1.42)	< 0.001	4.75	(+1.23)	< 0.001
FAI	16.50	(+11.53)	8.94	(+5.89)	< 0.001	4.93	(+4.20)	< 0.001
Prolactin	19.98	(+9.55)	30.14	(+32.42)	< 0.001	35.06	(+22.33)	< 0.001
LH/FSH ratio	2.29	(+0.78)	2.12	(+0.67)	0.005	1.27	(+0.41)	< 0.001

*Comparison between the means before and one week after laparoscopy.

** Comparison between the means before and three months after laparoscopy.

Table 4. Means of the hormones, one week, and three months after LOD

	A week after		**Three months after**		
	Mean	**(+SD)**	**Mean**	**(+SD)**	**P**
LH	11.44	(+3.20)	7.17	(+1.85)	< 0.001
FSH	5.53	(+1.05)	5.88	(+1.25)	0.001
T	0.65	(+0.37)	0.46	(+0.30)	< 0.001
SHBG	28.50	(+13.76)	38.09	(+17.01)	< 0.001
AMH	5.89	(+1.42)	4.75	(+1.23)	< 0.001
FAI	8.94	(+5.89)	4.93	(+4.20)	< 0.001
Prolactin	30.14	(+32.42)	35.06	(+22.33)	0.029
LH/FSH ratio	2.12	(+0.67)	1.27	(+0.41)	< 0.001

Discussion

LOD regarded as one of the mode of PCOS treatment and this surgical treatment renovated by assumption of different surgical technique with use of different energy modalities to increase the success rate and minimize the complications[11].

In the current study menstrual cycle after LOD reported improvement from 89.3% to 19.5% this is in agreement with result of Seyam et al[12] and other studies[13,14]. Also hair suite, has a significant change and improvement in our study these results are in agreement with the study of Ashrafinia et al [13]. In another study [15] prevalence of hair suite from 60% after intervention become 40%. Also acne improvement from 50.9% to 12.4% these findings similar to results in many other previous studies [13,15], although many authors in their studies with laparoscopic surgery not reporting on this outcome and other clinical characteristics like acanthosis nigricans, greasy skin and scalp hair loss in our study($p=0.238$, $p<0.001$, $p=0.001$) respectively, more studies required to know about them after this modality of treatment.

Improvement in the endocrine data in our work is a remarkable observation are comparable with those previously reported showing a significant decrease in LH, testosterone, LH/FSH ratio[11,16,17], significant increase of LH($p<0.001$) few days post operatively in our study confirming report of the same phenomena by[16], this finding is against those found in previous studies[9,18]showed no change in the level of LH and testosterone weeks and months after operation. Significant increase in SHBG in the current work confirmed by study [19], furthermore another study demonstrated no change in this hormone[9].The obtained result in the present study confirmed previous report[17,20] of significant reduction of FAI.

Elevation of FSH is observed in the current and different studies[16,17], secondary increase in FSH is controversial, studies reported no change[11,13,21] although one study done by Elgafor demonstrated reduced FSH in his results[22] this variability in the results may be due to different age groups, sample size and technique in their study. Hormones produced by ovaries immediately after intervention restores feedback to the hypothalamus and pituitary lead to increased pituitary sensitivity and temporarily higher LH and particularly FSH levels.

Folliculogenesis initiation is induced by the increased FSH levels, in combination with decrease number of follicle and reduced intra-ovarian androgen levels [23].

As mentioned by Farzadi et al risk of ovarian tissue damage may not be significant statistically and decrease in AMH to the level of normality without any effects on the ovarian reserve[18].In our study decrease in AMH to a significant level but within normal range from mean of (7.45 before to 4.75 after the drilling) may be due to the significant increase in FSH and this may affect the negative feedback of the AMH secretion and also in the present study the mean AMH pretreatment was higher compared to the mean of AMH in[18].

The ovulation and pregnancy rate in the present study were the two main outcome measures (56.2% and 26%) respectively near to the results observed in the study [12]were(60% and 27.5%) respectively, these results in agreement with other studies[15,18].In several other studies described ovulation and pregnancy success results ranging from 26.5%-94%[9,11,24] and 20%-84%[9,16,25] respectively. In the present study despite of 56.2% ovulation rate but the conception rate was not high during the six months follow up compared to the most other studies may be related to the duration of follow up after the operation reaching up to 12-18 months and this explain the long term effects of LOD, number of punctures used in each study and the last may be due to hyper prolactinemia observed in our study in some of the patients and this is in accordance to the previous finding[26] while another study observed no change in this hormone[17], so follow up of prolactin level after ovarian surgery is important.

Conclusions

Thus LOD not only helps in regulating ovulation and enhancing conception rates but also helps much in regulation of menstruation and hormone level improvement for future steps of infertility management for those failed to conceive a period after LOD.

Conflicts of Interest : No conflicts of interest

Ethical Clearance: The Research Ethics Committee of HMU, College of Medicine, approved the study proposal**.**

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