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Comparative Study Between Lod Versus Medical Therapy In Polycystic-Ovarian Disorder

Obstetrics & Gynecology

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ABSTRACT

Background: Polycystic-ovary syndrome (PCOS) is the commonest endocrinopathy influencing reproducing age females, with occurrence ranged from 6-15% of population. PCOS is multifaceted with reproduction, metabolic and psychological conditions. It is marked by chronic anovulation, bio-chemical and/or clinical indication of hyper-androgenism and expanded polycystic ovary.

Aim of the work: To compare laparoscopy ovarian drilling (LOD) and medical therapy in PCOS regarding efficacy and safety of both interventions.

Patients and methods: This prospective interventional report was performed on total 100 infertile women diagnosed with PCOS attending the infertility outpatient clinic at Sayed Galal university hospital in period between April 2021 and September 2021 and cases have been allocated into 2 equal groups with random allocation to Group-A for Metformin, Clomid and Group-B for laparoscopic drilling with inclusion and exclusion criteria.

Results: There was no indication of a variance in gestational rate when LOD in comparison to medical therapy. There was indication of significantly lesser live birth rate subsequent to LOD in comparison to medical therapy. The rate of multi gestations was significantly lesser in the LOD arm in comparison with the medical therapy arm.

Conclusion: As evident from the current study, The LOD in PCOS cases can prevent or decrease the OHSS risk and the multi gestation rate persuaded by medical therapy and the cost effectiveness of procedure after an attractive treatment for PCOS cases. But, LOD may be measured as secondary treatment thereafter clomiphene Citrate therapy failures and /or resistant.

Keywords: *PCOS; Anovulation; Infertility; Clomiphene citrate.*

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INTRODUCTION

PCOS impacts about 6 to 15% of females of reproduction ages and comprise 72 to 84% of adults with hyper-androgenism. PCOS is multifaceted with reproduction, metabolic and psychological factors [1]. It is marked by chronic anovulations, bio-chemical and/or clinical evidence of hyper-androgenism and expanded poly-cystic ovaries [2].

Three universal conferences have advanced slightly dissimilar but overlying diagnosing criteria for females: the conference criteria of National Institutes of Health (NIH) (1990), the Rotterdam consensus criteria (2003), and the Androgen Excess-PCOS-Society consensus criteria (2006) [3].

The NIH criteria comprised hyper-androgenism, chronic anovulation, and exclusions of other reasons of these signs. The Rotterdam criteria are the widest and comprise the features of other descriptions. They permit PCOS to be detected with combinations of chronic anovulation and poly-cystic ovaries morphology (PCOSM) with no hyper-androgenism [4].

The PCOS is accompanying with cardiometabolic anomalies and maybe an elevated risk of cardio-vascular disorder. Among females with this condition, 50 -80 % are obesity cases [4].

Reduced glucose tolerance is found in 30-35 % of USA females with classic PCOS, and T2DM was found in 8-10 %; the danger of these disorders is impacted by age, adiposeness, and a DM family history. Females with the PCOS have subordinate HDL-C and higher triglyceride and LDL-C level than cases with no PCOS. Variances in LDL-C level are at minimum partly non-dependent of variances in BMI [5].

Sub clinical vascular disorder (e.g., reduced endothelial purpose, elevated carotid-artery intima–media breadth, and raised coronary-artery calcium score) was as well found in PCOS cases and seems to be at minimum partially non-dependent of adiposeness. While some

reports propose elevated frequency of cardio-vascular conditions between post-menopausal females with a supposed PCOS history, information are inadequate to determine rates of cardio-vascular conditions between pre-menopausal cases with this condition [6].

The danger of endometrial tumor is assessed to be 2.7-fold as high between PCOS cases as among cases with no PCOS, and the life-time risk of endometrial tumor between PCOS cases was found to be at most as 9 % [7].

Risk factors for endometrial tumor between PCOS cases comprise anovulation, obese, and insulin resistances; the danger connected to chronic anovulation mirrors extended estrogen-mediated mitogenic stimulations of the endometrium with insufficient progesterone exposures for endometrial differentiations. PCOS cases as well have elevated complication risks of gestation (e.g., gestation diabetes and pre-eclampsia), disruptive sleep apnea, and emotional distress [8].

PATIENTS AND METHODS

After ethical committee approval and written consents from the cases, this prospective randomized study was performed on total 100 infertile women diagnosed with PCOS attending the infertility outpatient clinic at Sayed Galal university hospital in period between April 2021 and September 2021 and cases were allocated into 2 equal groups with random allocation to Group-A for Metformin, Clomid and Group-B for laparoscopic drilling with the following criteria.

Inclusion criteria included cases with age between 19- 40 years, polycystic ovary (existence of ≥12-follicles in each ovary measurement 0.2–0.9 cm in diameter, and/or expanded ovarian size >10 mL), history of non-fertility for at minimum a year, irregular menstruation and cases giving consent for either types of intervention.

Exclusion criteria included disorders that can interrupt clinical and hormonal response, BMI >30 or <17, Drug resistance women, Absence of consent to be involved in the study, Previous exposure to ovarian hyper stimulation syndrome.

Study Procedures: All participants were submitted to the following:

History: including

Personal history including: Name, Age, marital state, address

Menstrual history: including age of Menarche, menstrual disturbance, dysmenorrhea, related symptoms.

Present history: of chronic disorders and medication.

Past history of HTN, DM.

Family history of similar condition or diabetes.

History of allergy to any medication.

Surgical history of operation, laparoscopic interference, treatment of hirsutism by Laser.

Examinations:

General examinations: BMI, underweight if the case BMI from 15 to 19.9 kg/m2, normal if between 20 and 24.9, over-weight between 25 and 29.9, and between 30 and 35 or more.

Abdominal and local clinical examination

Laboratory investigation:

Complete blood picture (CBC): Hb (%), RBCs, WBCs, platelets.

A 5-ml of venous blood collected from every case for determination of FSH, E2, LH, DHEA, free and testosterone and prolactin by means of ELISA before and 6 mths after the interventions.

Procedure:

After review of all inclusion and exclusion criteria, the 100 eligible cases will randomly divided into 2 equal groups (n=50) with random allocation, for treatment with metformin, clomid or LOD.

Group-A for Metformin, Clomid and Group-B for laparoscopic drilling.

A 5-mL sample of venous blood will be drawn from all of the cases for measurement of FSH and LH using enzyme-linked immunosorbent assay (ELISA) before and 6 months after the intervention

follow up by ultrasound (measurement of endometrial thickness, antral follicle count) .

Cases will be requested to document their menstrual cycle and bleeding days for 6 mths post intervention.

Ages and BMI of the cases will be collected.

Cases in the metformin therapy group will take an everyday dosage of 1500 gm of metformin for 6 mths .

Clomiphene citrate should be stared with dosage of 50 mg for 5-day, taken from 5^{th} to 9^{th} day of the cycle for 6 monthes. May give Clomiphene citrate up to 250 mg.

Cases in treated by LOD will undergo laparoscope underneath overall anesthesia. The two ovaries will be checked for indications of PCOS. The ovarian tendon will be held by Babcock forceps and ovarian boring will be performed by means of uni-polar diathermy .

The boring needle is utilized to enter the ovarian capsule at right angle to a typical depth of 0.8 cm with a 60 Watt cutting power, and coagulated with a 40-Watt power if hemorrhage happened. Drilling will be accomplished 4 time in every ovary for 2 to 4 sec each time. The ovaries will cool with saline.

Outcome measures: The primary outcomes measures were menstrual orderliness

Ethical Considerations: The patient data were anonymous. Data presentation were not be by the patient's name but by diagnosis and patient confidentiality was protected. An informed agreement was collected from all cases, it win Arabic language and confirmed by date and time. confidentiality was preserved by assigning a number to cases initials and only the investigator knew it

Conflict of interest: the candidate declared that there is no conflict of interests and the cost of the research was paid by the candidate.

Statistical analysis: Analysis is to be performed using SPSS for windows v20.0, Data to be introduced as range, mean and SD (for numeric parametric data); range, median and IQR (for numeric non-parametric data); or numbers and percentages (for categorical data). Variance amid 2 non-dependent groups is to be investigated by means of in-dependent student's t-testing in addition to the mean change and its 95% CI (for numeric parametric data); or chi-squared testing in addition to the RR and its 95% CI (for categorical variables). Binary logistic regression analysis is to be performed for estimating the association between good/poor response and the measured variables ROC curves are to be constructed for estimating the validity of measured variables as predictors of good or poor response validity is to be presented in terms of sens., spec., PPV and NPV and their corresponding 95% C. result significant at p<0.05.

RESULTS

Table (1) shows that both groups were similar regarding age. The ages mean of group-A was 27.88± 3.76 (22 to 35) years, the age of group-B was ranged from 21 to 33 years with mean27.24± 3.68 years with nonsignificant change among both groups.

Table (2) shows that nonsignificant change was found among the study groups as regard weight (p value= 0.590), height (p value= 0.986) or BMI (p value=0.777). 60% females in group-A and 56% women in group-B were overweight.

Table (3) shows that a nonsignificant change was found among the study groups regarding duration of infertility (p= 0.139). The majority of cases in both groups (64% in group-A & 60% in group-B) had primary infertility with nonsignificant change (pvalue= 0.680).

Table (4) shows that a significant reduction was found in serum LH levels pre and post medical therapy (p<0.001). Also, a significant reduction was found in s.LH levels pre and post-LOD (p<0.001). In contrast, a nonsignificant change was found between group-A & B regarding LH level neither before (p= 0.230) nor after intervention (p= 0.363).

Table (5) shows that a significant reduction was found in median levels serum FSH pre and post medical therapy (pvalue=0.003) but there was nonsignificant variance in s.FSH pre and post LOD (p value=0.890). In contrast, there was nonsignificant variance among group-A & B regarding FSH level neither before (p= 0.117) nor after intervention (p= 0.347).

Table (6) shows that a significant variation was found in LH/ FSH ratio after medical therapy (p<0.001) in comparison with before medical therapy. Also, a significant alteration was found in LH/ FSH ratio pre and post LOD (p value<0.001) regarding LH/ FSH ratio. In contrast, a nonsignificant change was found among A & B-groups regarding LH/ FSH ratio neither before (p= 0.789) nor after intervention (p= 0.852).

Table (7) shows that a significant reduction was found prolactin level after medical therapy (p<0.001) in comparison with before medical therapy. Also, a significant reduction was found in prolactin level pre and post LOD (p= 0.02). Instead, a nonsignificant change was found between group-A & B regarding prolactin level neither before (p= 0.073) nor after intervention (p= 0.825).

Table (8) shows that a significant rise was found in E2 level after medical therapy (p value<0.001) in comparison with before medical therapy. Also, a significant rise was found in E2 level pre and post LOD (p value<0.001). In contrast, there was nonsignificant change was found between group-A & B regarding E2 level neither before (p= 0.679) nor after intervention (p= 0.524).

Table (9) shows that a significant reduction was found in testosterone total level after medical therapy (pvalue<0.001) in comparison with before medical therapy. Also, a significant reduction was found in testosterone total level pre and post LOD (p<0.001). In contrast, a nonsignificant change was found between group-A & B regarding testosterone total level neither before (p= 0.304) nor after intervention (p= 0.756).

Table (10) shows that a significant reduction was found in testosterone free level after medical therapy (p<0.001) in comparison with before medical therapy. Also, a significant reduction was found in testosterone free level pre and post LOD (p<0.001). In contrast, a nonsignificant change was found between group-A & B regarding testosterone free level neither before (p= 0. 767) nor after intervention (p= 0. 730).

Table (11) shows that a significant reduction was found in DHEA-S level after medical therapy (p<0.001) in comparison with before medical therapy. Also, a significant reduction was found in DHEA-S level pre and post LOD (p<0.001). In contrast, a nonsignificant change was found between group-A & B regarding DHEA-S level neither before (p= 0. 879) nor after intervention (p= 0. 730).

Table (12) shows that both groups were similar as regard pregnancy rate. A nonsignificant change was found among the study groups (p value= 0.198).

Table (13) shows that both groups were similar as regard complication. It was observed significant increase in the incidence of pain in group-B (LOD) in comparison with group-A (p= 0.05). Besides, there wincrease in the incidence of bleeding and infection in group-B (LOD) in comparison with group-A but didn't reach the significant level.

Variable		Group-A (N=50)		Group-B (N=50)		Test value	P-value	Sig.
		No.	%	No.	%			
Age (years)	< 25	9	18.0%	13	26.0%	X^2= 3.33	0.189	NS
	25 - 30	23	46.0%	27	54.0%			
	> 30	18	36.0%	10	20.0%			
	Mean± SD	27.88± 3.76		27.24± 3.68		^{Z}MWU= 0.782	0.434	NS
	Median (IQR)	27.5 (25.0 - 31.0)		27.5 (24.0 - 31.0)				
	Range	22.0 - 35.0		21.0 - 33.0				

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing

Table 1: Comparing among the study groups as regard age

Variable		Group-A (N=50)		Group-B (N=50)		Test value	P-value
		No.	%	No.	%		
Weight (kg)	Mean± SD	69.64± 9.22		68.98± 9.64		^{Z}MWU= 0.539	0.590
	Median (IQR)	68.5 (63.0 - 77.50)		68.0 (62.0 - 77.0)			
	Range	56.0 - 91.0		54.0 - 91.0			
Height (cm)	Mean± SD	162.98± 5.67		163.22± 6.16		^{Z}MWU= 0.017	0.986
	Median (IQR)	162.0 (159.0 - 166.0)		162.5 (158.0 - 169.0)			
	Range	154.0 - 176.0		155.0 - 176.0			
BMI (kg/m2)	Mean± SD	26.16± 2.58		25.85± 2.65		^{Z}MWU= 0.283	0.777
	Median (IQR)	27.29 (23.73 - 28.57)		26.03 (23.34 - 28.30)			
	Range	21.99 - 29.47		21.15 - 29.62			
	Normal	20	40.0%	22	44.0%	X^2= 0.164	0.685
	Overweight	30	60.0%	28	56.0%		
	Obese	0	0.0%	0	0.0%		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing

Table 2: Comparing among the study groups as regard weight, height and BMI

Variable		Group-A (N=50)		Group-B (N=50)		Test value	P-value
		No.	%	No.	%		
Duration of infertility (years)	Mean± SD	4.8± 2.5		4.2± 2.4		^{Z}MWU= 1.48	0.139
	Median (IQR)	4.0 (3.0 - 6.0)		3.0 (2.0 - 5.0)			
	Range	2.0 - 10.0		2.0 - 10.0			
Type of infertility	Primary	32	64.0%	30	60.0%	X^2= 0.170	0.680
	Secondary	18	36.0%	20	40.0%		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing

Table 3: Comparing among the study groups as regard type and duration of infertility:

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
LH (mIu/ml)	Before	Mean± SD	12.05± 3.69	11.24± 3.42	^{Z}MWU= 1.2	0.230
		Median (IQR)	12.35 (9.10 - 14.81)	10.22 (8.60 - 13.20)		
		Range	6.10 - 20.20	6.10 - 20.20		
	After	Mean± SD	6.92± 1.81	6.63± 1.57	^{Z}MWU= 0.910	0.363
		Median (IQR)	6.70 (5.30 - 8.10)	6.03 (5.6 - 8.0)		

		Range	4.20 - 10.50	4.20 - 10.50	
		Test value	6.155	6.156	
		P-value	<0.001	<0.001	

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing.

Table 4: comparing amid the studied groups in levels of LH and difference in LH in each group-Pre and post intervention:

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
FSH (mIu/ml)	Before	Mean± SD	6.33± 1.44	5.86± 1.20	^{Z}MWU= 1.566	0.117
		Median (IQR)	6.30 (5.40 - 7.40)	6.11 (4.70 - 6.70)		
		Range	3.90 - 9.15	4.10 - 8.80		
	After	Mean± SD	6.06± 1.26	5.85± 1.03	^{Z}MWU= 0.941	0.347
		Median (IQR)	5.90 (5.10 - 6.90)	5.90 (4.90 - 6.60)		
		Range	3.90- 8.90	4.10 - 8.40		
	Test value		2.984	0.138		
	P-value		0.003	0.890		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing..

Table 5: Difference between the two studied groups in FSH level and its difference in each group-Pre and post intervention.

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
LH/FSH ratio	Before	Mean± SD	1.89± 0.35	1.91± 0.40	T= 0.269	0.789
		Median (IQR)	1.96 (1.62-2.10)	1.93 (1.53 - 2.20)		
		Range	1.14 - 2.60	1.07 - 2.60		
	After	Mean± SD	1.14± 0.17	1.13± 0.17	T= 0.187	0.852
		Median (IQR)	1.13 (1.03 - 1.30)	1.15 (1.00 - 1.24)		
		Range	0.74- 1.46	0.74 - 1.46		
	Test value		21.22	15.84		
	P-value		<0.001	<0.001		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing..

Table 6: Difference between the two studied groups in LH/FSH ratio and its difference in each group-Pre and post intervention:

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
Prolactin (ng/ml)	Before	Mean± SD	13.52± 5.04	15.28± 5.16	^{Z}MWU = 1.793	0.073
		Median (IQR)	13.2 (9.0 - 16.0)	15.85 (12.00- 19.30)		
		Range	6.0 - 25.0	6.50 - 25.0		
	After	Mean± SD	17.70± 4.17	17.47± 5.79	^{Z}MWU = 0.221	0.825

	Median (IQR)	18.0 (14.0- 20.0)	18.20 (13.2 - 23.0)	
	Range	8.0- 26.7	6.0 - 26.0	
	Test value	4.37	2.33	
	P-value	<0.001	0.020	

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing.

Table 7: Difference between the two studied groups in prolactin level and its difference in each group-Pre and post intervention.

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
E2 (ng/ml)	Before	Mean± SD	29.25± 8.50	30.46± 15.21	^{Z}MWU= 0.414	0.679
		Median (IQR)	29.0 (22.00 - 34.80)	26.85 (22.00- 32.80)		
		Range	18.00 - 53.00	18.0 - 95.0		
	After	Mean± SD	37.25± 9.26	39.33± 14.90	^{Z}MWU= 0.637	0.524
		Median (IQR)	33.0 (30.0- 41.0)	32.5 (32.0 – 41.3)		
		Range	30.0- 41.0	30.0 - 100.0		
	Test value		5.19	4.814		
	P-value		<0.001	<0.001		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing.

Table 8: Difference between the two studied groups in E2 level and its difference in each group-Pre and post intervention.

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
testosterone total (ng/ml)	Before	Mean± SD	0.37± 0.11	0.46± 0.39	^{Z}MWU = 1.028	0.304
		Median (IQR)	0.39 (0.31 - 0.44)	0.40 (0.31 - 0.49)		
		Range	0.10 - 0.54	0.21 - 2.29		
	After	Mean± SD	0.16± 0.07	0.16± 0.07	^{Z}MWU = 0.311	0.756
		Median (IQR)	0.17 (0.11 - 0.20)	0.13 (0.09 - 0.22)		
		Range	0.07 - 0.32	0.07 - 0.31		
	Test value		6.157	6.159		
	P-value		<0.001	<0.001		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing.

Table 9: Difference between the two studied groups in testosterone total level and its difference in each group-Pre and post intervention:

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
Testosterone free (pg/ml)	Before	Mean± SD	5.28± 1.23	5.21± 1.09	^{Z}MWU = 0.297	0.767
		Median (IQR)	5.81 (4.80 - 6.04)	5.38 (4.50 - 6.16)		
		Range	2.01 - 6.90	2.90 - 6.71		
	After	Mean± SD	2.41± 0.57	2.52± 0.75	^{Z}MWU = 0.345	0.730
		Median (IQR)	2.16 (1.98 - 2.98)	2.15 (1.98 - 3.04)		
		Range	1.48 - 3.90	1.48 - 4.30		
	Test value		6.155	6.156		
	P-value		<0.001	<0.001		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing.

Table 10: Difference between the two studied groups in testosterone free level and its difference in each group-Pre and post intervention.

			Group-A (N=50)	Group-B (N=50)	Test value	P-value
DHEA-S (µg/dl)	Before	Mean± SD	190.89± 34.27	193.13± 31.68	^{Z}MWU = 0.152	0.879
		Median (IQR)	196.0 (4 169.00 - 207.30)	195.0 (176.0 - 209.0)		
		Range	120.30 - 270.40	112.0 - 270.4		
	After	Mean± SD	181.16± 32.79	179.67± 27.48	^{Z}MWU = 0.345	0.730
		Median (IQR)	185.5 (153.0 - 199.0)	184.5 (167.0 - 195.0)		
		Range	110.12 - 254.90	108.0 - 254.90		
	Test value		4.686	5.218		
	P-value		<0.001	<0.001		

Significant at p<0.05, highly significant p<0.001, IQR= Interquartile range, ZMWU = Mann- Whitney U testing, X2= Chi- Square testing.

Table 11: Difference between the two studied groups in DHEA-S level and its difference in each group-Pre and post intervention.

Variable		**Group-A (N=50)**		**Group-B (N=50)**		**Test value**	**P-value**
		No.	%	No.	%		
pregnancy rate	No	37	74.0%	0.198	62.0%	X^2= 1.654	0.198
	Yes	13	26.0%	19	38.0%		

Significant at p<0.05, highly significant p<0.001, X2= Chi- Square test.

Table 12: Comparing among the study groups as regard pregnancy rate.

Complications		Group-A (N=50)		Group-B (N=50)		Test value	P-value
		No.	%	No.	%		
Bleeding	No	50	100.0%	45	90.0%	X^2= 5.26	0.056 FET
	Yes	0	0.0%	5	10.0%		
Pain	No	46	92.0%	39	78.0%	X^2= 3.84	0.05
	Yes	4	8.0%	11	22.0%		
Infection	No	50	100.0%	46	92.0%	X^2= 4.17	0.117 FET
	Yes	0	0.0%	4	8.0%		

Significant at p<0.05, highly significant p<0.001, X2= Chi- Square test. FET= Fischer Exact Testing

Table 13: Comparing among the study groups as regard complications.

DISCUSSION

PCOS is a shared disorder between females of reproduction ages, with an occurrence of 5- 15% in populace universally [9].

PCOS is an endocrinal disorder, which is varied in clinical presentations with collection of symptoms and signs which comprise menstrual turbulences fluctuating from oligomenorrhoea to amenorrhea, existence of acne and hirsuteness, obese. Elevated testosterone levels, elevated L.H, IR, lipid profile variations and poly-cystic ovaries in US scans are the bio-chemical and image features seen with condition [10].

PCOS cases having an elevated incidence of atherosclerosis and cardio-vascular disorder, promoted from calorie restrictions even if it isn't associated by weight losing [11].

Low dosage collective oral contraceptive pill play to reason decreases of LH secretions, inhibitions of ovaries and adrenal androgen making and decrease of the free testosterone fraction minor to elevated SHBG productions in liver [12].

Progestin existing in oral contraceptive pills has defensive effects on the endometrium. Oral contracepting pills are measured the 1st line treatment in PCOSs, who need to not get gestation [13, 14].

Insulin sensitizing medication, Metformin is nowadays considered as 1st line treatment in PCOS cases. It decreases hyper-androgenemia and reinstates ordinary secretions of LH. Long-term administrations of Metformin are found to accomplish reductions in free as well as bound testosterone [13, 14].

In ovulation inductions Clomiphene citrate is the medication of choice and 1st line therapy. It is non-steroidal choosy estrogen receptor modulator. It is frequently given in 5 mg orally for 5 successive days starting from 2nd to 6th or 5th to 9th day. Gonadotropin to be utilized in clomiphene resistant/failures. Injectable preparations of Human Menopausal Gonadotropin comprising FSH (75-IU) and LH (75-IU) or we may as well utilize pure FSH (follitropin) [15].

Operative intervention of PCOS previous comprised bi-lateral ovarian wedge resections, resulting in resumptions of ordinary menstrual cycle and ovulation. In early series by Stein Leventhal the gestation rate was 85 %. Though following studies have reported lesser success rate and elevated risk of peri-ovarian adhesion [15].

Development in laparoscopy have led to attention in ovarian drilling. Several reports have focused in the success of utilizing technique of electrocautery and laser and all have revealed equal rate of success with recommencement of ovulation and menstrual cyclicity in about 80 % of cases, and 84% of cases were still ovulating 20-yrs postoperatively and that androgen levels remained regulated [16].

Possible benefit of laparoscopic method comprised longstanding result and repetitive ovulatory influence from single intervention. LOD is an operative intervention that could induce ovulation in cases with PCOS who haven't responses to weight losing and fertility medications. LOD is an operative technique in cases with clomiphene citrate resisting PCOS. It results in significant failure in testosterone levels, LH/FSH ratio with significant rise in FSH in responders as well as non-responders of clomiphene citrate [17].

So, the current study aimed to compare LOD and medical therapy in PCOS regarding ovulation of both interventions.

This randomized study was performed in the obstetrics and gynecology dep. at Al-Azhar University hospitals. The study included 100 women of polycystic ovary. Cases were allocated into 2 equal groups with random allocation. Group-A comprised cases on for Metformin and Clomid and Group-B for laparoscopic drilling.

The basic data of our study cases showed insignificant differences as regards age, weight, height, BMI, type and duration of infertility (p value >0.05) which indicate good randomization of the study groups.

In current work performed a comparison between the outcomes after medical and LOD interventions in PCOS. Both medical and operative interventions are effective in the improvement of ovulation and regularizing the menstrual cycles, androgen levels and insulin levels.

In the current work, a nonsignificant change was found between group-A & B regarding LH level neither before (p= 0.230) nor after intervention (p= 0.363). while a significant reduction was found in serum LH levels pre and post medical therapy (p<0.001). Also, a significant reduction was found in serum LH levels pre and post LOD (p<0.001).

Also, in the current report, a significant reduction was found in median levels serum FSH pre and post medical therapy (p=0.003). but a nonsignificant alteration was found in s.FSH levels pre and post

LOD (p=0.890). In contrast, a nonsignificant change was found between group-A & B regarding FSH level neither before (p= 0.117) nor after intervention (p= 0.347).

This is in agreement with Verma and Srivastava, [17] study which found that impacts on ovulation post medical and operative treatments was significant in the study groups separately but variance among group-A and -B was nonsignificant [17]

On contrary to our findings, Onofriescu et al. [18] revealed a significant increase of FSH levels post LOD during the follow up period. The cause of elevation could be because of long period of following-up can be >12 months, different technique of LOD, they had performed their investigations on various age groups, various patients' number and criteria [18].

Regarding LH/ FSH ratio, the current work revealed that a significant reduction was found in LH/ FSH ratio after medical therapy (p<0.001) in comparison with before medical therapy. Also, a significant reduction was found in LH/ FSH ratio pre and post LOD (p<0.001) with nonsignificant change among A & B groups regarding LH/ FSH ratio neither before (p= 0.789) nor after intervention (p= 0.852).

Our findings were agreed with Farquhar et al, Gomel V et al, Gabor Kovacs et al, Palomba S et al, and Saleh AM et al, who revealed no change in ovulation post medical and operative intervention [14, 15, 16, 19].

Paramu, [20]. report showed that a significant reduction was found in s.testosterone, LH, and LH:FSH ratio, at 7th day post LOD.

Response of treatment on androgen level showed significant decrease in testosterone total level after medical therapy and after LOD (p<0.001) with nonsignificant change among groups regarding testosterone total level neither before (p= 0.304) nor after intervention (p= 0.756).

This is in the same line with Verma and Srivastava,[17] study in which Hyperandrogenemia showed significant decrease after medical and surgical treatment but statistical association amid group-A and -B post intervention was nonsignificant.

The findings were comparable to the report of Farquhar et al, Gabor Kovacs et al, Homed HO et al who revealed a comparable impact on androgen levels post medical and operative interventions [14, 15, 16, 19].

Our study results about LOD were similar to a recent study which included 50 cases, among them 31(64.60%) menstruated consistently and 26 (54.20%) ovulated impulsively and 9(18.80%) of them consider impulsively post LOD within 3 mths post operatively. The hormones serum level, pre, 1 day post and 3 mths postoperatively, for FSH (IU/L) were 5.2±1.7, 6.6±2.0 and 7.2±2.0, (p= 0.000), resp. For the LH (IU/L) were 10.2±21, 10.7±4.5 and 7.2±2.2, (p =0.000), resp. For the testosterone level (ng/ml) was 1.16±0.7, 0.44±0.2 and 0.34±0.1, (P = 0.000), resp [21].

Effects of treatment on conception were comparable in our study with respect to pregnancy rate (26%) with medical therapy and (38%) with LOD. A nonsignificant change was found among the study groups (p= 0.198).

In agreement with another study in which impacts of intervention on conceptions was as well significant in the two the group separately, but association among group-A and -B was nonsignificant [17].

The results were comparable with Bayram et al, [(22)]. Pirwany et al, [(23)]. Palomba et al, [19]. Hamed et al [24] who revealed no change in conceptions post medical and operative interventions [19. 22, 23, 24].

A long-term following-up by Naether et al. described a total of 211 gestations, counting 50 % impulsive gestations [25].

Malkawi et al. couldn't prove any significant change among the treatments with metformin 2×850 mg every day and LOD as regard ovulation rate (70.70 versus 83.50%) and gestation rate (64.10 versus 59.80%) [25].

Additional report matched a following-up of 8 yrs post ovarian drilling via thermo-coagulation in 116 cases, with 34 cases post hormonal therapy. Around 31 cases of drilling and 7 controls were lost to following-up, the others were followed for 3 to 9 yrs. At the end of the follow-up period, cases post drilling exhibited ovulatory cycles in 55.0% in comparison with 8% pre operation, ovulatory cycle rate of the controls was 26.0%. Throughout the 1st year post-operatively, 49.0% of the cases get gravid. In total, 56.0% of cases post-operatively had live births in comparison with 44.0% of hormonal therapy [27].

This is in line with other reports that have revealed that ovulation and gestation rates in cases treated with uni-lateral LOD of 30–90 % and 13–88 %, resp, based on the following-up retro. Variations as regard the re-productive outcome is frequently because of the haeterogeneity of the study samples and the dissimilar methods utilized [28, 29].

In another report, ovulation and gestation rates in cases treated using uni-lateral LOD are (67.70 and 54.80 %, resp.). ovulation and gestation rates were improved in the uni-lateral drilling cases in comparison to metformin that can be understood by the excessive decrease of luteinizing hormones that is detected in LOD, which has an significant function in reinstating ordinary intra-ovarian paracrine signaling and decreasing local androgen productions [30].

This study reported a significant reduction DHEA-S and prolactin levels post medical therapy in comparison with pre medical therapy. As well, a significant decrease was found in DHEA-S and prolactin levels pre and post LOD with nonsignificant change amid group-A & B regarding prolactin level neither before nor after intervention.

This is similar to case report in which the patient of similar twin sisters presented with signs PCOS. But, on evaluations, they were as well revealed to have hyper-prolactinemia, which was established on repetitive sampling. There was no medications intakes to clarify secondary hyper-prolactinemia, no clinical or bio-chemical evidences of acromegaly, and no clinical or radiologic indication of mass lesions in the sellar area. Both hyper-prolactinemia and PCOS may result in androgen excessing and

existing with anovulation. While androgen excessing in PCOS can be of ovarian or adrenal origins, the hyper-androgenic state in hyper-prolactinemia is maybe intermediated by elevated adrenal androgen productions, which advances with dopamine agonist therapy. Case T was manged with Metformin (1g a day), whereas case S was managed with dopamine agonist Cabergoline (0.5 mg weekly). Both cases advised on nutritional and life-style changes to lose weights. There was significant decrease in prolactin levels thereafter the usage of metformin and weight decrease. Bio-chemistry showed normalizations of prolactin, testosterone and DHE In case S, whereas all these factors sustained to continue elevated in case T [31].

The reduction of s.prolactin post LOD revealed in our results came in agreement with the study performed by Elmashad, [32] Abuelghar et al, [33] Elnaaggar & Abo Elwan, [34] observed reduction in s.Prolactin level post LOD [32, 33, 34].

We found that a significant rise was found in E2 level post medical therapy (pvalue<0.001) in comparison with before medical therapy. Also, a significant rise was found in E2 levels pre and post LOD (p<0.001). A nonsignificant change was found between group-A & B regarding E2 level neither before (p= 0.679) nor after intervention (p= 0.524).

Our study results regarding LOD was similar to another study which included fifty infertile women diagnosed with PCOS attending the infertility outpatient clinic at Syed Galal university hospital were selected for prospective interventional study. Hormonal assessment for FSH, LH, E2, prolactin and androgens (total & free test oster on and DHEA-S) were done before LOD (LOD), and 3month after LOD. Main outcome measures were changes in hormonal profile including LH, LH/FSH ratio, E2, Prolactin and androgens (total &free testosterone and DHEA-S). LOD was successfully used with no any complications 3 mths postoperatively. Throughout the following up, levels of serum prolactin and E2 have significantly increased. (LH, LH/FSH ratio, total & free Testosterone and DHEA-S) have significantly reduced and FSH level persisted unaffected postoperatively [(35)]. This may be due to operative stress that causes an elevated prolactin level which is a common finding during and after operation with the peak of prolactin levels.

In this study, both groups were similar as regard complication. It was observed significant increase in the incidence of pain in group-B (LOD) in comparison with group-A (p= 0.05). Besides, there wincrease in the incidence of bleeding and infection in group-B (LOD) in comparison with group-A but didn't reach the significant level.

In agreement with a prospective parallel randomized double-blind placebo-controlled trial, Palomba et al. matched metformin therapy for at most of 6 mths, as well as a 6 mths following-up post LOD. No change in the hemorrhage pattern was found [19].

CONCLUSION

From the current work results we reported that, medical therapy and LOD are similarly effective in management the cases of PCOS. Results of both the treatments are analogous in this work. But medical therapy must be the 1st line treatment, it has significant advantage for usage in OPD, cost effective, no hospitalization and suitability to the cases. But, when medical therapy fails on cases with medical therapy resistance, LOD might be favored.

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