ORIGINAL RESEARCH

Evaluation of effect of oral contraceptive pills (OCP) and metformin on metabolic and endocrine parameters in PCOS

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ABSTRACT
Background: PCOS, or polycystic ovarian syndrome, is a prevalent endocrine disorder affecting women in the reproductive age range. The present study was conducted to evaluate the effect of oral contraceptive pills (OCP) and metformin on metabolic and endocrine parameters in PCOS. **Materials & Methods:** The study was conducted at Nalanda Medical College and Hospital, Patna from December 2021 to December 2023. 80 female patients with PCOSwere divided into 2 groups. Group I (40) received lifestyle intervention and 500mg oral metformin and group II received lifestyle intervention, and was given OCP (fixed dose combination of ethinyl estradiol 50 micrograms and cyproterone acetate 2 milligrams per day for six months). Parameters were evaluated at baseline, 2nd month and 6th month. **Results:** At baseline, 2 months and 6 months mean weight (kg) in group I was 58.2, 57.6 and 54.1 and in group II was 50.3, 51.3 and 52.8 respectively. BMI (kg/m2) in group I was 29.4, 28.1 and 26.4 and in group II was 24.8, 25.3 and 26.1. The mean waist/hip ratio in group I was 0.92, 0.91 and 0.89 and in group II was 0.80, 0.82 and 0.84 respectively. The difference was significant (P< 0.05). At baseline, 2 months and 6 months, FBS (mmol/L) in group I was 5.6, 4.4 and 4.9 and in group II was 4.2, 4.3 and 4.8 respectively. PPBS (mmol/L) in group I was 5.8, 5.4 and 5.1 and in group II was 5.1, 5.3 and 5.7. HbA1c (%) in group I was 7.4, 7.2 and 6.8 and in group II was 5.7, 5.4 and 5.2. Total cholesterol (mmol/L) in group I was 5.6, 5.8 and 5.9 and in group II was 5.3, 5.6 and 5.1. TG (mmol/L) in group I was 2.7, 2.8 and 2.5 and in group II was 2.2, 2.1 and 2.1. HDL (mmol/L) in group I was 0.90, 0.92 and 0.94 and in group II was 1.2, 1.4 and 1.5. LDL (mmol/L) in group I was 4.5, 4.6 and 4.6 and in group II was 3.2, 3.4 and 3.4 respectively. The difference was significant (P< 0.05). At baseline, 2 months and 6 months, the mean TSH (IU/L) in group I was 3.7, 3.9 and 3.6 and in group II was 3.6, 3.5 and 3.6 respectively. Testosterone (mmol/L) in group I was 2.6, 2.4 and 2.2 and in group II was 2.9, 2.9 and 2.2. Prolactin (ng/mL) in group I was 19.4, 19.2 and 18.5 and in group II was 18.6, 18.4 and 18.5 respectively. **Conclusion:** For PCOS patients, oral metformin and oral contraceptive tablets are both effective therapeutic options that significantly reduce menstruation symptoms within six months of starting therapy.
Keywords: polycystic ovarian syndrome, Prolactin, Testosterone

INTRODUCTION

PCOS, or polycystic ovarian syndrome, is a prevalent endocrine disorder affecting women in the reproductive age range.[1,2]Its multifactorial and polygenic genesis makes it a difficult endocrine disorder.[3] Hyperandrogenism and insulin resistance are traits of PCOS. A condition known as insulin resistance occurs when normal insulin concentrations have abnormal effects on glucose balance and utilization. PCOS individuals have abnormal lipid profiles, obesity, and type 2 diabetes as a result of insulin resistance. Women with PCOS who are overweight tend to have more severe insulin resistance, whereas those who are slim have less severe insulin resistance.[4]

An insulin resistant state is indicated by decreased levels of apolipoprotein, high density lipoprotein cholesterol, and triglycerides and increasing levels of triglycerides, Apolipoprotein B (Apo-B), and very low- density lipoprotein.[5] Which of these two conditions—hyperandrogenism or insulin resistance—should be held responsible for these issues is hard to say. Increased insulin causes the ovaries' capillary cells to release more testosterone, which is the primary androgen source in PCOS, through the action of luteinizing hormone (LH). Adipose tissue contains an enzyme called aromatase, which changes testosterone into estradiol and androstenedione into estrone. PCOS individuals produce more estrogens and androgens because they have an excess of fat tissue.[6] Increased prolactin increases the generation of

adrenal androgen in 20% of instances due to increased pulsatility of gonadotropin-releasing hormone (GnRH). This creates a vicious cycle. While PCOS and subclinical hypothyroidism have been linked, they also have certain characteristics in common, such as anovulatory periods and high BMI.[7] The present study was conducted to evaluate the effect of oral contraceptive pills (OCP) and metformin on metabolic and endocrine parameters in PCOS.

MATERIALS & METHODS

The study was conducted at Nalanda Medical College and Hospital, Patna from December 2021 to December 2023. The present study was conducted on 80 female patients with PCOS. All were informed regarding the study and their written consent was obtained.

Data such as name, age, etc. was recorded. They were divided into 2 groups. Group I (40) received lifestyle intervention and 500mg oral metformin and group II received lifestyle intervention, and was given OCP (fixed dose combination of ethinyl estradiol 50 micrograms and cyproterone acetate 2 milligrams per day for six months). Polycystic ovaries were assessed using ultrasound sonograpghy (USG). For the metabolic parameters, fasting blood sugar (FBS), postprandial blood sugar (PPBS), haemoglobin A1C (HbA1c), and lipid profile (total cholesterol, high density lipoprotein, low density lipoprotein, triglycerides) were recorded. And for the endocrine parameters testosterone, prolactin and Thyroid Stimulating Hormone (TSH) levels were measured. They were evaluated at 2nd month and 6th month. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS
Table I Assessment of parameters

Parameters	Groups	Baseline	2 months	6 months	P value
Weight (kg)	Group I	58.2	57.6	54.1	0.09
	Group II	50.3	51.3	52.8	
BMI (kg/m2)	Group I	29.4	28.1	26.4	0.84
	Group II	24.8	25.3	26.1	
Waist/hip ratio	Group I	0.92	0.91	0.89	0.17
	Group II	0.80	0.82	0.84	

Table I shows that at baseline, 2 months and 6 months mean weight (kg) in group I was 58.2, 57.6 and 54.1 and in group II was 50.3, 51.3 and 52.8 respectively. BMI (kg/m2) in group I was 29.4, 28.1 and 26.4 and in group II was 24.8, 25.3 and 26.1. The mean waist/hip ratio in group I was 0.92, 0.91 and 0.89 and in group II was 0.80, 0.82 and 0.84 respectively. The difference was significant (P< 0.05).

Table II Assessment of metabolic parameters

Parameters	Groups	Baseline	2 months	6 months	P value
FBS (mmol/L)	Group I	5.6	4.4	4.9	0.09
	Group II	4.2	4.3	4.8	
PPBS (mmol/L)	Group I	5.8	5.4	5.1	0.84
	Group II	5.1	5.3	5.7	
HbA1c (%)	Group I	7.4	7.2	6.8	0.17
	Group II	5.7	5.4	5.2	
Total cholesterol (mmol/L)	Group I	5.6	5.8	5.9	0.42
	Group II	5.3	5.6	5.1	
TG (mmol/L)	Group I	2.7	2.8	2.5	0.04
	Group II	2.2	2.1	2.1	
HDL (mmol/L)	Group I	0.90	0.92	0.94	0.01
	Group II	1.2	1.4	1.5	
LDL (mmol/L)	Group I	4.5	4.6	4.6	0.03
	Group II	3.2	3.4	3.4	

Table II, graph I shows that at baseline, 2 months and 6 months, FBS (mmol/L) in group I was 5.6, 4.4 and 4.9 and in group II was 4.2, 4.3 and 4.8 respectively. PPBS (mmol/L) in group I was 5.8, 5.4 and 5.1 and in group II was 5.1, 5.3 and 5.7. HbA1c (%) in group I was 7.4, 7.2 and 6.8 and in group II was 5.7, 5.4 and 5.2. Total cholesterol (mmol/L)in group I was 5.6, 5.8and5.9 and in group II was 5.3, 5.6 and 5.1. TG (mmol/L) in group I was 2.7, 2.8 and 2.5 and in group II was 2.2, 2.1 and 2.1. HDL (mmol/L) in group I was 0.90, 0.92 and 0.94 and in group II was 1.2, 1.4 and 1.5. LDL (mmol/L) in group I was 4.5, 4.6 and 4.6 and in group II was 3.2, 3.4 and 3.4respectively.The difference was significant (P< 0.05).
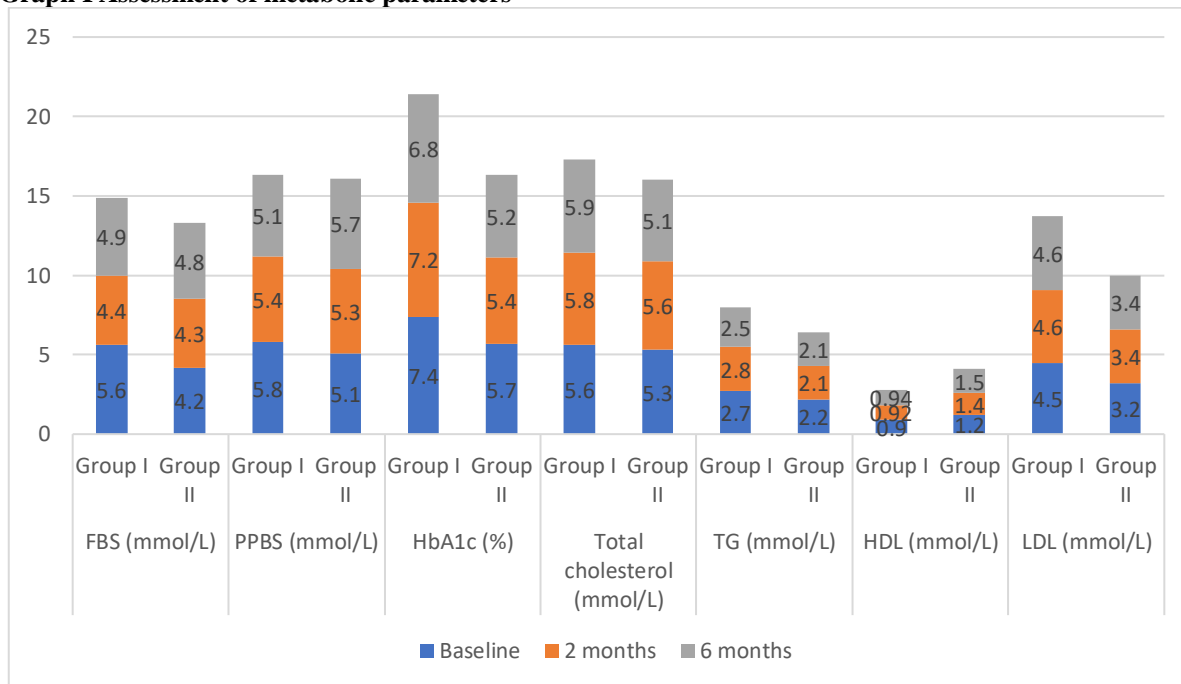
Graph I Assessment of metabolic parameters

Table III Assessment of endocrine parameters

Parameters	Groups	Baseline	2 months	6 months	P value
TSH (IU/L)	Group I	3.7	3.9	3.6	0.92
	Group II	3.6	3.5	3.6	
Testosterone (mmol/L)	Group I	2.6	2.4	2.2	0.85
	Group II	2.9	2.9	2.2	
Prolactin (ng/mL)	Group I	19.4	19.2	18.5	0.05
	Group II	18.6	18.4	18.5	

Table III shows that at baseline, 2 months and 6 months, the mean TSH (IU/L) in group I was 3.7, 3.9 and 3.6 and in group II was 3.6, 3.5 and 3.6respectively.Testosterone (mmol/L) in group I was 2.6, 2.4 and 2.2 and in group II was 2.9, 2.9 and 2.2. Prolactin (ng/mL) in group I was 19.4, 19.2 and 18.5 and in group II was 18.6, 18.4 and 18.5respectively.

DISCUSSION

Insulin Resistance Syndrome, also known as Syndrome X, is a medical condition that has been linked to PCOS in up to 33% of cases.[8] Low adiponectin levels have been associated with insulin resistance syndrome in PCOS.[9] Adiponectin plays a role in glucose and fatty acid metabolism, which predisposes people to the long-term consequences of diabetes, dyslipidemia, obstructive sleep apnea, and cardiovascular illnesses.[10] Three or more of the following criteria, such as a waist circumference of more than 88 cm or 35 inches, fasting plasma glucose of at least 100 mg/dL, blood pressure of at least 130/85 mm Hg, fasting triglycerides of at least 150 mg/dL, and high-density lipoprotein [HDL-C] of less than 50 mg/dL, must be met in order to diagnose metabolic syndrome.[11]The present study was conducted to evaluate the effect of oral contraceptive pills (OCP) and metformin on metabolic and endocrine parameters in PCOS.

We found that at baseline, 2 months and 6 months mean weight (kg) in group I was 58.2, 57.6 and 54.1 and in group II was 50.3, 51.3 and 52.8 respectively.

BMI (kg/m2) in group I was 29.4, 28.1 and 26.4 and in group II was 24.8, 25.3 and 26.1. The mean waist/hip ratio in group I was 0.92, 0.91 and 0.89 and in group II was 0.80, 0.82 and 0.84 respectively. Asad et al[12]assessed the effect of Oral Contraceptive Pills (OCP) and metformin on metabolic and endocrine parameters in PCOS. A total of 162 patients were recruited for the present study with the mean age in group A was 23.75±1.7 years and in group B was 22.40±1.6 years. The mean HbA1c levels of group A before the initiation of the treatment was found to be 7.51±0.89% which was reduced to 7.45±0.49% and 6.83±0.34% at the end of two months and six months, respectively (p-value=0.001). In group B, serum testosterone was significantly reduced from 2.86±0.48 to 2.18±0.42, however the glycaemic control worsened.

We found that at baseline, 2 months and 6 months, FBS (mmol/L) in group I was 5.6, 4.4 and 4.9 and in group II was 4.2, 4.3 and 4.8 respectively. PPBS (mmol/L) in group I was 5.8, 5.4 and 5.1 and in group II was 5.1, 5.3 and 5.7. HbA1c (%) in group I was 7.4, 7.2 and 6.8 and in group II was 5.7, 5.4 and 5.2. Total

cholesterol (mmol/L) in group I was 5.6, 5.8 and 5.9 and in group II was 5.3, 5.6 and 5.1. TG (mmol/L) in group I was 2.7, 2.8 and 2.5 and in group II was 2.2, 2.1 and 2.1. HDL (mmol/L) in group I was 0.90, 0.92 and 0.94 and in group II was 1.2, 1.4 and 1.5. LDL (mmol/L) in group I was 4.5, 4.6 and 4.6 and in group II was 3.2, 3.4 and 3.4 respectively. Tao T et al[13]in their study 63 patients were randomly distributed into three treatment groups: the first treatment group received metformin, saxagliptin was given to the second group and the third group received both the drugs. In the third group, reduction in HbA1c was significant as compared to the first and the second group (saxagliptin vs. combination treatment vs. metformin: -1.1 vs. -1.3 vs. -1.1%, p-value=0.016), whereas HbA1c reduction was similar between the first and the second group. All the three groups significantly reduced the homeostasis model assessment- insulin resistance index and increased the deposition index (p-value 0.05 for all) had no change.

We found that baseline, 2 months and 6 months, the mean TSH (IU/L) in group I was 3.7, 3.9 and 3.6 and in group II was 3.6, 3.5 and 3.6 respectively. Testosterone (mmol/L) in group Iwas 2.6, 2.4 and 2.2 and in group II was 2.9, 2.9 and 2.2. Prolactin (ng/mL) in group I was 19.4, 19.2 and 18.5 and in group II was 18.6, 18.4 and 18.5 respectively.Medeiros SF et al.[14], conducted a meta-analysis to examined the impact of subclinical hypothyroidism on the characteristics of PCOS patients. Total of 1,537 euthyroid PCOS patients and 301 subclinical hypothyroid PCOS patients were selected from nine studies. Both groups had similar anthropometrical parameters. Patients with subclinical hypothyroidism hypothyroid PCOS had higher total cholesterol and triglyceride and low high-density lipoprotein cholesterol. In euthyroid PCOS, fasting glucose was less. In both the groups androgen levels were similar.

The shortcoming of the study is small sample size.

CONCLUSION
Authors found that for PCOS patients, oral metformin and oral contraceptive tablets are both effective therapeutic options that significantly reduce menstruation symptoms within six months of starting therapy.

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