Original Article

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Effect of Oral Contraceptive Pill and Metformin on Metabolic and Endocrine Parameters in Polycystic Ovarian Syndrome: A Prospective Interventional Study

Pharmacology Section

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ABSTRACT

Introduction: Polycystic Ovarian Syndrome (PCOS) is one of the most common endocrinopathies, affecting women of reproductive age group worldwide. There is no comprehensive data, regarding the outcome of various treatment modalities.

Aim: To assess the effect of Oral Contraceptive Pills (OCP) and metformin on metabolic and endocrine parameters in PCOS.

Materials and Methods: It was a prospective interventional study, done over a period of 12 months from January 2017 to January 2018 at the Outpatient Department (OPD) of Gynaecology and Obstetrics, Medical College, Kolkata, West Bengal, India. A total of 162 PCOS patients were recruited. The selected patients were divided into two groups A and B, based on the clinician's assessment with respect to the patient profile. Group A received lifestyle intervention plus metformin (started at 500 mg/day and according to patient's response and the clinical judgement titrated upto 2000 mg/day for six months) and group B received lifestyle intervention plus oral contraceptive pill. (fixed dose combination of ethinyl estradiol 50 micrograms and cyproterone acetate 2 milligrams per day for six months). The patients were assessed for metabolic parameters [Fasting Blood Sugar (FBS), Post-Prandial Blood Sugar (PPBS), Haemoglobin A1c (HbA1c), lipid profile] and endocrine parameters [testosterone, prolactin and Thyroid Stimulating Hormone (TSH)]. The Student t-test, Chi-square test and Analysis of Variance (ANOVA) test were used to compare the data.

Results: 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 (p-value=0.0001), however the glycaemic control worsened.

Conclusion: The OCPs and metformin do not significantly correct metabolic abnormalities associated with PCOS, although, gynaecological symptoms are improved significantly. Comparatively, metformin helps in control of blood sugar levels but high Body Mass Index (BMI) and deranged lipid profile remains unaltered by both metformin and OCP.

Keywords: Insulin resistance, Lipids, Testosterone

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrinopathies of women of reproductive age group [1]. It is a complex endocrine condition, because of its multifactorial and polygenic etiology [2]. Insulin resistance and hyperandrogenism are characteristics of PCOS [3]. Insulin resistance is defined as a state in which the normal concentration of insulin produces subnormal effects on glucose homeostasis and utilisation. Because of insulin resistance there is obesity, type 2 diabetes, and abnormal lipid profile in PCOS patients [4]. Insulin resistance in women with PCOS is more severe, in those who are overweight whereas, lean women with PCOS have less severe insulin resistance [5-7]. Decreased levels of high density lipoprotein cholesterol, and apolipoprotein; and increased levels of triglycerides, Apolipoprotein B (Apo-B) and very low density lipoprotein is consistent with an insulin resistance state [8-10]. It is difficult to determine, which of these two (insulin resistance or hyperandrogenism) should be implicated as the cause of these problems [11,12]. Increased insulin stimulates theca cells of ovaries via Luteinising Hormone (LH), to produce excess testosterone which is the main source of androgen in PCOS [13]. An enzyme called aromatase, which converts androstenedione to estrone and testosterone to estradiol is present in the adipose tissue. Since, PCOS patients have excess of adipose tissue, there is an increased production of androgens and estrogens [14]. In 20% cases, increased pulsatility of Gonadotropin Releasing Hormone (GnRH) causes increased prolactin which further stimulates adrenal androgen production, thus setting up a vicious cycle [2]. Although, subclinical hypothyroidism was found in association with PCOS, [15] and they share certain common features of anovulatory cycles and high BMI [16].

Upto 33% of patients of PCOS have an association with a syndrome of medical disorder known as Syndrome X or Insulin Resistance Syndrome. Insulin Resistance Syndrome in PCOS has been linked to low adiponectin levels, which has a role in fatty acid metabolism and glucose metabolism thus predisposing to long term sequelae of Cardiovascular diseases, diabetes, dyslipidaemia and obstructive sleep apnoea [17]. For diagnosis of metabolic syndrome three or more of the criteria like waist circumference of >88 cm or >35 inches, fasting plasma glucose of ≥100 mg/dL, blood pressure ≥130/85 mm Hg, fasting triglycerides ≥150 mg/dL and High-Density Lipoprotein [HDL-C] <50 mg/dL should be present [18]. Metabolic syndrome is also seen in 10-15% lean PCOS patients [19,20]. Hyperandrogenism, oligo-ovulation and insulin resistance are the main features of PCOS and the treatment is directed towards these three.

First line of treatment is lifestyle intervention and exercise [21-24]. For the management of weight and obesity exercise is recommended by Endocrine society [25] and Royal College of Obstetricians and Gynaecologists (RCOG) [26]. Patients of PCOS have high prevalence of central obesity [27]. Symptoms of PCOS can be improved through weight loss and diet [28,29]. Oral contraceptives, clomiphene, gonadotropins, metformin, spironolactone and pioglitazone are

the agents for medical management of PCOS [18]. Metformin is an insulin sensitiser and it improves both metabolic parameters and ovarian function [30,31]. For the treatment of hyperandrogenic symptoms, combined oral contraceptives with Ethinyl Estradiol [EE] and Cyproterone acetate are considered as the first line therapy [32,33].There is no comprehensive data regarding the outcome of various treatment modalities. This study intends to find out the effect of OCP and metformin on metabolic and endocrine parameters in patients with PCOS.

MATERIALS AND METHODS

This prospective interventional study was performed in the OPD of Obstetrics and Gynaecology at Medical College, Kolkata, West Bengal, India for a duration of 12 months from January 2017 to January 2018. Ethical Clearance (MC/Kol/IEC/Non-spon/369/11-2016) was obtained from the Institutional Ethics Committee.

Sample size calculation: The PCOS patients were diagnosed using the Rotterdam criteria [34]. The following formula was used to calculate the sample size:

$$n = \frac{Z^2 P_{(1-2)}}{d^2}$$

n=Sample size, Z=Statistic level of confidence, P=Prevalence, d=Precision, For the level of confidence of 95%, which is conventional, Z value is 1.96. Prevalence=12% [35,36], Precision=5%.The minimum sample size required was 162.

Inclusion and Exclusion criteria: Patient's with PCOS, aged 15-35 years, who were not pregnant at the time of inclusion or anytime during the study period, patients who were not on any medications which can alter glucose levels and sex hormone levels (e.g.: Oral contraceptives, Metformin etc.) were included in the study. The women who were suffering from any other pre-existing or co-existing gynaecological diseases, patients with pre-existing diabetes, hypertension, dyslipidaemia or any other medical conditions were excluded from the study.

Study Procedure

Patients selected were divided into two groups based on the clinician's assessment with respect to the patient's profile. A total of 71 patients were allotted in group A and 91 patients in group B. Counselling about healthy lifestyle and dietary advice for weight reduction was given to all the selected patients. Counselling was provided by nutritionist, regarding a balanced diet and adequate exercise. It was advised to have a low carbohydrate diet with high fibre content, with a total calorie intake of 1400 kcal/day and 150 minute of moderate exercise a week (as per RCOG standard).

Group A received lifestyle intervention and oral metformin. At the initiation of the study, a dose of 500 mg was given and according to patient's response and clinical judgement, the dosage of metformin was adjusted to a maximum of 2000 mg per day for 6 months. Group B was advised lifestyle intervention, and was given OCP (fixed dose combination of ethinyl estradiol 50 micrograms and cyproterone acetate 2 milligrams per day for six months). Each patient recruited in the study, was followed-up with all the relevant clinical and laboratory parameters for a period of six months. During the follow-up period, they were evaluated at 2nd month and 6th month from the date of initiation of the specific treatment. None of the patients developed serious adverse reaction to the given medication.

Study measures: After the written informed consent was taken, following data were collected from the participants- demographic profile of the patient, weight, hirsutism; detailed menstrual history which included duration of cycle, intermenstrual spotting, dysmenorrhoea, amount of flow as guided by number of pads used and passage of clots if any, symptoms of androgen excess, and drug history. Body Mass Index (BMI) was calculated as weight in kilograms divided by height in metres squared. A detailed general examination was conducted for the identification of acne, hirsutism (scored by the Ferriman and Gallwey system [37]), acanthosis nigricans.

Polycystic ovaries on Ultrasound Sonograpghy (USG) were defined as presence of 12 or more follicles in each ovary, measuring 2-9 mm in diameter, and/or increased ovarian volume >10 mL [38]. Improvement in USG was considered, if the number of follicles decreased to less than 12 in number and/or the ovarian volume reduced to less than 10 cc during the two scheduled follow-up visits.

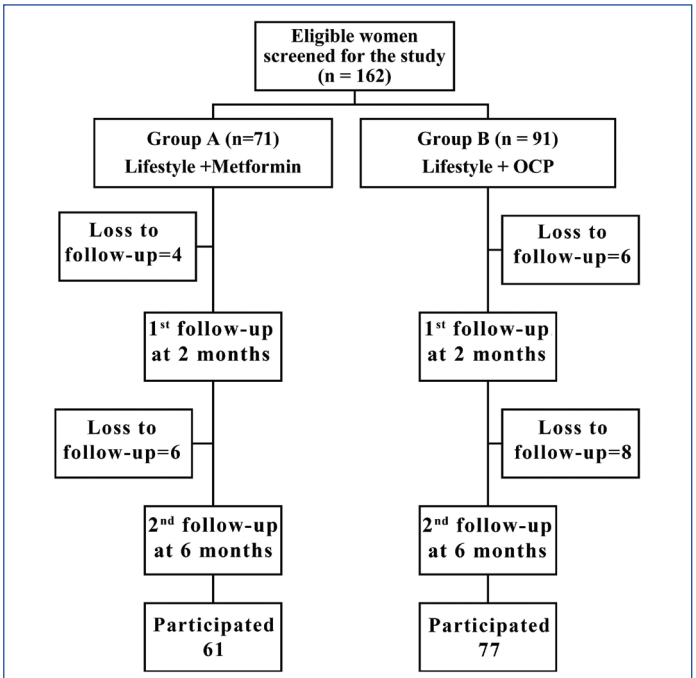
For the metabolic parameters, Fasting Blood Sugar (FBS), Post-Prandial Blood Sugar (PPBS), Haemoglobin A1C (HbA1c), and lipid profile (total cholesterol, high density lipoprotein, low density lipoprotein, triglycerides) were recorded. And for the endocrine parameters testosterone, prolactin and Thyroid Stimulating Hormone (TSH) levels were measured.

STATISTICAL ANALYSIS

Statistical analysis was performed with Statistical Package For The Social Sciences software version 26.0 software (version 26). Data were presented as mean±standard deviation and percentages (numbers). The Student's t-test, Chi-square test and ANOVA test were used to compare the data. A p-value of <0.05 was considered to be statistically significant.

RESULTS

A total of 162 patients were recruited for the present study of which 24 did not follow-up. The mean age in group A was 23.75±1.7 years and in group B was 22.40±1.6 years. Group A (n=61) received lifestyle intervention plus metformin and group B (n=77) received lifestyle intervention plus OCP. A flow chart of the study is depicted in [Table/Fig-1]. There was no significant difference in the socio-economic status between both the groups [Table/Fig-2].



[Table/Fig-1]: Flow diagram to depict recruitment of the study participants.

Socio-economic scale	Group A n (%)	Group B n (%)	p-value
Upper	01 (1.6%)	02 (2.6%)	0.7
Upper middle	05 (8.2%)	07 (9.1%)	0.8
Lower middle	10 (16.4%)	13 (16.9%)	0.9
Upper lower	20 (32.8%)	23 (29.9%)	0.8
Lower	25 (41%)	32 (41.5%)	0.9

[Table/Fig-2]: Comparative data between Group A and group B according to Modified Kuppuswamy Scale (N=138).
Test used: Chi-square test

The mean weight of group A at the starting of the treatment was 58.40±2.63 kg which reduced to 53.84±1.77 kg at the end of the 6 months (p=0.001). The mean weight of group B at the starting of the treatment was 49.39±2.21 which increased to 52.34±2.06 (p=0.001). This difference was again statistically significant. Frequency of hirsutism and acne was more in group B at the initiation of the treatment. At the end of the treatment in both the groups, hirsutism and acne reduced. However, only the reduction in the prevalence of acne in group B at the end of the treatment was statistically significant [Table/Fig-3,4].

Clinical parameters	Before treatment	At 2nd month	At 6th month	p-value
Weight (kg) (mean±SD)	58.40±2.63	57.04±2.97	53.84±1.77	<0.001
BMI (kg/m^2) (mean±SD)	29.05±2.73	28.87±2.80	26.77±2.25	<0.001
Waist/hip ratio	0.91±0.03	0.90±0.04	0.89±0.06	0.03
Acanthosis Nigricans n (%)	18 (29.5%)	17 (27.8%)	17 (27.9%)	0.36
Hirsutism	27 (44.3%)	25 (41%)	24 (39.3%)	0.09
Acne	35 (57.4%)	33 (54.1%)	32 (52.4%)	0.09

[Table/Fig-3]: Clinical parameters of study population in group A before and after treatment (n=61).
Test used: ANOVA

Clinical parameters	Before treatment	At 2nd month	At 6th month	p-value
Weight (kg) (mean±SD)	49.39±2.21	50.75±2.28	52.34±2.06	<0.001
BMI (kg/m^2) (mean±SD)	24.74±2.22	25.44±2.51	26.21±2.25	<0.001
Waist/hip (mean±SD)	0.79±0.02	19 (24.7%)	0.85±0.03	<0.001
Acanthosis Nigricans	19 (24.7%)	19 (24.7%)	18 (23.4%)	0.36
Hirsutism n (%)	41 (53.2%)	41 (53.2%)	40 (51.9%)	0.37
Acne n (%)	44 (57.1%)	40 (51.9%)	36 (46.7%)	<0.001

[Table/Fig-4]: Clinical parameters of group B study population before and after treatment (n=77).
Test used: ANOVA

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) [Table/Fig-5].

Metabolic parameters	Before treatment (Mean±SD)	At 2nd month (Mean±SD)	At 6th month (Mean±SD)	p-value
FBS (mmol/L)	5.08 (0.24)	4.77 (0.60)	4.43 (0.43)	0.001
PPBS (mmol/L)	5.85 (0.35)	5.60 (0.20)	5.36 (0.17)	0.001
HbA1c (%)	7.51 (0.89)	7.45 (0.49)	6.83 (0.34)	0.001
Total cholesterol (mmol/L)	5.77 (0.20)	5.73 (0.17)	5.72 (0.21)	0.3242
HDL (mmol/L)	0.97 (0.17)	0.94 (0.19)	0.99 (0.10)	0.2161
LDL (mmol/L)	4.31 (0.57)	4.48 (0.67)	4.42 (0.52)	0.2743
TG (mmol/L)	2.68 (0.44)	2.63 (0.56)	2.57 (0.36)	0.4200

[Table/Fig-5]: Metabolic parameters of study population in group A before and after treatment (n=61).
Test used: ANOVA; FBS: Fasting blood sugar; PPBS: Post prandial blood sugar; HbA1c: Haemoglobin A1c; HDL: High density lipoprotein; LDL: Low density lipoprotein; TG: Triglycerides

Before the initiation of treatment, the mean TSH level of group A was found to be 3.67±0.52 IU/L which marginally increased to 3.72±0.38 IU/L and then reduced to 3.57±0.45 IU/L at the end of 2nd month and 6th month, respectively (p-value=0.1803) [Table/Fig-6].

The mean HbA1c levels of group B before the initiation of the treatment was found to be 5.51±0.39% which became 5.52±0.28% and 5.48±0.26% at the end of 2nd months and 6th months, respectively (p-value=0.7151) [Table/Fig-7].

Among the endocrine parameters, only the serum testosterone was reduced significantly at the end of the treatment in group B [Table/Fig-8].

Endocrine parameters	Before treatment Mean (SD)	At 2nd month Mean (SD)	At 6th month Mean (SD)	p-value
Testosterone (mmol/L)	2.79 (0.79)	2.69 (0.95)	2.47 (0.70)	0.0907
Prolactin (ng/mL)	19.37 (1.4)	19.01 (1.60)	18.73 (1.47)	0.0623
TSH (IU/L)	3.67 (0.52)	3.72 (0.38)	3.57 (0.45)	0.1803

[Table/Fig-6]: Distribution of endocrine parameters among the study population in Group A (n=61) before and after the treatment.
Test used: ANOVA

Metabolic parameters	Before treatment (Mean±SD)	At 2nd month (Mean±SD)	At 6th month (Mean±SD)	p-value
FBS (mmol/L)	4.68 (0.18)	4.71 (0.20)	4.71 (0.21)	0.5525
PPBS (mmol/L)	5.22 (0.26)	5.25 (0.29)	5.20 (0.19)	0.4601
HbA1c (%)	5.51 (0.39)	5.52 (0.28)	5.48 (0.26)	0.7151
Total cholesterol (mmol/L)	5.22 (0.56)	5.11 (0.67)	5.29 (0.55)	0.1700
HDL (mmol/L)	1.07 (0.30)	1.03 (0.20)	1.02 (0.21)	0.3965
LDL (mmol/L)	3.18 (0.35)	3.27 (0.31)	3.29 (0.40)	0.0905
TG (mmol/L)	2.15 (0.27)	2.16 (0.47)	2.11 (0.32)	0.6654

[Table/Fig-7]: Metabolic parameters of study population in group B before and after treatment (n=77).
Test used: ANOVA

Endocrine parameters	Before treatment Mean (SD)	At 2nd month Mean (SD)	At 6th month Mean (SD)	p-value
Testosterone (mmol/L)	2.86 (0.48)	2.80 (0.27)	2.18 (0.42)	0.0001
Prolactin (ng/mL)	18.74 (1.91)	18.72 (1.57)	18.35 (1.62)	0.2814
TSH (IU/L)	3.54 (0.51)	3.49 (0.52)	3.56 (0.40)	0.6479

[Table/Fig-8]: Distribution of endocrine parameters among the study population in group B (n=77) before and after the treatment.
Test used: ANOVA

The mean HbA1c levels among the study subjects in group A at the end of the study were 6.83±0.34% as compared to 5.48±0.26% among group B study population. The difference was found to be highly significant (p=0.0001). Among the lipid profile, the differences in total cholesterol, LDL and TG was statistically significant [Table/Fig-9].

Metabolic parameters	Group A (n=61) Mean (SD)	Group B (n=77) Mean (SD)	p-value
FBS (mmol/L)	4.43 (0.43)	4.71 (0.21)	0.0001
PPBS (mmol/L)	5.36 (0.17)	5.20 (0.19)	0.0001
HbA1c (%)	6.83 (0.34)	5.48 (0.26)	0.0001
Total cholesterol (mmol/L)	5.72 (0.21)	5.29 (0.55)	0.0001
HDL (mmol/L)	0.99 (0.10)	1.02 (0.21)	0.0228
LDL (mmol/L)	4.42 (0.52)	3.29 (0.40)	0.0001
TG (mmol/L)	2.57 (0.36)	2.11 (0.32)	0.0001

[Table/Fig-9]: Comparative analysis of metabolic parameters between group A and group B at the end of the study.
Test used: Unpaired t-test

The mean testosterone levels among the study subjects in group A at the end of the study were 2.47±0.70 mmol/L as compared to 2.18±0.42 mmol/L among group B study population. The difference was found to be statistically significant (p-value=0.001) [Table/Fig-10].

Endocrine parameters	Group A (n=61) Mean (SD)	Group B (n=77) Mean (SD)	p-value
Testosterone (mmol/L)	2.47 (0.70)	2.18 (0.42)	0.001
Prolactin (ng/mL)	18.73 (1.47)	18.35 (1.62)	0.1633
TSH (IU/L)	3.57 (0.45)	3.56 (0.40)	0.8927

[Table/Fig-10]: Comparative analysis of endocrine parameters between group A and group B at the end of the study.
Test used: Unpaired t-test

A total of 25 (40.1%) of the study population in group A had USG changes, suggestive of PCOS before initiation of the treatment, which

got reduced to 23 (37.7%) and 22 (36.1%) at the end of 2nd month and 6th month of treatment, respectively. The rate of improvement of the USG changes of PCOS among the study population was found to be not statistically significant (p-value=0.09). Similarly, 47 (61%) of the study population in group B had USG changes suggestive to PCOS before initiation of the treatment, which got reduced to 35 (45.4%) and 29 (37.7%) at the end of 2nd month and 6th month of treatment, respectively. The rate of improvement of the USG changes of PCOS among the study population was found to be highly significant (p-value <0.001).

DISCUSSION

Polycystic ovarian syndrome is one of the most common endocrinopathies affecting woman of reproductive age group. The first line of therapy for all women with PCOS is lifestyle modification, including diet and exercise [38]. Lifestyle intervention is particularly important in individuals with dyslipidaemia [18,39]. In a meta-analysis done by Sirmans SM et al., it was shown that the prevalence of PCOS varies, depending on which criteria are used to make the diagnosis, but is as high as 15-20% [40]. The study also highlighted, that PCOS women are more prone to metabolic derangements and infertility related issues. They also emphasised, that PCOS patients are more likely to have increased coronary artery calcium scores and increased carotid intima-media thickness. The current study showed that the metabolic difference mean in FBS in the two study groups were 5.08±0.24 mmol/L and 4.68±0.18 mmol/L (p=0.0001), respectively whereas the mean PPBS was 5.85±0.35 mmol/L and 5.22±0.26 mmol/L (p=0.0001), respectively at the beginning of the study.

In a study conducted by Kocer D et al., in Turkey, it was shown that metformin decreases oxidative stress and improve insulin resistance, dyslipidaemia and endothelial dysfunction [41]. The present study also showed that lifestyle intervention plus oral metformin improves the glycaemic control and dyslipidaemia in PCOS patients.

In another study conducted by Aydogmus H et al., it was shown that total testosterone (p-value=0.01), LH (p-value <0.00), total cholesterol (p-value=0.02), insulin (p-value <0.00) and triglyceride (p-value <0.00) were significantly more among the PCOS patients as compared with healthy women having polycystic ovarian morphology with regular menstrual cycle [42].

Another institution-based study was done by Tao T et al., in an urban set up in Northern China. This was a randomised, parallel, open-label study, in which 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 (p-value> 0.05) [43]. All the three groups significantly reduced the homeostasis model assessment- insulin resistance index and increased the deposition index (p-value <0.01 for all). Homeostasis Model Assessment-Insulin Resistance Index (HOMA-IR)- cell function among the metformin and combination groups, had no significant change also the insulinogenic index among all three groups (p-value >0.05 for all) had no change. However, BMI and high-sensitivity C-reactive protein levels (p-value <0.01 for both) was significantly reduced in saxagliptin and metformin group. Similarly, the present study also demonstrated that oral metformin significantly improved the glycaemic parameters (p-value=0.0001). Metformin however, did not improve significantly the endocrinological parameters (p-value >0.05). The follow-up time of the present study was only six months as compared to 24 months for the study conducted by Tao at al. The present study also could not evaluate the HOMA-IR and other high-end parameters for insulin resistance due to logistic reasons.

Medeiros SF et al., conducted a meta-analysis in Brazil to examine the impact of subclinical hypothyroidism on the characteristics of PCOS patients [44]. 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 (p-value=0.036 and p-value=0.012) and low high-density lipoprotein cholesterol (p-value=0.018). In euthyroid PCOS, fasting glucose was less (p-value=0.022). In both the groups androgen levels were similar (p-value >0.05). The present study showed that the mean TSH levels did not show any significant improvement at the end of the study period with oral metformin and lifestyle modification (p-value=0.1803). The same findings were echoed in the study population who received OCP with lifestyle modification (p-value=0.6479) at the end of study period of six months. The mean TSH at the end of the study period when compared between the two groups also showed no significant difference (p-value=0.1503). These findings suggest that the standard modalities of treatment, namely metformin and OCP, do not have any significant bearings on the thyroid profile of PCOS patients.

Metabolic and endocrine sequelae of PCOS as explained are morbid and incurs high mortality rates. Diabetes affects macro and microvasculature leading to end organ damage in eyes, kidneys and heart. Dyslipidaemia accounts for premature atherosclerosis and a prothrombotic state, which is life-threatening. Central obesity causes obstructive sleep apnoea which is itself an independent risk factor for cardiac failure, pulmonary arterial hypertension and arrhythmias, that severly impair quality of life. Most women tend to ignore these co-morbidities once menstrual irregularities are relieved with OCPs or fertility is achieved with ovulation induction drugs like metformin and clomiphene [45-48]. It should be emphasised that management of PCOS should also seek to correct or prevent these clinical consequences by appropriate early screening of high-risk individuals. A small reduction in weight (2-5%) can result in significant improvement in metabolic and endocrine parameters, thus reducing disease progression. Incorporation of moderate exercise in daily activities and low-calorie diet intake, reduces risk of developing diabetes and cardiovascular diseases [49]. However, the currently available treatment modalities i.e., OCP and metformin, though may be of undisputed benefit in resolving menstrual irregularities and infertility in PCOS, they are largely ineffective in treating these health issues once developed, as seen in the present study.

Limitation(s)

Randomisation was not done for the recruitement of the subjects, which might have lead to selection bias. A limitation of present study might have been the short duration of follow-up and logistic restrictions of our centre.

CONCLUSION(S)

Both oral metformin and oral contraceptive pills are efficacious treatment modalities for PCOS patients and cause significant improvement in menstrual symptoms within six months of initiation of treatment. However, patients with poorer metabolic parameters have been more benefitted with oral metformin therapy whereas patients with good metabolic parameters and poorer endocrinological profiles have been comparably further improved with oral contraceptive pills Further recommendations for treatment options may be combination therapy of OCP and metformin or addition of statins with lifestyle modification.

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