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Original Research

Effect of oral contraceptive pill and metformin on metabolic and endocrine parameters in PCOS: A prospective interventions study

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ABSTRACT

Aim: This study aimed to evaluate the effects of oral contraceptive pills (OCPs) and metformin on metabolic and endocrine parameters in patients with polycystic ovary syndrome (PCOS). The objective was to compare their impact on hormonal regulation, insulin sensitivity, lipid profile, and clinical symptoms such as menstrual irregularities, acne, and hirsutism.

Materials and Methods: A prospective interventional study was conducted at the Department of Obstetrics and Gynecology, A.N.M.M.C.H, Gaya, from January 2023 to December 2024. A total of 100 women (aged 18-35 years) diagnosed with PCOS using the Rotterdam criteria (2003) were randomly divided into two groups: Group A (OCPs, n=50) received a combination pill of ethinyl estradiol (30 mcg) and cyproterone acetate (2 mg) daily, and Group B (Metformin, n=50) received metformin 1500 mg/day in divided doses for six months. Endocrine (LH, FSH, testosterone, DHEA-S), metabolic (FBG, insulin, HOMA-IR, lipid profile), and clinical parameters (menstrual regularity, acne, hirsutism, ovarian morphology) were assessed at baseline and post-intervention. Data were analyzed using SPSS 25.0, and $p<0.05$ was considered statistically significant.

Results: Both treatments significantly improved hormonal and metabolic parameters, but their effects varied. OCPs were more effective in reducing LH (12.5 to 8.2 mIU/mL, p=0.002), testosterone (65.4 to 45.3 ng/dL, p=0.003), and DHEA-S (p=0.02), leading to better menstrual regulation (80% vs. 65%, p=0.001) and improvements in acne (p=0.02) and hirsutism (p=0.03). In contrast, Metformin was superior in lowering fasting insulin (16.1 to 12.8 µIU/mL, p=0.002), HOMA-IR (3.89 to 2.95, p=0.001), and LDL cholesterol (p=0.01), demonstrating greater metabolic benefits. Both groups showed a significant reduction in ovarian volume (OCP: 10.5 to 8.2 mL, Metformin: 10.7 to 9.4 mL, p=0.03) and follicle count (p=0.01).

Conclusion: This study concludes that OCPs are more effective in regulating menstrual cycles, reducing hyperandrogenism, and improving ovarian morphology, whereas Metformin is superior in enhancing insulin sensitivity and metabolic parameters in PCOS patients. A combination approach may provide a more comprehensive management strategy, addressing both endocrine and metabolic dysfunctions in PCOS.

Keywords: Polycystic Ovary Syndrome (PCOS), Oral Contraceptive Pills (OCPs), Metformin, Insulin Resistance, Hyperandrogenism

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age. It is a complex condition characterized by a range of metabolic, hormonal, and reproductive disturbances, with symptoms including irregular menstrual cycles, hyperandrogenism, insulin resistance, and polycystic ovarian morphology. PCOS is not only a reproductive concern but also a metabolic disorder that significantly increases the risk of conditions such as type 2 diabetes, obesity, dyslipidemia, and cardiovascular diseases. The underlying pathophysiology of PCOS involves a complex interplay between hormonal imbalances, insulin resistance, and genetic and environmental factors, making its management challenging and multifaceted.[1]

Among the various treatment approaches available, oral contraceptive pills (OCPs) and metformin are widely used to address different aspects of PCOS. OCPs, primarily prescribed for regulating menstrual cycles and managing hyperandrogenic symptoms such as hirsutism and acne, work by suppressing ovarian androgen production and increasing sex hormone-

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binding globulin (SHBG). This leads to a reduction in free androgens, thereby alleviating the clinical manifestations of hyperandrogenism. Additionally, OCPs contribute to menstrual cycle regularity, which is particularly beneficial for women with PCOS who experience oligomenorrhea or amenorrhea.[2]

Metformin, on the other hand, is an insulin-sensitizing agent commonly used in the management of type 2 diabetes, but it has gained considerable attention for its role in improving metabolic dysfunctions in PCOS. It enhances insulin sensitivity, reduces hepatic glucose production, and decreases circulating insulin levels, which are often elevated in women with PCOS. By improving insulin resistance, metformin indirectly helps in lowering androgen levels and restoring ovulatory function, thereby addressing both metabolic and reproductive aspects of the syndrome. Given that insulin resistance plays a central role in the pathogenesis of PCOS, metformin has emerged as an important therapeutic option, particularly for women with impaired glucose tolerance or those at risk of developing diabetes.[3]

Despite the widespread use of OCPs and metformin in PCOS management, their comparative effects on metabolic and endocrine parameters remain a topic of ongoing research. While OCPs are effective in controlling hyperandrogenic symptoms and menstrual irregularities, concerns have been raised regarding their potential impact on metabolic health. Some studies suggest that OCPs may contribute to weight gain, worsening insulin resistance, and unfavorable lipid profile changes, which could increase the long-term risk of metabolic disorders in women with PCOS. Conversely, metformin has been shown to improve insulin sensitivity and lipid profiles, but its effects on androgen levels and menstrual regulation may be less pronounced than those of OCPs.[4-6]

The choice of therapy for PCOS is often individualized, depending on the patient's primary concerns, whether they are reproductive, metabolic, or both. While OCPs are typically recommended for women seeking menstrual cycle regulation and cosmetic relief from androgen excess, metformin is preferred for those with insulin resistance, obesity, or metabolic complications. However, the comparative effectiveness of these two treatments in addressing the broader spectrum of PCOS-related metabolic and endocrine disturbances remains an area of interest.

This prospective interventional study aims to evaluate and compare the effects of OCPs and metformin on key metabolic and endocrine parameters in women with PCOS. By assessing parameters such as insulin resistance, lipid profile, androgen levels, and menstrual cycle regularity, this study seeks to provide a comprehensive understanding of the therapeutic impact of these interventions.

Materials and Methods

This prospective interventional study was conducted in the Department of Obstetrics and Gynecology at Anugrah Narayan Magadh Medical College and Hospital (A.N.M.M.C.H), Gaya, from January 2023 to December 2024. The study aimed to evaluate the effects of oral contraceptive pills (OCPs) and metformin on metabolic and endocrine parameters in patients with polycystic ovary syndrome (PCOS).A total of 100 female patients diagnosed with PCOS based on the Rotterdam criteria (2003) were enrolled in the study. Patients were recruited from the outpatient department (OPD) and inpatient department of the hospital.Ethical approval for the study was obtained from the Institutional Ethics Committee of A.N.M.M.C.H, Gaya. Written informed consent was obtained from all participants before enrollment. Confidentiality of patient data was ensured.

Inclusion Criteria:

- Women aged 18–35 years
- Diagnosis of PCOS based on at least two of the following criteria:

1. Oligo/anovulation
2. Clinical and/or biochemical hyperandrogenism
3. Polycystic ovaries on ultrasound

- No use of hormonal therapy or insulin-sensitizing agents in the last 3 months

Exclusion Criteria:

- Presence of other endocrine disorders (e.g., Cushing's syndrome, thyroid dysfunction)
- Diabetes mellitus or other metabolic disorders
- Use of hormonal contraceptives or metformin within the last three months
- Pregnant or lactating women
- History of cardiovascular disease, liver dysfunction, or renal impairment

Study Groups and Intervention

Participants were randomly assigned into two groups:

- **Group A (OCP group, n=50):** Received a combination oral contraceptive pill containing ethinyl estradiol (30 mcg) and cyproterone acetate (2 mg) daily for six months.
- **Group B (Metformin group, n=50):** Received metformin at a dose of 1500 mg/day in divided doses for six months.

Data Collection and Outcome Measures

Baseline and post-intervention assessments were conducted at 0 and 6 months. The following parameters were evaluated:

1. Endocrine Parameters

- Serum luteinizing hormone (LH)
- Serum follicle-stimulating hormone (FSH)
- LH/FSH ratio
- Serum testosterone
- Serum dehydroepiandrosterone sulfate (DHEA-S)

2. Metabolic Parameters

- Fasting blood glucose (FBG)

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- Fasting insulin levels
- Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)
- Lipid profile (total cholesterol, LDL, HDL, triglycerides)
- Body mass index (BMI)
- Waist-to-hip ratio (WHR)

3. Clinical Parameters

- Menstrual regularity
- Acne score (Global Acne Grading System)
- Hirsutism (Ferriman-Gallwey score)
- Ultrasonographic assessment of ovarian morphology

Statistical Analysis

Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation (SD). Paired t-tests and independent t-tests were used for intra-group and inter-group comparisons, respectively. A p-value of <0.05 was considered statistically significant.

Results

Baseline Characteristics of the Study Population (Table 1)

The baseline characteristics of the participants were comparable between the OCP group and the Metformin group. The mean age of participants in the OCP group was 25.4 years, while it was 24.9 years in the Metformin group, with no statistically significant difference (p=0.62). Similarly, BMI and waist-to-hip ratio (WHR) were nearly identical between the two groups (p=0.74 and p=0.81, respectively), indicating that both groups had similar metabolic profiles at baseline. This suggests that any observed changes post-intervention are likely due to the treatment effects rather than baseline differences in the patient groups.

Endocrine Parameters Before and After Intervention (Table 2)

Luteinizing hormone (LH) levels significantly decreased in both groups, but the reduction was more pronounced in the OCP group, where levels dropped from 12.5 mIU/mL to 8.2 mIU/mL (p=0.002**).** In contrast, the Metformin group exhibited a decrease from 12.8 mIU/mL to 10.5 mIU/mL**,** indicating that while both treatments had an impact, OCPs were more effective in suppressing LH secretion.

Follicle-stimulating hormone (FSH) levels remained relatively unchanged in both groups, with no statistically significant difference between baseline and post-treatment values **(**p=0.34**).** This suggests that neither OCPs nor Metformin had a notable effect on FSH levels. However, the LH/FSH ratio showed a significant reduction in both groups**,** with a more pronounced decline in the OCP group (2.05 to 1.26, p=0.001**)** compared to the Metformin group (2.03 to 1.64). This finding highlights that OCPs contribute to improved gonadotropin regulation, a critical factor in managing PCOS-related reproductive dysfunction.

In terms of androgen excess, both groups exhibited a reduction in serum testosterone levels**,** but the effect was stronger in the OCP group, where levels dropped from 65.4 to 45.3 ng/dL (p=0.003**).** The Metformin group also showed a decrease **(**67.1 to 55.6 ng/dL**),** but to a lesser extent. Similarly, DHEA-S levels decreased significantly in both groups**,** yet the decline was greater in the OCP group **(**p=0.02**),** reinforcing the superior role of OCPs in addressing hyperandrogenism.

Metabolic Parameters Before and After Intervention (Table 3)

Metformin was more effective in improving metabolic parameters compared to OCPs. While both groups exhibited a decline in fasting blood glucose (FBG) levels, the reduction was more significant in the Metformin group (99.1 to 92.3 mg/dL, p=0.04**).** This suggests that Metformin plays a more substantial role in enhancing insulin sensitivity compared to OCPs. Additionally, fasting insulin levels showed a marked decline in the Metformin group, decreasing from 16.1 to 12.8 µIU/mL (p=0.002)**,** along with a significant reduction in HOMA-IR (3.89 to 2.95, p=0.001**).** These results confirm Metformin's well-established role as an insulin-sensitizing agent, whereas OCPs showed only a slight improvement in insulin resistance.

In terms of lipid profile, both groups experienced a reduction in total cholesterol and LDL levels**,** but the Metformin group exhibited a more significant improvement **(**p=0.03 for cholesterol and p=0.01 for LDL**).** While the OCP group demonstrated a mild increase in HDL levels (p=0.05)**,** Metformin showed a greater enhancement in HDL levels, increasing from 44.9 to 50.1 mg/dL**.** Additionally, triglyceride levels decreased in both groups**,** but the reduction was more pronounced in the Metformin group (**p=0.02**), reinforcing its positive impact on metabolic health.

Clinical Parameters Before and After Intervention (Table 4)

Menstrual regularity significantly improved in both groups, with the OCP group showing a greater increase from 35% to 80%, compared to the Metformin group, which improved from 32% to 65% (p=0.001). This highlights the strong role of OCPs in regulating menstrual cycles by modulating hormonal imbalances. Given that irregular menstruation is a hallmark feature of PCOS, these findings reinforce the superior ability of OCPs in restoring menstrual cyclicity through their direct effects on ovarian hormone regulation.

In addition to menstrual regulation, acne and hirsutism symptoms improved in both groups, but the effect was more pronounced with OCPs. The acne score decreased significantly in the OCP group from 3.8 to 2.2 (p=0.02), while Metformin led to a milder

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reduction. Similarly, hirsutism scores (Ferriman-Gallwey score) decreased from 12.1 to 8.6 in the OCP group, whereas the Metformin group showed a more modest reduction from 12.5 to 10.3 (p=0.03). These results indicate that OCPs are more effective in reducing hyperandrogenic symptoms, such as acne and excessive hair growth, due to their androgen-suppressing effects.

Ultrasonographic Findings Before and After Intervention (Table 5)

Ovarian volume significantly decreased in both groups, with a greater reduction in the OCP group (10.5 mL to 8.2 mL, p=0.03) compared to the Metformin group (10.7 mL to 9.4 mL). This suggests that OCPs have a more direct effect on ovarian structure, likely due to their ability to suppress gonadotropin secretion, thereby reducing follicular stimulation and overall ovarian enlargement. The reduction in ovarian size is clinically relevant, as enlarged ovaries are a hallmark feature of PCOS and are associated with persistent anovulation.

In addition to ovarian volume, there was a notable decrease in follicle count post-treatment in both groups. The OCP group showed a greater reduction, but the Metformin group also exhibited a significant effect, with follicle count decreasing from 16.1 to 13.2 (p=0.01). This indicates that while Metformin does contribute to improvements in ovarian morphology, its effect is less pronounced than that of OCPs. The reduction in follicle count in the Metformin group may be attributed to its role in improving insulin sensitivity, which in turn helps restore normal ovarian function

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Table 1: Baseline Characteristics of the Study Population

Parameter	OCP Group (n=50)	Metformin Group (n=50)	p-value
Age (years)	25.4 ± 3.2	24.9 ± 3.1	0.62
BMI (kg/m²)	27.8 ± 4.1	28.1 ± 4.3	0.74
Waist-to-Hip Ratio	0.85 ± 0.03	0.86 ± 0.02	0.81

Table 2: Endocrine Parameters Before and After Intervention

Parameter	OCP Group (Baseline)	OCP Group (6 Months)	Metformin Group (Baseline)	Metformin Group (6 Months)	p-value
LH (mIU/mL)	12.5 ± 2.3	8.2 ± 1.8	12.8 ± 2.1	10.5 ± 2.0	0.002
FSH (mIU/mL)	6.1 ± 1.0	6.5 ± 1.1	6.3 ± 1.1	6.4 ± 1.2	0.34
LH/FSH Ratio	2.05 ± 0.5	1.26 ± 0.4	2.03 ± 0.4	1.64 ± 0.5	0.001
Testosterone (ng/dL)	65.4 ± 10.2	45.3 ± 8.4	67.1 ± 9.8	55.6 ± 7.6	0.003
DHEA-S (µg/dL)	220.3 ± 25.7	180.5 ± 22.3	225.7 ± 26.1	200.2 ± 24.5	0.02

Table 3: Metabolic Parameters Before and After Intervention

Parameter	OCP Group (Baseline)	OCP Group (6 Months)	Metformin Group (Baseline)	Metformin Group (6 Months)	p-value
Fasting Blood Glucose (mg/dL)	98.4 ± 7.2	96.8 ± 6.8	99.1 ± 7.5	92.3 ± 6.9	0.04
Fasting Insulin (µIU/mL)	15.2 ± 2.8	14.1 ± 2.5	16.1 ± 3.1	12.8 ± 2.7	0.002
HOMA-IR	3.71 ± 1.1	3.35 ± 1.0	3.89 ± 1.2	2.95 ± 0.9	0.001
Total Cholesterol (mg/dL)	190.3 ± 18.6	185.6 ± 17.2	192.7 ± 19.3	180.2 ± 16.8	0.03
LDL (mg/dL)	120.4 ± 15.2	115.3 ± 13.9	122.1 ± 14.7	110.7 ± 12.5	0.01
HDL (mg/dL)	45.2 ± 5.3	47.8 ± 5.9	44.9 ± 5.1	50.1 ± 5.7	0.05
Triglycerides (mg/dL)	150.8 ± 18.4	145.2 ± 17.1	152.3 ± 19.6	138.9 ± 16.2	0.02

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Table 4: Clinical Parameters Before and After Intervention

Parameter	OCP Group (Baseline)	OCP Group (6 Months)	Metformin Group (Baseline)	Metformin Group (6 Months)	p-value
Menstrual Regularity (%)	35	80	32	65	0.001
Acne Score	3.8 ± 1.2	2.2 ± 1.0	3.9 ± 1.3	2.8 ± 1.1	0.02
Hirsutism Score (Ferriman-Gallwey)	12.1 ± 3.2	8.6 ± 2.8	12.5 ± 3.4	10.3 ± 3.0	0.03

Table 5: Ultrasonographic Findings Before and After Intervention

Parameter	OCP Group (Baseline)	OCP Group (6 Months)	Metformin Group (Baseline)	Metformin Group (6 Months)	p-value
Ovarian Volume (mL)	10.5 ± 2.1	8.2 ± 1.7	10.7 ± 2.0	9.4 ± 1.8	0.03
Follicle Count	15.8 ± 4.2	11.6 ± 3.8	16.1 ± 4.5	13.2 ± 3.9	0.01

Discussion

The present study aimed to evaluate the effects of oral contraceptive pills (OCPs) and Metformin on metabolic and endocrine parameters in patients with polycystic ovary syndrome (PCOS). Our findings demonstrated that while both treatments were effective in improving hormonal and metabolic profiles, OCPs were superior in reducing hyperandrogenism and regulating menstrual cycles, whereas Metformin was more effective in improving insulin sensitivity and metabolic parameters.

The baseline characteristics of participants in the OCP and Metformin groups were comparable, with no significant differences in age, BMI, or waist-to-hip ratio (WHR) ($p>0.05$). This ensures that any observed differences in outcomes are likely due to the treatment effect rather than baseline disparities. Similar findings have been reported in previous studies where matched baseline characteristics were used to compare OCPs and Metformin in PCOS treatment (Legro et al., 2013).7

The OCP group showed a greater reduction in LH levels (12.5 to 8.2 mIU/mL, $p=0.002$) compared to the Metformin group (12.8 to 10.5 mIU/mL), confirming that OCPs are more effective in suppressing LH secretion. This is consistent with the findings of Diamanti-Kandarakis et al. (2007), who reported that OCPs significantly suppress LH secretion by inhibiting gonadotropin-releasing hormone (GnRH) pulsatility, thereby reducing ovarian androgen production.8

In contrast, FSH levels remained unchanged in both groups ($p=0.34$), suggesting that neither OCPs nor Metformin has a direct impact on FSH regulation. However, the LH/FSH ratio showed a significant reduction, particularly in the OCP group (2.05 to 1.26, $p=0.001$). This aligns with findings from Azziz et al. (2016), who suggested that a decreased LH/FSH ratio is an indicator of improved gonadotropin regulation in PCOS patients receiving hormonal therapy.9

Furthermore, serum testosterone levels decreased significantly in both groups, with a greater reduction observed in the OCP group (65.4 to 45.3 ng/dL, $p=0.003$) compared to the Metformin group (67.1 to 55.6 ng/dL). This supports previous research by Morin-Papunen et al. (2000), which demonstrated that OCPs effectively suppress ovarian androgen production, leading to improved hyperandrogenic symptoms. Additionally, DHEA-S levels also decreased significantly, reinforcing the androgen-lowering effects of both treatments, though OCPs exhibited a stronger effect ($p=0.02$).10

Our study demonstrated that Metformin was superior to OCPs in improving metabolic parameters. Fasting blood glucose levels significantly decreased in the Metformin group (99.1 to 92.3 mg/dL, $p=0.04$), whereas the OCP group showed a more modest reduction. Similarly, fasting insulin levels declined more substantially in the Metformin group (16.1 to 12.8 µIU/mL, $p=0.002$), along with a significant reduction in HOMA-IR (3.89 to 2.95, $p=0.001$). These findings are consistent with those reported by Lord et al. (2003), who conducted a meta-analysis showing that Metformin significantly improves insulin sensitivity and glucose metabolism in women with PCOS.11

Regarding lipid profiles, Metformin led to a greater reduction in total cholesterol ($p=0.03$) and LDL ($p=0.01$) compared to OCPs. Additionally, Metformin significantly increased HDL levels (44.9 to 50.1 mg/dL), while OCPs only had a mild effect ($p=0.05$). This is in agreement with findings from Harborne et al. (2005), who reported that Metformin positively affects lipid metabolism and reduces cardiovascular risk in women with PCOS.12

Both OCPs and Metformin resulted in significant improvements in menstrual regularity, acne, and hirsutism, though the effects varied between the groups. Menstrual regularity improved more in the OCP group (35% to 80%) compared to the Metformin group (32% to 65%, $p=0.001$), confirming that OCPs are more effective in restoring menstrual cyclicity. This aligns with studies by Legro et al. (2007), who reported that OCPs regulate menstrual cycles by suppressing ovarian androgen production and endometrial proliferation.13

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Additionally, acne and hirsutism scores improved significantly in both groups, with a greater reduction in the OCP group (p=0.02 for acne, p=0.03 for hirsutism). This is supported by studies from Redmond et al. (1997), which found that OCPs are effective in reducing androgen-related symptoms such as acne and hirsutism due to their anti-androgenic properties. While Metformin also showed improvements, its effects were milder compared to OCPs.14

These findings suggest that OCPs are more effective for patients with clinical manifestations of hyperandrogenism, while Metformin offers moderate benefits in managing these symptoms.

Both treatments led to a significant reduction in ovarian volume and follicle count, indicating a positive response to intervention. The OCP group exhibited a greater reduction in ovarian volume (10.5 mL to 8.2 mL, p=0.03) compared to the Metformin group (10.7 to 9.4 mL). This suggests that OCPs have a stronger impact on ovarian morphology, likely due to their ability to suppress gonadotropin stimulation, thereby reducing follicular growth.

A significant decrease in follicle count was observed in both groups, with the Metformin group showing a reduction from 16.1 to 13.2 (p=0.01). Similar findings have been reported by Baillargeon et al. (2004), who suggested that Metformin reduces ovarian follicle number by improving insulin sensitivity, which indirectly restores normal ovarian function.15 However, OCPs had a stronger direct effect on reducing ovarian size and follicular excess, reinforcing their role in managing ovarian morphology in PCOS patients.

Conclusion

This study concludes that OCPs are more effective in regulating menstrual cycles, reducing hyperandrogenism, and improving ovarian morphology**,** while Metformin is superior in enhancing insulin sensitivity and metabolic parameters in women with PCOS. Both treatments showed significant benefits, but their effects varied based on the primary clinical presentation. OCPs are preferable for patients with hormonal and menstrual irregularities, whereas Metformin is more suitable for those with metabolic disturbances**.** A combination approach may offer comprehensive management**,** addressing both endocrine and metabolic aspects of PCOS.

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