



THE EFFECT OF OCP AND METFORMIN ON DOPPLER INDICES OF UTERUS AND OVARIES IN POLYCYSTIC OVARIAN SYNDROME

Obstetrics & Gynaecology

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ABSTRACT

Background: Polycystic Ovarian Syndrome (PCOS) is a prevalent endocrine disorder in reproductive-age women, often associated with anovulation, insulin resistance, and altered pelvic blood flow. Elevated vascular resistance in ovarian and uterine arteries has been demonstrated using Doppler ultrasound. Oral contraceptive pills (OCPs) and metformin are common treatments, yet their individual and combined effects on uterine and ovarian hemodynamics remain underexplored. **Objectives:** To assess and compare the effects of OCP and metformin on Doppler indices of uterine and ovarian blood flow in women with PCOS, aiming to evaluate their vascular modulation potential. **Methods:** This randomized controlled trial included 120 women aged 18–35 years diagnosed with PCOS as per Rotterdam criteria. Participants were allocated into three groups: OCP alone, OCP plus metformin, and control. Doppler ultrasonography was used pre- and post-treatment to measure resistance index (RI), pulsatility index (PI), and peak systolic velocity (PSV) in ovarian and uterine vessels. Data were analyzed using paired t-tests and ANOVA. **Results:** OCP significantly increased ovarian RI and decreased PSV, while improving uterine artery perfusion. Metformin further enhanced uterine blood flow and attenuated OCP-induced ovarian vascular resistance. Combination therapy demonstrated a more balanced vascular response. **Conclusion:** Both OCP and metformin significantly affect uterine and ovarian blood flow. Their combination offers synergistic benefits, supporting individualized therapy for PCOS.

KEYWORDS

Polycystic Ovary Syndrome; Doppler Ultrasound; Metformin; Oral Contraceptives; Uterine Artery Blood Flow

INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is a multifactorial endocrine disorder affecting approximately 4–10% of women globally [1] and up to 11.34% in India [2], making it one of the leading causes of infertility and metabolic dysfunction in women of reproductive age [1,2]. It is clinically defined by hyperandrogenism, oligo/anovulation, and polycystic ovarian morphology, as per the Rotterdam criteria (2003) [3]. The condition is associated not only with reproductive complications but also with insulin resistance, obesity, and long-term cardiovascular risks [4]. Recent advances in color Doppler ultrasonography have enabled detailed, non-invasive assessment of uterine and ovarian blood flow, which is often altered in PCOS due to increased vascular resistance and impaired perfusion [5]. Elevated resistance index (RI) and pulsatility index (PI) in uterine arteries and reduced ovarian stromal flow are commonly observed hemodynamic patterns. Oral contraceptive pills (OCPs) and metformin are widely used therapeutic agents in PCOS. OCPs regulate the menstrual cycle and suppress androgen levels, while metformin improves insulin sensitivity and restores ovulatory function [6]. However, their effects on uterine and ovarian Doppler indices remain underexplored.

This study aimed to evaluate and compare the effects of OCP and metformin on Doppler parameters of uterine and ovarian blood flow in women with PCOS, to understand their impact on reproductive hemodynamics and optimize individualized treatment strategies.

MATERIALS AND METHODS

This randomized controlled trial was conducted over six months in the Department of Obstetrics and Gynecology at Subharti Medical College, Meerut, to assess the effects of oral contraceptive pills (OCP) and metformin on Doppler indices of uterine and ovarian vasculature in women diagnosed with polycystic ovary syndrome (PCOS). A total of 120 women between the ages of 18 and 35 years, fulfilling the Rotterdam criteria for PCOS, were recruited from the outpatient clinic.

Eligible participants presented with clinical features such as irregular menstruation, anovulation, hyperandrogenism, or polycystic ovaries on ultrasonography. Women were excluded if they had received hormonal treatment in the past six months, were lactating, had congenital adrenal hyperplasia, systemic illnesses affecting the hypothalamic-pituitary-ovarian axis, or contraindications to oral contraceptives. Known cases of diabetes mellitus were also excluded.

After obtaining informed consent, participants were randomized into three groups: the first group received a daily dose of combined OCP (ethinyl estradiol 30 mcg + levonorgestrel 0.15 mg), the second group received both OCP and metformin, and the third served as a control group. All interventions were administered for a duration of three months.

Baseline assessments included a thorough clinical evaluation, hormonal profile testing, and pelvic ultrasound using Doppler to evaluate blood flow parameters. Doppler indices such as Resistance Index (RI), Pulsatility Index (PI), and Peak Systolic Velocity (PSV) were recorded for uterine and ovarian arteries, ovarian stroma, and endometrial vessels. Blood samples were collected via venipuncture and centrifuged for hormonal analysis using automated enzyme-linked fluorescent assays, with specific commercial kits for luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and estradiol. After three months, participants underwent follow-up assessments using the same Doppler parameters, along with endometrial thickness and ovarian morphology evaluations. Hormonal changes and improvements in clinical symptoms such as menstrual regularity, acne, and hirsutism were also documented.

Data analysis was performed using SPSS software. Statistical tests, including paired t-tests and ANOVA, were applied to compare pre- and post-treatment findings within and across the groups. A p-value less than 0.05 was considered statistically significant. The study was ethically approved by the Institutional Review Board, and all protocols adhered to the principles of the Declaration of Helsinki.

RESULTS

In our study, the age-wise distribution revealed a predominance of younger women (18–22 years) in both groups, with no statistically significant difference between them, suggesting a well-matched baseline population (Table 1). OCP therapy significantly increased ovarian vascular resistance, especially in the left ovary, while reducing peak systolic velocity (PSV), and simultaneously improved uterine artery perfusion with significant decreases in RI and PI and an increase in PSV (Table 2). Metformin led to a significant improvement in uterine blood flow parameters and reduced PSV in ovarian vessels, with left ovarian RI and PI showing a notable increase, indicating its role in modulating both ovarian and uterine hemodynamics (Table 3). Combination therapy with OCP and metformin demonstrated a

significantly lesser rise in ovarian RI and stromal resistance compared to OCP alone, while further enhancing uterine artery PSV, indicating a more balanced vascular response with combined treatment (Table 4).

Table 1: Age Distribution of Patients Among Groups

Age Group	Group A	Group B	Total	P-value
18-22	34	22	56	0.07
23-27	20	27	47	
28-33	6	11	17	

Table 2: Effect of OCP on Right Ovary Doppler, Left Ovary Doppler, Uterine Artery Doppler

Parameter	Pre (Mean ± SD)	Post (Mean ± SD)	P-value
Right Ovary Doppler			
RI	0.902 ± 0.309	1.071 ± 0.378	0.038
PI	2.03 ± 1.22	2.45 ± 1.2	0.246
PSV	12.5 ± 1.729	10 ± 0.968	< 0.001
Left Ovary Doppler			
RI	0.798 ± 0.205	1.316 ± 0.226	< 0.001
PI	2.17 ± 1.232	2.95 ± 0.941	0.00029
PSV	12 ± 1.73	10.7 ± 1.33	0.01444
Uterine Artery Doppler			
RI	0.688 ± 0.0948	0.658 ± 0.0718	0.03752
PI	1.65 ± 0.316	1.46 ± 0.249	0.01747
PSV	30.3 ± 4.75	34.1 ± 5.04	0.0076

Table 3: Effect of Metformin on Ovarian Stromal Vascularity Doppler, Left Ovary Doppler, Uterine Artery Doppler

Parameter	Pre (Mean ± SD)	Post (Mean ± SD)	P-value
Ovarian Stromal Vascularity Doppler			
RI	0.935 ± 0.28	1.029 ± 0.376	0.78785
PI	2.07 ± 1.19	2.51 ± 1.37	0.45157
PSV	12.3 ± 1.781	10.1 ± 0.968	< 0.001
Left Ovary Doppler			
RI	0.800 ± 0.179	1.331 ± 0.228	< 0.001
PI	1.75 ± 1.06	2.98 ± 0.952	< 0.001
PSV	12.2 ± 1.38	10.5 ± 1.01	< 0.001
Uterine Artery Doppler			
RI	0.682 ± 0.0931	0.627 ± 0.0799	0.00427
PI	1.76 ± 0.337	1.47 ± 0.25	0.00002
PSV	29.6 ± 4.98	34.2 ± 4.66	0.04565

Table 4: Comparison of OCP vs OCP+Metformin (Doppler Changes)

Parameter Category	Parameter	OCP (Δ Mean ± SD)	OCP + Metformin (Δ Mean ± SD)	P-value
a) Right Ovarian RI	RI	0.169 ± 0.08	0.094 ± 0.05	< 0.001
	PI	0.42 ± 0.21	0.44 ± 0.22	0.888
	PSV	-2.5 ± 1.0	-2.2 ± 1.0	0.720
b) Left Ovarian RI	RI	0.518 ± 0.20	0.531 ± 0.19	0.477
	PI	0.78 ± 0.39	1.23 ± 0.49	< 0.001
	PSV	-1.3 ± 0.8	-1.7 ± 0.7	0.049
c) Uterine Vessel	RI	-0.030 ± 0.006	-0.055 ± 0.007	< 0.001
	PI	-0.19 ± 0.15	-0.29 ± 0.17	0.360
	PSV	3.8 ± 0.059	4.6 ± 0.063	< 0.001
d) Stromal Vascularity	RI	0.17 ± 0.04	0.10 ± 0.01	< 0.001
	PI	0.42 ± 0.15	0.44 ± 0.18	0.367
	PSV	-2.5 ± 0.21	-2.2 ± 0.25	< 0.001

DISCUSSION

The present study demonstrates significant alterations in Doppler indices of ovarian and uterine vessels following administration of oral contraceptive pills (OCP), metformin, and their combination in women with polycystic ovarian syndrome (PCOS). OCP therapy significantly increased resistive index (RI) in both right and left ovarian arteries, with a more pronounced effect on the left side (p < 0.001), accompanied by a significant decline in peak systolic velocity (PSV), suggesting elevated vascular resistance and reduced perfusion. This pattern aligns with the studies by Sahu et al. [6] and Okyay et al. [7], who reported similar increases in RI and reductions in PSV in

PCOS patients undergoing hormonal therapy. However, while these studies often reported statistically significant increases in pulsatility index (PI) bilaterally, the current study noted a non-significant PI increase on the right side, possibly reflecting lateralized variability in ovarian hemodynamic response. A comparable asymmetry was also noted by Ozay et al. [8], emphasizing the heterogeneous impact of hormonal suppression on ovarian vasculature. Importantly, OCP therapy led to improved uterine artery perfusion, evidenced by significant decreases in RI and PI and a rise in PSV. These findings are consistent with the work of Khalaf et al. [9] and Farshchian et al. [10], who reported enhanced endometrial receptivity and uterine blood flow following treatment with hormonal or insulin-sensitizing agents. This dual vascular response—ovarian suppression and uterine enhancement—was also highlighted in the meta-analysis by Ganesh et al. [11], suggesting differential site-specific vascular effects of OCPs. Metformin monotherapy similarly resulted in significant improvement in uterine artery Doppler indices (p < 0.05 for all parameters), which parallels observations by Khalaf et al. [9] and Yuan et al. [12]. These studies demonstrated increased endometrial blood flow and thickness, reinforcing metformin's role in promoting endometrial receptivity. On the ovarian side, the left ovary showed significant increases in RI and PI and decreased PSV, mirroring findings by Abd EL-Sattar et al. [13]. However, the right ovary and stromal indices showed non-significant changes in RI and PI, suggesting variability in response, a phenomenon also reported by Sahu et al. [6], potentially due to inter-ovarian anatomical or physiological differences. The comparison between OCP monotherapy and combination therapy (Table 4) further underscores metformin's moderating influence. The combination therapy significantly attenuated the rise in right ovarian RI (p < 0.001) and showed a less pronounced decrease in stromal PSV, suggesting that metformin may reduce the vasoconstrictive impact of OCP on ovarian vessels. These findings corroborate the vascular balancing effect discussed by Okyay et al. [7] and provide mechanistic insight into the clinical superiority of combination therapy in enhancing follicular microenvironment and ovulatory outcomes.

Strengths of the Study

The strengths of the study include its prospective design, use of objective Doppler ultrasound parameters, and inclusion of both monotherapy and combination therapy groups for comparative analysis. Additionally, the assessment of both ovarian and uterine vascular changes offers a comprehensive view of pelvic hemodynamics. The study also enhances clinical relevance by directly correlating treatment effects with vascular changes, thereby supporting individualized therapeutic strategies in PCOS.

Limitations of the Study

The limitations of the study include a relatively small sample size and short follow-up duration, which may limit the generalizability and long-term interpretation of vascular changes. The study also did not assess hormonal or metabolic markers alongside Doppler indices, which could have provided a more holistic understanding. Additionally, interobserver variability in ultrasound measurements was not accounted for, potentially affecting measurement precision.

CONCLUSION

We concluded that both oral contraceptive pills and metformin significantly affect uterine and ovarian Doppler indices in women with PCOS. OCP increased ovarian vascular resistance while enhancing uterine perfusion. Metformin further improved uterine blood flow and moderated the vascular resistance induced by OCP. The combination therapy provided a more balanced hemodynamic response. This study's findings highlight the complementary roles of hormonal and insulin-sensitizing agents in optimizing vascular and reproductive outcomes in PCOS management.

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Consent: Written consent secured.

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