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Effect of oral contraceptive containing ethinyl estradiol combined with drospirenone vs. desogestrel on clinical and biochemical parameters in patients with polycystic ovary syndrome

Alka Kriplani[a,*], Anurekha Janaki Periyasamy[a], Nutan Agarwal[a], Vidushi Kulshrestha[a], Anand Kumar[b], Ariachery Chinnama Ammini[c]

[a]*Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi 110029, India*
[b]*Department of Reproductive Endocrinology, All India Institute of Medical Sciences, New Delhi 110029, India*
[c]*Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi 110029, India*

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Abstract

Background: A prospective randomized trial was conducted to compare efficacy of a drospirenone-containing combined oral contraceptives (COC) with desogestrel-containing COC in women with polycystic ovary-syndrome (PCOS) not desirous of child-bearing.
Study Design: Sixty women were randomized into study group [ethinylestradiol (EE) 30 mcg+drospirenone 3 mg] and control group (EE 30 mcg+desogestrel 150 mcg), treated for 6 months and followed up at 1 month, 3 months, 6 months, during treatment and 3 and 6 months post-treatment. Acne and hirsutism scoring, bodyweight, body mass index (BMI), blood pressure (BP), ultrasound parameters, lipid profile, glycemic profile and hormonal profile were compared.
Results: Cycles were regular in both groups during treatment. Effect of regular cycles persisted in 44.83% (13/30) vs. 17.24% (5/30) in study vs. control group at 6 months post-treatment with 33.3% decreased hirsutism score in the study group (versus no change in control group) even at 6 months after stopping treatment. With treatment, BMI fell by 0.52 kg/m^2 in the study group; systolic and diastolic BP fell in the study group while it rose in the control group. Low-density lipoprotein significantly decreased and high-density lipoprotein was elevated in the study group ($p<.05$). The study group showed a significant fall in fasting/postprandial blood sugar and insulin and total testosterone against a rise in the control group.
Conclusion: In women with PCOS, a drospirenone containing COC has better outcome in terms of persistent regular cycles, antiandrogenic effect, fall in BMI and BP, better lipid profile, favorable glycemic and hormonal profile than desogestrel-containing COC.

Keywords: COCs; PCOS; Drospirenone; Desogestrel

1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder of young women occurring globally in 6% to 10% of the population [1]. Combined oral contraceptives (COCs) had been the traditional option for those presenting with menstrual irregularity and not wanting conception. Estrogen increases the circulating levels of sex hormone binding globulins (SHBG), which in turn decreases the serum concentration of free testosterone. The progestin component inhibits 5α-reductase activity and acts as antagonists at the androgen receptor level [2–5].

A recently developed COC contains 30 mcg ethinylestradiol (EE) and 3 mg drospirenone, a new progestogen. Drospirenone is derived from 17α-spirolactone. Unlike most other current progestogens which are derived from 19-nortestosterone, drospirenone has anti-mineralocorticoid, antiandrogenic effects [6,7] and favorable metabolic effects, including potential to reduce blood pressure and body weight. Only a few Western trials have been done with drospirenone-containing pills. Therefore, this study was conducted to evaluate the effects of drospirenone-containing pills on clinical, endocrine and metabolic indices in Indian women with PCOS.

* Corresponding author. Tel.: +91 11 26594933, +91 26589883, +91 9810828717; fax: +91 11 26588641, +91 26588663.
E-mail address: kriplanialka@gmail.com (A. Kriplani).

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2. Materials and methods

2.1. Study design

Prospective randomized clinical trial was conducted after obtaining ethical approval from the institute's Ethics Committee.

2.2. Participants

Sixty women not desirous of conception for at least 6 months and diagnosed with PCOS by Rotterdam ESHRE/ASRM Workshop criteria [8].

Inclusion criteria (Rotterdam) were oligomenorrhea and/or anovulation, clinical or biochemical signs of hyperandrogenism, polycystic ovarian morphology on ultrasonography scan defined as presence of 12 or more follicles in each ovary (with one ovary sufficient for diagnosis) measuring 2–9 mm in diameter or increased ovarian volume >10 mL. Any two of these three were considered to be PCOS.

Exclusion criteria were hypothyroidism, hyperprolactinemia, history of exogenous hormonal agent within past 6 months, smoking, alcohol, recent history of surgical treatment for PCOS, contraindications to combined oral contraceptives or associated renal or adrenal insufficiency on drugs that increase serum potassium (ACE inhibitors, AT II blockers).

2.3. Randomization

After obtaining informed consent, participants were randomized using a computer-generated randomization table into two groups. The study group was given EE 30 mcg+drospirenone 3 mg and the control group received EE 30 mcg+desogestrel 150 mcg for 6 months as 21/7-day regimen.

2.4. Workup

A detailed history, including menstrual history and past medical history, was taken and thorough physical and gynecological examination with acne scoring [9] and hirsutism assessment with Ferriman–Gallwey (FG) scoring [10] were done. By FG scoring, the extent of hair growth was quantitated in nine key anatomic sites, by subjective assessment by a single clinician for all the patients. Hair growth was graded using a scale from 0 (no terminal hair) to 4 (maximal growth), for a maximum score of 36. Patients with a score of 8 or more were diagnosed as hirsutism. Patients were requested not to use shaving or other methods for hair removal during the study period. The same clinician assessed the patients during follow-ups.

Body weight and height of patients were measured with patients wearing loose clothes and without shoes and BMI was calculated as weight (in kg)/height^2 (in m). Blood pressure was measured after patient has seated quietly for 5 min.

Blood samples were taken at baseline for hemoglobin, lipid profile, fasting blood sugar and insulin, 2-h postprandial glucose and insulin after 75 g glucose ingestion along with hormonal parameters including follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid stimulating hormone, prolactin, total testosterone, SHBG, dehydroepiandrosterone sulfate (DHEAS) and 17-hydroxyprogesterone on Days 2–5 of the cycle. Ultrasound of the pelvis was performed on Days 5–7 of the cycle for features of PCOS in the ovaries.

2.5. Analysis of blood components

Total testosterone was determined by microparticle assay on the Axsym autoanalyzer using commercial kits manufactured by Abbott Laboratories (Abbott Park, IL, USA). DHEAS was analyzed by enzyme immunoassay using Demeditec DHEA-S/ELISA (Demeditec diagnostics, Germany). SHBG was measured in serum samples by chemiluminescent immunometric assay (Immulite/Immmulite1000 systems, PILKSH-9, EURO/DPC). Fasting and postprandial insulin were measured by ELISA immunoassay (Mercodia, Uppsala, Sweden). Normal values were as provided by respective manufacturers. Free androgenic index and bioavailable testosterone were calculated [11]. Lipid profile [total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), very low-density lipoprotein (VLDL)] was analyzed by Beckman Coulter CX9,CX4 autoanalyzer (RANDOX Laboratories, Crumlin, UK) based on spectrophotometry. Blood glucose was measured by glucose oxidase method adapted to auto-analyzer.

2.6. Follow-up

Patients were followed-up at 1, 3 and 6 months during treatment and then 3 and 6 months post-treatment. Lipid profile and ultrasound were repeated at 3 and 6 months of treatment and then 3 months post-treatment. Glycemic and hormonal profile were repeated at the end of 6 months of treatment.

2.7. Statistical analysis

Analysis was done using STATA 9.0 (College Station, TX, USA). Data are presented as number (%) or mean±S.D./median (range) as appropriate. Paired *t* test/Wilcoxon signed rank test (for non-parametric data) were used to compare changes in follow-up values from baseline. $p<.05$ was considered statistically significant.

3. Results

The age of patients was 22.5±4.7 years (mean±S.D., range 16–40 years). At baseline, all patient parameters were comparable between the two groups except weight ($p=.04$); however, BMI was comparable ($p>.05$). All women were normoprolactinemic, normotensive, had normal thyroid function and were without evidence of any other major medical disorder. Fig. 1 shows the

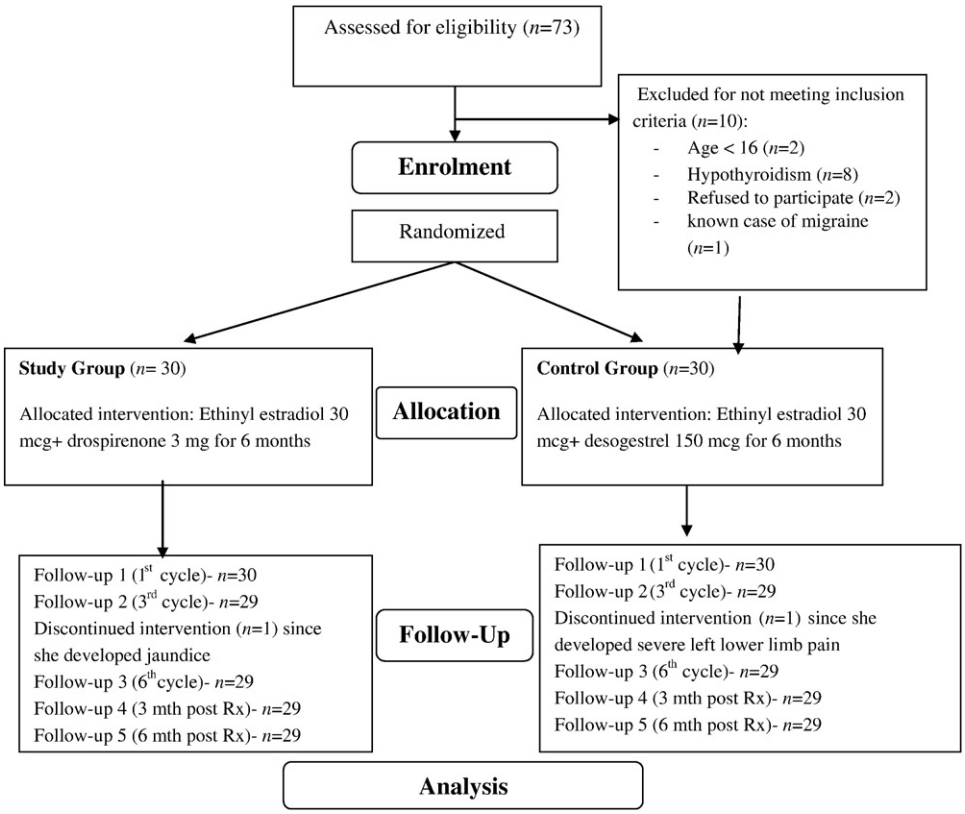

Fig. 1. CONSORT flowchart of the study.

CONSORT flowchart of patients screened, excluded, randomized, treated and followed up.

3.1. Menstrual regularity

Details of menstrual pattern of patients at baseline, at 6 months of therapy and at 6 months post-treatment are shown in Fig. 2. Prior to treatment, two thirds of patients, 20 of 30, in both groups had oligomenorrhea; eight (26.7%) and nine (30%) patients in the study and control group, respectively, presented with amenorrhea, and only two patients (6.7%) in the study group and one patient (3.3%) in the control group had regular cycles. During treatment, cycles became regular in all patients in both groups. In the study group 13/29 (44.8%) continued to have regular cycles vs. 5/29 (17.2%) in the control group ($p<.01$) for 6 months after stopping treatment. The number of cycles per 6 months increased from 4±1.78 at the baseline to 5±1.29 ($p=.0003$) in the study group at 6 months post-treatment; however, they increased insignificantly from 3±1.07 at baseline to 3±1.26 at 6 months in control group ($p=.16$).

3.2. Acne

One third of patients (10/30, 33.3%) had acne in both groups. Out of 10 patients with acne, 50% responded to treatment in the study group vs. 30% in the control group at the end of 6 months treatment ($p=.87$). The changes were statistically not significant between the groups. After stopping treatment, the number of patients with acne did not increase at 6 months in the study group; however, it increased to eight of 10 in the control group.

3.3. Hirsutism

In the study group, 23 of 30 patients (76.7%) and 22 of 30 patients (73.3%) in the control group complained of hirsutism, though on the basis of the Ferriman-Gallwey score (>8) hirsutism was diagnosed only in 5 and 4 patients in the study and control group, respectively. In the study group, hirsutism score as evidenced by the extent of hair growth was reduced significantly from a baseline value of 12.6±4.5 (mean±S.D.) to 8±4.3 (36.5%) at the end of 6 months of treatment ($p=.04$) and remained decreased at 8.4±3.8 (mean±S.D.) at 6 months post-treatment. There was no change in hirsutism score in the control group throughout the study period.

3.4. Body mass index and body weight

At baseline, 19 of 30 (63.3%) patients in the study group, and 20 of 30 (66.7%) in the control group were overweight/obese (BMI >25). Mean change in weight in both groups are depicted in Fig. 3. There was a significant weight loss in the study group from 68.3±12.4 (mean±S.D.) to 65.82±12.1 kg (3.63%, $p<.01$) at 3 months and 66.9±12.3 kg (2% fall, $p=.01$) at the end of 6 months of treatment against a mean weight gain in the control group from 60.4±7.6 (mean±S.D.) to

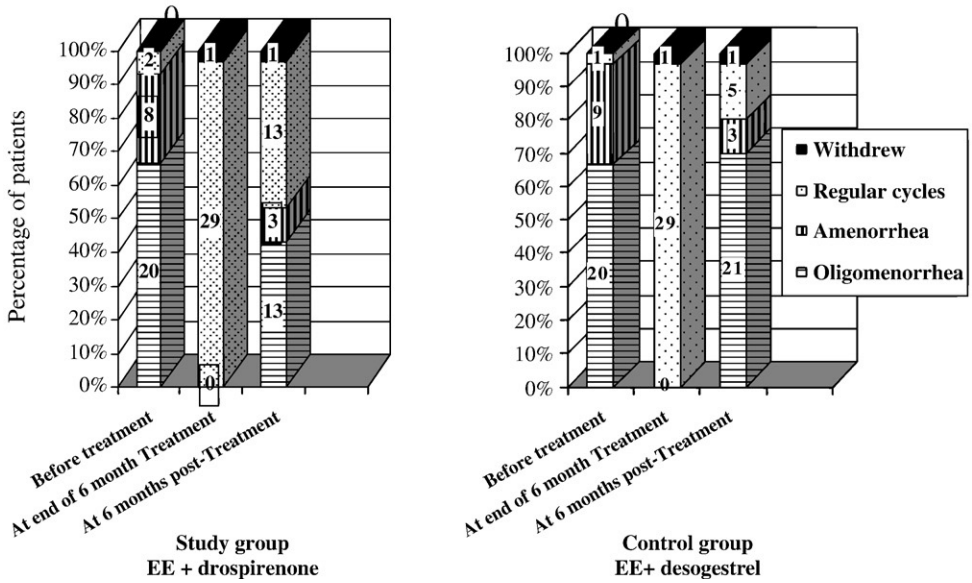

Fig. 2. Menstrual pattern with treatment in study and control groups.

62.4±7.2kg (3.3%, p<.01) at 3 months and 63.7±7.3 kg (5.3% rise, p<.01) at 6 months. At the end of 6-month treatment, BMI was reduced from 27.6±5.4 (mean±S.D.) to 27±5.3 kg/m^2 (1.9% fall) in the study group, whereas it increased from 26.1±3.6 to 27.5±3.6 kg/m^2 (5.3% rise) in the control group. The fall in BMI in the study group and rise in BMI in the control group were statistically significant (p=.01). The trend continued even at 6 month post-treatment with 1.7% fall and 1.8% rise in the study and control groups, respectively.

3.5. Blood pressure

As compared to baseline, blood pressure (BP) showed a falling trend during treatment in the study group; systolic BP reduced from 120.3±12.5 (mean±S.D.) to 118.4±7.5 (1.9 mmHg or 1.6% fall) and diastolic BP from 76.1±5.5 to 75.7±5.3 (0.4 mmHg or 0.5% fall) at end of 6 months of treatment (p>.05). Maximum fall in diastolic BP was noted as early as the first month of treatment. At 6 months post-treatment, both systolic/diastolic BP were found to be elevated from baseline in the study group, with mean increase by 1.39 mmHg (1.1%) and 3.24 mmHg (4.2%), respectively. While the rise in systolic BP was insignificant from baseline, that of diastolic BP was significant (p=.005).

In the control group, there was a significant rising trend in both systolic/diastolic BP throughout the study (p<.01 from baseline). Systolic BP rose from 114.7±9.4 (mean±SD) to

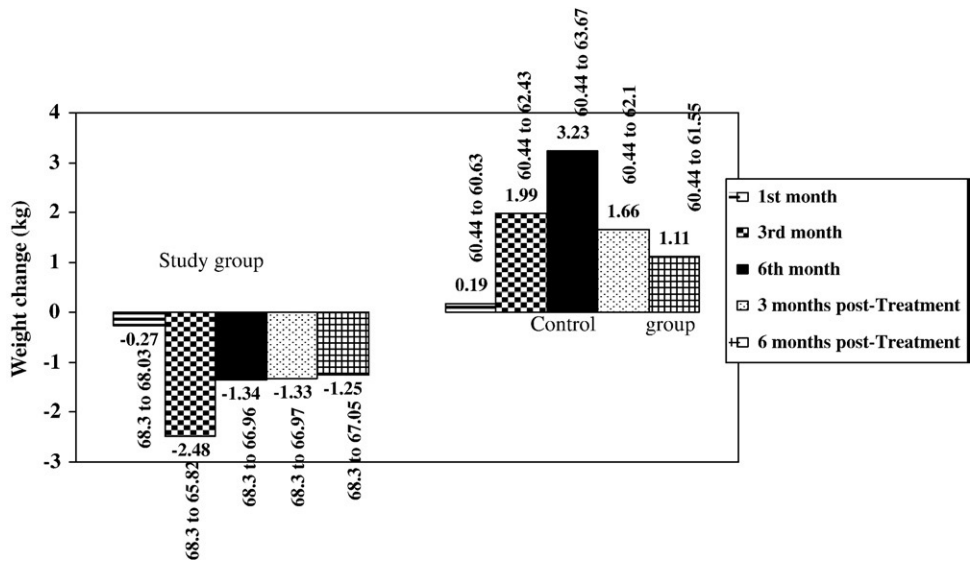

Fig. 3. Mean change in weight in both groups during the study.

116.4±7.8 (1.7 mmHg or 1.4% rise); diastolic BP was elevated from 73.1±7.4 to 76.1±5.0 (3 mmHg or 4.2% rise) at the end of 6 months of treatment. At 6 months post-treatment, BP remained above baseline values, with mean increase in systolic BP of 2.16 mmHg (1.8%) and in diastolic BP of 3.1 mmHg (4.2%).

One patient in the study group had a baseline BP of 150/80 mmHg and, during her treatment, had normal BP values. But at 3 months post treatment, her BP rose to 160/110 mmHg for which anti-hypertensives were given by the physician after evaluating for secondary causes. No patient in the control group had hypertension during the study.

3.6. Ultrasound parameters

Ultrasonographic features of PCOS were present in 25 of 30 (83.3%) patients in the study group and 20 of 30 (66.7%) in the control group. At end of 6 months treatment, 16 of 25 (64%) vs. 11 of 20 (55%) patients in the study and control group, respectively, reverted to normal sonographically. There was a significant decrease in mean ovarian follicle number from baseline of 10.2±3.6 (mean±S.D.) to 6.6±3.3 (35.1% fall, p<.01) in the study group and from 8.8±2.1 to 8 ±1.8 (8.3% fall) in the control group at end of 6 months of therapy. This reduction remained significant (p<.01) in the study group at 29.2% vs. 6.2% in the control group at 6 months post-treatment. Ovarian volume decreased significantly (p=.01) from baseline to 3 months of treatment in the study and control groups, 10.3% vs. 11.8%, respectively; the fall persisted at 7% and 5.3% in both groups until the end of 6 months of treatment; the control group showed a minimal rise of 0.8% at 3 months post-treatment. Endometrial thickness decreased from baseline by a maximum of 13.8% vs. 7.1% at the end of 6 months of treatment in the study and control group, respectively.

3.7. Lipid profile

Effects of treatment on lipid profile are shown in Table 1. There was a significant rise (p<.01) in total cholesterol (8.5% vs. 6.7%) and triglycerides (11.8% vs. 14.4%) from baseline in the study and control group, respectively, at the end of 6 months of treatment. It persisted even after 3 months of stopping the drug. Mean LDL decreased significantly from baseline by 7.2% in the study group (p<.01) at end of 6 months of treatment. This fall persisted at 3 months after treatment at 0.3%. But in the control group LDL levels significantly increased (p<.05) from baseline by 6.5% at the end of 6 months of treatment and persisted at 6.3% above baseline after 6 months post-treatment. HDL levels increased significantly from baseline in both groups (p<.01 in study group, p<.05 in control group) with more marked effect in the study group (12.3% vs. 5.4% at the end of 6 months of treatment) and persisted 3 months post-treatment. VLDL increased by 14.2% vs. 16.9% at the end of 6 months of treatment in the study and control groups, respectively; rise of VLDL being significant in the study group (p<.05) at 3 months of therapy, while in the control group it was significant throughout the study (p<.05).

3.8. Glycemic profile

Effects of treatment on glycemic profile are shown in Table 2. There was a significant decline of fasting blood sugar and insulin (p<.01) and postprandial blood sugar and insulin (p<.05) from baseline in study group. In control group, there was insignificant rise in fasting and postprandial sugar from baseline with significant rise (p<.01) of fasting and postprandial insulin. However, there was no significant difference between the groups at the end of 6 months treatment. One patient in the study group who had impaired fasting blood sugar had normal value at the end of treatment.

Table 1
Effects of treatment on lipid profile in both groups

Parameters (normal values in non-PCO women) (mg/dL)	Group	Baseline Mean±S.D. (range)	6 months treatment Mean±S.D. (range)	% Change	3 months post-treatment Mean±S.D. (range)	% Change
Cholesterol (100–200)	Study	160.3±20.1 (126–194)	173.9±19.9 (139–219.6)	↑8.5%#	172.4±18.9 (140–208)	↑7.5%#
	Control	150.9±23.0 (101–193)	162.1±25.8 (98–219)	↑6.7%#	160.3±18.9 (102–199)	↑6.2%#
	p value	.09	.04*		.02*	
Triglycerides (50–150)	Study	105.6±28.8 (54–167)	118.1±30.7 (67–190)	↑11.9%#	116.9±26.9 (76–184)	↑10.7%#
	Control	90.8±31.0 (48–199)	103.9±29.4 (66–186)	↑14.4%#	103.7±27.7 (63–183)	↑14.2%#
	p value	.054	.07		.07	
LDL (<130)	Study	96.7±22.5 (61–147)	89.6±17.8 (62–133.8)	↓7.3%#	96.3±17.1 (70–129)	↓0.3%
	Control	94.6±17.9 (52–124)	100.8±16.8 (58–128)	↑6.5%#	100.6±13.2 (70–120)	↑6.3%#
	p value	.69	.008**		.22	
HDL (>35)	Study	44.7±7.1 (29.7–59)	50.3±7.3 (40–67.1)	↑12.3%#	48.6±6.2 (31–60)	↑8.7%#
	Control	41.7±4.7 (33–53)	44±4.4 (40–56)	↑5.4%#	43.4±3.3 (40–51)	↑3.9%
	p value	.05	.000**		.000**	
VLDL (10–30)	Study	23.6±7.4 (12.8–42)	26.9±11.0 (11–55.2)	↑14.2%	25.8±8.7 (13–40)	↑9.3%
	Control	19.6±9.2 (9–50)	22.9±8.22 (11–46)	↑16.9%#	22.7±7.5 (14–45)	↑15.5%#
	p value	.06	.07		.08	

* p<.05, statistically significant.
** p<.01, statistically very significant.
# p<.05, from baseline.

Table 2
Change in glycemic profile with treatment in both groups

Parameter (normal values in non-PCO women)	Group	Baseline	At 6 months of treatment	% change	p
Fasting blood sugar (70–110 mg/dL)	Study	84.8±9.2 (70–110)	80.6±6.2 (70–95)	↓ 3.8%#	.22
	Control	81.3±7.4 (67–97)	81.9±6.1 (70–96)	↑0.6%	
postprandial blood sugar (70–140 mg/dL)	Study	89.7±9.8 (70–114)	87.0±11.7 (75–130)	↓2.7%#	.17
	Control	89.2±9.5 (75–118)	91±10.3 (78–126)	↑2.1%	
Fasting insulin (3–22 μIU/mL)	Study	11.3±4.4 (3.9–21.8)	8.7±3.6 (3.5–17.6)	↓23.1%#	.07
	Control	10.3±5.4 (3.2–21.9)	11.7±6.2 (4.1–24.8)	↑12.6%#	
Postprandial insulin (5–80 μIU/mL)	Study	24.7±11.5 (9.1–58)	22.1±10.4 (7.3–54.9)	↓10.5%#	.07
	Control	23.6±9.9 (9.8–44.7)	27.8±11.5 (10.4–54)	↑17.8%#	
HOMA IR[a] (<2.6)	Study	2.3±0.9 (0.7–4.42)	1.7±0.7 (0.7–3.5)	↓ 29.2%	.1
	Control	1.6±1.2 (0.7–5.1)	1.8±1.3 (0.7–5.3)	↑15.8%	

[a] HOMA IR=serum fasting insulin (mcg IU/mL)×fasting blood glucose (mmol/L)/22.5.
# p<.05 from baseline.

Two patients in the study group and 1 patient in the control group with high postprandial insulin at baseline had decrease in values to normal at the end of treatment. Three patients in the control group with normal postprandial insulin at baseline had higher values at the end of treatment. No patient was found to be diabetic either at baseline or at the end of treatment.

3.9. Hormonal profile

Effects of treatment on hormonal profile are shown in Table 3. Testosterone levels of all patients at baseline were within normal range (0.05–0.78 ng/mL) except three of 30 in the study group and two of 30 in the control group which also lowered to normal range at the end of treatment.

3.10. Side effects

Side-effects noted in both group of patients were nausea, headache, abdominal pain, breakthrough bleeding, spotting and breast pain. The most common side effect was nausea seen in three (10.3%) in the study group vs. five (16.7%) in the control group at the first month of treatment; nausea persisted in one (3.4%) vs. three (10.3%) in the study and control group, respectively, at 3 months of therapy. Two (6.7%) patients in the control group had vomiting at 1 month of treatment, though none had vomiting in the study group. Patients were managed with anti-emetics and no patients withdrew from the study. On and off headaches were a complaint of one (3.4%) patient in the study group from 3 months of therapy which persisted until the end of 6 months of treatment which was relieved by pain killers and she continued with treatment. The patient did not complain of headaches in the post-treatment period. Abdominal pain was noted less in the study group than in the control group five (16.7%) vs. six (20.7%), respectively, which persisted in two (6.9%) patients in both groups through 3 months of treatment. Breakthrough bleeding was reported by two of 30 (6.7%) patients in each group at one month of treatment as an episode of 3–4 days which recurred in only one of 30 (3.3%) patients in the control group at 3 months of treatment, whereas no patient in the study group had breakthrough bleeding until the end of 6 months treatment. Four (13.3%) patients missed pill intake for more than 2 days and spotting was noted in two (6.7%) vs. three (10.3%) in

Table 3
Change in hormonal profile with treatment in both groups

Parameters (normal values in non-PCO women)	Group	Baseline	At 6 months of treatment	% Change	p
FSH (4–13 mIU/mL)	Study	5.1±2.0 (1.5–12.2)	4.5±1.7 (0.4–9.6)	↓12.3%	.5
	Control	5.3±1.6 (1.9–9.2)	4.7±2.9 (2.1–9.1)	↓11.9%	
LH (1–18 mIU/mL)	Study	7.8±4.5 (1.2–21.6)	3.8±2.8 (0.1–11.9)	↓51.2%	.06
	Control	6.0±2.7 (3.0–16.5)	5±1.2 (2.3–8)	↓17.1%	
LH/FSH ratio (<2)	Study	1.3±1.4 (0.3–6.4)	0.9±0.7 (0.1–4.1)	↓34.8%	.06
	Control	1.3±0.4 (0.6–2.1)	1.1±0.2 (0.3–1.5)	↓18.7%	
Total testosterone (0.05–0.8 ng/mL)	Study	0.6±0.3(0.1–1.4)	0.5±0.2(0.1–0.9)	↓21.3%#	.049*
	Control	0.6±0.2 (0.1–0.9)	0.6±0.2 (0.3–0.9)	↑3.2%	
SHBG (18–114 nmol/L)	Study	20±12.0 (12–62)	62.3±50.3 (13.1–221)	↑211%	.5
	Control	22.5±17.2 (7.6–7)	60±41.0 (20–199)	↑166%	
Free androgenic index	Study	8.9±7.9 (1.6–40.5)	2.8±4.9 (0.2–19.5)	↓68.7%	.12
	Control	8.3±6.9 (1.2–32.8)	3.9±1.9 (0.749.5)	↓52.7%	
Bioavailable testoterone (0.2–2.5 nmol/L)	Study	0.7±0.3 (0.1–1.7)	0.4±0.2 (0.1–1.01)	↓33.8%	.25
	Control	0.6±0.2 (0.1–1.1)	0.5±0.1 (0.2–0.7)	↓16.9%	

* p<.05, statistically significant.
# p<.05, from baseline.

the study and control groups, respectively, at 1 month of treatment. One (3.4%) patient in the study group had spotting at 3 months of therapy also but no spotting thereafter. Bloating was complained by four of 29 (13.79%) patients in the control group and none in the study group. Breast pain was complained by two patients (6.7%) in both groups at one month of treatment, but only one (3.4%) patient in the study group continued to have breast pain until 3 months of treatment. None of the patients had any serious side effect except one (3.4%) patient in the control group who had severe left lower limb pain. Doppler evaluation showed no evidence of thrombosis, but the patient discontinued treatment.

4. Discussion

In PCOS, although all COCs achieve some reduction in androgen levels, clinical benefit is blunted by variable androgenic activity of progestins within the formulations [12–14]. The new drospirenone-containing COC is considered a fourth-generation OC. Besides the antiandrogenic benefits similar to the physiological effects of progesterone in the luteal phase of spontaneous cycles, drospirenone is able to induce sodium excretion and a compensatory increase in renin secretion, plasma renin activity, angiotensin II and plasma aldosterone, thus minimizing the estrogen-related flluid retention [15].

In the present study, patients underwent treatment for 6 months and were followed-up for 6 months post-treatment. There was a significant increase in the number of withdrawal bleeding episodes cycles per 6 months in the study group during and months after stopping treatment (p=.0003). Two other studies have also reported good cycle control with drospirenone in PCOS patients with 6 and 12 months treatment, but the drug-free period after treatment was not included in their study [16,17].

The effect of treatment on acne is in accordance with other studies [16]. In a randomized control trial with 125 patients with mild to moderate acne, median reduction in total facial acne lesions was 62% for drospirenone-containing pills and 59% for cyproterone acetate-containing pills after 9 cycles [18].

A period of 6 months is usually sufficient to observe some benefit in body and limb hair. However, facial hair which are most distressing may take a couple of years of antiandrogen therapy to show improvement [16]. In the present study, improvement in hirsutism score was assessed by reduction in extent of hair growth (FG score). A significant decrease in the mean score of hirsutism from baseline was observed in study group (p<.05) at all visits, with 36.5% reduction at the end of 6 months of treatment and remained decreased at 6 months post-treatment. No change in hirsutism score was noted in control group. Most prominent effect was noted on the chest and abdomen, followed by the upper lip and chin. The lowest effect was observed on the back and arms. A similar finding was noted in the study by Batukan and Muderris [19].

In accordance with a previous study, our study group showed a significant (p=.01) fall in body weight and BMI in contrast to gain in the control group [17]. Another study reported no overall change in BMI [16]. Reduced weight persisted even after 6 months of stopping treatment in our study group though none of the other studies have reported the effect in the post-drug period. Hence, a COC which can reduce or at least maintain weight, like those containing drospirenone, are promising in the management of PCOS patients who are reportedly obese in 41% cases [20,21].

Similar to the present study, there is another report showing a fall of 2 mmHg in both mean systolic/diastolic BP (p>.05) at the end of 6 months of drospirenone-containing pills in 17 PCOS women [16], while mean systolic/diastolic BP remained stable during the treatment in another study [17]. One retrospective study analyzed the combined daily administration of drospirenone and estradiol valerate, and found a slight reduction in BP [22]. The post-treatment period was not studied in any of the above studies. In our study, the finding of a rise in BP from baseline after stopping treatment might be due to small sample size and because one patient developed hypertension, this aspect needs further evaluation in larger studies.

Drospirenone has been shown to decrease endometrial thickness both morphometrically as well as sonographically when given for 13 cycles [23] which correlates well with our study. Ovarian follicle number decreased significantly from baseline at the end of 6 months of treatment in the study group and so did the ovarian volume which was significantly decreased even at 3 months of treatment. None of the previous studies had evaluated the ovarian volume in PCOS patients as a parameter of comparison between drugs. The original PCOS pattern returned in the patients within a few months following treatment. Similar finding was reported by a previous report by European Society of Human Reproduction and Embryology [24].

In various studies including the present study on drospirenone-containing pills, there was elevated total cholesterol and triglyceride levels, raised VLDL, lowered LDL and a significant rise of HDL at the end of 6 months of treatment [15,17,25,26]. One study showed a rise in LDL by 34.2% in the first six cycles and thereafter a fall of 27% in the next six cycles [17]. A study comparing drospirenone combination pills with flutamide-metformin continuation over 9 months in PCOS patients, showed a similar increase of triglycerides and HDL in both groups, but they reported a more pronounced fall of LDL and a favorable adipocytokine pattern with the addition of flutamide-metformin to drospirenone-containing pills [27]. A rise in cholesterol of 31.4% in the study by Guido et al. [17] vs. 8.4% in our study and elevation of triglycerides of 18–80% in various studies vs. 11.5% in our study can be explained by shorter duration of treatment in our study as well as by the influence of various dietary and environmental factors on lipid profile.

Our study group showed an improvement in insulin sensitivity with drospirenone similar to few other studies [16,17]. Other studies have shown that blood glucose values and insulin remained unchanged or showed an insignificant rise [15,26,28]

Decrease in FSH and LH due to pituitary suppression was noted in both the groups in our study. But the LH levels decreased more in the study group than in the control group (51.2 vs. 17.1%) at the end of 6 months of treatment, as have been reported by a previous study in hirsute women with PCOS [17]. In accordance with various other studies, there was a significant fall in total and free testosterone in the study group. SHBG levels were elevated in both groups and hence free androgenic index decreased in both groups [16,27,29].

Nausea, abdominal pain and breakthrough bleeding was less frequent in the patients treated with drospirenone-containing pills, as was also seen in other studies [17,28,30].

5. Conclusion

In women with PCOS, a drospirenone-containing COC had better outcome measures in terms of persistent regularity of cycles, antiandrogenic effect, fall in BMI and BP, better lipid profile and favorable glycemic and hormonal profile than a desogestrel-containing COC. Drosperinone-containing COCs are a good option for treatment in obese PCOS patients with hirsutism.

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