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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

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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.

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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