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AN OBSERVATIONAL STUDY TO EVALUATE EFFECT OF SIX-MONTH USE OF ORAL CONTRACEPTIVE PILLS ON PLASMINOGEN ACTIVATOR INHIBITOR-1 & FACTOR VIII AMONG WOMEN WITH POLYCYSTIC OVARY SYNDROME

[1]Fahad Qureshi, [2]Dr.Rashmeen Khan Afridi, [3]Dr.Sidra Ashraf

[1]Continental Medical College Lahore, [2]Yusra Medical & Dental College Islamabad, [3]Quaid E Azam Medical College, Bahawalpur.

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Abstract:

Polycystic ovary disorder (PCOS) is an endocrinopathy, a lasting individualized treatment through way of life pharmacological specialists and, over every oral prophylactic (OCP), legitimizes. The point of this examination was to explore the impacts of OCP on plasminogen-1 inhibitor-activator (PAI-1) and on factor VIII (FVIII) in PCOS ladies for a half year.

Strategies: *Women with PCOS analyzed in Rotterdam 2003 criteria, regardless of whether OCP (ethinyl estradiol 0.03 mg, 0.15 mg levonorgestrel) for a time of a half year (n = 40) or medications (n = 42), were incorporated into this investigation. Blood was taken to evaluate glucose, insulin levels and lipid profile. Chemiluminescent immunoassays (LH, FSH, PRL, T4) were utilized to gauge hormones. Plasma dimensions of PAI-I and FVIII were estimated with business packs.*

Results: *the consistency of monthly cycle, the Ferriman-Gallwey score and serum absolute testosterone improved fundamentally in the OCP bunch contrasted with the gathering without medications (P <0.01). No noteworthy contrasts were seen in the PAI-1 dimensions of the two gatherings; In the OCP gathering, be that as it may, a huge reduction in FVIII levels was watched contrasted with the gathering without medications. PAI-1 dimensions of the OCP bunch related decidedly with two-hour glucose, triglycerides and insulin two hours while the FVIII bunch OCP level associated adversely with fasting insulin and insulin opposition for homeostatic model.*

Elucidation and conclusion: *the utilization of OCPs differently affects markers that advance coagulation in ladies with PCOS. To elucidate the adequacy and wellbeing of OCP in the treatment of PCOS, well-planned, long haul, forthcoming and enormous scale considers are required.*

Corresponding author:

Fahad Qureshi,

Continental Medical College, Lahore.

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INTRODUCTION:

Polycystic ovary disorder (PCOS) is a typical endocrine issue in ladies of childbearing age. Other than the various ones .Regenerative clutters (endless anovulation and hyperandrogenism), these ladies will in general create insulin obstruction (IR), compensatory Hyperinsulinemia, dyslipidemia, hypertension, Fettleibigkeit3, metabolic disorder (MS), type 2 diabetes mellitus (DM2) and high danger of cardiovascular malady (CVD) 4. A few investigations have appeared of the haemostatic framework, for example, a genius thrombotic condition, including hypofibrinolysis, hypercoagulability5,6 and endothelial and platelet dysfunction5,7.

The inhibitor plasminogen-1 activator (PAI-1), a key controller of fibrinolysis, is a marker for IR, since dimensions of PAI-1 antigen and movement in plasma in IR conditions, for example, heftiness in the stomach depression, MS and T2DM8 frequently expanded. In perspective on the higher commonness of IR in ladies with PCOS, plasma dimensions of PAI-1 have been contemplated in ladies with PCOS9-11 and now and again expanded dimensions of PAI-1 have been accounted for. Factor VIII (FVIII) is a coagulation factor subject to nutrient K which is combined fundamentally in the liver and circles in plasma in a non-covalent complex with von Willebrand factor. Coronary vessel sickness and gemeldet stroke 12,13 FVIII is a successive hazard factor for venous thrombosis, in which raised qualities with a high weight list (BMI), plasma glucose, insulin, fibrinogen and Triglyceridspiegeln14 detailed. FVIII has constrained information; It has not been concentrated broadly in ladies with PCOS. Oral contraceptives (OCPs) are viewed as the treatment of decision in PCOS, as these operators are helpful in directing menstrual cycles and improving androgenic symptoms15. Be that as it may, OCPs have been related with the interruption of lipid and glucose digestion notwithstanding venous thrombosis 16,17. This pilot consider was directed to analyze the plasma dimensions of PAI-I and FVIII in ladies with PCOS who got OCP for at any rate a half year with ladies without PCOS.

MATERIAL AND METHODOLOGY:

This pilot investigation of individual perception was led from January 2015 to March 2016 at the Department of Endocrinology at the Services Institute Of Medical Sciences. The ladies needed to meet the Rotterdam 200318 criteria for the finding of PCOS before taking an interest in the investigation. Consequently, of the 200 ladies inspected amid this period, just those were chosen for this investigation that met the consideration criteria. Ladies were separated into two gatherings: OCP gathering (n = 40); Women who got OCP (ethinyl estradiol - 0.03 mg, levonorgestrel-0.15 mg) for in any event 24 ± 2 weeks after conclusion and medication treatment (n = 42), including

Ladies with PCOS and have not taken medications.

Clinical assessment:

Consecutive ladies who took an interest in centers with grievances of oligomenorrhea, undesirable hair development or skin inflammation vulgaris were educated about the investigation, and the individuals who volunteered to take an interest in the examination were approached to sign an assent structure. Subtleties of menstrual history, weight increase, undesirable hair development, skin break out vulgaris, and so on. They have been taken note. Oligomenorrhea was characterized as the quantity of cycles under eight every year or interim of> 35 days, while amenorrhea was viewed as ready to interfere with the menstrual cycle for a half year. Anthropometry (estimation of stature, weight, midriff hip proportion and blood vessel weight) and point by point fundamental examination were performed in all ladies. The hirsutism score was performed utilizing the Ferriman-Gallwey 19 score tallying nine showed body territories. A score> 8 was viewed as critical. The prohibition criteria were diabetes or hypertension, Cushing's disorder, hypothyroidism, hyperprolactinaemia and tumors that discharged androgens.

Assay: glucose (mg/dl) was estimated by the glucose oxidase oxidation strategy (DiaSys Diagnostic Systems, Germany). Plasma insulin was estimated by electrochemiluminescence (Cobase411, Roche Diagnostics Limited, Germany) utilizing economically accessible units. Lipid parameters, for example, cholesterol, triglycerides, low thickness lipoprotein (LDL) and high thickness lipoprotein (HDL) were (DiaSys Diagnostic Systems, Germany) was estimated with a colorimetric strategy. Immunological chemiluminescence (ECLIA, Meditron, USA) was utilized for LH, FSH, PRL, T4, TSH, cortisol and business all out testosterone packs utilizing (Beckman Coulter Uicel DXI 800, USA) to investigate in copy. ELISA was utilized to dissect 17-OHP utilizing business units (Diagnostics Biochem, Canada). Plasma PAI levels were estimated in copy utilizing an ELISA unit (SYMANSIS, New Zealand). The FVIII plasma was evaluated utilizing a coagulometric strategy utilizing a financially accessible pack (SIEMENS, USA).

IR was evaluated utilizing the homeostatic IR model

appraisal (HOMA-IR), which as a result of the fasting insulin esteem (μIU/ml) and the fasting glucose esteem was (mg/dl) partitioned by 40520 is determined. quantitative insulin affectability control file (QUICKI)) was utilized to gauge insulin affectability, and as 1/fasting insulin log (μIU/ml) + determined fasting blood glucose (mg/dl) 21 The proportion fasting glucose and insulin (FGIR) is gotten as fasting glucose (mg/dl)/fasting insulin (μIU/ml) 22 determined

Measurable investigation:

factual examination was performed with SPSS 20 programming (SPSS 20, IBM, Armonk, NY, USA). Different parameters, for example, anthropometry, fundamental biochemical estimations, hormonal and insulin estimations were thought about among cases and controls utilizing a two-example t-test. The Pearson relationship coefficient (r) was utilized to dissect the relationship between the examination factors.

RESULTS:

The fundamental attributes of the investigation bunches are abridged in tables I and II. Attributes, for example, mean age (years) and BMI (kg/m2) were tantamount in the two gatherings. Be that as it may, a noteworthy distinction was seen between the quantity of cycles every year and serum testosterone levels (P <0.01) among OCP and medication autonomous gathering. Absolute cholesterol, LDL cholesterol, insulin two hours (P <0.01) and QUICKI (P <0.05) were essentially higher than in the medication free gathering in the OCP gathering. The distinction in plasma dimensions of PAI-1 was not huge between members treated with OCP and those medication guileless. Plasma FVIII levels, in any case, were essentially lower in the OCP-treated gathering than in medication credulous ladies (P <0.01). PAI-1 in the OCP bunch a critical positive connection with glycaemia two hours (r = 0.26, p = 0.02), insulin demonstrated two h (r = 0.28, p = 0.03) and triglyceride levels (r = 0.24, P = 0.01). Notwithstanding, the FVIII level demonstrated a noteworthy negative connection with fasting insulin (r = - 0.34, p = 0.02) and HOMA-IR (r = - 0.32, p = 0.030).

Table I. Comparison of various clinical and biochemical parameters of drug-naïve group and oral contraceptive pill group

Parameters	OCP group (n=40)	Drug-naïve group (n=42)
Mean age (yr)	21.69±4.23	22.01±5.04
Number of cycles/yr	11.70±2.93**	7.33±3.90
Ferriman-Gallwey score	9.12±6.47	11.29±7.33
Weight (kg)	60.30±6.7	59.92±8.28
WHR	0.92±0.08	0.94±0.09
BMI (kg/m2)	24.30±3.56	23.81±3.11
Systolic BP (mmHg)	124.89±7.37	122.44±6.99
Diastolic BP (mmHg)	83.6±4.99	81.9±6.62
Serum total cholesterol (mg/dl)	189.87±38.43**	156.48±26.17
Serum triglycerides (mg/dl)	120±36.54	115.08±40.68
Serum HDL (mg/dl)	49.41±10.13	46.45±8.74
Serum LDL (mg/dl)	120.77±42.56**	86.21±24.99

***P*<0.01 compared to drug-naïve group, values are mean±SD. WHR, waist-hip ratio; BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OCP, oral contraceptive pill

Ladies with PCOS are because of expanded dimensions of markers that advance coagulation, for example, fibrinogen and PAI-1, which advance atherogenic procedures and increment the danger of CVD in these women23. A few examinations have detailed larger amounts of PAI-1 in ladies with PCOS, which associated decidedly with the segments of IR9.10. Moreover, the proof recommends that the utilization of OCP may additionally corrupt the coagulation state and the danger of CVD24,25.

There are constrained examinations assessing the impact of OCPs on PAI-1 plasma dimensions, and the outcomes are preferably disputable over conclusive26-28. In the present examination, a slight increment in plasma dimensions of PAI-1 was seen following a half year of OCP organization. Be that as it may, the PAI-1 dimensions of the OCP bunch were decidedly associated with the MS and IR markers. Past information recommend that OCP application may decrease PAI-126.27 dimensions or have no effect28. Teede et al 26 announced a further diminishing in PAI-1 levels in ladies with PCOS utilizing OCP containing cytoprotone acetic acid derivation. Like our revealed outcomes Küçük et al.29 have about an immaterial contrast in PAI-1 levels between ladies taking levonorgestrel-containing OCPs, and control ladies who had not gotten OCPs, despite the fact that this examination was led in ladies not PCOS.

Table II. Comparison of oral glucose tolerance test derived insulin resistance parameters, gonadotropins, total testosterone and pro-coagulant markers between drug-naïve group and oral contraceptive pill group

Parameters	OCP group (n=40)	Drug-naïve group (n=42)
Blood glucose - fasting (mg/dl)	89.57±10.28	88.85±16.91
Blood glucose - 2 h (mg/dl)	115.87±26.31	110.77±38.31
Serum insulin - fasting (µIU/ml)	18.33±24.75	13.18±10.19
Serum insulin - 2 h (µIU/ml)	65.64±54.53*	45.63±32.55
FGIR	6.74±5.84	4.88±10.30
HOMA-IR	2.89±3.04	4.05±3.99
QUICKI	0.31±0.02**	0.32±0.01
Serum LH (IU/l)	6.94±4.59	7.73±5.54
Serum FSH (IU/l)	6.23±3.32	6.16±2.00
Serum total testosterone (ng/dl)	53.57±17.03**	67.35±29.47
Plasma PAI-1 (ng/ml)	1.28±0.62	1.15±0.45
Plasma factor VIII (%)	0.57±0.33**	0.78±0.28

*P**<0.05, ****<0.01 compared to drug-naïve group. OGTT, oral glucose tolerance test; FGIR, fasting glucose insulin ratio; QUICKI, quantitative insulin sensitivity index; LH, luteinizing hormone; FSH, follicular-stimulating hormone; PAI-1, plasminogen activator inhabitor-1; HOMA-IR, homoeostatic model assessment-IR; IR, insulin resistance

It is realized that the grouping of FVIII is the expanded coagulant action and the utilization of OCP further builds the grouping of FVIII30. In the use of OCP with ethinyl estradiol and levonorgestrel, a huge abatement in plasma FVIII level contrasted with PCOS patients without medications was watched, and the OCP FVIII bunch associated in the present examination with negative IR markers. One examination revealed that OCPs don't seem to have any effect on FVIII31 levels. Ladies taking OCP demonstrated an expansion in fibrinogen and FX and a lessening in antithrombin III qualities with regard to their control values 28. This gathering likewise revealed little however noteworthy increments in

triglyceride-rich triglycerides and lipoproteins28. In rundown, the consequences of this pilot consider can't be unequivocal because of various restrictions, for example, the absence of essential information of the OCP gathering, less subjects and no control bunch with longitudinal investigations, it very well may be said. Notwithstanding these constraints, the information can make ready for well-structured and randomized longitudinal investigations with an enormous associate of ladies with PCOS.

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