Original Article

EFFECT OF COMBINED ORAL CONTRACEPTIVE PILLS ON LIPID PROFILE, BLOOD PRESSURE AND BODY MASS INDEX IN WOMEN OF CHILD BEARING AGE

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ABSTRACT

Objective: To find out the effect of combined oral contraceptives pills (COCPs) on lipid profile, blood pressure and body mass index in females of reproductive age.

Methodology: This cross sectional study was conducted from January 2011 to December 2011 in Family Planning Department of tertiary referral health care hospitals of Peshawar.

A total of 200 married fertile women of child bearing age (14-49 years) participated in the study. They were divided in two groups: Group 1 (COCPs users at least for six months) and *group 2* (age matched controls not using COCPs). Fasting levels of serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) were analyzed using chemistry analyzer. Haemoglobin (Hb) and platelets counts were measured on haematology analyzer. Body Mass Index (BMI) and blood pressure (BP) were measured in all subjects. Various parameters were compared among oral and control groups by using SPSS version 10.

Results: Comparing females of group-1 vs group-2, there was significant increase of cholesterol (185±3.27mg/dl vs 158.26±2.81mg/dL; p=0.0001), triglycerides (207.33±4.92mg/dL vs 135.63±4.49mg/dL; p=0.0001), LDL-C (98.20± 3.11mg/dL vs 85.19±2.65mg/dL; p= 0.002), BMI (27.52±0.371 vs 24.79±0.34 Kg/m2; p=0.0004), systolic BP (133.30±1.71 vs 122.69±1.35 mmHg; p=0.0007) and diastolic BP (84.85±1.16 vs 80.79±0.89 mmHg; p=0.009). Changes in the HDL-C (46.18±0.82 vs 45.92±0.91mg/dL; p=0.833), Hb (12.95± 0.16 vs 12.47±0.17 g/dL; p=0.045) and platelet count (262510.00±8822.64 vs 258882.63±9843.44 thousand/uL) were not significant.

Conclusion: Significantly elevated lipid profile, BP and BMI were recorded in women using COCPs.

Keywords: Combined Oral Contraceptive Pills, Lipid Metabolism, BMI

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INTRODUCTION

The oral contraceptive hormones, introduced in 1960, have undergone much modification. Worldwide, the contraceptive pills are used by 100 millions of women in child bearing age and about 11.6 million women of United States used combined oral contraceptive pills (COCPs). About 80% of child bearing age American women have used oral contraceptives in their life at some time.[1] In Pakistan, the prevalence of contraceptive use is 5.5% and this use of contraception is more common in urban area (9.8%) than rural area (3.9%).[2] According to data of Pakistan Population Planning Council and Ministry of Population Welfare/Population Council, the contraceptive prevalence rate in Pakistan was 5% during 1974-75[3] which increased up to 18.7 percent in 1994-95[4] due to continuous efforts of family planning service in Pakistan.

Two types of oral contraceptive pills are available in market, the *combined oral contraceptives* containing both estrogen and progesterone and *Progestin* containing only progesterone. The combined oral contraceptive pills are prepared in three different formulations, i.e. monophasic, biphasic, triphasic depending on the concentration of estrogen and progestin in menstrual cycle. COCPs are classified into three (first, second and third) generations.[5] Since its introduction, efforts have been directed to balance its risks and benefits. First-generation COCPs preparations combined high-dose ethinyl estradiol (≥50μg) and androgenic progestins, and were associated

with several adverse effects, the most acute being strokes and thromboembolic events.[6] In addition COCPs were found to be associated with cardiovascular risk factors that promote myocardial infarctions in its users. In order to reduce these adverse effects, COCPs with lower doses of estrogen (≤50 μg ethinyl estradiol) and less androgenic progestins were developed. In the United States, most low-dose COCs have estrogens in the range of 20–35μg. Although these low-dose COCPs are having lesser side effects but still the cardiovascular and thromboembolic risks have not been eliminated.[7,8] Mostly used COCPs in developed countries are the third generation; while in Pakistan second generation monophasic COCPs are still in use.[3]

Studies have shown that COCPs have effects on lipid & carbohydrate metabolism, liver proteins and coagulation.[9] The effect of COCPs on the level of serum lipid depends upon the concentration of estrogen and the concentration and type of progestogens.[9]

The COCPs changes the serum lipoprotein profile, HDL increase and decrease in LDL due to estrogen (a desirable occurrence), whereas these beneficial effects of estrogen are negated by progestogens.[9] Therefore, the preparations having dominant estrogen is best for individuals with elevated serum cholesterol. The third generation COCs had little impact on lipid profile.[10-12] Weight gain with combined oral contraceptives is also reported in earlier studies along with rise in BMI in COCs user.[13,14]

Progesterone can affect blood pressure by hormone cascades and direct effect on small blood vessels. Estrogen is primarily responsible for the rise in the blood pressure, but studies have suggested that progestogens may also contribute to the raised blood pressure. Estrogens induce the hepatic production of renin substrate, angiotensinogen, with a subsequent increase in angiotensin.[11]

For evaluation of the metabolic effect very few studies have been conducted in developing countries like Pakistan and almost none in Peshawar. The current study will help to reduce the mentioned metabolic risk factors for cardiovascular disease.

This study was conducted to find out the effect of combined oral contraceptive pills on lipid

Profile, platelets count, blood pressure and body mass index in females of reproductive age group in our set up.

METHODOLOGY

This cross sectional/analytical study was conducted during the year 2011. Ethical approval of the study was taken from the institutional research ethical board (IREB) Postgraduate Medical Institute (PGMI) Hayatabad Medical Complex, Peshawar. A total of 200 women of reproductive age (14-49 years) were randomly selected and included in the study from the Family Planning Departments of tertiary care hospitals (Khyber Teaching Hospital, PGMI Lady Reading Hospital and PGMI Hayatabad Medical Complex) of Peshawar. Aim of the study was explained and written informed consent was taken. These women were divided in two groups: group-I included 100 women of child bearing age (14-49 years) using combined oral contraceptives pills for at least 6 months and group-2 included same number of age matched control group not using COCPs. Women without history of hypertension, diabetes mellitus, stroke, renal/heart diseases taking hormonal contraceptives attending family planning department were randomly selected. We studied the effect of second generation monophasic combined oral contraceptive pills (28 days pack), which contains 0.3mg norgestrel and 0.03mg ethinyl estradiol in 21 white tablets, and 7 brown tablets contain 75mg ferrous fumarate. The specimen analysis was done in Pakistan Medical Research Council (PMRC) Research Centre, Khyber Medical College Peshawar and Institute of Basic Medical Sciences Khyber Medical University.

Biochemical analysis of lipoprotein included total serum cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, very low density lipoprotein cholesterol, triglycerides, while haematological parameters included haemoglobin and platelet count. Serum lipids were analyzed enzymatically by using Chemistry auto analyzer, and haematological parameters were measured by three dimensional, fully automated Haematology Analyzer Humacount Plus.

Serum triglycerides and total cholesterol were measured using enzymatic method of Elitech Diagnostic kits (France). Serum HDL-C was measured [Using Merck Diagnostics kit]. Serum LDL-C was calculated by Frederickson-Friedwald's formula according to which LDL-C = TC - HDL cholesterol – VLDL cholesterol. VLDL cholesterol was calculated as 1/5 of triglycerides.

The BMI was calculated from the measurement of weights and heights by using the following formula: BMI = Weight in Kg/Heights in (meter)^2. Finally the data was analysed using SPSS version 10.

RESULTS

In table-I the comparison of different socio demographic and reproductive characteristic of the two groups was done using student-t test. The age of both groups was comparable. The highest significance was seen in BMI (27.52±0.371 vs 24.79±0.34 Kg/m2; p=0.0004), systolic BP (133.30±1.71 vs 122.69±1.35 mmHg; p=0.0007) and diastolic BP (84.85±1.16 vs 80.79±0.89 mmHg; p=0.009).

Comparison of various biochemical and haematological parameters between group-I and group-2 is given in table II. Highest significantly increased values (p<0.00001) were seen in cholesterol (185.00±3.27mg/

TABLE I: COMPARISON OF DIFFERENT SOCIODEMOGRAPHIC AND REPRODUCTIVE CHARACTERISTICS BETWEEN GROUP 1 (WOMEN USING COMBINED ORAL CONTRACEPTIVE PILLS) AND GROUP 2 (CONTROL)

Variables	Group 1 (Oral COCP) Mean + SEM	Group 2 (Control) Mean + SEM	P value t-test
Age (years)	33.76± 7.01	33.41± 7.43	0.97
Menarche age (years)	12.55± 0.95	12.49± 0.70	0.95
Marriage age (years)	16.91 ± 2.80	18.87 ± 3.52	0.66
Age at 1st delivery (years)	18.47 ±2.59	20.29 ± 3.33	0.66
BMI Kg/m2	27.52 ±0.371	24.79 ±0.34	0.0004
Systolic B.P mmHg	133.30 ±1.71	122.69 ±1.35	0.0007
Diastolic B.P mmHg	84.85 ±1.16	80.79 ±0.89	0.009

TABLE-II: COMPARISON OF VARIOUS BIOCHEMICAL AND HAEMATOLOGICAL PARAMETERS BETWEEN GROUP 1 (WOMEN USING COMBINED ORAL CONTRACEPTIVE PILLS) AND GROUP 2 (CONTROL)

Parameters	Group 1 (COCPs group) Mean + SEM	Group 2 (Control group) Mean + SEM	P value t-test
T- Cholesterol mg/dL	185.00+ 3.27	158.26+ 2.81	0.0001
HDL mg/dL	46.18+ 0.82	45.92+ 0.91	0.833
LDL mg/dL	98.20+ 3.11	85.19+ 2.65	0.002
VLDL mg/dL	41.50+ 0.93	27.41+ 0.86	0.0001
Triglycerides mg/dL	207.33+ 4.92	135.63+ 4.49	0.0001
Hb% g/dL	12.95+ 0.16	12.47+ 0.17	0.045
Platelets count (thousand/uL)	262510.00 + 8822.64	258882.63+ 9843.44	0.78

TABLE III: COMPARISON OF BMI BETWEEN GROUP 1 (WOMEN USING COMBINED ORAL CONTRACEPTIVE PILLS) AND GROUP 2 (CONTROL)

BMI (kg/m2)	Group 1 {Oral COCP} (n)	Group 1 {Control group} (n)	OR (CI)	$\chi 2$	P value
<22.99	10	15	Referent		
23 – 24.99	19	41	1.57(0.53-4.69)	0.49	0.51
25 – 26.99	18	23	1.90(0.62-5.90)	1.01	0.32
>27	53	21	2.90(0.91-9.80)	3.18	0.07

TABLE IV: COMPARISON OF VARIOUS BIOCHEMICAL AND HAEMATOLOGICAL WITH SYSTOLIC B.P. >120MM HG AND DIASTOLIC B.P. >80MM HG BETWEEN GROUP 1 (WOMEN USING COMBINED ORAL CONTRACEPTIVE PILLS) AND GROUP 2 (CONTROL)

Blood concentrations	Group 1 (COCPs group) Systolic BP >120 (n=87)	Group 2 (Control group) Systolic BP >120 (n=25)	P value t-test	Group 1 (COCPs group) Diastolic BP >80 (n= 54)	Group 2 (Control group) Diastolic BP >80 (n=27)	P value t-test
Cholesterol mg/dL	185.63± 3.76	159.13± 3.39	0.0001	192.15± 4.69	163.89± 6.186	0.002
HDL mg/dL	46.07 ± 0.88	46.19± 1.01	0.926	45.74 ± 1.09	46.56± 1.90	0.712
LDL mg/dL	97.63 ± 3.45	84.41± 3.27	0.009	105.35± 4.27	88.50± 5.48	0.040
VLDL mg/dL	41.93 ± 1.10	28.88 ± 1.00	0.0001	41.06± 1.34	28.83± 1.87	0.0001
Triglyceride mg/dL	209.56 ± 5.50	142.50 ± 5.30	0.0001	205.13± 6.72	143.72± 9.25	0.0008
Hb% g/dL	13.93 ± 0.17	12.41± 0.21	0.0001	13.22± 0.16	12.46± 0.42	0.045
Platelets thousand/uL	254885.06 ± 9098.49	257071.42 ± 11347.91	0.880	254851.85 ± 9937.00	295388.88 ± 21296.71	0.058

dl vs 158.26±2.81mg/dL; p=0.0001), triglycerides (207.33±4.92mg/dL vs 135.63±4.49mg/dL; p=0.0001), LDL-C (98.20± 3.11mg/dL vs 85.19±2.65mg/dL; p= 0.002). Changes in the HDL-C (46.18+0.82 vs 45.92+0.91mg/dL; p=0.833), Hb (12.95+ 0.16 vs 12.47+0.17 g/dL; p=0.045) and platelet count (262510.00+8822.64 vs 258882.63+9843.44 thousand/uL) were not significant.

The women in COCPs group were found almost three times more obese BMI>27 kg/m^2 (53% in oral vs.16% of control group) with OR 2.90, CI (0.91-9.80), χ^2 3.18, p-value 0.074 (Table III).

Comparison of different parameters with systolic B.P >120 mmHg and diastolic B.P >80mmHg in oral and control groups has been given in table IV. The result showed highly significant p-value of the cholesterol, VLDL, Triglyceride and haemoglobin by p<0.00001, p<0.00001, p<0.00001 and p<0.00001 respectively when systolic B.P of the oral and control groups were compared and t- test was applied. When the lipoproteins of diastolic B.P >80 mmHg of oral and control groups were compared, the highly significant p-values of 0.00008 and 0.0001 were recorded for triglycerides and VLDL respectively.

DISCUSSION

The combined oral contraceptives have been in use in Pakistan for the last more than 50 years and proved to be highly effective but their components steroidal hormones i.e. the estrogens and progestogens have various metabolic effects, including lipid metabolism impairment. Evidence suggests that the individual composition of different COCs, in terms of estrogens dose and progestogen type, also influences their respective effects on lipids and lipoproteins.[15] The estrogen increases HDL-C and decreases LDL-C and progestrogen have opposite effect so these effects taken into consideration by keeping a balance in the dosage of two hormones in combined hormonal contraceptives.

In our study it was noted that the mean serum cholesterol level of women using COCs was increased with a p- value of high significance (0.0001). In a study conducted on the Nigerian women using COCs showed increased level of cholesterol with p<0.001.[16] Similar results of elevated cholesterol levels have been shown by others.[17,18]

The high level of lipids parameters, raised BMI and systolic and diastolic blood pressure pose an increased risk to cardiovascular diseases (CVD). Our study revealed these risk factors in COCs users. HDL-cholesterol level increases with COCs use because estrogens inhibits hepatic lipase activity, the enzyme responsible for clearing HDL-cholesterol from the circulation.[19] In our study the HDL-C was not changed significantly (p> 0.83), while the mean LDL and VLDL was increased with significant p-value of 0.002 and 0.0001 respectively. The levels of HDL, LDL, VLDL and TGs were observed to be elevated in hormonal contraceptives users. In a study conducted on the women receiving monophasic oral contraceptives reported reduction in HDL-C and an elevation in LDL-C and total triglycerides.[20] Our results are consistent with those observed in previous studies on combined oral contraceptives users.[7,18]

In our study the levels of triglycerides were found significantly elevated (p=0.0001) in COCs users Therefore, by causing an increase in TG levels, COCs use may be worsening cardiovascular risk. The increased level of triglycerides in the COCs using group was also reported by others.[7]

In our study the BMI in the women using COCPs was found to be significantly high (p<0.0004) when compared with control of their respective age groups. Analysis of the literature reports either minimal weight increase or little evidence for a causal relationship with oral contraceptive pills.[18, 21]

The mean systolic and diastolic B.P was found to be high in women taking combined oral contraceptive pills when compared with controls. Our study revealed an increase in the mean systolic blood pressure and diastolic blood pressure with p-value of 0.0007 and 0.009 respectively. This finding was also supported by Nicholas M et al in a study conducted on normotensive women using COCPs. [22]

CONCLUSION

It is concluded that the use of combined oral contraceptive pills, which contain estrogen and progestrogen and are provided by the government sector of Khyber Pakhtunkhwa Province causes elevation in lipid profile, B.P and BMI in women using COCs which are metabolic risk factors for the development of cardiovascular diseases (CVD). The women should be screened for lipid profile and blood pressure before starting COCs and followed up regularly to prevent the risk of cardiovascular diseases in these women and to decrease disease burden on the country.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

NSM: Conception and design, acquisition of data, drafting the manuscript, and final approval of the version to be published

RN: Supervision, critical Revision, drafting the manuscript and final approval of the version to be published

MAK: Analysis and interpretation of data and final approval of the version to be published

TA: Critical Revision and final approval of the version to be published

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CONFLICT OF INTEREST

Author declares no conflict of interest

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NIL

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