Orginal Article

Effect of Two Combined Oral Contraceptives on Serum Lipid Profile

M T G Mustafa[1], S Zabeen[2], M Monirujjaman[3], T Bashar[4]

Abstract:

Alterations in the composition of the plasma lipids caused by estrogens are characterized by an increase in the high-density lipoproteins (HDL) and plasma triglyceride, a slight reduction in the low-density lipoproteins (LDL), and a reduction in total plasma cholesterol levels. Oral Contraceptive pills(OCP) having different doses of hormones may affect blood lipids differently. The present study was designed to see the effect of two combined oral contraceptives on lipid levels. 68 females of the reproductive age who were advised to do lipid profile before and after using oral contraceptives were included in this study. One group of 38 females was advised to take 30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the form of Desogestrel while another group of 38 females was advised to take 0.05 mg of oestrogen in the form of Ethinylestradiol and 1 mg of progesterone in the form of Lynestrenol. Cholesterol(P<0.0001) and LDL(P<0.0001) decreased while HDL(P<0.0001) increased in the group which received 30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the form of Desogestrel. Cholesterol(P<0.0001) and LDL(P<0.0001) also decreased and HDL(P<0.0001) increased in the group which received 0.05 mg of oestrogen in the form of Ethinylestradiol and 1 mg of progesterone in the form of Lynestrenol. OCPs have a beneficial effect on blood lipid profile.

Keywords: Oral Contraceptive Pill (OCP), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Cholesterol, Triglyceride

Introduction

Estrogens decrease hepatic oxidation of adipose tissue lipid to ketones and increase synthesis of triglycerides. Estrogens increase serum triglycerides and free and esterified cholesterol. Phospholipids are also increased, as are HDL; levels of LDL usually decrease. Although the effects are marked with doses of 100 mcg of mestranol or ethinyl estradiol, doses of 50 mcg or less have minimal effects. The progestins (particularly the "19-nortestosterone" derivatives) tend to antagonize these effects of estrogen. Preparations containing small amounts of estrogen and a progestin may slightly decrease triglycerides and HDL.[1] The effect of oestrogens is on balance favorable, but the addition of a progestogen (unless gestodene or desogestrel) reverses the balance.[2] Estrogens have many effects on lipid metabolism; of major interest are their effects on serum lipoprotein and triglyceride levels.[3] In general, estrogens slightly elevate serum triglycerides and slightly reduce total serum cholesterol levels. More importantly, they increase HDL levels and decrease the levels of LDL and Lipoprotein A. The presence of estrogen receptors in the liver suggests that the beneficial effects of estrogen on lipoprotein metabolism are due partly to direct hepatic actions.[4] Progesterone stimulates lipoprotein lipase activity and seems to enhance fat deposition. Progesterone and analogs such as Medroxy Progesterone Acetate (MPA) have been reported to increase LDL and cause either no effects or minimum reductions in serum HDL levels. The 19-norprogestins may have more pronounced effects on plasma lipids because of their androgenic activity. In this regard, a large prospective study has shown that MPA decreases the favorable HDL increase caused by conjugated estrogens during postmenopausal hormone replacement, but does not significantly affect the beneficial effect of estrogens to lower LDL. In contrast, micronized progesterone does not significantly affect beneficial estrogen effects on either HDL or LDL profiles.[5] In African-American women, OCP use is associated with an increase in markers of cardiovascular risk manifested by increased insulin resistance, glucose intolerance, and elevated TGs.[6] An open, prospective, noncomparative study of a contraceptive combination of ethinyl estradiol (30 μg) and gestating (75 μg) continuously for 24 weeks in 45 women aged 25±3.7 years revealed a reduction in the levels of cholesterol and LDL and an increase in HDL and triglycerides in Sao Paulo.[7] The different oral contraceptives available in Bangladesh have different doses of oestrogen and progesterone, therefore in this study we analysed the effect of two combined oral contraceptives on lipid profile.

Materials and Methods

This study was carried out in different Gynaecology outdoor chambers of private practitioners in Dhaka. Only those patients who were advised to do lipid profile by the gynaecologists before and after using OCP were enrolled in the study. Healthy subjects (n=68) aged within the reproductive age group 18 to 45 with no history of cardiovascular diseases were included in this study. Subjects using lipid lowering agents, steroids or other hormonal preparations were excluded from this study. After the subjects were advised to do lipid profile we gathered the data by questionnaire.

1. Dr. Md Tarek Golam Mustafa, MD Resident, Department of Pharmacology, BSMMU.

2. Dr. Shahana Zabeen, Associate Professor, Department of Biochemistry, AKMMC.

3. Md Monirujjaman, Research Officer, Department of Nutritional Biochemistry, ICDDR,B.

4. Dr. Tahmina Bashar, Research Assistant, Department of Pharmacology, BSMMU.

Corresponding Author

Dr. Tarek Golam Mustafa e-mail: tarekgolammustafa@yahoo.com

Samples with preexisting hyperlipidaemia were also excluded from the study. After 3 months when these subjects came for follow up in Gynaecology outdoor and were again advised to do a lipid profile we recorded the data once more. Statistical analysis was performed using SigmaStat 3.[1] (San Jose, CA). Descriptive statistical analysis was performed to examine the distribution of each of the major baseline and outcome variable. The effects of OCPs on serum lipid levels were analyzed by paired t-test. Correlation or differences was considered significant at P=<0.05

Results

Subjects with moderate socio economic status were recruited in this study. Sixty eight female subjects were advised to take either 30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the form of Desogestrel or 0.05 mg of oestrogen in the form of Ethinylestradiol and 1 mg of progesterone in the form of Lynestrenol. The baseline characteristics of the subjects did not differ in age, years of education, family income, etc. between these two groups (Table 2). 30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the form of Desogestrel decreased the serum cholesterol level from 147.94±32.05 mg/dl to 143.32±31.39 mg/dl (P<0.0001) and serum LDL level from 80.73±20.45 mg/dl to 75.44±20.23 mg/dl (P<0.0001), while increased serum HDL level from 40.26±7.80 mg/dl to 45.94±5.11 mg/dl (P<0.0001) but the change in serum

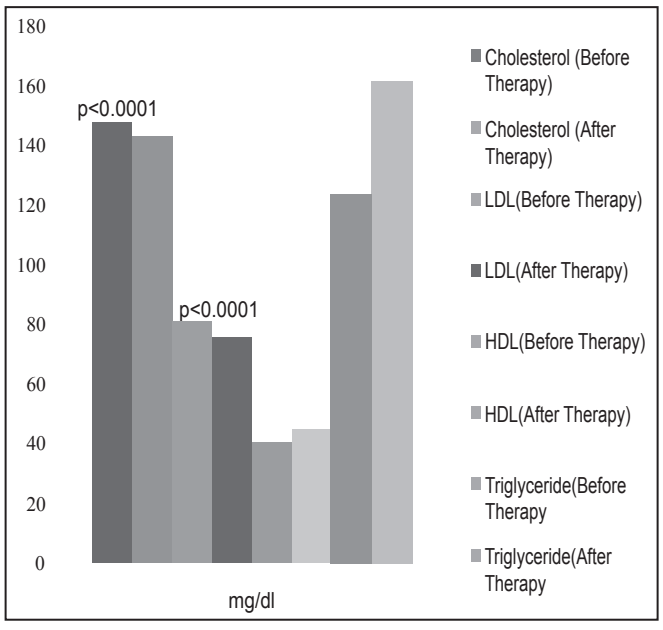

Figure 1: Effect of 30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the formof Desogestrel on Serum Lipids. triglyceride from 123.97±43.08 mg/dlto 131.85±46.77 mg/dl was not statistically significant (P=0.1216) as shown in figure 1.

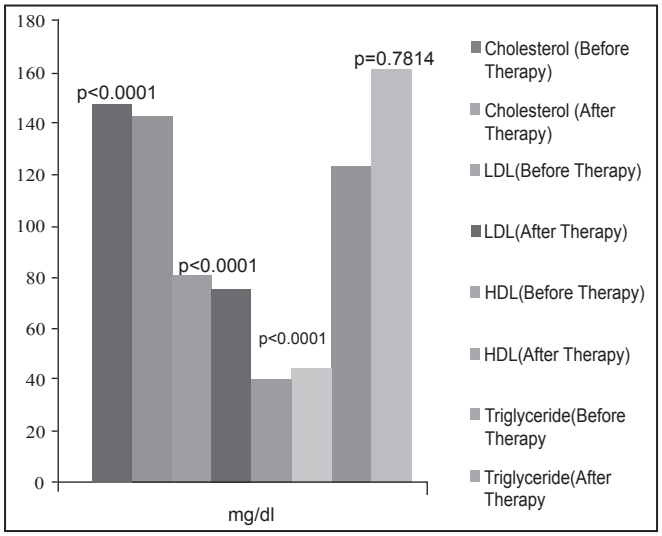

Figure 2: Effect of 0.05 mg of oestrogen in the form of Ethinylestradiol and 1 mg of progesterone in the form of Lynestrenol on Serum Lipids

0.05 mg of oestrogen in the form of Ethinylestradiol and 1 mg of progesterone in the form of Lynestrenol decreased the serum cholesterol level from 155.11±21.08 mg/dl to 149.11±19.90 mg/dl (P<0.0001) and serum LDL level from 81.85± 22.04 mg/dl to 75.67± 23.31 mg/dl (P<0.0001), while increased serum HDL level from 40.26± 7.42 mg/dl to 44.70± 5.9 mg/dl (P<0.0001) but the change in serum triglyceride from 162.91± 62.02 mg/dl to 162.05± 60.97 mg/dl (P=0.7814) was not statistically significant as shown in figure.2 Figure3 shows the statistically significant change in BMI in both the groups

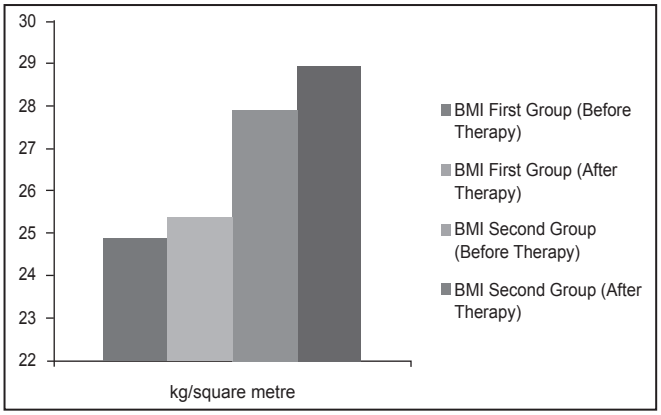

Figure 3: Effect of 30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the form of Desogestrel and 0.05 mg of oestrogen in the form of Ethinylestradiol and 1 mg of progesterone in the form of Lynestrenol on BMI

Discussion

OCP alone led to a 5% increase of total cholesterol without effect on low-density lipoprotein cholesterol in a study in Poland8. Studies on the use of oral contraceptives in the West have shown that they induce changes in total serum cholesterol, triglycerides, high density lipoproteins, low density lipoproteins, and very low density lipoproteins --

atherosclerosis.[9] In Bangladesh, however, women consume low fats, low cholesterol and fewer calories; they drink less alcohol and rarely smoke; and they engage in more physical activities. [2] groups of Bangladeshi women were tested for lipid metabolism alterations during and after use of oral contraceptives prescribed by gynaecologists.[1] group of 34 women received low dose oral contraceptives containing 30 mcg of Ethinylestradiol and 150 mcg of Desogestrel and their serum lipid levels were tested after 3 months of use. A 2nd group of 34 women received low dose oral contraceptives containing 0.05 mg of Ethinylestradiol and 1 mg of Lynestrenol and their serum lipid levels were tested after 3 changes which are implicated in the development of months of use. Results showed that both the OCPs decreased the serum cholesterol level (P<0.0001) and serum LDL level (P<0.0001), while increased serum HDL level (P<0.0001). But the increase in serum triglyceride was not significant. BMI increased in both the groups which was also statistically significant.

Conclusion

The findings of both OCP reinforce the need to monitor changes in these factors within the context of the treated patient's risk-benefit profile. However, because the magnitude of these differences was small, relative to normative ranges, it may be concluded that OCPs are unlikely to markedly affect cardio metabolic risk. In conclusion, to the best of current knowledge, in this area, this is the first study of OCP on lipid profile in Bangladesh. Although sample size is low (n=68), more studies with larger sample size are required to verify the repeatability of these findings.

Table 1 Data Summarisation

	Before Therapy	After Therapy	P Value	Significance
30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the form of Desogestrel				
Cholesterol	147.94±32.05	149.11±19.90	0.0001	Significant
LDL	80.73±20.45	75.67± 23.31	0.0001	Significant
HDL	40.26±7.80	45.94±5.11	0.0001	Significant
Triglyceride	123.97±43.08	131.85±46.77	0.1216	Not Significant
BMI	24.87±4.01	25.36±3.80	0.0004	Significant
0.05 mg of oestrogen in the form of Ethinylestradiol and 1 mg of progesterone in the form of Lynestrenol				
Cholesterol	155.11±21.08	149±20.23	0.0001	Significant
LDL	81.85± 22.04	75.65± 23.56	0.0001	Significant
HDL	40.26± 7.42	44.70± 5.9	0.0001	Significant
Triglyceride	162.91± 62.02	162.05± 60.97	0.7814	Not Significant
BMI	27.88±4.55	28.93±3.56	0.001	Significant

Table 2. Socio-economic status of the study population

	Group taking 30 mcg of oestrogen in the form of Ethinylestradiol and 150 mcg of progesterone in the form of Desogestrel	Group taking 0.05 mcg of oestrogen in the form of Ethinylestradiol and 1mcg of progesterone in the form of Desogestrel
Number of Subjects	34	34
Age (years)	29.00± 7.85	28.00± 2.83
Education (years)	12.83 ±2.00	13.50 ± 3.54
Income per month (Tk)	20000±1000	21000±1000
Total family income (Tk)	50583± 2538	51000± 2070
No. of people eation form the same pot	4.50 ± 1.05	4.50 ± 0.71
No. of rooms per household	6.17 ± 0.41	6.00 ± 0.00
No. of people living in one room	1.17 ± 1.47	1.50 ± 0.71

References

1. Bertram G. Katzung (2006) The Gonadal Hormones and Inhibitors In Basic and Clinical Pharmacology 10th Edition San Francisco.
2. Bennett & Brown (2003) Hypothalamic, pituitary and sex hormones In Clinical Pharmacology 9th Edition Page-718 Bath, Cambridge.
3. Walsh, B.W., Li, H., and Sacks, F.M. (1994) Effects of postmenopausal hormone replacement with oral and transdermal estrogen on high density lipoprotein metabolism. J. Lipid Res., 35:2083-2093.
4. Louis S. Goodman, Alfred Gilman (2006) Estrogens And Progestins In The Pharmacological Basis of Therapeutics 11th Edition New Haven, Connecticut.
5. Writing Group for the PEPI Trial. (1995)Effects of estrogen or estrogen/progestin regimens on heart disease risk factors in postmenopausal women. The Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. JAMA, 273:199-208.
6. Barbara A. Frempong, Madia Ricks, Sabyasachi Sen, Anne E. Sumner (2008) Effect of Low-Dose Oral Contraceptives on Metabolic Risk Factors in African-American Women The Journal of Clinical Endocrinology & Metabolism vol. 93 no. 6 2097-2103.
7. Rogério Bonassi Machado, Paula Fabrini, Achilles Machado Cruz Edna Maia, Álvaro da Cunha Bastos. (2004) Clinical and metabolic aspects of the continuous use of a contraceptive association of ethinyl estradiol (30 µg) and gestodene (75 µg) Contraception Volume 70, Issue 5, Pages 365-370.
8. Banaszewska B, Pawelczyk L, Spaczynski RZ, Dziura J, Duleba AJ.(2007) Effects of simvastatin and oral contraceptive agent on polycystic ovary syndrome: prospective, randomized, crossover trial. J Clin Endocrinol Metab. 92(2):456-61.
9. Arora S, Arora RC, Garg RK, Agarwal N, Nautiyal A (1988) Effect of administration and withdrawal of oral contraceptive pills on serum lipids and lipoproteins. Indian J Physiol Pharmacol. 32(1):67-71.