Effect of Oral Contraceptives on Lipid Profile in Premenopausal Indian Women

Authors

Dr Harmohinder Kumar Attri (Assistant Prof.)¹, Dr Tejinder Singh²
Department of Biochemistry, Government Medical College, Amritsar

Corresponding Author
Dr Tejinder Singh
Department of Biochemistry, Government Medical College, Amritsar

Abstract

Background: Fertility regulation has acquired great importance in the field of human reproduction. The use of synthetic progestogens has completely revolutionized the field of contraception as these offers a reliable, safe, easy and reversible method of contraception. We aim to examine the lipid and lipoprotein changes in women taking low dose oral contraceptives.

Aim: To study the effect of oral contraceptives on Lipid profile of Premenopausal Indian women.

Material and Method: This hospital-based study was conducted on 100 pre-menopausal women, 50 as control and 50 as cases, age and gender matched. Blood Sample were taken in plain vial and lipid profile was done on each sample on Semiautoanalyzer. Results were collected and analyses statically.

Result: The mean value of serum cholesterol in cases group and control group were 193.48±14.49 mg% and 184.46±13.58 mg% respectively with p value of <0.001 serum triglyceride is 91.16±11.04 mg% and 85.26±11.03 mg% respectively with p value of <0.01. Mean value of HDL in cases and control were 44.70±5.12 mg% and 46.62±5.11 mg% with p value of >0.05. This shows that serum total cholesterol and serum triglyceride shows statically significant association while serum HDL shows no association.

Conclusion: Tablet Mala-D causes very significant increase in total serum cholesterol and LDL cholesterol, triglycerides while there was no significant change in HDL cholesterol levels and it is almost 100% effective in preventing pregnancy.

Keywords: Mala –D, Serum Cholesterol, Serum Triglyceride, HDL.

Introduction

Fertility regulation has acquired great importance in the field of human reproduction, since it aims not only at finding out an ideal method of contraception but at the same time equal importance has been given to the treatment of infertile couples.¹

Approximately 95% of the growth of the world population is occurring in the developing countries. The rampant population growth has been viewed as the greatest single obstacles to the economic and social advancement of majority of people in the underdeveloped world.

The use of synthetic progestogens has completely revolutionized the field of contraception as these offers a reliable, safe, easy and reversible method of contraception. At present time, most formulations of the combined pills contain no
more than 3-35 ug of synthetic oestrogen and 0.5 to 1.0 mg of progestogen.

Whereas, there is no doubt as to the superior efficacy of progestogens or combined pill, over that of previous methods of fertility control, their wide spread use has raised the question of long term safety in addition to the short term side effects like nausea, vomiting, break-through bleeding, weight gain etc. They after the endocrinial hemostatic mechanism of body and may affect various metabolic processes. One such field is their effects on plasma lipids.

Morries et al (1989) studied the lipid and lipoprotein changes in women taking low dose, triphasic oral contraceptives for 12 months. His data indicated that use of both oestrogen & progestogen preparation were accompanied by increase in cholesterol, LDL cholesterol and triglycerides and also a decrease in HDL cholesterol.

The primary action of the combined oral contraceptives is suppression of synthesis or secretion of the pituitary gonadotrophins or both. The oestrogen component of oral contraceptives was chiefly responsible for the suppression of secretion of follicular stimulating hormone resulting in incomplete maturation of follicles and thus interference with ovulation. It also produced changes in the cervical mucosa rendering it hostile to sperm penetration. Progestogens prevented the secretion of L.H., necessary to trigger ovulation.

Serum lipids begin to rise during the third month of pregnancy and increase progressively to a value 40 to 50% above the normal value at term, and decrease to normal after delivery. Watson, 1957 found a greater increase in the beta lipoprotein as compared to the alpha lipoprotein fraction. Many factors are held responsible for this rise in serum lipids. The hormonal status is changed during pregnancy. As oestrogens are formed in large amounts by the foeto-placental unit they were implicated as the cause of the rise particularly total cholesterol, phospholipids, beta and alpha lipoproteins.

Hence administration of synthetic oestrogens has been shown to be associated with changes in lipid transport in plasma with lowering of low density lipoproteins, and raising of high density lipoproteins, while various synthetic androgens exert an opposite effect. When oestrogen therapy is combined with orally active androgens, a sharp increase in low density and a fall in high density lipoprotein occurs, Russ et al, 1955.

**Material and Method**

A Hospital based cross-sectional study was carried out in Department of Biochemistry, Guru Nanak Hospital, Amritsar on 100 subject including 50 control which were taken from OPD/Wards. The 50 females, as cases were taken up from Post-partum unit of and were aged 30 to 40 years, who had been using MALA-D, which contains D-Norgestrol 0.50mg and Ethinyl oestradiol, 0.04mg for the last 3 months. The subjects were age and gender matched. In our study, Lipid profile consisting of Serum Cholesterol ,Serum Triglyceride and HDL were estimated.

Serum Sample were taken in plain vial and serum cholesterol, serum triglyceride and HDL were estimated by Semi-auto analyzer method. The result were collected and analyzed.

**Result**

The mean value of serum cholesterol in cases group and control group were 193.48± 14.49 mg% and 184.46± 13.58 mg% respectively with p value of <0.001 serum triglyceride is 91.16±11.04 mg% and 85.26±11.03 mg% respectively with p value of <0.01. Mean value of HDL in cases and control were 44.70±5.12 mg% and 46.62±5.11 mg% with p value of >0.05. This shows that serum total cholesterol and serum triglyceride shows statically significant association while serum HDL shows no association.
### Discussion

It is apparent that oral contraceptives taken by most normal women raise the levels of triglycerides, phospholipids and increase cholesterol. The mechanism of increase of these serum lipids is not clear. It has been suggested by Gershberg (1968) that oestrogens are the major cause of increase in plasma lipids. Progestogens may have an indirect effect on serum lipids because they are metabolized in the body into substances having oestrogenic activity, Pincus et al, 1964. Wynn and Doar (1966) concluded that the 19-nor-progestational compounds though not having much of androgenic activity, had sufficient chemical similarity to methyl testosterone, to have some of the effects observed with androgens and could likewise reverse or nullify the action of oestrogens. Hood and Cramer (1959), showed that as little as 10mg of methyl testosterone could reverse the effect of as large a dose of oestrogens as 1mg of ethinyl estradiol daily. Hence this androgen like action of progestational compounds may be responsible for the increase in cholesterol, produced by oral contraceptives. Oestrogens and oral contraceptives in liver function by Muellaar (1964), Sherlock (1966). Relative hypertriglyceridemia observed after oral contraceptives may be related to an increase in non-esterified fatty acids, impaired glucose tolerance test (Paola et al, 1968) increase in basal immune-reactive insulin (Paoal et al, 1968 and Spellacy, 1969). The role of non-esterified fatty acids in the genesis of hypertriglyceridemia and metabolism deserves careful consideration. Increase in non-esterified fatty acids levels have been shown to stimulate production of lipoprotein according to Nestgel and Steinberg (1963). This could be due to increase hepatic uptake of free fatty acids (Reaven et al 1967). Insulin may be responsible for this increase in the uptake of free fatty acids by the liver (Shoemaker, 1962). Therefore increase in hepatic utilization of free fatty acids could be secondary to the raised insulin levels resulting from oral contraceptive therapy. This may represent the most important mechanism whereby oral contraceptives elevate endogenous production of triglycerides. This theory is further strengthened by the correlation shown between insulin and triglycerides in obesity (Bagdade et al, 1968). OCs alter the lipid profile via the genomic pathway, in which ER alterations affect hepatic apolipoprotein up-regulation. Studies...
in pre-menopausal women using OCs have shown a dose related response in the lipid profile. Women using a 20-µg EE/100-µg LNG OC demonstrated reductions in high density lipoprotein cholesterol (HDL-C) and small increases in LDL-C and triglycerides, in contrast to a 30-µg EE/150-µg LNG OC. The amount of lipid alteration also depends on the delivery route, where transdermal contraceptive hormone delivery is relatively less potent compared with oral. Barkfeldt et al conducted a randomized, double-blind study that evaluated the effects of lipid metabolism on 98 women who received 2 different types of progestin-only pills, desogestrel 75 µg/day or LNG 30 µg/day. There were minimal changes seen to the lipid profile except for decreasing trends with levels of HDL-C, its subfractions, and the apolipoproteins apolipoprotein-I and -II. No differences were observed between the 2 formulations despite the higher progestin dose found in desogestrel, including no changes in LDL-C or apolipoprotein-B.

Spearman’s rho correlation showed significant influence of HC use on TG (P=0.026), TC (P=0.000), LDLC (P=0.004), and VLDLC (P=0.026) over time. In one of the study it was shown that greater the duration of oral contraceptive use the higher is the chance of dyslipidaemia. To decrease the side effects, now a day’s oral contraceptive tablets contains Levonorgestrol 0.15mg and Ethinyl oestradiol, 0.03mg. So concentration of both the hormones reduces in oral contraceptive pills.

**Conclusion**

When tab. Mala-D was taken by for 3 months there was a significant increase in total serum cholesterol and triglycerides while there was no significant change in HDL cholesterol levels.

**Reference**