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EEFECT OF DURATION OF USE OF HORMONAL CONTRACEPTIVE PILLS ON TOTAL LIPID AND LIPOPROTEINS IN NIGERIAN WOMEN.

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ABSTRACT

The study seeks to determine the effect of duration of oral contraceptive use on lipid and lipoproteins in Nigerian women. The study group was made of 120 women (mean age 24.1±5 years) who were on biphasic lofeminal tablets for a period ranging from 1- 48 months, while 50 age matched women with regular menstruation with no history of hormonal use within the last six months before the investigation were used as controls. Total lipid, triglyceride, total cholesterol, LDL-cholesterol and HDL-cholesterol were determined using standard colorimetric techniques. Statistically significant increases were observed for triglyceride, LDL-cholesterol, and VLDL cholesterol with the duration of oral contraceptive use. The level of total lipid did not increase beyond 24months of oral contraceptive intake while the level of HDL cholesterol was significantly decreased ($p<0.05$) with the duration of use. The atherogenic index of serum lipid declined with duration of oral contraceptive use and thus hormonal induced dyslipidaemia may not be regarded as proatherogenic . The study suggests that Oral contraceptive pills may not necessarily lead to pathologic concentration of lipid within 4 years duration of use in Nigerian women.

KEYWORDS

Lipid, lipoprotein, Oral contraceptive pills.

INTRODUCTION

The use of oral contraceptive pill (OCP) by women the world over is on the increase, especially in recent years when various governments and organizations are campaigning for its use in order to space pregnancies especially in developing countries like Nigeria. Several authors have observed that OCP use may increase the risk of cardiovascular disease by increasing the levels of triglyceride[1] but the position over the cholesterol has been much less clear. Wynn et al[2]reported a significant differences in cholesterol levels in young women on OCP. Other authors observed a significant increase in all lipid fractions in women on OCP[3]. In our previous study, we observed that OCP may be a risked factor for cardiovascular disease in African women because of increase serum cholesterol, the haemoglobin S gene may protect against this effect[4]. On the contrary, Syed et al.[5] reported no significant variations in serum triglyceride, LDL cholesterol and VLDL cholesterol in a group of women on OCP. The cardiovascular effects of long term use of hormonal contraception have continued to generate interest

from scientists, unfortunately, most of the studies have focused mainly on the evaluation of changes in serum lipids[6] and not much has been reported on long term effects of OCP on Nigerian users. This present study seeks to determine the effect of duration of OCP use on lipids and the relationship between lipids and age of women on OCP.

MATERIALS AND METHODS

Subjects: All subjects consecutively recruited for this study gave informed consent. They consisted of 120 women on OCP for a period ranging from one month to 4years and 50 control subjects made up of staff and students of University of Benin and university of Benin Teaching Hospital, Benin City. The study group (mean age 24.1±5) have been receiving combined biphasic lofemenal tablets (Wyeth laboratory inc, Philadelphia, USA) containing 0.3mg norgestrel and 0.03mg ethinyloestradiol from the family planning clinic of the University of Benin Teaching Hospital, Benin city, Nigeria. The control group (mean age 26.2±4years) was made up of apparently healthy women with regular menstruation with no history of hormonal therapy within the last six months before the investigation. The weight and blood pressure of both subjects on OCP and controls were measured. The blood pressure was measured on the right arm with the subject seated after 10 minutes of rest. Other demographic data were obtained with the help of a structured questionnaire. None of the subjects admitted to smoking of cigarette but 20% of them drink alcohol beverages occasionally.

Laboratory Methods: Blood was withdrawn after 9-10 hr fast and near as much as possible to their mid-cycle from the antecubital vein into a clean plastic plain container. The blood was allowed to clot at room temperature for one hour and serum collected immediately after centrifugation. The sera were stored at -20^{oC} and analyzed within five days. Serum triglyceride, total cholesterol and HDL-cholesterol were determined by enzyme colorimetric technique using kits supplied by Randox Laboratories, UK. LDL-cholesterol was calculated using Friedwald equation[7]. Total lipid was determined using the method of Zollner and Kirsch[8]. Students't- test was used to compare the mean, results were expressed as means±SEM. Values were considered statistically significant at $p<0.05$.

RESULTS

Table 1 shows the effect of duration of OCP intake on serum lipid in women. The levels of triglyceride, total cholesterol, LDL-cholesterol and VLDL-cholesterol were significantly elevated ($p<0.001$) while decreased level of HDL-cholesterol was statistically significant ($p<0.05$) in women on OCP compared with controls. However, the level of total lipid was only significantly increased ($p<0.001$) in women on OCP intake for up to 24 months and the levels began to decline thereafter from 25-36months to 37-48months. The atherogenic index of plasma (AIP), calculated as log (TG/HDL-C) decline with duration of OCP intake. Table 2 shows the relationship between lipid and age of women on OCP intake. The percentage change of lipid and lipoproteins declined as the age of women on OCP increases. The mean systolic blood pressure of women on OCP was 107.8±0.9 and controls were 103.1±0.9. While the diastolic blood pressure for study group on OCP and control were 67.7±0.6 and 65.0±0.6 respectively. Statistically significant increases were observed for systolic blood pressure ($p<0.002$) and diastolic blood pressure ($p<0.05$) when compared with controls. The mean weight of women on OCP was 56.4±0.85kg and control was 50.3±0.8kg. Statistically significant increase ($p<0.01$) was also observed when compared with the controls.

Table 1: Effect of duration of OCP intake on serum lipid in women (mean±SEM)

		Duration of OCP intake in months			
	Controls	1-12	13-24	25-36	37-48
No of Subjects	50	45	30	25	20
Triglyceride (mmol/L)	0.96±0.03	1.10±0.03[a]	1.20±0.07[a]	1.31±0.04[a]	1.34±0.07[a]
Total cholesterol (mmol/L)	3.55±0.02	3.75±0.05[a]	3.88±0.05[a]	4.04±0.07[a]	4.16±0.08[a]
HDL-cholesterol (mmol/L)	1.88±0.02	1.80±0.06	1.75±0.04[b]	1.70±0.08[c]	1.65±0.07[c]
LDL-cholesterol (mmol/L)	1.25±0.04	1.45±0.1	1.60±0.06[a]	1.74±0.10[a]	1.94±0.06[a]
VLDL-cholesterol (mmol/L)	0.18±0.02	0.23±0.01[a]	0.25±0.01[a]	0.27±0.02[a]	0.27±0.01[a]
Total lipid(g/L)	6.20±0.1	7.38±0.2[a]	8.00±0.5[a]	6.91±0.50	6.70±0.40
AIP	0.29	0.21	0.16	0.11	0.09

AIP= Atherogenic index of plasma lipids.
a=p<0.001, b=0.005, c=p<0.05

Table 2: **Relationship between lipid and age of women on OCP intake**

Age group (years)	Triglyceride (mmol/L)	Total cholesterol (mmol/L)	HDL-cholesterol (mmol/L)	LDL-cholesterol (mmol/L)	VLDL-cholesterol (mmol/L)	Total lipid (mmol/L)
15-20						
Controls (n=10)	0.76±0.05	3.57±0.07	1.70±0.03	1.42±0.01	0.15±0.04	6.20±0.32
Women on OCP (n=15)	1.10±0.04	4.14±0.14	1.50±0.04	2.01±0.03	0.22±0.07	7.26±0.30
% increase	44.7	16.0	-11.8	41.5	46.7	17.1
21-25						
Controls (n=20)	0.90±0.02	3.64±0.05	1.66±0.03	1.44±0.01	0.18±0.01	6.24±0.1
Women on OCP (n=50)	1.20±0.03	4.21±0.06	1.62±0.04	1.89±0.03	0.23±0.01	7.00±0.4
% increase	33.3	15.7	-2.4	31.2	27.8	12.2
26-30						
Controls (n=15)	1.02±0.01	3.85±0.05	1.68±0.02	1.56±0.05	0.20±0.02	6.48±0.12
Women on OCP (n=30)	1.24±0.08	4.08±0.15	1.58±0.08	1.90±0.02	0.24±0.01	7.30±0.4
% increase	21.6	6.0	-6.0	21.8	20	12.7
Above 31						
Controls (n=5)	1.08±0.3	3.85±0.16	1.68±0.03	1.52±0.07	0.21±0.01	6.51±0.10
Women on OCP (n=25)	1.24±0.05	3.90±0.07	1.56±0.02	1.79±0.02	0.23±0.02	6.94±0.30
% increase	14.8	1.30	-7.1	17.8	9.5	6.6

DISCUSSION

One of the main reported effects of combined OCP is an increased risk of cardiovascular disease (CVD). The progressive change in the composition and dosages in the OCP and more careful selection of women who are to use these products have resulted in a lower risk of CVD associated with their use[9]. The World Health Organization (WHO) study of CVD and steroid hormone contraception conducted in developing and developed countries revealed a higher overall risk of Ischaemic stroke among OCP users in developing countries than those in developed countries of Europe. These differences were attributed to the type of OCP used and the frequency with which users reported that their blood pressure had been checked prior to or during OCP use[10-11].The result of the effect of low dose OCP on lipid shows an increase in weight, systolic and diastolic blood pressure in OCP users compared with non users. This observation is consistent with other studies[12].It was suggested that blood pressure check reduces the OCP attributable mortality, the impact is however insignificant in women under 35years. Much has been written implicating cardiovascular disease with OCP intake[13-15]. Most of these studies were on Caucasians but not much is known about the effect of duration of OCP use on lipids in Nigerian women. Our results show that the levels of triglyceride,

LDL-cholesterol and VLDL-cholesterol increased with duration of OCP intake in the study group. This result is in agreement with other studies[16-18].This observation is however different from that reported by other investigators.[5,19-20] They observed that serum triglyceride, LDL and VLDL cholesterol did not show significant variations. Significant decrease ($p<0.05$) level of HDL-cholesterol was observed within the duration of OCP use. HDL-cholesterol is involved in the reverse cholesterol transport from peripheral cells to the liver, prevents oxidation of LDL-cholesterol because of the presence of paraoxonase in HDL-cholesterol. Paraoxonase is synthesized in the liver and is HDL-associated enzyme that inhibits the oxidation of LDL-cholesterol[21]. The variations in the observation by the different investigators may be due to the chemical composition of the different OCP the women were given. Changes seen in lipid and lipoproteins with combined oral contraceptives vary according to progestogen type[9]. The OCP induced increased triglyceride is due to increased synthesis rather than decreased clearance. These observed changes in lipid and lipoproteins were sustained with duration of OCP use but the levels were still within normal or acceptable range. However, there was no significant association between duration of OCP use and risk of cardiovascular disease because the atherogenic index of plasma lipids declined with duration of OCP use. Although it was suggested that a long term (>6years) current use of OCP may be associated with CVD in old women[16]. In our study the duration of current OCP use was not more than 4years and the age of users were not more than 40years. This study also indicated that total lipid was not significantly increased beyond 24months of OCP use. The OCP effect on total lipid was short lived and started to decline towards levels in control subjects after 24months of administration. Since the effects caused by OCP intake are short lived, it could be said that the effects of these hormonal preparation may be physiologic rather than pathogenic[16]. The percentage increase in the lipid and lipoproteins were highest in the young OCP users. The percentage change also decreases with increase in age of the women (table 2).Since the incidence rates of CVD events are low in younger women of reproductive age these observed changes are not likely to have adverse effects. The dyslipidaemia induced by OCP use may not be regarded as proatherogenic since the AIP of lipid plasma did not change significantly with duration of use.

In conclusion, OCP intake produce changes in lipid metabolism in women, but does appear that such changes may necessarily lead to pathogenic concentration that could result in CVD with prolong use of not more than 4 years.

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