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Effect of oral contraceptive brands on risk markers of cardiovascular dysfunction

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ABSTRACT

Today, research interest is increasing in the study of the changes in plasma triacylglycerol (TAG) and lipoprotein lipids as possible cardiovascular disease risk factor among Nigerian users of oral contraceptive pills (OCPs). This study investigates the changes in serum TAG : HDL - cholesterol ratio and LDL-cholesterol levels among Nigerian users of OCPs. Three hundred and forty-eight non-smoking women in apparent good health currently receiving either monophasic (n= 204) or triphasic (n=144) formulation of OCPs were selected from 13 primary health care centres and twenty-nine clinics/hospitals operating within the Urhobo and Isoko communities in the Central /Senatorial District of Delta State, Nigeria. Niger-Delta region. The control subjects (n=207) were women using non-hormonal contraceptive device (condom, diaphragm, IUD). Both categories (i.e. test and control subjects) have been using the respective contraceptive agents for 12- 18 months. Results show that OCPs significantly ($P<0.05$) increased serum TAG and LDL-cholesterol concentrations, but reduced HDL-cholesterol ($P>0.05$) levels. OCPs increase serum TAG : HDL-cholesterol ratio by 52% when compared with control ratio after about 18 months of continuous use. Since these parameters have been implicated in atherogenic reactions, then, the cardiovascular disease risk of using OCPs need further investigation among Nigerian women who use the pills.

Key words: Triacylglycerol, cholesterol, oral contraceptive pills, lipoprotein.

INTRODUCTION

Sixteen years ago, it was estimated that about 14 million women in the United States and about 60 million in the world use oral contraceptives (Hillard, 1989). Steroidal oral contraceptive pills (OCPs) are of different formulations, and they contain synthetic female hormones, oestrogen and progestin. These active synthetic agents are similar to the natural hormones, and so, they prevent pregnancy by suppressing ovulation (Timmons and Tyrer, 1979). The use of steroidal OCPs is becoming popular and is presently having overwhelming impact in the society including ours. For over two decades, it has remained the most effective drug ever marketed (Droegemiller and Bressler, 1980). The active components of OCPs are catabolized into cholesterol, and the use of OCPs appears to inhibit the conversion of dietary folate to folate derived coenzymes, metabolically involved in haematopoetic function. As such, the accumulating reports on the effects of OCPs centre around the analyzes of blood cholesterol, a well established heart disease risk factor, and haematological parameters, in order to unravel any associated anaemic condition. A number of such previous studies have reported that OCPs do not significantly increase blood total cholesterol (Burkman, *et al.,* 1988), and anaemia is not a well documented disease associated with OCPs use.

However, some epidemiological studies have demonstrated a relationship between OCPs use and myocardial infarction, and other vascular disorders (Slone, *et al.,* 1981; Stadel, 1981). Two European studies have shown blood triacylglycerol (TAG) to be a risk factor for coronary heart disease (CHD) (Jick, et *al.,* 1978; Layde, *et al.,* 1985). Some investigators now feel that plasma TAG (Mercola, 1997) and Lipoprotein (Thomas, *et al.,* 2001) levels may actually be more important than cholesterol levels in establishing heart disease risk. Today, attention is being directed to the investigation of the changes in plasma TAG and lipoprotein - cholesterol as possible risk factors of cardiovascular diseases.

This article therefore, reports the observations of the investigation into the effect of OCPs on TAG : HDL-cholesterol ratio and LDL-cholesterol content in Nigerian users belonging to different age groups and currently, receiving either the monophasic or triphasic formulation of the pills.

MATERIAL AND METHODS

Selection of subjects

Three hundred and forty-eight (348) non-smoking women in apparent good health currently receiving either the monophasic (n=204) or the triphasic (n=144) formulation of OCPs were randomly selected from subjects regularly attending the Family Planning Clinic operating in thirteen primary health care centres and twenty nine clinics/hospitals in the Urhobo and Isoko communities in Central Senatorial District of Delta State, Nigeria. The subjects were separated into three (20 - 30, 31-40 and 41 - 50) age (yr) groups. Two hundred and seven age-matched and weight - matched women in apparent good health presently using non-hormonal contraception (condom, IUD, diaphragm) were included as control subjects. The subjects selected were individuals using any of the different contraceptive agents for the first duration that has lasted for a continuous period of between 12-18 months.

Blood collection

Volunteers participation was approved by the Ethics Committee on Human Experimentation, and blood was drawn by a qualified Nursing Officer from the consenting participants according to guidelines approved by the Clinical Research Practices Committee. Blood was collected into sterile plain bottle, allowed to clot and then, separated by centrifugation. The separated serum was decanted into bijou bottle and stored frozen for analysis which was conducted within 48 hours of collection.

Analysis of serum

Serum TAG (Searcy, 1961), total cholesterol (Allain, *et al.,* 1974), and HDL-cholesterol (Burstein and Mortin, 1969) were measured in a spectrophotometer (Photomech 301-A:OPTIMA) by the end-point colorimetric method using reagent test kits supplied by Randox Laboratories Limited, Ardmore, United Kingdom. LDL - cholesterol was estimated mathematically (Friedewald, *et al.,* 1972).

Measurement of blood pressure

Blood pressure was measured in a well-seated position after about 10min of rest by a medical practitioner using Aneroid Sphygmomanometer (ACCOSSON MERCURY, CE 0120) as previously documented (Moreira,, *et al.,* 1998).

Statistics

Statistical significance among groups was assessed using ANOVA. A Student's *t*-test assuming unequal variances was used to assess the significance of the results between groups.

RESULTS

The results obtained from the investigation into the effect of OCPs on cardiovascular parameters (Serum TAG, total cholesterol, HDL-cholesterol, LDL-cholesterol, blood pressure and TAG: HDL-cholesterol ratio) are shown on Table 1.

Table 1 shows that OCPs increased serum TAG, total cholesterol, LDL- cholesterol and blood pressure (BP), but reduced HDL-cholesterol when compared with the matching control value. These changes were influenced by the subject's age and the OCP brand. The observed increase in serum TAG and LDL - cholesterol for the oldest (41-50 years) users of either formulation were demonstrated to be statistically significant ($P<0.05$).

Table 1: Changes in mean serum lipids and lipoprotein-cholesterol induced by oral contraceptive pills (OCPs)

Age (Yr)	n	Serum Lipids (mmol/L)		Lipoprotein-chlesterol (mmol/L)		Blood	TAG:HDL-Cholesterol	
		TAG	Total cholesterol	HDL-Cholesterol	LDL-Cholesterol	Pressure (mmHg)	Ratio	% increase from control ratio
Monophasic Brand of OCPs								
20-30	33	1.32±015	4.96±1.12	1.46±0.31	2.90±1.01	110±6/80±3	0.91	30%
31-40	103	1.57±0.17	5.11±1.06	1.39±0.27	3.01±1.11	116±8/88±5	1.13	51%
41-50	68	1.66±0.13*	5.24±1.21	1.41±0.33	3.07±1.15	122±4/83±3	1.18	49%
Triphasic Brand of OCPs								
20-30	29	1.44±0.18	5.04±1.31	1.43±0.35	2.96±0.84	115±7/76±6	1.04	49%
31-40	72	1.72±0.21	5.21±1.27	1.37±0.35	3.06±1.04	121±8/83±4	1.26	68%
41-50	43	1.75±0.13*	5.30±1.36	1.34±1.19	3.16±1.03*	124±8/78±6	1.31	66%
Control: non hormonal contraceptive device								
20-30	38	1.13±0.10	4.40±1.01	1.61±0.13	2.28±0.82	102±8/70±4	0.70	
31-40	93	1.18±0.09	4.38±1.31	1.58±0.20	2.26±0.93	105±7/81±4	0.75	
41-50	76	1.21±0.11	4.43±1.24	1.54±0.26	2.34±1.03	110±10/83±6	0.79	

[Values are expressed as mean ± SD for 'n' number of subjects.

* P<0.05

Note: Average duration of continued contraceptive use = 15± 3 months.

TAG=Triacylglycerol

HDL=High Density Lipoprotein

LDL = Low Density Lipoprotein

DISCUSSION

Majority of studies on OCP monophasic formulation and other trials on sex hormones suggest that increase in serum LDL-cholesterol or decrease in HDL-cholesterol content may be caused by the androgenic potency of the progestogen in the formulation, while the increase in serum TAG could be due to the oestrogen component (Knopp, *et.al.,* 1982). The results of this study appear to further confirm these initial claims.

The effect of OCPs on LDL- and HDL-cholesterol contents (Table 1) may have some health implications. High plasma concentrations of HDL are associated with a reduced risk of atherosclerosis, and reverse cholesterol transport from peripheral tissues back to the liver is generally assumed to be the major antiatherogenic role of HDL. Most of the lipids deposited in the artery wall of humans come from LDLs, and several studies have shown that the severity of the atherosclerotic lesion may be directly related to the amount of lipid oxidation products in a plaque. Penn and Chisolm (1994) have proposed that the peroxidation of LDL lipids may play an important role in the development of atherosclerosis. Several reports have suggested that HDLs retard atherosclerosis by slowing the oxidation of LDL or by removing the preoducts of lipid oxidation (Christison, *et al.,* 1996). OCP- induced increase in LDL-cholesterol may enhance the vulnerability of this lipoprotein fraction to oxidation, and the protective capacity of HDL may be low due to its reduced level. These conditions may aggravate the atherogenicity of LDL and its associated lipid oxidation products in especially older users.

The OCP-induced increase in serum TAG and TAG: HDL-cholesterol ratio (Table 1) again, could be predictive of cardiovascular complications. There is growing body of evidence linking plasma TAG to the "clogging" of arteries, which may increase the risk of heart attack or stroke. High TAG alone increases the risk of heart attack nearly three-fold, and people with high ratio of TAG: HDL the "good" cholesterol-had 16 times the risk of heart attack as those with low ratio (Mercola, 1997). The mechanisms of how OCP affect these emerging cardiovascular disease risk factors (TAG and atherogenic lipoproteins) are presently being refined.

Although, the changes in the cardiovascular parameters so obtained (Table 1) are not alarming, the trends of the data presented do not altogether indicate that the use of OCPs may be without some health risk. It is therefore, suggested that the study be extended to include subjects with longer duration of OCP continuous use and varied ethnic background. Cardiovascular disease morbidity and mortality rates among women who had use the pills earlier in life should be documented. This is important in order to establish a complete health safety of the pills among Nigerian users.

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