

Original research article

## Evaluation of lipid profile in adolescents during long-term use of combined oral hormonal contraceptives

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### Abstract

The study evaluated the effects of the long-term use of a combined oral hormonal contraceptive containing 30 µg ethinyl estradiol and 75 µg gestodene in adolescents. Thirty-three volunteers, aged from 14 to 19 years, who used the oral contraceptive for three consecutive years, were studied. Evaluation of total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides was made before use and after 1, 2 and 3 years. During the 3-year study period, total cholesterol, HDL-C, LDL-C and triglyceride levels were significantly higher than previous measurements, but average values did not exceed the normal range.

Compared to the first year, the second- and third-year cholesterol, HDL-C, LDL-C and triglyceride levels were not significantly different. © 2005 Elsevier Inc. All rights reserved.

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### 1. Introduction

Combined oral contraceptives (COC) are popular among adolescents since they are highly efficient and easy to use. Although the consequences of their use have been extensively reviewed in adult women, there have been few studies involving adolescents. The most feared complications of oral hormonal contraceptives include thromboembolic phenomena and cardiovascular disease [1].

Previous studies have demonstrated that atherosclerosis is a process that begins in young adults and can be accelerated by the presence of risk factors such as smoking, alcohol, obesity and oral hormonal contraceptives [2].

The objective of this study was to evaluate the effects of the long-term use of monophasic combined hormonal oral contraceptives on the lipid metabolism of adolescents.

### 2. Materials and methods

All adolescents attending the Family Planning Clinic of São Paulo Federal University who elected COC as their method of choice were invited to participate in the study. Of the initial 80 participants, 58 completed 1 year of study, 50 completed 2 years and 33 completed 3 years. Therefore, the study population consisted of 33 adolescents who used monophasic oral hormone contraceptive (21 tablets monthly containing gestodene 75 µg and ethinyl estradiol 30 µg each) who were prospectively evaluated for 3 years. The study was approved by the Ethics Committee of UNIFESP (Universidade Federal de São Paulo) and all participants signed an informed consent form.

The exclusion criteria were: WHO medical eligibility criteria categories 3 and 4 [3]; use of an oral hormonal contraceptive in the three previous months prior to entry in the study; concomitant use of medications that might interfere in lipid metabolism (thiazides, corticosteroids, β-blockers, cyclosporine); smoking; cholesterol values higher than 199 mg/dL at baseline [4]; hemoglobin lower than 12 g/dL; body mass index (BMI; weight/height<sup>2</sup>) higher than

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95th percentile; family history of thromboembolic diseases or myocardial infarct before 50 years of age in men and 60 years in women.

All participants were healthy and had normal physical and gynecological exams before starting contraceptive use. These were repeated every 3 months during the 3-year study period.

The lipid profile consisted of total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides before (T0) and after 1 (T1), 2 (T2) and 3 (T3) years of oral hormonal contraceptive use. The levels of each parameter obtained at baseline were considered as control values for each patient. Total cholesterol values below 199 mg/dL and LDL-C below 129 mg/dL were considered normal and triglyceride levels were classified as adequate when lower than 131 mg/dL [4].

Measurements were made throughout the 3 years of the study, immediately after each sample collection.

### 2.1. Laboratory assays

Enzyme kits and an auto-analyzer were used to determine total cholesterol, HDL-C and triglyceride levels. Cholesterol was measured on supernatant using the ADVIA 1650-Bayer colorimetric enzyme kit. According to solution characteristics, concentrations up to 500 mg/dL were detectable. HDL-C was quantified using the same technique as for cholesterol, after precipitation with dextran sulfate. VLDL-C was obtained dividing triglyceride values by 5. This method could be used since triglycerides levels were <400 mg/dL in all samples.

### 2.2. Statistical analysis

The sample size was calculated as a minimum of 30 patients followed-up for 3 years, with a 90% power to detect differences of 1 standard deviation comparing the four annual averages. Significance was established at 5%.

A paired *t* test was used to compare average values of each variable (total cholesterol, HDL-C, LDL-C and triglycerides). Confidence intervals were set at 95% ( $\gamma=0.95$  or 95%).

## 3. Results

The mean age at entry was 16.6 years and average age at menarche was 12.4 years with a standard error of 0.2 years. The mean age at first intercourse was 15.4 and 72.7% of the patients had no previous pregnancies.

Compared to baseline values, total cholesterol levels increased significantly after 1 (T1), 2 (T2) and 3 (T3) years of contraceptive use (Table 1), as did HDL-C values. At baseline, 11 adolescents had HDL-C below 35 mg/dL. After starting contraceptives and throughout the study period, only four measurements were lower than 35 mg/dL.

In five adolescents, total cholesterol level rose above normal limits (199 mg/dL) during the 3-year study period. None of these patients had BMI above the 95th percentile.

Triglycerides and LDL-C also increased significantly after 1, 2 and 3 years of oral hormonal contraceptive use (Table 1).

In the second and third years of the study, cholesterol, HDL-C, LDL-C and triglyceride levels did not differ significantly from those obtained in the first year.

## 4. Discussion

Atherosclerosis is an important cause of adult mortality and its prevention can be initiated in childhood through adequate evaluation of family history (hypercholesterolemia or early myocardial infarct) and periodic exams of cholesterol levels. Several additional risk factors have been identified, such as smoking, obesity, hypertension, diabetes and high levels of cholesterol [1].

Adolescence is a time of great personal changes and frequently marks the beginning of undesirable habits such as smoking, sedentary lifestyle and improper eating patterns, such as the ingestion of large amounts of food rich in saturated fat. Frequently, it is also the period of sexual initiation, hence the need for contraceptive methods. Adolescents frequently prefer oral hormonal contraceptives because they are highly efficient, reduce dysmenorrhea and improve menstrual cycle control [5].

Consequences of oral contraceptive use have been widely studied in adult women but the adolescent population has been less studied. Therefore, recommendations for the prescription of OC to adolescents are largely based on guidelines originally designed for adult women [6].

In this study, we observed a statistically significant elevation in total cholesterol, HDL-C, LDL-C and triglycerides levels. Although this increase alone may not jeopardize the health of a young adult, it could increase the effect of other risk factors [6].

Table 1  
Lipid profile of 33 adolescents using oral hormonal contraceptives for 3 years

| Parameter     | Baseline (T0) | After 1 year (T1) | After 2 years (T2) | After 3 years (T3) |
|---------------|---------------|-------------------|--------------------|--------------------|
| Cholesterol   | 148.06±23.78  | 178.82±36.36*     | 184.06±35.05*      | 184.15±36.35*      |
| HDL-C         | 40.24±10.07   | 47.97±10.51*      | 50.85±10.6*        | 53.94±14.59*       |
| LDL-C         | 91.7±19.15    | 111.21±30.08*     | 113.55±32.35*      | 111.39±37.51**     |
| Triglycerides | 80.52±32.34   | 98.30±40.54**     | 98.33±43.61**      | 99.45±44.74**      |

\*  $p<.001$  paired *t* test in comparison with baseline values.

\*\*  $p<.05$ .

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