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Original research article

Effect of oral contraceptive use on lipid profile in Korean women aged 35–55 years☆

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Abstract

Background: Although oral contraceptives (OCs) are widely used, their effects on lipid profile need monitoring according to current usage in different populations.
Study Design: A cross-sectional study was conducted using data from 1541 participants aged 35–55 years collected by the 2005–2009 Korea National Health and Nutrition Examination Surveys. OC use, demographic characteristics and dietary intake were obtained from the participants by questionnaire, and lipid levels were determined by analysis of blood samples.
Results: Longer duration of OC use was positively associated with increasing levels of high-density lipoprotein cholesterol (HDL-C) and decreasing levels of low-density lipoprotein cholesterol (LDL-C). After adjusting for demographic and dietary factors, the odds ratio (OR) of low HDL-C (<50 mg/dL) was significantly decreased in the longer-term (>12 months) OC users (OR=0.36, 95% confidence interval 0.24–0.52) compared with those who never used OCs. However, use of OCs was not associated with a risk of high total cholesterol (≥240 mg/dL), high LDL-C (≥130 mg/dL), high triglycerides (≥150 mg/dL) or high ratio of triglycerides to HDL-C (>3.8).
Conclusions: These data suggest that the use of OCs may reduce the risk of dyslipidemia, mainly due to the decreased risk of low HDL-C, in Korean women.

Keywords: Oral contraceptive; Dyslipidemia; Cholesterol; Triglyceride; KNHANES

1. Introduction

Oral contraceptives (OCs) are an important and widely accepted contraceptive modality worldwide [1]. In Korea, most OCs contain 20–40 mcg ethinyl estradiol as the estrogen component. OCs containing low-dose ethinyl estradiol are associated with fewer adverse effects than those containing higher doses, which are known to contribute to the development of adverse health effects, including cardiovascular conditions [2–4].

Although the detailed mechanism of the cardiovascular risk of exogenous estrogen remains to be elucidated, estrogen is known to regulate many cellular functions and to modulate cellular metabolic homeostasis [5]. Estrogens acting on both estrogen receptors α and β are recognized as especially important regulators of lipid metabolism. Many experimental studies have demonstrated that estrogens regulate lipogenesis, lipolysis and adipogenesis in fat tissue [6–8]. Moreover, the type and dose of progestin in OCs can also influence lipid profile [9,10].

Furthermore, several epidemiological studies have indicated that exposure to OCs may alter lipid metabolism. OCs have been reported to cause alterations in the serum concentrations of some lipid compounds, including total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides, causing dyslipidemia in various study designs of short- and long-term administration modalities [11–14].

However, findings from epidemiological studies of the association between OCs and lipid profile have been less consistent according to the population studied; different levels of total cholesterol, HDL-C, LDL-C and triglycerides

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have been reported following the administration of OCs. In particular, relatively little information is available about the effect of commonly used OCs containing both estrogen and progestin on lipid profile or the prevalence of dyslipidemia in Korean women. Alteration of lipid profile may represent an important and potentially etiological component in the pathogenesis of many disorders, including cardiovascular diseases [15,16]; thus, it is important to elucidate the correlation between OC use and dyslipidemia profiles.

The aim of the present study was to investigate this association in Korean women using data from the Korea National Health and Nutrition Examination Survey (KNHANES), a nationally representative survey conducted in the Republic of Korea.

2. Materials and methods

2.1. Study population

This study was based on data from the 2005–2009 KNHANES, which were provided by the Korea Centers for Disease Control and Prevention. The sample for KNHANES was selected using a stratified, multistage, cluster-sampling design with proportional allocation based on the National Census Registry. Seven hundred sampling units were randomly sampled, and 2278 women aged 35–55 years who did not take drugs for hormone replacement therapy were included. Of these 2278 participants, 693 who did not provide sufficient blood for lipid analysis or had missing responses on the questionnaire were excluded from the analysis. In addition, 44 participants were excluded because they were taking medication for dyslipidemia ($n=41$) or were pregnant ($n=3$). Therefore, the final analysis included a total of 1541 subjects. Information on OCs use, including number of months of use, was obtained by self-administered questionnaire, and OCs were used by 578 (37.5%) participants.

2.2. Data collection

The KNHANES included well-established questions to determine the demographic and socioeconomic characteristics of the subjects. These included questions on age, gender, education level, income, physical exercise, smoking habit and alcohol consumption. Daily energy and nutrient intakes were assessed using 24-h recall and food-intake frequency methods. Height and weight were measured with the participants wearing light clothing and no shoes. Body mass index (BMI) was then calculated as weight (in kilograms) divided by the square of height (in meters). Then, subjects were categorized as underweight (BMI<18.5), normal (18.5≤BMI<23.0), overweight (23.0≤BMI<25.0) or obese (BMI≥25.0) according to the World Health Organization definitions for Asian populations. Blood samples were collected by venipuncture after 10–12 h of fasting. Then, total cholesterol, HDL-C and triglycerides were measured by enzymatic methods using commercially available kits (Bayer Diagnostics or Sekisui Medical) within 2 h of blood sampling. LDL-C levels were calculated using the Friedewald formula when triglyceride levels were ≤400 mg/dL and were measured directly using commercially available kits (Cholestest® LDL; Sekisui Medical, Tokyo, Japan) when these levels were >400 mg/dL. Blood analyses were carried out by a laboratory certified by the Korean Ministry of Health and Welfare. The study protocol was approved by the Korean Ministry of Health and Welfare and was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects, as defined by the Helsinki Declaration. All study participants provided written informed consent.

2.3. Variable definitions

Dyslipidemia included three lipid abnormalities: decreased HDL-C levels and increased LDL-C and triglyceride levels. According to the cutoff values for plasma lipids established by the Adult Treatment Panel III guidelines published by the US National Institutes of Health [17], a low HDL-C level was defined as <50 mg/dL, a high LDL-C level was defined as ≥130 mg/dL, and a high triglyceride level was defined as ≥150 mg/dL. In addition, the ratio of triglycerides to HDL-C was used as a measure of dyslipidemia because a ratio >3.8 is known to correlate with LDL-C phenotype B, which is a reliable predictor of the risk of cardiovascular disease [18,19].

As a covariate, education level was categorized as less than a high school diploma, high school diploma, and college or higher. Alcohol consumption was assessed by questioning the subjects about their drinking behavior during the month before the interview. The subjects were asked about the average frequency and amount of alcoholic beverage intake. The average amount and number of alcoholic beverages consumed were converted into the amount of pure alcohol (ethanol) consumed per day.

2.4. Statistical analysis

Means and standard deviations (SDs) or standard errors (SEs) of the demographic and dietary characteristics were calculated according to the duration of OC use. Estimate statements in linear regression models were used to determine the adjusted mean and 95% confidence intervals (CIs) of each lipid measure with increasing duration of OC use. For triglyceride level, based on a normal probability plot, geometric means were used to improve the approximation of a normal distribution. The prevalence of dyslipidemia measures was compared among categories of OC consumption using multivariate logistic regression after adjusting for potentially confounding variables. The presence of a linear trend was evaluated by defining a linear contrast in each linear and logistic regression model. All statistical analyses were conducted using SAS software (version 9.2; SAS Institute, Cary, NC, USA).