

Original Article**Evaluation of Serum Cholesterol and Copper in Women Taking Oral Contraceptive**

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For Correspondence*Abstract**

Background: Birth control pills alter women's reproductive cycle and suppress various endocrine functions. Primary alterations of endocrine functions have secondary effects on other chemical and enzyme functions of the body. A general lowering of the body's nutrient base occurs in women on hormonal contraception. The biochemical profile of oral contraceptive pill user women showed different changes in plasma total protein, albumin and various trace minerals like serum zinc, copper, magnesium etc. Trace minerals are necessary for endocrine function. The pill can effectively prevent pregnancy and alleviate menstrual disorder while used correctly. Many biochemical profiles of women taking oral contraceptives are disturbed due to metabolic alterations induced by its hormone content. **Objectives:** To find out the relationship between serum cholesterol, serum copper with the use of oral contraceptive.

Materials and Methods : The case control study was carried out in the Department of Biochemistry, Mymensingh Medical College, Mymensingh, during the period of July 2015 to June 2016 to evaluate the status of serum cholesterol and copper in women taking oral contraceptive. For this study, 100 age-matched women were selected and grouped as 50 oral contraceptive user and 50 non oral contraceptive user. Data were analyzed with the help of SPSS version 21.

Results: Mean \pm SD level of serum fasting cholesterol and copper were 216.96 ± 16 mg/dl and 153.96 ± 15.6 μ g/dl in oral contraceptive user women, while in normal healthy women the levels were 163.44 ± 18.9 mg/dl and 106.34 ± 16.73 μ g/dl respectively. Serum cholesterol and copper were significantly increased in oral contraceptive user group when compared with that of normal healthy group ($p < 0.001$). **Conclusion:** The study showed increased trend of serum cholesterol and copper in oral contraceptive users when compared with non-oral contraceptive users. Hence, it can be concluded that there may be significant association of serum cholesterol and copper level with oral contraceptives.

Keywords: Oral contraceptives, Serum cholesterol, Serum copper.

Introduction

Contraceptives are devices or techniques that permit sexual union without resultant pregnancy.¹ In Bangladesh among the available modern methods of contraceptives, about 30% couples use oral contraceptives.² Combined oral contraceptives are highly effective, reversible and popular one.³ Available and heavily used contraceptive in Bangladesh has been the oral pill (Sukhi) containing estrogen and progestin.⁴ Oral contraceptive pill stops ovulation by preventing the ovaries from releasing ovum. They also thicken cervical mucus making it harder for sperm to enter the uterus.⁵ The major side effects were found to be dreaded conditions like malignancy and thromboembolic cardiovascular disease. Among the cardiovascular disorders, hypertension, myocardial infarction, hemorrhagic or ischemic strokes and venous thromboembolic conditions were mentionable.⁶ There has been interest in recent years about alterations in various metabolic processes and trace elements profiles associated with the use of contraceptives. Changes in life style, environmental factors, dietary habits and active ingredients of hormonal agents have been known to affect status of micronutrients in humans.⁷ Changes in tissue level or bioavailability of those elements could play a significant role in health risk and the pathogenesis of some disorders such as cardiovascular complications, the aging process at certain cancers have been associated with the use of contraceptives.⁸

The relationship between abnormal high plasma lipid and estrogen progesterone combination oral contraceptive has been known for many decades & it also increases the risk of coronary heart disease.⁹ The increasement was progressive relating with duration of oral contraceptives use.¹⁰ Many scientists were in the same opinion that oral contraceptives can induce changes in lipid and carbohydrate metabolism due to change in insulin levels.¹¹ Some of the researchers found increased cholesterol in OCP users. It appears to be the estrogen component of oral contraceptive pill that is responsible for the abnormality.¹²

Copper is one of the important trace elements, essential co-factor, enzyme involved in metabolic reactions,

angiogenesis, oxygen transport and antioxidant protection, including catalase, super oxide dismutase (SOD) and cytochrome oxidase.¹³ There is an association between use of OCP and increase absorption of copper, resulting in increase of serum copper concentration. Increased level of copper in individuals on oral contraceptives may be related to a saturation of ceruloplasmin or a reduction in plasma ceruloplasmin level. Excess level of circulating copper may have adverse effect on liver. Use of oral contraceptive pill has been associated with alteration of serum copper level, which may lead to hepatolenticular degeneration.¹⁴ So, the present study is carried out to see the effect of OCP on serum cholesterol and serum copper, excess of which may cause many metabolic derangements leading sometime to dire consequences. Findings of this study may aware the clinician and gynecologist in prescribing copper supplement in women taking OCP for contraception and also help them in better management of those cases.

Materials and Methods

This cross sectional study was carried out in the Department of Biochemistry, Mymensingh Medical College, and the subjects were collected from the Model Family Planning Clinic of Mymensingh Medical College Hospital during the period of July 2015 to June 2016. For this 50 apparently healthy married women with age ranging from 20 to 35 years taking no hormonal contraceptives for at least one year selected as controls (Group-I) and age matched 50 married women taking oral contraceptive pill for at least six months were taken as cases (Group-II). Subjects having systemic illness like diabetes mellitus, hypertension, tuberculosis, kala-azar were excluded from the study. Apparently looking obese, taking other hormonal contraceptive pill other than combined estrogen progesterone preparation was excluded.

Informed written consent was taken from each study subject and ethical approval for the study was obtained from the Ethical Committee of Mymensingh Medical College and Hospital.

Height, Body weight and Blood pressure were measured and Body Mass Index (BMI) was calculated.

Serum cholesterol: Serum total cholesterol was determined by enzymatic end point method.

Serum copper was estimated by colorimetric method with the 3,5-DiBr-PAESA stain. In an acid solution (pH 4.7),copper is released from the Ceruloplasmin protein and reduced. Afterwards the cuprous ion reacts with the 3,5-DiBr-PAESA stain, and forms coloured complex,which is photometrically measured at 582 nm.The colour intensity is directly proportional to the copper ions concentration present in the sample.

Data were analyzed with the help of SPSS version 21. Quantitative data were expressed as mean and standard deviation and comparison between groups was done by Student’s unpaired ‘t’ test.

Results

In this study, age range was from 20 to 35 years for both case and control group. It was observed that the mean age of Group-I and Group-II was 26.16±3.38 and 26.12±3.28 years respectively and the level of significance was 0.47 (p>0.05). Thus difference in mean age was not significant between OCP users case and apparently healthy control group.

In this study, mean ± SD age of controls (Group-I) and cases (Group-II) were 26.16±3.38 and 26.12±3.28 years respectively, which showed no significant difference (p>0.05). Mean ± SD BMI of controls and cases were 21.63±2.11 kg/m² and 21.67±2.11 kg/m² respectively, which showed no significant difference (p>0.05); as shown in **Table I:**

Table I: Demographic features of study subjects.

Demo graphic features	Group I (control) Mean± SD	Group II (case) Mean± SD	p value
Age (years)	26.16±3.38	26.12±3.28	0.47 ^{ns}
BMI (kg/m ²)	21.63 ±2.11	21.67±2.11	1.000 ^{ns}

Data were expressed as mean and standard deviation and comparison between groups were done by Student’s unpaired ‘t’ test.

Table II shows the level of serum fasting cholesterol and serum copper in study subjects. The study revealed that mean (± SD) of serum fasting cholesterol level (mg/dl) were 216.96±16 and 163.44±18.9 in cases and control respectively which was significantly higher in cases (p<0.001). Mean± SD of serum copper (µg/dl) were 153.96±15.6 and 106.34±16.73 in cases and controls respectively which was significantly higher in cases (p<0.001).

Table II: Serum cholesterol and copper levels of the study subjects.

Biochemical parameters	Group -I (control) Mean± SD	Group -II (case) Mean± SD	p value
Cholesterol (mg/dl)	163.44±18.9	216.96±16	<0.001**
Copper (µg/dl)	106.34±16.73	153.96±15.6	<0.001**

Data were expressed as mean and standard deviation and comparison between groups were done by Student’s unpaired‘t’ test.

Discussion

The oral contraceptive pill fulfills the great human need for birth control with unrivalled effectiveness.¹⁵ The pill can effectively prevent pregnancy and alleviate menstrual disorder while used correctly.¹⁶ Many biochemical parameters of women taking oral contraceptives are disturbed due to metabolic alterations induced by its hormone content. Researches had been continuing for many decades to explore risk versus benefits of different contraceptive methods. The present study was designed to observe some biochemical alterations in women taking combined oral contraceptives containing 30- μ g ethinyl estradiol and 150- μ g levonorgestrel. Combined oral contraceptives (Sukhi) is the mostly used brand in rural community as it is distributed free of cost.¹⁷ Therefore, metabolic alteration might be initiated earlier that go on silently without developing any overt clinical abnormality. On the contrary, long time use of hormones such as oral contraceptives can affect various metabolic pathways to such an extent that would cause detectable clinical abnormality.¹⁸

In the present study serum total cholesterol were found to be significantly increased in OCP user as compared to healthy woman. These findings were in agreement with the result of Barry et al.¹²

Some studies, have found the increase serum cholesterol was progressive relating with duration of oral contraceptives use. They found no correlation among age, length of therapy, degree of obesity, day of cycle.¹⁹

They found an increase in mean total lipids above control value during the first 3 cycles that showed further increase through subsequent cycles. Mean serum cholesterol level showed no significant change up to 6 cycles, but significant elevation in comparison to controls were noted after 6 cycles and onwards. It appears to be the estrogen component that is responsible for the abnormality.¹²

The mechanism by which contraceptive steroids bring about changes in serum copper levels is not clearly understood. Researchers suggested that estrogen-induced synthesis of ceruloplasmin in the liver is responsible for the increase in serum copper levels. The estrogen component is mainly responsible for the increased level of serum ceruloplasmin while

progesterone causes a less drastic rise. Estrogen acts as an inducer for synthesis of ceruloplasmin RNA templates causing subsequent increase in synthesis of the protein. For this reason, the increasing in ceruloplasmin level cause an increase in serum copper concentration.¹⁸

Conclusion

The present study showed significant alteration in serum cholesterol and copper levels. This study was done within the context of the facilities available to us. Our sample size was small due to limitation of time and fund. Considering the side effects, close biochemical monitoring and follow up must be emphasized for women on oral contraceptive.

It may be recommended to carry out a large scale prospective study with the application of modern sophisticated technology to elucidate alteration in biochemical parameters including other trace elements and organ function test which can give a conclusive decision. As a preliminary study, our data may raise enthusiasm and interest in future researcher for studying with trace minerals.

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