

Effect of Oral Contraceptive on some Serum Biochemical Parameters

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الملخص

يتضمن البحث الحالي تقدير مستوى بعض المتغيرات الكيموحيوية: (الفوسفاتيز القاعدي, ALK والكرياتين كايينيز, CK واسبارتيت امينوترانسفيريز, AST وحامض اليوريك واليوريا والبيليروبين الكلي والألبيومين والبروتين الكلي) في مصل 47 امرأة سليمة ممن يتناولون حبوب موانع الحمل ولمدة تتراوح من 1 الى 3 سنوات التي كانت أعمارهن بين 20-45 سنة وممن يراجعن مركز تنظيم الاسره في مستشفى الخنساء التعليمي في الموصل و30 امرأة سليمة من ذات الفئة العمرية وذات مؤشر كتلة الجسم ممن لا يستعملن موانع الحمل باعتبارهن مجموعة سيطرة.

أشارت النتائج الى وجود انخفاض معنوي في كل من: ALP وCK وAST والألبومين والبروتين الكلي بينما اظهر حامض اليوريك ارتفاعا معنويا مع عدم حدوث تغيير معنوي في تراكيز كل من اليوريا والبيليروبين الكلي لدى مجموعة النساء المستعملات لحبوب موانع الحمل مقارنة مع مجموعة السيطرة.

الكلمات ألدالة : موانع الحمل الفموية , المتغيرات , الانزيمات , البروتين.

ABSTRACT

The present study were aimed to determine the level of some biochemical parameters: (alkaline phosphatase ALP, creatine kinase CK, aspartate aminotranferase AST, urea, total bilirubin, albumin and total protein) in serum of 47 healthy women who took oral contraceptive pills (OCPs) during the period 1 to 3years. Their ages ranged between 20-45 years. They were attending to Al-Khanssa Family Planning Center in Mosul. The study also aimed to compare the results with those of another 30 healthy women who did not use any hormonal contraceptive.

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They were matched for age and weight with the OCPs user groups. Results obtained in this study showed a significant decrease in the activities of ALP, CK, AST, albumin and total protein, while the uric acid value was significantly increased, and no significant differences in the concentration of urea and total bilirubin in OCPs user group compared to control group.

Key words: Oral Contraceptive, Biochemical , Enzymes, Protein.-

INTRODUCTION

Oral contraceptives are medicines taken by mouth to help in preventing pregnancy ,They are artificially made from two hormones naturally produced in the body (Estrogen and progesterone) so called OCPs ⁽¹⁾.They are the most effective ,safe ,reliable and popular form of reversible contraceptive ⁽²⁾.

They are highly efficacious ,with a theoretical effectiveness generally considered to be 99.9% ,and a use effectiveness (missed pills, starting the active pills cycle early or late, sporadic use or discontinuation) of 97% to 98% ⁽³⁾.

It has been accepted for well over a decade that OCPs have substantial health benefits unrelated to their contraceptive use⁽⁴⁾ .In addition to their high contraceptive efficacy OCPs have many other contraceptive benefits ,these include: a lower risk of incidence of the menorrhagia ,iron deficiency anemia ,benign breast disease and functional ovarian cysts and endometriosis ⁽⁵⁾.The incidence of ovarian and endometrial cancer is reduced for each by 50% ⁽⁶⁾.

The OCPs has a positive effect on bone mineral density, and the benefit is related to estrogen dose and duration of OCPs use. Also the incidence of post-menopausal hip fracture is reduced possibly for women who use OCPs in their 30 s ⁽⁷⁾.

Given the growth promoting effects of estrogen, there has been long-standing concern that OCPs might increases the incidence of endometrial , ovarian , breast and other cancers. However , it is now clear that there is not a widespread association between OCPs use and cancer ⁽⁸⁾.

The aim of this investigation was to clear controversial effects of the various formulations on the some biochemical parameters of the contraceptive user's women. Thus the present study was performed to evaluate the effects of hormonal contraceptive on some biochemical parameters among OCPs users and non-users (Control) healthy women.

MATERIALS AND METHODS

Samples:

The samples included apparently (47) healthy women with age range between (20-45) years, who were attending Al-Khanssa Family Planning Centers in Mosul and used oral contraceptives during the period 1 to 3 years, in addition to 30 healthy women who did not use any hormonal contraceptive and were drawn from the same population and matched for age.

The weight and the height were measured for each participant in the study. The body mass index (BMI) was also calculated according to the equation:

$$\text{BMI} = \text{weight (kg)} / \text{height (m}^2\text{)} .$$

Any women with over weight (BMI/25) according to the classification of adult according to BMI, was excluded from the study.

Blood samples:

About 5 milliliters of venous blood was withdrawn, using a disposable syringe on the inner wall of plain tube to avoid hemolysis. The blood was allowed to clot and the serum was separated by a centrifugation and divided in aliquot and at -20 °C for the measurement of enzymatic activities and other biochemical tests.

Measurement of biochemical parameters:

- Activities of alkaline phosphatase, aspartate aminotransferase and urea concentration were assayed using kit manufactured by BioMerieux.
- Activity of creatine kinase was assayed using kit manufactured by Randox.
- Uric acid concentration was estimated by using the uricase enzymatic method ⁽⁹⁾.
- Total bilirubin, albumin and total protein were measured by the colorimetric method using kit manufactured by Syrbio.

RESULTS AND DISCUSSION

The oral contraceptives users included in this investigation were apparently healthy fertile married women with regular period. OCPs represent the most commonly method of contraception in Iraq especially among younger women as it had been found by Khalil ⁽¹⁰⁾, that 54% of pills users.

The results in table (1) showed that there is no significant difference between mean heights of OCPs users and control group.

Table (1) Anthropometric measures between OCPs users and control groups.

Measure	Control group (Mean ± SD) n=30	OCPs users (Mean ± SD) n=47
Height (cm)	154.20 ± 4.52	151.32±2.48 NS
Body weight(kg)	61.32 ± 6.78	63.38±6.81 NS
BMI(kg/m ²)	25.78 ± 2.95	27.67±3.82 NS

NS=Non significant

The results in table (1) also indicated that OCPs causes a non-significant increase in the body weight among the OCPs users in comparison with the non-user women.

The OCPs although cause a non-significant increase in the BMI of the OCPs users in comparison with control women ,as shown in table (1).

These results were in agreement with other reports who found that there is no adverse effects of cardiovascular risk modifiers (age, body mass index, cigarette smoking, alcohol intake, exercise habit, family history of heart disease or diabetes, number of pregnancies and duration of OCPs) on metabolic risk markers⁽¹¹⁾. Also, the results of Al-Banna emphasized the lack of association of OCPs use with weight gain, even no weight changes due to OCPs use was found ⁽¹²⁾. On the other hand, there is another studies changes in body weight were reported which are in contrast with the finding of the present work , which they found that there was a significant increase in body weight of OCPs users in comparison to non-users ⁽¹³⁾.

The results in table (2) illustrates that there is a significant increase in serum uric acid on OCPs users in comparison with control group at (p < 0.001). The percent increment was about 53 %.

Table 2: Effect of OCPs on some biochemical parameters .

Parameters	Control group (Mean±SD) n=30	OCPs users (Mean±SD) n=47
Uric acid (mmol/L)	0.19±0.08	↑0.29±0.09 ***
Urea (mmol/L)	5.20±0.15	4.99±0.09 NS
Total bilirubin(μmol/L)	11.48±4.26	9.24±3.96 NS
Total protein (gm/L)	65.41±8.75	↓60.25±10.92 ***
Albumin (gm/L)	50.5±5.50	↓39.1±1.10 ***

***significant difference between control at(p≤0.001)

NS=Non significant

This increasing in uric acid concentration may be due to the increased de novo purine synthesis; increased purine nucleotide degradation diminished renal excretion of urate and oral combination of these defects ⁽¹⁴⁾. The causes of the increment could be due to the increased nucleoprotein production and catabolism which are important in the hyperuricemia that occurs with OCPs users ⁽¹⁵⁾, or due to that the uric acid is one of the antioxidant which present in plasma in high concentration. It efficiently scavenges radicals. Urate might be particularly important in providing protection against certain oxidizing agents ⁽¹⁶⁾.

Our results were in agreement with the study of Al-Youzbaki ⁽¹⁷⁾, while they were in disagreement with the study of Jayasri *et al.* ⁽¹⁸⁾ who found that the uric acid value were significantly reduced in OCPs users when compared to non-users.

The present investigation showed that the use of OCPs causes non-significance decreased in the concentration of urea when compared to control group, as shown in table (2).

The concentration of total bilirubin showed that there are non-significant changes in OCPs users when compared to non-users groups. This result was in agreement with other previous studies ^(19, 17). Some studies have shown that bilirubin is a powerful endogenous anti-oxidant that scavenges peroxy and hydroxyl radicals. Bilirubin thereby protects linoleic acid, lipid of membranes, its own carrier protein albumin and other protein from oxidation. Other studies mentioned that bilirubin as an important cytoprotector for tissues that are poorly equipped with antioxidant defense systems such as myocardium and nervous tissue ⁽²⁰⁾.

The present study showed that the albumin level was reduced in women who used OCPs than non-user as shown in table (2). The decrement of the concentration of serum albumin was serve as an index to the effect of contraceptive hormones on the liver, these changes suggested that biochemical profile of long term OCPs user be assessed periodically ⁽²¹⁾. On the other hand, albumin is the main constituent of protein which plays several roles in the human body. Albumin may be considered as an important component of plasma with anti-oxidant activity, primarily, binding free radicals, free fatty acid, divalent cations, hypochloride and bilirubin ⁽²²⁾.

The results of the present study are in agreement with many others studies of decrement of albumin concentration ^(21, 23) which reported hypoalbuminemia in subjects treated with OCPs and they attributed the hypoalbuminemia to the direct effect of OCPs on the metabolism of proteins.

The total protein was also measured in this study and the results indicated that there was a significant decrease in its concentration of it in OCPs users compared with non-users. The results was corresponding with other reporters which noted that the total protein concentration was decreased in women who used hormonal contraceptive⁽²⁴⁾. These studies indicate that the intake of PCPs could cause metabolic changes in carbohydrate, protein and lipid macromolecules⁽²¹⁾.

Alkaline phosphatase belongs to a class of enzymes called phosphatases .They are very important in determining normal liver function. The results showed that there was a significant decrease in the activity of ALP in OCPs users when compared to control group, as shown in table(3). These results were comfortable with other results which indicated a significant reduction in ALP activity in women who used the OCPs pills compared to non-users ⁽²⁵⁾.

The abnormally low level of ALP in the serum is indicative of genetic disorder known as hypophosphatasia . This is a bone disorder where, due to the deficiency of phosphorus the body exhibits bone deformities⁽¹⁴⁾. The low levels of ALP have been observed in women who are under medication such as OCPs, which indicated that the bone turnover were influenced by OCPs and cognitive dietary restraint among this population of young women in dependent of body composition and physical activity ⁽²⁵⁾.

**Table (3) Comparison between some enzymes activity
in OCPs users and control group**

Enzymes	Control group (Mean ± SD) n=30	OCPs users (Mean ± SD) n=47
Alkaline phosphatase (U/L)	58.32±1.80	↓50.74±1.63 ***
Creatine phosphokinase (U/L)	97.53±7.32	↓76.53±9.84 ***
Aspartate aminotransferase (U/L)	38.49±5.97	↓31.28±8.65 ***

***Significant differences between controls at (p≤0.001)

The present study also concluded the effect of OCPs use on serum creatine phosphokinase (CK) activity. The results indicated that the OCPs group had significantly lower CK activity when compared to the control group. These results were in agreement with other results ⁽²⁶⁾. The lower levels of serum CK activity indicated a possible role of estrogens in the CK response. Moreover, research on animals has indicated a role of estradiol in reducing membrane permeability⁽²⁷⁾. Hinderks and Frohlich reported an association between low serum creatine kinase values and

administration of steroids in patients suffering from various diseases. Steroids reportedly prevent the rise in serum CK in experimental myocardial ischemia due to their " membrane stabilizing effect"⁽²⁶⁾. Other reported that progesterone decreased the myometrial CK activity in no gravid human subjects. This might explain the lower value for serum CK in contraceptive steroid users ⁽²⁷⁾.

The results on table (3) showed that the AST activity was significantly decreased among OCPs uses when compared to control group. The percent of decrement was 23%. These result was in agreement with Jayarama *et al.*,⁽²⁸⁾,others reported that the serum aspartate aminotransferase is slightly decreased among hormone uses (9%) but is significantly increased (27%) in pregnancy⁽²⁹⁾.

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