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# PHYSIO-CHEMICAL STUDY OF SOME LIVER ENZYMES IN THE PROVINCE OF NAJAF WOMEN'S USED LOW DOSE COMPOUND ORAL CONTRACEPTIVES PILLS (COCS)

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**ABSTRACT**

This study was evaluate to find out the effect of low-dose compound oral contraceptives on some liver function in women employed by conducting some special liver function tests. The study included 30 women employed to pills in addition to 20 age matched healthy women included as control group. ALT, AST and ALP were estimated in sera levels for threads examined. A significant elevation found for ALT, AST, While ALP it observed decrease significantly in users when compared with non-users. In addition, study the effect of duration of use on hepatic parameters examined. The results showed significant differences in the effectiveness of ALT, AST and ALP. In addition, it has been observed correlation relationships between these significant parameters and duration of use. Therefore, which is used for birth control may have a negative effect on the liver function and safety.



## INTRODUCTION

During half a century, many of the studies dealt with the combined oral contraceptives (COCS) because it is have become a key component of modern fertility regulation programmers. At present more than 100 million women in the world use contraception[1]. Most combined hormonal methods including the pills, contain synthetic Ethinylestradiol, which is much more effect than the naturally occurring estrogens. Which means they remain present a long time in the blood after taking them and influence a greater on the liver[2,3]. Studies indicated that more than 14% of the world's women and 6% of women in developing countries using oral contraceptives [4].

There are three types of oral contraceptives:-

A single hormone (Progesterone only pills).
A grain that contains progesterone only.

Grain compound (Combined Pills): It is containing the progesterone and estrogen together.

Pregnancy Sequential Oral Contraceptive contain estrogen, which is given in the first half of the session, then given Progestin in the second half [5].

## LITERATURE SURVEY

The liver is one of the most important organs in the body. As th e body's "chemical factory" it regulate the levels of most of the main blood chemicals and acts with the kidneys to clear t he blood of drugs and toxic substances. Liver function tests are used to determine if the liver has been damaged or its function impaired. Elevations of certain liver tests in relation to others aids in that determination[6,7,8] .

### *Alanine aminotransferase*

Alanine aminotransferase (ALT), formerly called serum glutamate pyruvate transaminase, or SGPT, is an enzyme ecessary for energy production. It is present in a number of tiss ues, including the liver, heart, and skeletal muscles, but is found in the highest concentration in the liver. Because of this, it used in conjunction with other liver enzymes to detect liver disease, especially cirrhosis of the liver without jaundice. Additionally, in conjunction with AST; it helps to distinguish between damage the heart and liver tissue damage [9].

### *Aspartate aminotransferase*

Aspartate aminotransferase (AST), formerly called serum gluta mic- oxaloacetic transaminase, or SGOT, is anotherenzyme necessary for energy production. Too, it may be high in the liver and heart disease. In liver disease, increased AST is usually less than the increase ALT. However, in the liver diseases caused by alcohol abuse, and increased AST maybe two or three times ALT Increased [10.11].

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***Alkaline phosphatase***

Alkaline phosphatase (ALP) levels usually include two similar enzymes (isoenzymes) that mainly come from the liverand bon e and from the placenta in pregnant women. In some cases, doctors may order a test to differentiate between thealkaline ph osphatase that originates in the liver and the alkaline phosphata se originating in bone. If a person haselevated ALP, does not h ave bone disease and is not pregnant, he or she may have a pro blem with the biliary tract, thesystem that makes andstores bile. Bile is made in the liver, then passes through ducts to the gall bladder, where it is stored [12,13].

Liver principal organ of drug metabolism [14]. The biochemical pathway responsible for the great portion of drug metabolism is hepatic mixed function[15]. Therefore the liver plays a central role in the metabolism of estrogens and progestogens and it is becoming obvious that these substances can act directly or indirectly on the liver to produce a variety of biological effects that have both physiological and pathological significance[16.]

The aim of this study was to indicate the association between low dose hormonal contraception use and the effect on function of the liver and to determine if the duration of use may be directed changes in liver function tests of users.

## MATERIALS AND METHODS

This study was conducted in the province of Najaf on a group of women were used 50 and women between the ages of convergent revisions, in outpatient clinics for a number of doctors.

As they were distributed into two groups A and B groups, depending on the nature of the study.

Group A: - comprised 20 women divided depending on the use of the compound oral contraceptive pills.

Patient group: - includes 10 women who are ingestion of COCS.

The control group included 10 women who are not ingestion of COCS.

While Group B included 30 women distributed in three groups: The first group included 10 women who are not ingestion of the compound oral contraceptives pills. (Control group)

The second group included 10 women who they are taking COCS for one year.

The third group included 10 women who they are taking COCS for two years.

The study included measurement of some liver function (AST, ALT and ALP) and the effect of The period for taking pills, according to Special regulations all subject in this study suffered from any disease interferes with the data obtained were excluded.

***Sample analysis***

Liver functionality was indicated by the Serum aspartate amino transferase (AST) and alanine amino transferase (ALT) activities were estimated for liver integrity using Randox reagent kit using 2, 4-dinitrophenylhydrazine substrate[17]. Alkaline phosphatase (ALP) activity was determined for biliary integrity with the Randox reagent kit using the p-nitrophenylphosphate substrate as described by [18].

***Data analysis***

The Mean Standard deviation (mean ±S.D.) was determined and one-way ANOVA analyses of variance were performed using SPSS version 17 software. The significance level was set at $p<0.05$.

## RESULT AND DISCUSSION

The effect on some liver function parameters in female administered low dose OCC are as show in table 1. (AST, ALT and ALP) in patients group than control. AST and ALT. Ware observed to be increasing significantly between the group , presented significantly higher ($p<0.05$)levels of ALT (9.88 ± 0.33U/L), AST(17.5±0.88 U/L) and ALP(9.88± 3.8 U/L), compared to controlled group ALT (6.2 ± 0.8 U/L) ,AST(14.5 ± 5.5 U/L)and ALP(9.20 ±4.6 U/L).

**Table 1** serum liver enzyme activities in females used low dose combination oral contraceptive and the control group.

| Parameters | Patients Mean ±SD | Control Mean ±SD |
|---|---|---|
| ALT U/L | 9.88 ±0.33 | 6.2 ±0.8 |
| AST U/L | 17.5 ±0.88 | 14.5 ±5.5 |
| ALP U/L | 8.8 ±3.8 | 9.20 ±4.6 |

ALT: Alanine-amino transferase AST: Aspartate-amino transferase, ALP: Alkaline phosphatase; Values are Mean± Standard deviation and values within each liver and biliary integrity parameters having different superscript are statistically significant at $p<0.05$.

The Liver is particularly likely to develop because of its functions related to and dealing with many metabolites, drugs, and toxic substances[19]. Enzymatic activities plasma indicate liver cell membrane damage instead of functions, because these enzymes are also present in other tissues [20.]

The results of the present study, a significant increase in the activities of the two enzymes. Approximately percent of abnormally high and are rarely observed activity in another case of liver diseases parenchymal[21]. In addition, the ALP excreted in the bile-induced or released when canalicular membrane damage that occurs blockage of bile ducts[22]. ALP derived mainly from liver and bone in approximately equal properties[20].

It can be understood to limit the ALP activity when the total effect of estrogen on bone. Estrogen as is known inhibitor of the potential for thyroid hormone (PTH), particularly in its work. However, in female used oral contraceptives containing estrogen, the PTH activity is inhibited and ALP being significantly reduced[23]. In the liver cell integrity period, the findings of this study are in line of considering contraindications reported with the use of OCP[24, 25, 26, 27].

Judging by the dose was vested in increased serum concentrations of liver enzymes in this study; one can affirm that the dose-dependent manner, OCPs induces changes in the liver cell integrity.

This confirmation is the sequel to the importance of serum concentrations of liver enzymes and that these signs of leakage

into the circulation when there is necrosis or hepatic cell damage[28, 29].

The table 2. Show the effect of duration of use on serum liver enzyme activities of women used low dose compound oral contraceptive and control group.

The results were (7.2± 2.5 U/L),(16.5± 7.6 U/L) and (8.4 ±8.13 U/L)for ALT,AST and ALP respectively in first year. While the results in second years were (12.1 ± 29.2 U/L), (18.3 ± 17.9 U/L), and (6.4 ±34.2 U/L) for same parameters respectively. Compare with the controlled group were (6.2 ±0.8 U/L),(14.5 ±5.5 U/L) and(9.20 ± 4.8 U/L) for ALT,AST and ALP respectively.

**Table 2** Effect of duration of use on serum liver enzyme activities in females used low dose combination oral contraceptive and the control group.

| Parameters | Control Mean ±SD | Duration | |
|---|---|---|---|
| | | One year Mean ±SD | Two year Mean ±SD |
| ALT U/L | 6.2 ±0.8 | 7.2 ± 2.5 | 12.1 ± 29.2 |
| AST U/L | 14.5 ±5.5 | 16.5 ±7.6 | 18.3 ± 17.9 |
| ALP U/L | 9.20 ±4.8 | 8.4 ± 8.13 | 6.4 ± 34.2 |

Our results pointed out ALT and AST activities increased significantly in the third group only.

However, ALT showed an increase morally higher than AST. This observation may be due to the half-life of the two enzymes. Since then, his ALT longer half-life of AST[30]. Large variations of activities. ALT and AST between groups 1 and 2, with three and a positive correlation with duration of use may reflect the ongoing changes in the integrity of the liver with the progress.

Such changes management may remove when the liver is being well adapted for contraceptive oral[31]. It may be due to the induction of the synthesis of an enzyme in the liver this rise[32].

Steroids of contraceptives are powerful inhibitors of PTH, which is the driving force of the ALP to rise from the bones. Thus, continuous administration may lead to reduced bone loss and reduce the Alp activity[33]. Have noted [34] increased ALT and AST with lowered ALP activities during three months treatment of oral contraceptives.

In fact, based on the results of this study, the remarkable results on the nature of the liver of OCPs seems to have challenged the normal physiological function and integrity of the liver. Thus, taking low doses of synthetic even OCP may affect the functionality of the liver and cellular integrity and system biliary dose-dependent manner[35].

## CONCLUSION

Depending on the observed changes in proteins and enzymes in the liver and therefore suggested that he that OCPs administration to patients suffering from liver problems with care.

### *Future Scope*

Based on what has been reached there is a need to further investigation of other biochemical parameters hepatic cells, and most importantly, the tissue of the liver with respect to OCPs. Expand the study to include different organs of the body. Thyroid function tests evaluated, kidney function tests and bone.

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