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## Effect of oral contraceptive on thyroid hormones and lipid profile of male rats

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### ABSTRACT

This study is designed to investigate the effect of oral contraceptive on thyroid hormones triiodothyronine (T<sub>3</sub>) and thyroxin (T<sub>4</sub>), and lipid profile by using 18 Wister albino male rats divided into three groups: group A received normal saline (0.9% NaCl) as a control group. Group B and group C administered contraceptive pills at (0.32 mg/rat/day and 0.64 mg/rat/day) respectively for 60 days. The results showed a significant decrease ( $p < 0.05$ ) in level of T<sub>3</sub> and a significant increase in level of T<sub>4</sub> in B and C groups compared with the control group, while there was non-significant difference in T<sub>3</sub> and T<sub>4</sub> of group B compared with group C. The results indicated non-significant decrease in cholesterol, Triglycerides (TG) and low density lipoprotein (LDL) in both groups B and C, and a significant decrease in level of high density lipoprotein (HDL) in group C when compared with the control group, also non-significant different in these parameters between B and C groups.

**Key words:** Oral contraceptive, T<sub>3</sub>, T<sub>4</sub>, Lipid profile, Rats.



### INTRODUCTION

Oral contraceptives (OC) called also (birth control pills) are compounds consist of steroid hormones synthetic estrogen and progesterone (progestin) together (COCs) or contain progesterone only. OC used by women to prevent pregnancy [1]. Most estrogen in COC is ethinylestradiol and progesterone which used in COC is norethynodrel (norethisterone) or levonorgestrel (norgestimate) or gestodene (desogestrel) or drospirenone [2]. The action of COCs depended on inhibition of ovulation process by inhibition of follicle stimulating hormone (FSH) and luteinizing hormone (LH) which produced by the anterior lobe of pituitary gland, these hormones responsible on development and release egg from the ovary [3]. Progesterone in COCs act through negative feedback mechanism and cause decrease release of gonadotropin releasing hormone (Gn-Rh) from hypothalamus gland, the last is responsible on the secretion of FSH and LH, in the end the ovulation is stop [4].

One of the functions of progesterone in COCs prevents sperms penetration the ovum by increasing the cervical mucus and become thick, also progesterone prevent transport of ovum [3]. Estrogen and progesterone in COCs used also in other conditions such as: endometriosis,

amenorrhea, polycystic ovary syndrome (PCOS) and menorrhagia, hormones in COCs treat these cases [5]. Combined oral contraceptive decrease the risk of ovarian cancer and endometrial cancer [6]. In other side, COCs caused venous thromboembolism in women taking this drugs [7] and also COCs reduced level of testosterone [8]. Many studies refer to relationship between COCs and thyroid gland hormones [9, 10, 11]. They suggested that estrogen found in COCs caused increase of thyroxin binding globuline (TBG) concentration which increase the thyroid hormones (Triiodothyronine and Thyroxine). In the same veins, COCs effects on adrenal gland, blood pressure and thyroid function [12]. This study performed to investigate the effect of oral contraceptive on T<sub>3</sub> and T<sub>4</sub> and lipid profile of male rats.

### MATERIALS AND METHODS

**Animals and experimental design:** Eighteen male Wister albino rats (*Rattus norvegicus*) at age (10-12) weeks and weighting (200-250g) were obtained from the animals house of Department of Biology, College of Science, University of Thi-Qar, Iraq. Animals were housed in standard plastic cages and kept in room with temperature of (24-28°C) with 12 hrs light and 12 hrs darkness. Animals given free access to food and water *ad libitum*. Animals were

divided into three groups (each group contain 6 rats) as following:-

- Group A: the control group treated orally with normal saline (0.9%NaCl) for 60 days.
- Group B: treated orally with contraceptive pills (The drug that used in this experiment is microgynon (levonorgesterl and ethinylestradiol) Schering AG, Germany) for 60 days at dose (0.32mg/rat) daily.
- Group C: treated orally with contraceptive pills for 60 days at dose (0.64mg/rat) daily for 60 days.

**Blood Collection:** After sixty days of treatment, blood samples were taken by cardiac puncture and blood was collected in tubes without EDTA and centrifuged at 3000 (rpm) for 15 minutes, then serum was separated and kept in refrigerator at -20 °c until time of assay.

**Thyroid hormones (T<sub>3</sub>& T<sub>4</sub>) and lipid profile analysis:** Level of T<sub>3</sub> (triiodothyronine) and T<sub>4</sub> (thyroxin) were measured by ELISA kit from Monobind, USA. Serum levels of total cholesterol was measured according to [13] and triglyceride was measured according to [14], while high density lipoprotein (HDL) was measured according to [15]. Low density lipoprotein (LDL) was calculated from the total cholesterol [16].

**Statistical analysis:** Data in this study were analyzed by using SPSS (version 17). The different between groups determined by using one way ANOVA test and calculated L.S.D. A probability value (P<0.05) was considered to be significant.

## RESULTS

The results showed a significant decrease (P<0.05) in level of T<sub>3</sub> in B and C groups compared with the control group, and there was non-significant difference between B and C groups, while the serum concentration of T<sub>4</sub> increased significantly (P<0.05) in both groups (B&C) relative to the control group, and there was non-significant difference between B and C groups (table 1). There was non-significant decrease in the serum levels of cholesterol, triglycerides (TG) and low density lipoprotein (LDL) in groups B and C compared with the control group, but the results showed a significant decrease in level of high density lipoprotein (HDL) (P<0.05) in group C only compared with the control group, and there was non-significant different between B and C groups (table 2).

## DISCUSSION

The results showed a significant decrease in T<sub>3</sub> level and a significant increase in T<sub>4</sub> level in both groups B and C compared with control group. The increase in level of T<sub>4</sub> in this study agree with study of [17], which reported a significant increase in T<sub>4</sub> level in women taking COCs for six weeks. This rise of T<sub>4</sub> may be due to estrogen of COCS which increase the ability of T<sub>4</sub> binding globulin [12]. Also increasing of estrogen level increases TBG synthesis [18]. Thus T<sub>3</sub> concentration must be increase too, but our results showed a significant decrease in T<sub>3</sub> concentration, this results interpreted in one of two possibilities: the first, COCs or one of its components affects the process by which one iodide remove from T<sub>4</sub> to form T<sub>3</sub> (the active form of thyroid gland hormone [19]. the second, COCs or one of its components increase the concentration of rT<sub>3</sub> (unbenefited to body) by remove one iodide from wrong position of T<sub>4</sub> [20].

The levels of cholesterol, triglyceride and LDL in this study decreased non-significantly, this reduction may be either directly by components of COCs or indirectly by T<sub>4</sub>. There is inversely relationship between thyroid hormones and cholesterol and triglyceride in plasma [19]. But the non-significant decrease of cholesterol, TG and LDL in this study related with decrease of T<sub>3</sub> level which bind to thyroid hormone receptors at 90% and the rise in T<sub>4</sub> level which bind to thyroid hormone receptors at 10 % only which not enough to result a significant decrease in cholesterol, triglyceride and LDL in plasma. Thyroid hormone decrease cholesterol by increase its secretion in bile and then come out with feces. Other mechanism by which thyroid hormone decrease cholesterol is that increase the number of LDL receptors on liver [20]. Many studies refer to affect COCs on lipid profile according to type of estrogen and progesterone in this drug. Estrogen reduces LDL oxidation and binding [21]. Also, estrogen increase level of lipoprotein lipase enzyme which hydrolysis TGs [22]. The results showed a significant decrease in high density lipoprotein (HDL) in group C, women used type of COCs demonstrated reduction in level of HDL and little increase in LDL and TGs [23]. Progesterin in COCs can reduced HDL by raises hepatic lipase activity [24].

## CONCLUSION:

The present study indicated the effect of oral contraceptive on thyroid hormones and lipid profile of male rats.

**Table 1** : Effect of oral contraceptive on serum levels of thyroid hormones (T<sub>3</sub>& T<sub>4</sub>) of male rats

| Parameters<br>Groups | T <sub>3</sub><br>(ng/dl) | T <sub>4</sub><br>(ng/dl)  |
|----------------------|---------------------------|----------------------------|
| Group A<br>(Control) | 0.70 ± 0.08 <sup>a</sup>  | 62.52 ± 4.76 <sup>b</sup>  |
| Group B<br>(0.32 mg) | 0.57 ± 0.06 <sup>b</sup>  | 77.03 ± 5.25 <sup>a</sup>  |
| Group C<br>(0.64 mg) | 0.48 ± 0.13 <sup>b</sup>  | 72.78 ± 10.63 <sup>a</sup> |
| L.S.D                | 0.10                      | 7.46                       |

Each value represent (mean±SD); The different letters refers to a significant differences at (P<0.05); The same letters refers to non-significant differences at (P<0.05).

**Table 2** : Effect of oral contraceptive on lipid profile levels of male rats

| Parameters<br>Groups | Cholesterol<br>(mg/dl)     | Triglycerides (mg/dl)     | HDL<br>(mg/dl)            | LDL<br>(mg/dl)            |
|----------------------|----------------------------|---------------------------|---------------------------|---------------------------|
| Control              | 87.50 ± 7.0 <sup>a</sup>   | 57.66 ± 9.83 <sup>a</sup> | 38.66 ± 1.63 <sup>a</sup> | 38.03 ± 8.29 <sup>a</sup> |
| First treatment      | 69.16 ± 11.23 <sup>a</sup> | 55.91 ± 8.22 <sup>a</sup> | 31.0 ± 2.60 <sup>ab</sup> | 26.26 ± 8.26 <sup>a</sup> |
| Second treatment     | 60.83 ± 4.53 <sup>a</sup>  | 51.50 ± 6.94 <sup>a</sup> | 29.66 ± 2.50 <sup>b</sup> | 20.86 ± 3.55 <sup>a</sup> |
| L.S.D                | 31.66                      | 32.99                     | 8.97                      | 27.69                     |

Each value represent (mean±SD); The different letters refers to a significant differences at (P<0.05); The same letters refers to non-significant differences at (P<0.05).

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