Evaluation of Serum Malondialdehyde, Glutathione peroxidase, Superoxide dismutase, and Catalase levels in Hormonal Contraceptives in Tikrit City

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Abstract

Background: Oxidative stress is associated with the development of several disorders including cardiovascular disease and cancer. Among conditions known to influence oxidative stress, the use of oral contraception (OC) in women has been a matter of ongoing discussion.

The aim of the study report to evaluate the impact of oral contraceptive formulation containing 30 mg oestrogen (ethyloestradiol) and 1 mg progestin (norethisterone acetate) on lipid peroxidation, GPx, SOD, and catalase levels.

Patients & Methods: The present study was conducted in Family planning in Salahalddin Teaching Hospital in Tikrit province during the period from Feb 2016 until March 2017, Serum glutathione peroxidase (GPx) and , malondialdehyde (MDA), Super oxide dismutase (SOD), and catalase levels were estimated in 50 women who were using oral contraceptives for at least 1 year. Fifty- contraceptive users participated in the study as a control group. They were drawn from the same population and matched for age with the contraceptive-users group.

Results: The serum level of MDA, and GPx was significantly higher in women were using oral contraceptive than control group(11.872 ± 1.13 µM vs. 9.148 ± 1.179 µM respectively, 45.140 U/g Hb ±2.265 vs. 29.86 U/g Hb ±2.31) respectively . On the other hand the serum SOD, catalase values in women using oral contraceptives were significantly lower than control group.(2.72 U/L ± 0.479 vs. 3.5599 U/L ± 0.496 , 22.452 K/ml ± 2.045 vs. 26.370 K/ml ± 1.523) respectively.

Conclusion: Oral contraceptive pills showed a significant decreasing effect on the antioxidant status of its users .Routine monitoring of the antioxidant status of women on oral contraceptive is recommended.

Keywords: Oral contraception, MDA, GPx , SOD, Oxidative stress.

Introduction:

Oxidative stress is associated with the development of several disorders including cardiovascular disease and cancer. Among conditions known to influence oxidative stress, the use of oral contraception (OC) in women has been a matter of ongoing discussion. Oxidative stress which is formed by the breakdown of the balance between free radicals and antioxidants in favor of free radicals, plays a significant role in the pathogenesis of many diseases and mechanisms of complications [(1)].Reactive oxygen species (ROS) have many physiological regulatory functions and are also implicated in the development of a wide spectrum of diseases [(2)].The mammalian cell has an adequate antioxidant system to cope with excessive ROS production under normal physiological conditions. This system consists of antioxidant (AO) vitamins, thiol containing compounds such as reduced glutathione (GSH), and antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR). Variations in antioxidant capacity may influence individual susceptibility to some diseases associated with the deleterious effects of oxidative reactions[(3)].

Hormonal contraceptives are synthetic biochemical substances that act on the endocrine system and permit sexual union without

resultant pregnancy. Hormonal contraceptives are used by millions of women worldwide. Although other methods of contraception exist, the use of oral and injectable contraceptives is the most popular. In the United States, 18% of women who adopted contraceptive methods to prevent conception relied upon hormonal contraceptives [4].There are two main classes of hormonal contraceptives and these include combined contraceptives which contain both an oestrogen and a progestin, most oral contraceptives fall under this category and progestogenonly contraceptives which contain only progesterone or a synthetic analogue (progestin) [5].

Patients & Methods

The study carried out on 100 women attending Family planning in Salahalddin Teaching Hospital in Tikrit province. They were divided into 2 groups: group 1: consists of fifty non- contraceptive users participated in the study as a control group. group 2: comprising fifty women who were using oral contraception containing 30 mg oestrogen (ethyloestradiol) and 1 mg progestin for at least 1 year. They were drawn from the same population and matched for age with the contraceptive-users group. Venous blood samples were taken from all subjects and were left to clot then centrifuged at 3000 rpm for 10 minutes; the blood serum samples were obtained and were preserved al -20°C temperature till the laboratory analysis was done by the colorimetric method.

Malondialdehyde was estimated by the thiobarbituric acid assay method of sterbauer[6].Superoxide dismutase activities were assayed according to the procedure described by Woollians [7].,and , G-Px by the method of Rotruck *et al*[8], and catalase by Aebi[9].

Statistical analysis was done by using SPSS software. Results were expressed as the mean ± standard

error of the mean (SEM). Data for multiple variable comparisons were analyzed by one-way analysis of variance (ANOVA). For the comparison of significance between groups, Duncan's test was used as a post hoc test according to the Statistical Package for the Social Sciences (SPSS version 17.0). All P values are two-tailed and P.

Results

The results of study showed significantly higher serum MDA, and GPx level in among users of oral hormonal in comparison with control group (, $P<0.05$), therefore the mean ± SE of serum MDA was (11.872 ± 1.13 µM vs. 9.148 ± 1.179 µM respectively), (45.140 U/g Hb ±2.265 vs. 29.86 U/g Hb)±2.31) respectively (Table 1,&2).

Women in group II had also significantly lower serum SOD, and Catalase levels ($P<0.01$) as compared to control group.(2.72 U/L ± 0.479 vs. 3.5599 U/L ± 0.496) (22.452 K/ml ± 2.045 vs. 26.370 K/ml ± 1.523) respectively(Table 3,&4).

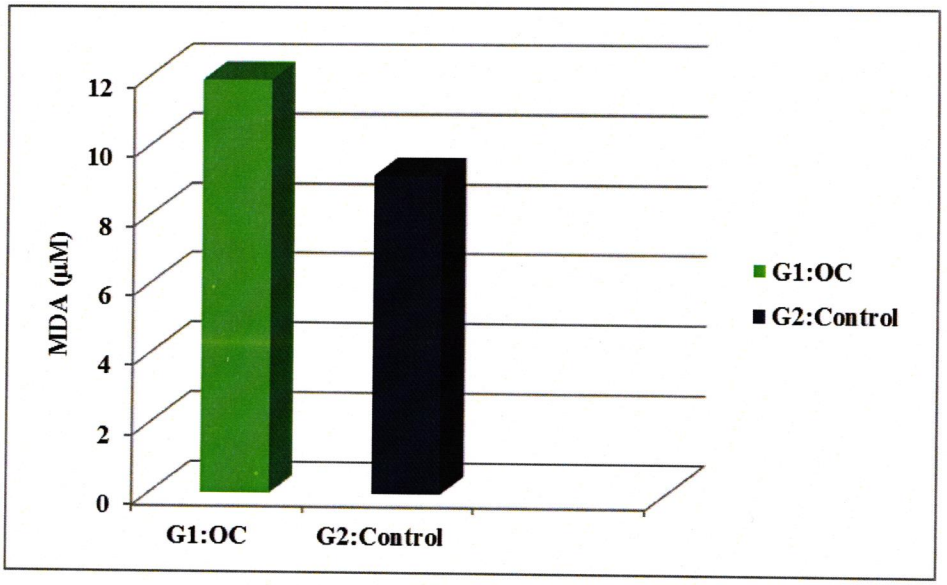

Table (1):- Effect of oral contraceptives pills on serum MDA levels.

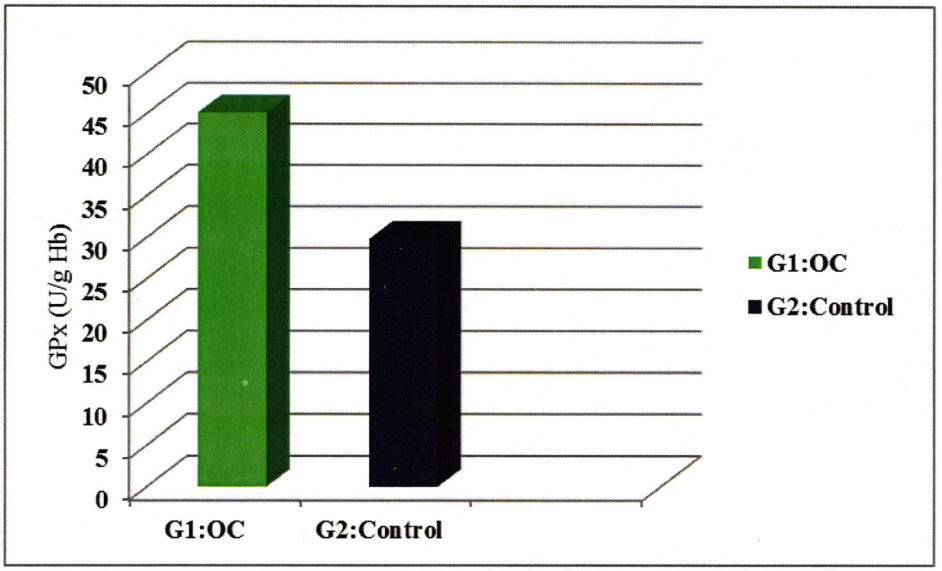

Table (2):- Effect of oral contraceptives pills on serum GPx levels.

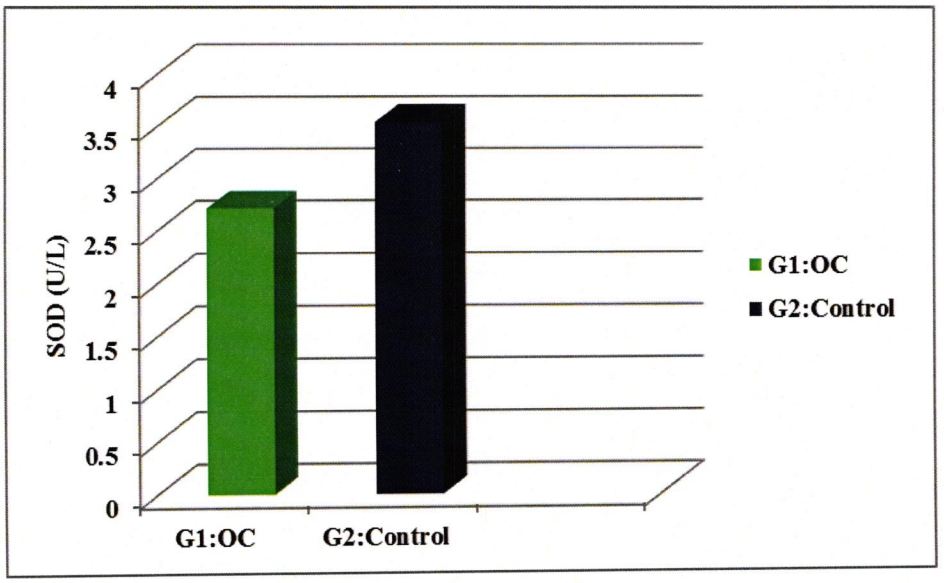

Table (3):- Effect of oral contraceptives pills on serum SOD levels.

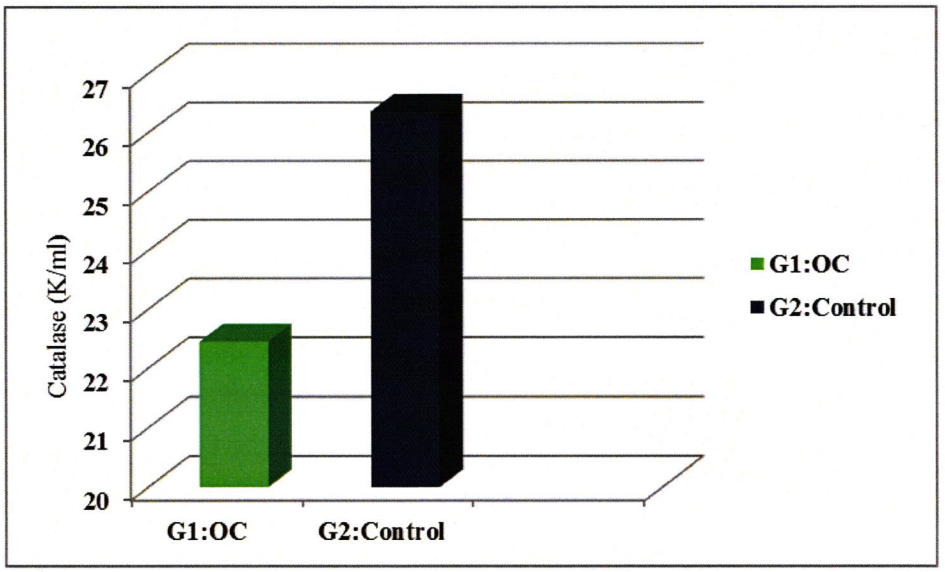

Table (4):- Effect of oral contraceptives pills on serum Catalase levels.

Discussion:

The results of the present study revealed that there was significantly higher levels of serum MDA, and GPx while lower levels SOD, and catalase in users of both oral hormonal contraceptives when compared with non-contraceptive users.

Recently, the possibility of alterations in various metabolic processes and antioxidant status, by hormonal contraceptives, has received much attention but unfortunately, there has been conflicting reports in this regard. The mechanisms responsible for the results of the present study are unclear, but there are several possible explanations. The behavior of molecules related to oxidative stress in circulating blood and at the cellular level can differ in the types and dosages of estrogen and progestin within the treatments may be important [10].

Oxidative stress occurs when an individual's antioxidant defense mechanism has been overwhelmed by destructive reactive oxygen species. Oxidative stress has been

implicated in the pathogenesis of many diseases including cardiovascular disease, cancer, diabetes complications, macular degeneration and arthritis. The antioxidant effect of oestrogen was observed in most of the in vivo studies performed on rats and women receiving hormone-replacement [11,14].The antioxidant activity of oestrogen has been attributed to prevention of expression and function of NADP+ /NADPH oxidase, increase in the expression and activation level of endothelial isoform of the nitric oxide synthase(eNOS) and stimulation of the expression and activation of manganese superoxide [15-17].

Contrarily, Bhat et al. (2003) and Gordon et al. (2005) reported the direct pro-oxidant effect of oestrogen in experimental model rats [18,19]. Prokai-Tatrai et al. (2005) attributed the pro-oxidant effects of oestrogens to the metabolic conversion of oestrogens to catecholoestrogens by cytochrome p450. Catecholoestrogens are easily auto-oxidized to ortho-quinone by-products which are powerful oxidizing agents capable of generating reactive oxygen species[20].

The administration of progesterone has anti-atherosclerotic effects with preferable lipoprotein profiles. Furthermore, progesterone may reduce ROS formation and cause vascular relaxation in a tissue-specific fashion; however; progesterone antagonizes the vasoprotective effects of estrogen on anti-oxidant enzyme expression and function, and enhances NADPH oxidase activity and the production of ROS[21]. In OCT, a progestogen-only contraceptive implant was reported to have no negative effects on cardiovascular risk factors (e.g., C-reactive protein, total/high-density lipoprotein cholesterol ratio and NO), suggesting progesterone does

not negatively impact cardiovascular risk factors in healthy young women.

A decrease in the activity of CAT could be due to increase in the lipid peroxidation product, malondialdehyde which can form cross links, thereby inactivating several membrane bound enzymes. The increase in circulating lipid peroxides may be related to a deficiency of SOD in tumor tissues. Decreased CAT activity could also be due to exhaustion of the enzyme because of increased peroxidation[22,23]. According to Wassman et al. (2005), the antioxidant effects of oestrogens are antagonized by progestins via the activation of NADPH oxidase and the inhibition of the expression and activity of manganese superoxide dismutase (MnSOD) and extracellular SOD[24].

Conclusion: The results of this study showed that OC is associated with a significantly altered oxidative status in women. The increase in MDA and GPx levels and decrease in SOD and catalase strongly support the hypothesis. Further research is suggested to elucidate its real impact as a cardiovascular risk factor in OCP users and routine monitoring of the antioxidant status of women may be beneficiary

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