Biomarkers of Oxidative Stress in Polycystic Ovary Disorder

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(Ann Coll Med Mosul 2019; 41 (2):112-116).
Received: 13th May 2019; Accepted: 8th Sept. 2019.

ABSTRACT

Background: oxidative stress(OS) happens when harmful reactive oxygen species (ROS) exceed antioxidants leading to damage of lipid, protein and DNA. OS was documented to participate in pathogenesis and complication of polycystic ovary syndrome(PCOS). PCOS is a common endocrine disorder, with incidence 4-12% between female at fertility period that leads to anovulation and infertility. This syndrome is accompanied with over production of androgen and dysfunction of ovaries which are associated by classical signs and/or symptoms and biochemical characteristics comprising hirsutism, acne, ultrasonic feature of polycystic ovaries, irregular menstrual period, adiposity, dyslipidemia, decrease insulin sensitivity and prediabetes.

Aim of the Study: to evaluate biomarkers levels of oxidative stress in women with PCOS and in healthy control women. This evaluation is necessary to show the effect of oxidative stress on sex hormonal profile of women with PCOS.

Participants and Methods: thirty women (16-38 year) with PCOS and thirty matched age women were enrolled to evaluate oxidative status by measuring serum levels of malondialdehyde(MDA) concentration and total antioxidant capacity(TAC) in all participants.

Results: Women with Polycystic ovary exhibited significantly increased means of MDA levels and significantly decreased mean of TAC levels when compared to healthy participants.

Conclusion: it concluded from this study there is a disturbance of oxidant and antioxidant profile in PCO women supposes a status of oxidative stress, guided by high level of oxidative stress biomarker of lipid peroxidation (MDA) and decreased antioxidant defense mechanism which indicated by TAC. Moreover, the oxidative stress biomarkers can be employed as indicator in early diagnosis of PCOS and utilization of them in monitoring and preventing further complication of it.

Keywords: Polycystic ovary syndrome, Oxidative Stress, MDA, TAC.

العلامات البيولوجية للجهد التأكسدي في اضطراب تكيس المبيض

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الخلاصة

الخلفية: تحدث حالة الجهد التأكسدي عندما تكون مستويات أنواع الأكسجين التفاعلية الضارة تتجاوز مستويات مضادات الأكسدة مما يؤدي الى تحطيم الدهون والبروتين و الحمض النووي. لقد اثبتت البحوث دور الجهد التأكسدي في الألية المرضية لمتلازمة تكيس المبيض ومضاعفاته, وهو اضطراب الغدد الصماء الاكثر شيوعا بين الإناث بنسبة 4-12% في فترة الخصوبة مما يؤدي الى عدم الإباضة والعقم ويرافق هذا الاضطراب الأفراط في انتاج هورمون الاندروجين وخلل وظيفي في المبايض و يصاحبه علامات واعراض سريرية وخصائص كيمائية حيوية المتضمنة الشعرانية وحب الشباب وتكيس المبايض واضطراب الطمث والسمنة واضطراب الشحوم بالدم ومقاومة الانسولين و عدم تحمل الجلوكوز.

الهدف من الدراسة: لتقييم العلامات البيولوجية للجهد التأكسدي في النساء المصابات باضطراب تكيس المبيض ومقارنتها مع المجموعة الضابطة, هذا التقييم ضروري لإظهار تأثير حالة الجهد التأكسدي على الهورمونات الجنسية للنساء المصابات باضطراب تكيس المبيض .

المرضى وطرق الدراسة: شملت الدراسة 60 امرأة تراوحت أعمارهم (16 - 38 سنه)، قسمت المشاركات الى مجموعتين المجموعة الأولى مثلت المجموعة الضابطة وشملت 30 امرأة من غير المصابات واللاتي ولا يعانين من أية مشاكل في الخصوبة ولديهن دورات حيضية منتظمة، أما المجموعة الثانية فشملت 30 امرأة من المصابات بمتلازمة تكيس المبايض والذين تم تشخيصهن بالاعتماد على الفحوصات الكيمياء الحيوية والكشف على المبيض بالموجات فوق الصوتية الذي يظهر وجود الأكياس في المبيض, تهدف الدراسة الى تقدير حالة الجهد التأكسدي من خلال قياس مستوى المالوندالديهايد(MDA) و السعة الكلية لمضادات الأكسدة (TAC).

النتائج: أظهرت نتائج التحري عن حدوث حالة الإجهاد ألتأكسدي في النساء المصابات, حيث بينت نتائج الدراسة الحالية ارتفاع معنوي في مستوى المالوندالديهايد (MDA) في مجموعة النساء المصابات مقارنة مع مجموعة سيطرتها بالإضافة الى وجود انخفاض معنوي في مستوى السعة الكلية لمضادات الأكسدة (TAC) في مجموعة النساء المصابات مقارنة مع مجموعة سيطرتها.

الاستنتاج: أستنتج من هذه الدراسة أن هناك اضطراب في توازن مواد التأكسد ومضادات الأكسدة حيث افترضت حالة الجهد التأكسدي في النساء المصابات بتكس المبيض وأستدل عليها من خلال ارتفاع مستوى المالوندالديهايد وانخفاض مستوى السعة الكلية لمضادات الأكسدة وعلاوة على ذلك يمكن أن تستخدام العلامات البيولوجية للجهد التأكسدي كمؤشر في التشخيص المبكر لاضطراب تكيس المبيض والاستفادة منها في رصد ومنع حدوث مضاعفات أكثر منه.

الكلمات المفتاحية: اضطراب تكيس المبيض والجهد التأكسدي والمالوندالديهايد والسعة الكلية لمضادات الأكسدة.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is endocrinologic and a reproductive abnormality disorder, affecting 4%–12% female during their reproductive period. Polycystic ovarian female usually have clinical signs of ovulatory dysfunction, adiposity, and over production of androgen[1]. Moreover, PCOS mostly accompanied with increased insulin resistance, glucose intolerance, dyslipidemia, type II diabetes mellitus, hypertension, cardiovascular complications, and cancer of endometrium[2,3]. Diagnosis of polycystic ovary disorder should be depending on the existence at least two of subsequent standards:(1)oligo or impaired ovulation, (2) clinical and/or biochemical features of overproduction of androgen, and (3) cystic ovaries on ultrasound[3]. Process of folliculogenesis in female with PCOS may be affected by oxidative stress (OS)[4]. The OS is a complicated process, resulting from an imbalance between oxidants and antioxidant defense system. Oxidants are chemical substances that acquire electrons. They include reactive oxygen species(ROS) and reactive nitrogen species that generate from nitric oxide (RNS). When, the disequilibrium prefers oxidants resulting in status of OS. The major aims of OS are proteins, lipids and DNA. Peroxidation of lipid by the free radicals producing Malondialdehyde (MDA) and hydroperoxides (FOX) which are good markers of oxidative stress[5,6]. MDA resulted from the peroxidation of polyunsaturated fatty acids used as good indicator of lipid peroxidation[7]. Oxidation and damage of protein can be evaluated by the measurement of advanced oxidation protein products (AOPP). Antioxidants are classified into categories: (i) Enzymatic antioxidants involve superoxide dismutase(SOD), catalase, and glutathione peroxidase(GPx). (ii) Non-enzymatic antioxidants involve reduced glutathione (GSH), Paraoxonase1 (PON1), α-tocopherol, β-carotene, ascorbate and others[8]. Total antioxidant capacity is the capability of serum to scavenge free radicals and prevent molecular damage of cell structure[9]. However, oxidative status is also showed to be significantly associated with adiposity, insulin resistance, over production of androgen, and chronic inflammation[10,11].

PATIENTS and METHODS

Thirty PCOS women with age (16-38) yrs. and thirty healthy counterparts were involved in this study, from February/ 2019 to May/ 2019. Women were diagnosed as polycystic ovaries by clinical features, polycystic ovaries detection by ultrasound and measuring a profile of sex hormones (Follicle stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL) and testosterone) that are attending to private clinics in Duhok City, Iraq. The healthy participants were volunteer's outpatient clinics, not receiving any medicine that influencing metabolism of adrenal hormone. Exception criterions are diabetes mellitus, impairment of hepatic and renal function, thyroid dysfunction, cardiovascular diseases, infection and inflammation cases.

Sample Collections and Measurements

Informed consent was gained from all participants and blood specimens were gathered in the first part of day (behind overnight refraining food for 14 hrs.) after that the blood is let stand for 1hour and serum is obtained by rotating samples at 3000 rpm for 15-20 minutes to assess serum MDA level using Colorimetric assay by using thiobarbituric acid reacting substances (TBARS) to measure absorbance of MDA- TBA at 530 nm, and TAC was measured using colorimetric assay at absorbance 570 nm. The sex hormones profile (FSH, LH, PRL, and testosterone) were measuring by Enzyme Linked Flourescent Assay using a BioMerieux (France) kits.

Statistical Study

The changeable values were recorded as Mean±SD and Chi($\chi 2$) square test was used to consider the variance among changeable values. The variances are regarding to be significant if $p \leq 0.05$. The Statistical study was carried out by using the statistical package SPSS collection (version 18).

RESULTS

There is a significant variance in MDA between patients (0.70 ± 0.60) and healthy participants women group (0.60±0.48) with *p*-value= 0.05. A mean serum level of TAC (13. 47± 1.48) is significantly decreased in PCO participants with (p =0.05) when comparison to controls(Table 1).

Table 1: A Comparison of mean demographical characteristic and biochemical variables between PCO women and healthy participant group.

Variables	Control group (n=30) Mean ± SE	PCOS group (n=30) Mean ± SE	P-value
Age	25.57 ± 1.24	22.71 ± 0.98	NS
MDA (Mmol/L)	0.60± 0.48	0.70 ± 0.60	0.05
TAC(Mmol/ L)	14.01 ± 1.34	13. 47± 1.48	0.05
LH(mIU/ml)	2.71 ± 0.19	6.22 ± 0.51	0.0001
FSH(mIU/m l)	4.77 ± 0.31	5.12 ± 0.42	NS
Testerone (ng/ml)	0.49 ± 0.05	0.78 ± 0.02	0.0001
Prolactin (ng/ml)	28.49 ± 0.59	24.8 ± 0.78	0.0001

Variables described as mean ±SD, NS (p- value >0.05), significant difference (p-value ≤ 0.05).

DISCUSSION

The present study shows that there is a status of oxidative stress in PCOS women. The mean of serum MDA is significantly increasing in the women with polycystic ovary disorder compared to healthy women. The finding of this study was similar to that of Maleedhu et al they had shown a significant increment in the level of serum MDA and a significant decreasing in the mean of serum TAC level in women with PCO when compared with control women[12]. It has been demonstrated that high production of ROS in PCOS which leading to tissue destruction[13]. Lipid peroxidation is considered to be outcome of the tissue damage by oxidative stress mechanisms and it has been detected as peroxidation of unsaturated fatty acids by free radicals and reactive oxygen species[14]. Over production of androgen in PCOS could be the cause for the rising in levels of MDA[13]. The result of this study is also in agreement with Shirsath et al who reported a significant increasing in a mean of MDA($p<0.001$)in PCO women than controls[15].

Kuscu et al researchers found similar result and contributed this rising in MDA levels to insulin resistance and hyperglycemia in polycystic ovary disease women[16]. However, Karadeniz M et al reported no statistically variance in regarding the mean of MDA level between PCO women and controls. Who attributed that their study were included only women with regular ovulatory cycles[17]. Antioxidants which are inhibit or reduce negative impact effects of free oxygen radicals have been recorded to play role in female fertility[18]. TAC is a defensive biomarker assessing the antioxidant status of body fluids and has been showed to be significantly decreased in this study. This result is matched with that of a subject field by Mohamadin et al, who demonstrated a significant decreasing in mean serum of TAC level in PCO group compared to controls[19]. Also Hilali et al study showed similar result diminishing TAC levels among PCO group compared to the healthy women[20]. Sulaiman et al, study reported lower levels of TAC in PCOS women than those in women controls, who contributed the oxidative stress in PCOS is outcome of disturbance in sex hormonal in PCO women[21]. There are many literatures on the role of oxidative stress in the PCOS pathogenesis. It has been showed that PCOS is accompanied with rising oxidative stress and reduced antioxidants. High oxidative stress causes defect in phosphorylation of insulin receptor, more serine phosphorylation and decreased tyrosine phosphorylation, that enhances insulin resistance and leading to hyperinsulinemia[22]. Veysel et al found that TAC levels were significantly lower in PCOS women than controls because TAC is an indicator to change in antioxidant status and predicting degree of oxidative stress[23]. This study is disagreeing with Al-Azzawie and Humadi who found that increased antioxidant capacity in PCOS women may be as a compensatory mechanism to the rising in oxidative stress status[24]. The possible reason of oxidative stress occurrence in PCOD is over production of ROS in the ovarian follicle that may overwhelm the antioxidant defense mechanism of follicular fluid and directly destruct immature ovum[25].

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