Coenzyme Q10 effects on body weight, serum testosterone level and oxidative stress in women with polycystic ovarian syndrome (PCOS)

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ABSTRACT
Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder among women. Insulin resistance is found in most women with PCOS. High insulin levels affect the hypothalamic-pituitary-ovarian axis causing increased GnRH release with high LH/FSH ratio and excessive ovarian androgen production. The aim of this study is finding the effects of CoQ10 on body weight, serum testosterone level and oxidative stress in women with PCOS. 80 patients assigned into two groups each contain 40 patients (CoQ10-metformin group) and (metformin group). In the first group the patients received CoQ10 soft gel capsules 200 mg once daily and metformin 850 mg twice daily and patients in the second group received metformin 850 mg twice daily. drugs administered for 3 successive months. Body mass index, serum testosterone, and serum malondialdehyde (MDA) level were measured at baseline and at the end of the study. At baseline, the results revealed significant differences in all parameters between the control group and the study group. At the end of the study, there was a significant reduction in the mean serum MDA, mean serum testosterone and mean BMI in both study groups compared to baseline but more significant in the CoQ10-metformin group compared to metformin group. It has been concluded that CoQ10 treatment produces good effects in PCOS patients mainly due to its effects as an antioxidant.

Keywords: CoQ10; MDA; Oxidative stress; PCOS

INTRODUCTION
About 2% to 20% of women between the ages of 18-44 are affected by Polycystic ovary syndrome (PCOS) which is the most common endocrine disorder among women (Teede et al., 2010; PCOS, 2014). According to Rotterdam Criteria (2003), two of the following are needed for the diagnosis of PCOS; oligo or anovulation, hyperandrogenism, and ultrasound features polycystic ovaries (Mortada et al, 2015). However, androgen excess should be a constant feature of PCOS regardless of ovarian condition or morphology as recommended by the Androgen Excess Society. Associated conditions as obesity may also present which increases the problem of hyperandrogenism (ESHRE/ASRM, 2004). Insulin resistance has been found in most women with PCOS. Elevated insulin levels affect the hypothalamic-pituitary-ovarian axis causing increased GnRH release with elevated LH/FSH ratio and excessive ovarian androgen production (Azziz et al., 2006). Metformin which is widely used for PCOS treatment is a biguanide that has been used for the treatment of T2DM. It increases the peripheral tissues sensitivity to insulin, so reducing the insulin levels, it inhibits gluconeogenesis in the liver and it also enhances the glucose uptake by peripheral tissues and reduces fatty acid oxidation (Kovacs et al., 2013).

The imbalance between oxidants and antioxidants is the oxidative stress (OS). The excessive highly reactive, free radicals result from the increase in oxidants they cause cellular damage by taking electrons from nucleic acids, lipids, carbohydrates, proteins, and other nearby molecules stability (Kirpichnikov et al., 2002). A number of investigations have compared OS in patients with PCOS with the normal and it was found to be increased in PCOS patients, when evaluated by circulating markers, such as malondialdehyde (MDA), glutathione peroxidase (GPx) and superoxide dismutase (SOD) (Murri et al., 2013).

MDA is widely employed as a biomarker for OS, it is a stable end product of lipid peroxidation (Dakhil, 2007). Many studies have shown that there is an increased level of MDA in PCOS women (Abuja et al., 2007). It has been shown that DNA mutations and alterations involved in the pathogenesis of cancer can result from OS. Recent studies show that risk of cancers mainly endometrial carcinoma is more in PCOS patients (Fader et al., 2009; Hardiman et al., 2003). ROS generation in the mitochondria mainly occurs in the electron transport chain (ETC) at complexes I (where NADH dehydrogenase acts),
Coenzyme Q10 (Co Q10) is an antioxidant agent essential for the cellular production of ATP which provides the energy for vital cellular functions and muscle contraction. The Co Q10 is bound to the enzymatic protein complexes. When oxidized it releases protons outside and takes up electrons and protons inside of the mitochondrial membrane (Yu et al., 1999). New study showed that Co Q10 may lower cholesterol and insulin levels (Samimi et al., 2017).

CoQ10 may lower cholesterol and insulin levels (Samimi et al., 2017)

PATIENTS & METHODS

The prospective study consisted of a 4-week screening phase and a 12-week treatment phase. 80 female patients (mean age 26±2.52, range from 22 to 31 years) selected at The High Institute for infertility diagnosis and Assisted Reproductive Techniques, Baghdad- Iraq from January 2017 to June 2017. 20 healthy women were included as control group. Informed consent from the patients and an ethical approval were obtained. The patients were diagnosed with PCOS according to international criteria by 2 of three of oligo or anovulation, high androgen, ultrasound evidence of polycystic ovaries. Patients with, hyperprolactinemia, diabetes mellitus, androgen-secreting tumors or receiving drugs as steroids, antipsychotic drugs were excluded from the study.

All patients underwent medical screening include history, physical examination, BMI measurement and investigations include serum MDA level, serum testosterone, FSH and LH, and prolactin.

TREATMENT ASSIGNMENT

The patients were divided into 2 groups each contain (40) patients (CoQ10-metformin group) and (metformin group). In the first group the patients received CoQ10 soft gel capsules 200 mg (Nature’s bounty inc., USA) once daily and metformin 850 mg (Julfar. UAE) twice daily and patients in the second group received metformin 850 mg twice daily. capsules administered for 3 successive months.

STUDY PARAMETER

Body mass index, serum testosterone, and serum MDA level.

STATISTICAL ANALYSIS

Collected data were analyzed using SPSS (statistical package for social sciences, version 20). Descriptive analysis of means and standard deviation (SD) were calculated on all demographic variables, and serum MDA, hormones and BMI. Multiple comparisons of paired series of data within groups were done using a paired t-test. Unpaired t-test was then used to evaluate the difference between the two group. A p-value <0.05 was considered the minimum for statistical significance.

RESULTS

At the end of the study, 12 patients were dropped out of the study so only 68 patients completed the study. 33 in the metformin-treated group and 35 in the metformin- CoQ10 treated group. In addition to the control group consisted of 20 healthy women. Baseline data of age, height, weight, and BMI (body mass index) for patients and controls were depicted in the table (1). When

**Table 1:** Description of general data for patients and control included in the study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± Std. Deviation</th>
<th>patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>26±2.52</td>
<td>25±2.976</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>62.32±5.389</td>
<td>69.62±9.389</td>
</tr>
<tr>
<td>Height (meter)</td>
<td>1.5831±0.05348</td>
<td>1.5531±0.05998</td>
</tr>
<tr>
<td>BMI (kg/meter²)</td>
<td>26.324±3.30118</td>
<td>28.8445±3.30118</td>
</tr>
<tr>
<td>Number</td>
<td>20</td>
<td>68</td>
</tr>
</tbody>
</table>

**Table 2:** Description of baseline hormonal profile and serum MDA level for all patients and control included in the study

<table>
<thead>
<tr>
<th>Parameter (baseline)</th>
<th>Mean ± Std. Deviation</th>
<th>patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.FSH</td>
<td>3.3412± 0.6231</td>
<td>4.2662± .93419</td>
</tr>
<tr>
<td>S.LH</td>
<td>5.2151±3.1241</td>
<td>10.4309 ±2.10878</td>
</tr>
<tr>
<td>S.testosterone</td>
<td>0.3279±0.2315</td>
<td>1.8669± 0.97102</td>
</tr>
<tr>
<td>S.PRL</td>
<td>8.321±1.3214</td>
<td>7.5803±1.69266</td>
</tr>
<tr>
<td>S.MDA number</td>
<td>7.2250±1.0858</td>
<td>11.8534 ± 1.86793</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>68</td>
</tr>
</tbody>
</table>

*significant (unpaired t-test) p value<0.05.
serum MDA level in the control group was compared with that in the PCOS patient’s groups at baseline, it was found that it is significantly higher in PCOS patients (11.8534±1.86793) than in healthy control group (7.2250±1.0858). table (2)

BMI serum testosterone level and serum MDA in both metformin-treated group and metformin-CoQ10 treated group compared at baseline and after treatment and also compared between the two groups at baseline and after treatment table (3). There was no significant difference in BMI between the two groups at baseline but it is significantly reduced in metformin-CoQ10 treated group between baseline and after treatment, while it reduced significantly after treatment in the metformin-CoQ10 treated group figure (3). There was a positive correlation between MDA level with BMI s.testosterone before and after treatment. Table (4) and (5)

**DISCUSSION**

PCOS is the most common endocrinological disorder in women reproductive life the common feature in PCOS women is hyperandrogenism. PCOS is multifactorial in origin. The main feature is increased insulin resistance regardless of the body mass index (BMI) (Norman et al., 2007). Oxidative stress(OS) is the imbalance between oxidants and antioxidants. More oxidants, lead to the generation of excessive reactive oxygen species which is harmful to the body (Agarwal et al., 2005) increased oxidant status has been shown to be correlated with insulin resistance. 25-60% of women with PCOS have insulin resistance (Azziz et al., 2003). OS levels can be increased by insulin resistance (IR) and hyperglycemia, but in non-obese PCOS patients without IR, high levels of total oxidant and antioxidant status was found (Verit et al., 2008). Lower antioxidant levels and lipid peroxidation have been shown to be induced by hyperglycemia (Uzel

| Table 3: Correlation between MDA with BMI and s.testosterone before treatment |
|-----------------------------|---|---|---|
| Variables                  | r  | p   | significance |
| S.MDA-BMI                  | 0.36 | <0.05 | significant |
| S.MDA-S.testosterone       | 0.41 | <0.05 | significant |

*Spearman correlation test.

| Table 4: Correlation between MDA with BMI and S.testosterone after treatment |
|-----------------------------|---|---|---|
| Variables                  | r  | p   | significance |
| S.MDA-BMI                  | 0.44 | <0.05 | significant |
| S.MDA-S.testosterone       | 0.52 | <0.05 | significant |

*Spearman correlation test.

Figure 1: Changes in BMI (body mass index between the groups: m1: metformin-treated group at baseline, m2 metformin-treated group after treatment, mq1: metformin-q10 treated group at baseline; mq2 metformin-q10 treated group after treatment)
MDA levels, a marker of OS, has been shown to be negatively correlated with insulin sensitivity as well as GSH (antioxidant) (Sabuncu et al., 2001). In the present study, CoQ10 administration for 3 months resulted in a significant decrease in BMI. It helps weight loss in three ways: (1) By increasing fat burning directly. Since it is required in the transport and breakdown of fat into energy (2) Patients become more likely to exercise due to increased energy levels (3) decrease appetite, so patients can stick to their eating plans easily (Saper et al., 2004). In a study, 52% of obese patients are deficient in CoQ10 and they lose about 8 kg of weight over a 9-week period when treated with CoQ10 (100-300mg/day) (Menke et al., 2004). In the present study CoQ10 administration was associated with significant reduction in androgen production by its well-known effects as antioxidants through the following actions (1) its major role respiratory chain and energy coupling (2) reducing fatty acid peroxidation and maintaining the phospholipid composition of cell membranes (3) preventing pathological apoptosis (Robert et al., 2009).

Studies showed that ROS generation is directly correlated with testosterone and androstenedione. So that ROS induces OS, leading to increased androgen production in PCOS women. Some in vitro studies showed that OS induces ovarian steroidogenic enzymes to lead to androgen production, while antioxidants as statins inhibit.
these enzymes (Piotrowski et al., 2005). In PCOS women invasion of ovaries by macrophages has been observed. glucose can activate mononuclear leading to the generation of OS provoke a local inflammatory response which in turn induce the generation of ovarian androgen (González et al., 2005).

Oxidative stress can be induced by insulin resistance because hyperglycemia and increased free fatty acids result in ROS production. insulin administration in obese individuals has resulted in inhibition of production of ROS. High levels of CoQ10 are produced from ovaries and the ovaries are able to uptake CoQ10 from external sources efficiently (Dandona et al., 2005).

CONCLUSION
It has been concluded that CoQ10 treatment produces good effects in PCOS patients mainly due to its effects as an antioxidant.

REFERENCES


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