Coenzyme Q10 Supplementation Reduces Oxidative Stress in Patients with Pre-Eclampsia

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Authors' contributions

This work was carried out in collaboration among all authors. Author FS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors HL, KAM, BS, SA, TS and AA managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Objective: To determine the effect of CoQ10 supplementation in reduction of oxidative stress by index marker, Malondialdehyde (MDA), super oxidase dismutase(SOD), catalase(CAT) and glutathione peroxidase (GPx) in patients with pre-eclampsia.
Methodology: A cross-sectional study was conducted at the Department of Biochemistry LUMHS, Jamshoro. During the period of January 2018 to June 2018. Total 200 pregnant women were

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recruited and divided into two groups. 50 females were normotensive pregnant women as a control group, 150 were pre-eclamptic patients as case group. Obstetric history, clinical data was gathered and then 5ml of blood sample was collected from each patient. The blood samples were taken before and after a 3 months' supplementation to analyse Malondialdehyde (MDA). The CoQ10 was evaluated by High performance liquid chromatography (HPLC-DAD) and MDA, SOD, CAT and GPx were performed on UV- spectrophotometer. Data was analysed by using SPSS version 22. Student t-test was used for analysed of continuous variables.

Results: The pre-eclamptic women treated with CoQ10 supplementation the plasma CoQ10 levels and MDA, SOD and CAT levels increased marked after 3 months(p<0.001). But the Glutathione Peroxidase was insignificant results as compared with controls (p=0.057).

Conclusion: The present study reflects that supplementation of CoQ10 decreased the oxidative stress and also helpful in improving the health of mother as well of her foetus by increase antioxidant activity.

1. INTRODUCTION

Preeclampsia (PE) is a pregnancy related complication which affects 3-8% of all pregnancies in developed countries [1]. PE is most common and fatal disorder of pregnancy. It is characterized by development of hypertension, proteinuria after 20th week of pregnancy with previously normal pregnancy [2]. In early pregnancy the endothelial and muscular layers of placenta progress and erode the spiral arteries, which supply the blood to placenta and nourish it for developing blastocyst accurately [3]. Endothelial dysfunction also leads to cause impairment of nitric oxide pathway, causes reduced blood flow and poor placentation results in oxidative stress and leads to cause potential damage to the cell [4]. Malondialdehyde (MDA) is an indicator of lipid peroxidation (LPO). The end products of lipid peroxidation are reactive aldehydes, such as MDA and 4-hydroxynonenal (HNE) [5]. MDA is three carbon aldehydes, which is increased in many diseases but greatly increased in pregnancy-induced hypertension [6]. When MDA levels increased, it produces free radicals which damages the cell membrane and effect on DNA, results in oxidative stress by production of free radicals [7]. The antioxidant enzymes such as, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), are the first line product of defence against free radicals (ROS). If these ROS decreased their activities results in oxidant attack on cells, especially individuals suffering from hypertension and other cardiovascular disorders [8,9].

Coenzyme Q10 (CoQ10) plays an important function as an antioxidant, stabilizes and protects the cell membrane [10]. It is also called as Ubiquinone, which is located in mitochondria. Due to its antioxidant property it protects the cell membrane from free radicals which causes the oxidative stress [11,12]. According to latest study the use of CoQ10 produce positive effects on various disorders by scavenging free radicals and inhibiting MDA production [13].

The objectives of this study are to analyze the beneficial effect of CoQ10 supplementation in preeclampsia and CoQ10 is help in reduction of oxidative stress in preeclampsia although Malondialdehyde is one of index biomarker of oxidative stress and to estimate and compare the Plasma levels of CoQ10 and MDA, CAT, SOD, GPx in normotensive pregnant women and pre-eclamptic patients before and after supplementation of CoQ10.

2. METHODOLOGY

The study was conducted at Department of Biochemistry LUMHS in collaboration with National Centre of Excellence and analytical Chemistry, university of Sindh, Jamshoro. The study population (n=300) was recruited from Department of Obstetrics & Gynecology, Liaquat University Hospital Jamshoro / Hyderabad during the period of January 2018 to June 2018. A cross sectional, comparative study. A simple random sampling technique was used to select the study subjects. Total 200 subjects were recruited for present study and divided into two groups. Group A: n = 50 Healthy pregnant women with normal B.P after 20th week of gestation and Group B: n = 150 patient with Pre-eclampsia before and after CoQ10 supplementation after 20th week of gestation. The study consists of two phases. In Phase 1, the recruitment of the participants and initial blood sampling was done, and in phase 2,

blood sample of the same participants was collected after three months of CoQ10 supplementation, all the sampling was done under aseptic measures, by venipuncture, and blood was collected into EDTA tubes. The blood was centrifuged at 3500 rpm for 10 min, fractionated and transferred to Eppendorf cups then stored at −20°C till required for analysis. Healthy pregnant women aged 20-35, after 20th week of gestation, and pregnant women with pre-eclampsia aged 20-35 years after 20th week of gestation were included in present study, whereas pregnant women below 20 or above 35 years, multiple Pregnancy, known hypertensive, diabetic, cardiac and renal, liver disease, smokers and any use of drug were excluded from the study.

2.1 Inclusion Criteria

Healthy pregnant women with normal B.P and pre-eclampsia patients were included in the study.

2.2 Exclusion Criteria

Patients who were unable to communicate properly or deaf and blind were excluded.

2.3 Formulations of CoQ10

CoQ10 is insoluble in water and commonly available in soft gel oil suspension capsules in Pakistan market as a dose of 500 mg of CoQ10 a day.

2.4 Estimation of CoQ10 on HPLC

The Determination of plasma CoQ10 was performed on HPLC-DAD (Thermo Finnigan, California, USA) by using Fabrizio Mosca method [14] and by Hamdy, et al. [15] while, MDA, Catalases (CAT) were measured by 250-x sodium phosphate buffer, superoxide dismutase (SOD), glutathione peroxides (GPx) were analysed by red blood cells were diluted with 25-x (sodium phosphate buffer) have previously been described [16] and measurements were performed on UV- spectrophotometer-1650 (*PC SHIMADZU*) at different wave length of 240 nm, 325 nm, and 340 nm, respectively.

2.5 Statistical Analysis

The data was entered and analyzed on SPSS (Statistical package for Social Sciences) Version 22.0. Student t-test for comparison between cases and control was used for continuous variable.

3. RESULTS

The result of present study was expressed as (Mean ± S.D) and summarized in Tables 1 and 2. Student t-test was used to calculate the level of significance.

3.1 Baseline Measurements of MDA, SOD, CAT, AND GPx Before CoQ10 Supplimentation

The Mean ± SD of gestational age of control and cases was (24.56±8.63 versus 26.94±6.18) weeks. The blood pressure was increased in pre-eclamptic patients as compared to control group. Systolic blood pressure of controls and cases were noted as (110±15.2 versus 150.5±20.7) mmHg, respectively while diastolic blood pressure of control and cases groups were noted as (70.6±12.5 versus 99.8±15.9) mmHg with highly significant difference ($p < 0.001$). The plasma Coenzyme Q10 was decreased in control group and cases subjects before intake of CoQ10, and it was noted as (1.19±0.45 versus 0.085±0.09) μg/dl, whereas plasma MDA levels were increased in pre-eclamptic patient as compared to control subjects and noted as (3.54 ± 1.71 versus 1.69 ± 0.42) nmol/dl with significant difference of ($p < 0.001$). Superoxide Dismutase activity was increased in pre-eclamptic subjects as compared to normotensive pregnant women (543.5±131.8 versus 654.9±143.7) U/mg of Hb with significant difference of ($p < 0.001$). The catalases activity was decreased in cases group as compared to control group with significant differences of ($p < 0.05$) but glutathione peroxidase activity in preeclamptic patient has not shown any change as compared to control group (17.18±4.1 versus 18.34±3.8) U/mg of Hb with insignificant results of ($p < 0.057$) as shown in Table 1.

3.2 Plasma MDA, SOD, CAT, and GPx Levels After Supplementation of CoQ10

The gestational age was increased as pregnancy proceed. The mean systolic and diastolic blood pressure was decreased in pre-eclamptic patients after supplementation of CoQ10 for three months with significant difference of ($p < 0.001$), as shown in Table-2 and Chromatogram-1. The plasma CoQ10 is markedly increased in pre-eclamptic patient after

Table 1. Base line comparative measurements between variable of Controls and Cases Groups Before CoQ10 Supplementation

Variable	Controls(n=50)	Cases(n=150) Before Supplementation	p-value
		Mean and standard deviation	
Gestational age (Weeks)	24.56±8.63	26.94±6.18	<0.05
Systolic BP (mmHg)	110±15.2	150.5±20.7	<0.001
Diastolic BP (mmHg)	70.6±12.5	99.8±15.9	<0.001
CoQ10 (µg/dl)	1.19±0.45	0.085±0.09	<0.001
MDA (mmol/dl)	1.69 ± 0.42	3.54 ± 1.71	<0.001
SOD (U/mg of Hb)	543.5±131.8	654.9±143.7	<0.001
CAT (U/mg of Hb)	9.52±4.9	7.13±2.4	<0.05
GPx (U/mg of Hb)	18.3±3.8	17.6±4.1	<0.057

Table 2. Effect of Coenzyme Q10 supplementation on Oxidative stress markers/variables

Variable	Controls(n=50)	Cases(n=150) (After Supplementation)	p-value
		Mean and standard deviation	
Gestational age (Weeks)	26.94±6.18	36.58±3.91	<0.001
Systolic BP (mmHg)	150.5±20.7	130.7±16.5	<0.001
Diastolic BP (mmHg)	99.8±15.92	84.33±5.39	<0.001
CoQ10 (µg/dl)	0.085±0.09	1.12±0.89	<0.001
MDA (mmol/dl)	3.54 ± 1.71	2.03 ± 1.5	<0.05
SOD (U/mg of Hb)	654.9±143.7	609.5± 45.9	<0.05
CAT (U/mg of Hb)	7.13±2.4	8.11±2.15	<0.05
GPx (U/mg of Hb)	17.6±4.1	17.3±3.01	=0.057

supplementation of CoQ10 as compared to before supplementation group and it was noted as (1.12±0.89 versus 0.085±0.09) µg/dl. The plasma MDA and SOD levels were reduced in pre-eclamptic patient as compared to after supplementation group. The mean value of MDA was (3.54 ± 1.71 versus 2.03 ± 1.5) nmol/dl, whereas SOD, as index marker of free radicals, was reduced to (427.2±145.1 versus 543.5±131.8) as compared after supplementation. CAT antioxidant activity enhances markedly after supplementation of CoQ10 (8.11±4.9 versus 7.13±2.4) U/mg of Hb with significant difference of (p<0.001). The GPx activity has no any drastic change after CoQ10 supplementation (17.6±4.1 versus 17.3±3.01) with insignificant results of (p<0.057) as shown in Table 2.

4. DISCUSSION

Coenzyme Q10 is a lipophilic quinone compound acting as antioxidant. Dietary supplement has recently gained attention due to its anti-oxidant property in the treatment of preeclampsia and eclampsia. CoQ10 reduces the oxidative stress by scavenging effects of preventing the production of free radicals during preeclampsia.

Boras M. et al. [17] revealed that oxidative stress during pregnancy enhance and CoQ10 has been prove to be helpful in the reduction of MDA, SOD, and Catalases and GPx. These results comply with present study results, except GPx, that is insignificant in present study.

Allali J et al., [18] reported that the intake of CoQ10 for four weeks, produced beneficial effects because they also performed exercise on trade mill and obtained significant results, as present study showed that CoQ10 supplementation reduces the MDA and others oxidative markers in pre-eclampsia. Xu X [19] and his coworkers reported that CoQ10 can alleviate the oxidative stress by enhancing mitrochondrial function and improve symptoms of preeclampsia, present study having same results. Liu H et al., [20] repoerted that CoQ10 has benefifical effects in Hepatic cancer patinets after surgery. The MDA, CAT, SOD and GPx shown significant results after intake of coenzyme Q10 but in our study MDA, SOD, CAT showed positive effects except GPx activity.
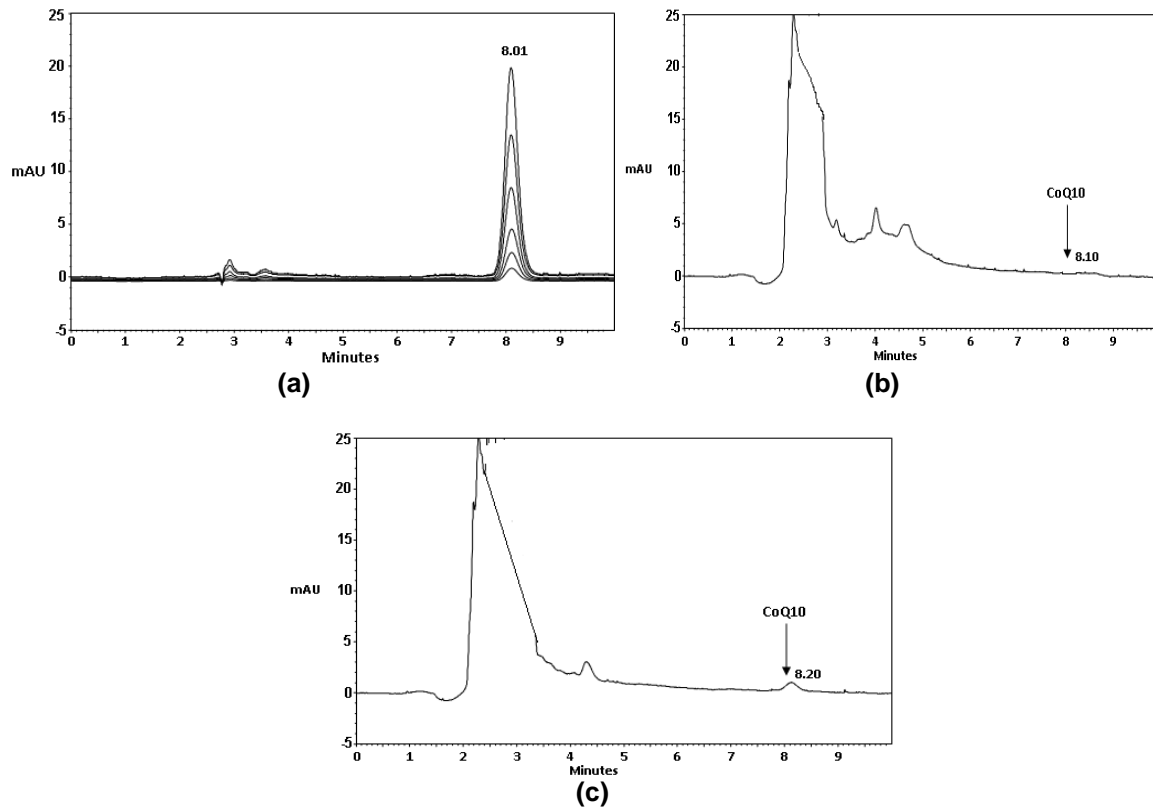
Fig. 1. Plasma CoQ10 levels in pre-eclamptic patients are shown; (a) CoQ10 standard calibration ranges from 200 ppm to 1.3 ppm, (b) Before supplementation of CoQ10, (c) after 3 months' supplementation of CoQ10 in pre-eclamptic patients

5. CONCLUSION

The intake of CoQ10 reduces the MDA, CAT, SOD in preeclampsia, which are index marker of oxidative stress. The significance of present study is CoQ10 improve the symptom of preeclampsia results in reduction of oxidative markers such as MDA, CAT and SOD.

6. RECOMMENDATION

Further advance studies will require to search the relationship of CoQ10 biosynthesis pathway and Malondialdehyde production from poly unsaturated fatty acid. Present study tries to fulfil the gap of oxidative stress by indication of biomarkers.

CONSENT

The pregnant women were recruited by filling proforma and written consent was taken.

ETHICAL APPROVAL

The study was conducted after the approval from Ethical Review Committee of LUMHS Jamshoro.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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