

# Evaluate the Effect of Coenzyme Q10 Supplementation on Reducing Oxidative Stress in Patients with Relapsing Remitting Multiple Sclerosis

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**Abstract:** Background: Multiple sclerosis it's a disease cause demyelination of the central nervous system (CNS). it's long duration result in individual, family tremendous & societal cost as well as reduction in life quality & work productivity. oxidative stress may play a key role in its pathogenesis. The aim of this study was to evaluate the effect of coenzyme Q10 (CoQ10) 200mg/day supplementation on oxidative stress and antioxidant enzyme activity in patients with relapsing–remitting MS (RRMS). Materials and Methods: the study was a single-blind, randomized (placebo-controlled) study to determine the effect of CoQ10 supplement (200 mg/day, n=20) versus placebo (control, n = 20) for 24 weeks. Blood samples were taken before and after a 24-week intervention to analyze malondialdehyde (MDA) and the antioxidant enzyme superoxide dismutase (SOD) activity, liver and renal function (aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AlkP), s. urea and s. creatinine) was measured to evaluate the safety of CoQ10. Results: Forty subjects with RRMS completed intervention study. After 24 weeks, CoQ10-treated patients had significant increase in SOD activity ( $p = 0.000$ ); and decrease in MDA levels ( $P=0.000$ ) compared with placebo group. CoQ10 supplementation have no significant effect on EDSS, liver and renal function. Conclusion: in the present study suggests that CoQ10 supplements at a dose of 200 mg/day for 24 weeks is safe and can decrease oxidative stress and increase antioxidant enzyme activity in patients with RRMS.

**Keywords:** Coenzyme Q10, Oxidative stress, Relapsing remitting MS patients

## 1. Introduction

Multiple sclerosis it's a disease cause demyelination of the central nervous system (CNS) [1]. The diagnosis required the occurrence of at least 2 neurological events that consist with CNS demyelination which separate temporally & anatomically. The onset of the disease early in life (occur typically between the age of 20 & 40 years) & it's long duration result in individual, family tremendous & societal cost as well as reduction in life quality & productivity in work [2]. Multiple sclerosis (MS) has characteristic, variable & unpredictable course, the symptoms could include visual loss, weakness, bowel & bladder incontinence, cognitive impairment, fatigue & mood symptoms.

2.5 million people in worldwide affected with MS approximately, four hundred thousand of people in United States, and 200 people and more to have diagnose with MS each week in the United States [3]. MS typically begins 20 to 40 years of age. In young adults it is consider the leading cause of non-traumatic disability. Initial symptom are rarely occur before the age 10 years or after the age of 60 yrs [4]. It affect women twice as often as men.

The true extent and nature of MS pathology within and between patients, and over time, remains unclear [5]. There is substantial evidence, however, to suggest it is a process of autoimmune that directed against oligodendrocytes (the cells that make CNS myelin) and myelin [6]. The mediator that actually cause destruction of myelin & axonal hasn't been

established, but it may reflects a combination of macrophage, reactive oxygen & intermediate of destructive cytokines. The clinical findings of MS are not unique, but the disease have some findings that are highly characteristic.

pathogenic evidence suggests a possible role for oxidative stress (OS) in the pathogenesis of MS [7]. Several studies indicate elevation of some markers of oxidation in cerebrospinal fluid and serum of patients with MS [8]. Reactive oxygen species ROS which is a small molecule that are highly reactive, due to presence of unpaired electron or their ability to give rise to new free radical production, that contributes to cellular injury [9]. Although, there are protective system against free radicals, these systems responses are overwhelms in pathological conditions like MS. This condition leads to the employment of many of antioxidants in order to enhance MS.

Experimental animal studies have demonstrated that dietary intake of exogenous antioxidants, reduce the progression and clinical signs of (experimental autoimmune encephalomyelitis) EAE [9]. Recently CoQ10 is used as a neuroprotective agent in the treatment of different neurodegenerative impairments such as Parkinson's disease (PD), Huntington's disease, amyotrophic lateral sclerosis (ALS) & Friedreich's ataxia [10]. Several studies have investigate CoQ10 role against ROS damage and apoptotic cell death [11]. In this study a try was made to evaluate CoQ10 effect and safety in RRMS patients.

## 2. Subject and Material

### 2.1 Patient Selection

40 patients (20 female and 20 male) with diagnosed MS were enrolled in this study in addition to 20 Healthy volunteers were served as control. Exclusion of smoking and alcohol drinking individuals, as well as individuals suffering from chronic diseases or any condition that may affect oxidative stress. The forty patients were divided into two groups randomly one group take CoQ10 (200)mg daily, the second group take placebo. Patients were evaluated at baseline and 24 weeks later. Patients were instructed to sustain their schedules of treatment.

### 2.2 Sample Collection

Venous blood was obtained for each individual (control and patient) by vein puncture before the initiation of therapy, as a baseline, and 24 weeks later. Estimation of Malondialdehyde (MDA) using (ELISA) kit apply the competitive enzymes immunoassay techniques. And superoxide dismutase (SOD) assessment by quantitative sandwich enzyme immune assay by (ELISA) kit to evaluate antioxidant activity of CoQ10, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALKP), serum urea and serum creatinine were determined by quantitation method to evaluate the safety of CoQ10. Expanded disability status scale (EDSS) has been evaluated before and after treatment.

### 2.3 Statistical Analysis

Statistical analysis performed by using SPSS-21 (Statistical Package for Social Sciences\_ V 21). Results are Means  $\pm$  SE, statistical analysis was performed by one - way analysis of variance (ANOVA).  $P < 0.05$  was considered statistically significant<sup>[13]</sup>.

## 3. Result

Of Fifty patients presented to the study only forty patients (20 male and 20 female) were complete the study. Their age were  $35.65 \pm 9.294$  years (as mean  $\pm$  SE). There were no apparent differences between the three groups with respect to demographic data (Table 1). At baseline there is no significant difference between Co Q10, placebo group in superoxide dismutase (SOD) level in compare with control, while malondialdehyde (MDA) was in RRMS patients differ significantly ( $P > 0.05$ ) in compare to control. However, after 24 weeks of treatment (MDA) was significantly decrease in CoQ10 group ( $p < 0.05$ ) compared to the baseline value, with significant difference between CoQ10 group and placebo.

**Table (1) Demographic data**

Parameter	CoQ10 group	Placebo group	Control group	P-value
Age	34.60 $\pm$ 8.66	35.65 $\pm$ 2.10	32.40 $\pm$ 1.98	NS
Female: Male (Female %)	10:10 (50%)	10:10 (50%)	10:10 (50%)	NS
BMI	24.29 $\pm$ 0.46	26.54 $\pm$ 1.26	24.90 $\pm$ 0.88	NS

Data expressed as mean $\pm$ SE, \*BMI= body mass index, which is calculated according to the following formula: BMI= weight (kilogram)/height<sup>2</sup> (meter), NS= non-significant ( $p > 0.05$ ).

Level of SOD was significantly increased in CoQ10 group from baseline with significant difference between CoQ10 and placebo.

Serum AST, ALT, AlkP, urea and creatinine have no significant difference between CoQ10, placebo and control group at baseline. After treatment there is no significant difference in compare to baseline, furthermore there was no significant difference between CoQ10 and placebo.

There was no significant differences in EDSSat baseline between CoQ10 group and placebo. However, there was no significant change among CoQ10 group after 24 weeks of treatment.

## 4. Discussion

Co Q10 involved in energy production<sup>41[14]</sup>, and acts as a primary scavenger of free radicals, protecting from oxidative damage and favoring the regeneration of other antioxidants<sup>[15]</sup>.<sup>42</sup> It has anti-inflammatory properties because it inhibits metalloproteinases and IL-6 production<sup>[16]</sup>. In this study a supplementation of 200 mg of CoQ10 over 24 wks resulted in a significant decrease ( $p > 0.05$ ) in MDA level compared with placebo in group of RRMS patients, this result is in constant with the result of Meisam Sanoobar and colleagues<sup>[17]</sup> who find that MDA level was reduced in RRMS patients taking supplement of CoQ10 (500 mg once daily) over 12 wks.

Level of SOD in this study was significantly increased ( $p > 0.05$ ) compare to placebo, in a study by Lee et al. in the same line<sup>[18]</sup>, activity of SOD increased in patient with coronary artery disease (CAD) after 12-week with CoQ10 supplementation. EDSS value show no significant change in CoQ10 group in compare to placebo this result is in an agreement with Maira Gironi et al., who suggest that antioxidant depletion as an intrinsic, probably a causative factor associated with MS course rather than a consequence<sup>[19]</sup>.

Monitoring of liver and renal functions showed the safety of use of CoQ10 cap. in RRMS patient. Comparing the measured levels of serum ALT, AST, AlpK, urea and creatinine between CoQ10 and placebo groups show no significant differences over 24 wks of treatment.

## 5. Conclusion

Administration of coenzyme Q10 (200mg/day) decrease lipid peroxidation and increase antioxidant enzyme activity and was safe in patients with MS, CoQ10 by its antioxidant activity, Enhanced antioxidant mechanisms may represent a natural compensatory mechanism protecting against direct oxidative damage. The antioxidant activity can be considered as one of the main factors responsible for the neuroprotective effect of CoQ10. Further larger and longer studies are warranted to confirm these findings.

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**Table 2:** Changes from baseline and after 24weeks in laboratory parameters for patients who completed the study

Parameter	Coenzyme 10 group 20 subjects	Placebo group 20 subjects	Control group 20 subjects
SOD(pg/ml) Before intervention After intervention	271.86±29.46 420.66±34.21*	363.99±51.62 249.63±28.64*	464.71±23.66
MDA (ng/ml) Before intervention After intervention	4.38±0.16** 3.32±0.18*	4.00±0.10** 4.53±0.16*	3.38±0.19
ALT(U/L) Before intervention After intervention	30.00±3.97 33.80±5.72	26.95±4.11 30.35±1.81	19.8±2.49
AST(U/L)Before intervention After intervention	28.45±2.87 32.05±6.51	29.25±2.72 26.25±1.93	20.60±1.08
AlkP(U/L)Before intervention After intervention	75.20±5.23 75.0±5.45	89.35±4.75 87.15±2.11	71.30±4.29
Urea (mg/dL)Before intervention After intervention	26.15±1.47 24.20±1.24	28.80±1.97 28.15±1.33	27.30±2.25
Cr(mg/dL) Before intervention After intervention	0.66±0.02 0.68±0.02	0.70±0.02 0.74±0.02	0.70±0.02

Data represented as mean±SE for baseline and end of study values; \* significantly different when compared to pre-treatment level within the same group (P<0.05); \*\* significantly different when compared to control group (p<0.05).