

Some Beneficial Effects of Coenzyme Q10 Supplementation on Patients with Chronic Obstructive Pulmonary Disease

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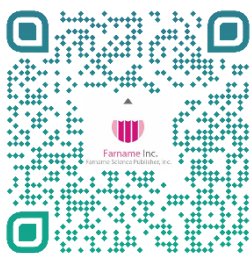
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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent airflow obstruction due to chronic parenchymal destruction and airway remodeling caused by persistent inflammation. Inflammation is not limited to the lungs and is associated with systemic inflammation that results in non-respiratory complications including cachexia, muscle dysfunction, and cardiovascular morbidities (1, 2). Serum levels of inflammatory markers, particularly C-Reactive Protein (CRP) levels, are directly related to disability in COPD (3).

CoQ10 is present in all living cells (4, 5). As a cofactor, it plays an essential role in the electron transport chain which is the main reaction participating in the biosynthesis of adenosine triphosphate (ATP) (6). Based on this functional role, Co q10 is an essential factor for all

ABSTRACT

Background & Objective: Chronic inflammation, dyspnea and activity limitation are common phenomena in patients with chronic obstructive lung disease. Clinical studies suggest that Ubiquinone has anti-inflammatory and energetic properties. Here the beneficial effect of CoQ10 in patients with COPD will be studied.

Materials & Methods: Baesd on the census method, 90 patients with moderate to severe COPD were divided into two identical placebo and CoQ10 groups. High sensitive-C-reactive protein (hs-CRP), Forced Expiratory Volume in 1 second, numerical rating breathlessness scale and "the time to get exhausted" were evaluated and recorded at baseline and the end of the study. The CoQ10 group received 120 mg of CoQ10 supplement per day versus the placebo group who also received a placebo (identical in look, size and taste to pharmaceutical sample) and were followed for 6 weeks. Data were analyzed using t-test, and nonparametric statistical tests. Qualitative variables were assessed by chi-square or Fisher exact tests.

Results: The study included 49(53.6%) women and 41(46.4%) men, collectively 90 patients with moderate to severe COPD. The mean age was 66.97±12.59 years in the placebo and 64.21±11.78 years in the CoQ10 group (p=0.30). Breathlessness scale was improved in CoQ10 group (p<0.001). hs-CRP significantly declined after intervention in the CoQ10 compared to the placebo group (p<0.001).No serious side effects were observed as a result of CoQ10 consumption.

Conclusion: Daily administration of CoQ10 in COPD patients increases hs-CRP and improves dyspnea and "the time to get exhausted" without side effect.

Keywords: Ubiquinone, COPD, hs-CRP, Shortness of breath

living cells and proper organ functions in the body. The main and sufficient source of Co Q10 in the body is usually provided by intracellular synthesis, although a small proportion is supplied through oral intake. In most cases, Co q10 deficiency is inherited as an autosomal recessive disorder with heterogeneous clinical manifestation (7). Researchers believe that in addition to inherited syndromes that reduce the level of CoQ10 in the body, aging and chronic diseases may also be associated with decreased CoQ10 levels (8). Multiple studies have been conducted on the anti-inflammatory and anti-oxidant properties of CoQ10.CoQ10 helps the immune system with better functioning (9). Co Q10 also increases energy production in the body (10). The potential anti-inflammatory effect of CoQ10 has been shown by

lowering effect on serum CRP levels and also decrease in mRNA expression of IL-6 and TNF- α (2).

Based on these findings, the hypothesis may be provided that CoQ10 supplementation could alleviate chronic disease-related disabilities (8).

For these reasons, CoQ10 supplementation has been considered as an attractive agent in the management of various chronic human diseases including cardiovascular diseases, metabolic syndromes and diabetes mellitus (10).

CoQ10 serum levels are lower in COPD patients than in normal individuals (11). The beneficial role of CoQ10 in respiratory diseases has been emphasized by reducing the need for corticosteroids in patients with asthma when these patients are supplemented with CoQ10 (12). It is claimed that CoQ10 provides more energy to the muscle and improves activity tolerance in patients with COPD (13). In general, due to persistent local and systemic inflammation in patients with COPD, similar inflammation-based comorbidities with COPD including muscle dysfunction, cardiovascular disease, osteoporosis and diabetes mellitus are conditions more common in these patients. (14). Limited studies have been conducted on the benefits of CoQ10 in COPD patients. Since most studies have not been able to independently confirm the effect of CoQ10 on improving various aspects (chronic inflammation, lung function and clinical presentations) of COPD patients, more studies are needed to get more definitive results about the usefulness of CoQ10 in COPD patients. (15) With progressive characteristics of COPD, it will be logical to cure symptoms in these patients, to reduce inflammation and also prevent comorbidities progression. The present study aims to analyze the effect of CoQ10 on the "high-sensitivity C-reactive protein (hs-CRP)", and also activity tolerance and shortness of breath in patient with COPD.

Materials and Methods

Participants

Based on the census method, 90 patients over the age of 18 years with moderate to severe COPD and without major comorbidities were selected. In order to match the two groups, the number of patients in terms of disease severity (moderate or severe) were selected equally in both groups. In case of exacerbation during the study period, the individual was excluded from the study. Informed consent was obtained from all participants in the study. The study was approved by the Office of Vice Chancellor for Research and Ethics Committee of Birjand University of Medical Sciences (Ethic Code: ir.bums.REC.1397.189; RCT code: IRCT20190618043934N1).

Blood pressure, pulse rate, and respiration rate, were recorded in all studied patients. Blood samples were taken and the Pars Azmoun kit Company (made in Iran-Tehran), the Prestige 24i device (Tokyo Bokei Company - Japanese) and Immuno-turbidimetric method were used to measure hs-CRP (mg/L). Forced Expiratory Volume in 1 second (FEV1) and Forced Expiratory Capacity (FVC) were measured by spirometry. Patients were asked to answer the numerical rating breathlessness scale by observing the shape of a numbered ruler from one to ten. Patients were also asked to walk as much as they could until exhaustion stopped moving, and their walking time (minutes), was recorded as "the time to get exhausted" (allowing maximum 6-minute walking). All studied parameters were recorded at baseline and end of the study.

Patients were divided into two identical placebo and CoQ10 groups (double blinded) (Figure 1). The CoQ10 group received 120 mg per day of CoQ10 supplement versus the placebo group who received a placebo (identical in look, size and taste to pharmaceutical sample) and both groups were followed for 6 weeks duration. Both groups underwent standardized basic treatments for COPD (fluticasone+salmeterol and ipratropium bromide or tiotropium bromide). In the case of the use of tiotropium or ipratropium, equalization between the two groups was considered.

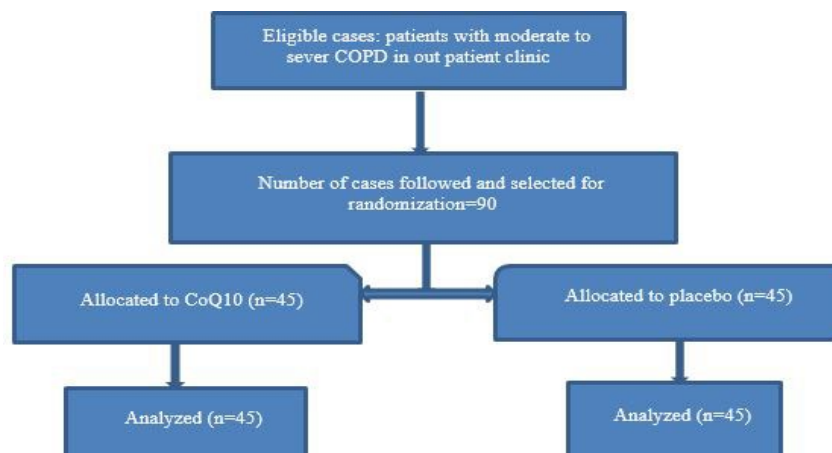


Figure 1. Study protocol flow chart

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) software version 16, (Parnian Engineering incorporated, Karaj, Iran) was used to perform statistical analysis. The normality of quantitative variables was assessed by Shapiro-Wilk test. Data with normal distribution were analyzed using independent t-test, but non-normal distribution variables were compared by Mann-Whitney U test. Associations between qualitative variables were assessed by chi-square or Fisher exact tests. The significance level for P value was considered to be less than 0.05.

Results

The study included 90 patients with moderate to severe COPD divided into two identical groups with equal numbers, including 45(50%) in the placebo and 45(50%) in the CoQ10 group. The study consisted of 42(46.7%) male and 48(53.3%) female cases respectively. The mean age was 65.59 ± 11.80 years. [Table 1](#) shows homogeneity of study groups in terms of demographic variables (Pgender=0.67, PAge=0.27, PLocation=0.67).

Table 1. Comparison of demographic factors between the CoQ10 and control groups

	Placebo group N(%)	CoQ10 group N(%)	P-Value
Gender			
Male	20 (44.4)	22 (48.9)	0.67
Female	25 (55.6)	23 (51.1)	
Age	66.98±12.16	64.20±11.38	0.27
Location			
Village	19 (42.2)	17 (37.8)	0.67
City	26 (57.8)	28 (62.2)	

* Mean±SD was reported

[Table 2](#) shows changes and comparison of studied parameter between the placebo and intervention groups. As it is seen, the "breathlessness" scale and "the time to get exhausted" scores showed statistically

significant improvement after intervention in CoQ10 group ($p < 0.001$). A decrease in hs-CRP was observed in CoQ10 group ($p < 0.001$).

Table 2. Comparisons of the differences in studied parameter between the CoQ10 and control groups

	Placebo group Q2 (Q1, Q3)	CoQ10 group Q2 (Q1, Q3)	P-Value
Systolic Blood pressure(mmHg)	-2 (-12.5, 0)	-5 (-15, 0)	0.84
Distolic Blood Pressure(mmHg)	0 (-10, 5)	-5 (-10, 2.5)	0.93
Pulse Rate/minute	-2 (-10, 4)	-5 (-13, 5)	0.50
Respiratory rate/minute	-2 (-4, 0)	1 (-1, 3)	0.26
Temperature(Degree of Celsius)	0 (0, 0)	0 (0, 0)	0.18
Breathlessness scale (The higher score the better codition)	1 (0, 2)	4 (2, 4)	<0.001
Activity tolerance(minute)	1 (0, 1)	3 (2, 3)	<0.001
FEV1(Percentage compared to normal values)	6 (0, 10)	7 (-3, 18.5)	0.57
hs-CRP(mg/L)	-20.66 (-10.73, 46.05)	-32.54 (-51.01, 0.675)	<0.001

Data presented as Q2 (Q1, Q3) or number (%). P-value is obtained by Mann-Whitney U Test (non-normally distributed variables) or Fisher's Exact Test (categorical variables). Significant bold values are < 0.05 levels.

Discussion

By daily administration of CoQ10, the noticeable finding in our study was improvement in "breathlessness" and "the time to get exhausted" in CoQ10 group of COPD patients compared to placebo group at the end of the study. COPD patients generally have lower scores of health sensation and quality of life (16). Decreased exercise tolerance is one of the main complaints in COPD patients. Several factors contribute to low physical performance in COPD patients (17). They often suffer from shortness of breath and chronic fatigue that lead to a vicious cycle of inactivity, further disability and reduction in quality of life (18).

Regarding the main role of CoQ10 as a cofactor in the electron-transport chain and energy production, adequate access to this substance is essential for good organ and muscle function. The primary source of CoQ10 in the human body is intracellular synthesis and concentration decrease during oxidation activity (6).

In addition to increased oxidative stress due to chronic and persistent inflammation, the COPD patients often suffer from malnutrition which parallels the severity of the disease (19).

Malnutrition also contributes to reduced availability of energetic substrates and to some extent CoQ10 for muscles energy production (17). Oxidative stress and inflammatory reactions along with reduced access to effective factors in energy production (such as CoQ10) lead to some decrease in the physical performance and activity tolerance of COPD patients. The effect of CoQ10 on improving the exercise tolerance, and physical performance has been considered for many years (20, 21). It was shown that CoQ10 supplementation can increase the time to get exhausted by increasing serum CoQ10 levels in both trained and untrained individuals (21). CoQ10 also improves activity tolerance, shortness of breath, and quality of life in COPD patients with chronic respiratory failure (22).

Design of the present study was based on the hypothesis of anti-inflammatory properties of CoQ10 (2). Based on this hypothesis, the valuable finding in our study was significant reduction of hs-CRP in CoQ10 group compared to the placebo group. While some researchers have not reported any difference (23), the others have shown higher level of serum hs-CRP levels in patients with COPD compared to the control group (24). Scientific databases were searched in English and did not yield any particular information about the effect of CoQ10 on hs-CRP serum levels in patients with COPD. According to some available evidence, CoQ10 can be useful in reduction of oxidative stress in COPD patients (25). Moreover, systemic inflammation manifested with high CRP levels contributes to higher prevalence of cardiovascular and cancer comorbidities in COPD patients ultimately leading to increased mortality in

these patients (26). Inflammation in COPD patients is not limited to the lungs and inhibition of local and systemic inflammation can potentially reduce mortality from the disease and /or related comorbidities (1, 3), (14). The investigation of the effect of CoQ10 on serum inflammatory markers and in particular on serum CRP levels in various chronic diseases has shown contradictory results. CoQ10 reduces hs-CRP levels in hemodialysis patients (27), however in cardiovascular disorders with high hs-CRP serum levels, there is no reduction in hs-CRP by prescribing of CoQ10 (28). At the same time, however, CoQ10 supplementation is associated with improved clinical outcomes in cardiovascular patients (28).

In the present study, CoQ10 administration did not show any effect on lung function and FEV1 value. In COPD patients, serum CoQ10 levels are lower than normal, but no correlation has been found between CoQ10 levels and lung function. At the same time, however, CoQ10 which is associated with improvement in PaO₂, provides more energy required for muscles, and increases activity tolerance in patients with COPD (29). In a study conducted under relatively similar conditions, 100 mg of CoQ10 supplementation per day significantly improved FEV1/FVC value in patients with asthma (30). This effect lasts up to 6 weeks after quitting CoQ10.

Regarding blood pressure, heart rate, and respiratory rate, there were no significant differences between the two groups in our study. In one study, CoQ10 supplementation in patients with COPD, while oxygen consumption remained unchanged during exercise, showed higher levels of PaO₂ and lower heart rates compared with an identical workload group (29). In the present study, no significant effect of CoQ10 on blood pressure was seen. Other studies do not also confirm the antihypertensive effect of CoQ10 (31).

Conclusion

Daily administration of CoQ10 (120 mg per day) in COPD patients has beneficial effects in terms of hs-CRP reduction and improvement in "the time to get exhausted" and shortness of breath. For more definite anti-inflammatory properties and clinically beneficial effects, more studies are recommended.

Limitations of the study and suggestions

In the present study, the total level of CoQ10 was not measured. We also did not include a healthy control group. In the future studies it is recommended to include a healthy control group, and measure serum level of CoQ10 before trial, so that appropriate candidates for treatment with CoQ10 would be determined.

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Conflict of Interest

All authors declare that they have no conflict of interest.

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