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Influence of ubiquinol on angina severity and dyspnea in patients with acute coronary syndrome

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ABSTRACT

Background: Co-enzyme Q10 (CoQ10) has highest concentration in the heart and a critical role in cellular energy production, but its physiological concentration decreases with aging. Ubiquinol is the active and most bioavailable form of CoQ10; this is extremely important for patients older than 20 years as the metabolic enzyme required for CoQ10 activation starts to decrease. Thus, ubiquinol may have a more potent beneficial impact on improving the health of acute coronary syndrome (ACS) patients. This study aimed to investigate the influence of ubiquinol on angina severity and dyspnea in patients who are receiving optimal medical therapy (OMT) after ACS.

Methods: In a randomized, controlled clinical trial, 50 patients who had undergone percutaneous coronary intervention (PCI) were prospectively assigned to either the control group (n=25) or the ubiquinol group (n=25). The control group received only OMT, while the second group also received a ubiquinol daily dose of 200 mg in addition to the OMT. Measurement of the patients' angina and dyspnea severity was achieved at baseline and at 2 months post-PCI via utilization of the Seattle Angina Questionnaire (SAQ) and the Rose Dyspnea Scale (RDS), respectively.

Results: After 8 weeks of intervention, a significant difference was revealed in health status improvement between the groups. In the ubiquinol group, 13 (52%) of patients became dyspnea-free, with 12 (48%) experiencing mild grade 1 dyspnea, while in the control group, residual dyspnea was still present in all patients, and 5 (20%) of them were still suffering from grade 4 dyspnea. Regarding the SAQ scores' improvement, a significant difference between the groups was observed in the mean changes from baseline, with greater mean changes in the ubiquinol group compared to the control group in all three SAQ sub-scales and summary scores (p value < 0.001). The mean change of the SAQ summary score in the ubiquinol group was 55.93 ± 19.71 compared to 11.47 ± 16.47 in the control group, and the ubiquinol group reported significantly larger reductions in angina episodes.

Conclusion: This study demonstrates that ubiquinol addition to OMT after ACS has a highly significant effect on improving clinical outcomes and patients' quality of life through greater reductions in angina frequency, physical limitations and dyspnea severity. This suggests an effective and safe strategy for optimizing therapeutic outcomes and secondary prevention.

Keywords: *Ubiquinol, Angina severity, Acute coronary syndrome*

INTRODUCTION

Cardiovascular disease (CVD) is a global health problem that results in an immense financial commitment in terms of both medical costs and the inability to work. According to the World Health Organization (WHO), CVD is currently the major cause of death in both advanced as well as developing countries and every year it claims more lives than both chronic lung disease and cancer combined.(1,2) Coronary artery disease (CAD) is a chronic pathological process involving progressive narrowing of coronary arteries and represents the most common CVD with a predominant serious prognosis that results in numerous clinical manifestations, which can be categorized as either acute or chronic coronary syndromes.(3)

Today, the management of acute coronary syndrome (ACS) is based on reperfusion and revascularization via the utilization of both pharmacologic and nonpharmacologic interventions, namely percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).(4) Although revascularization through PCI can effectively reduce angina, the incidence of death and recurrent myocardial infarction (MI) in patients presenting with an ACS, however, it has not the same impact in chronic stable patients and symptoms remain in approximately one-fourth of patients post PCI.(4–6) Furthermore, the residual angina impairs patient's quality of life and foretells a worse prognosis.(7)

It is well documented that the largest reductions in death and recurrent cardiovascular events can be achieved with optimization of secondary prevention management after acute MI or after revascularization.(8)

Following treatment of acute MI that focuses on limiting myocardial necrosis and preventing death, the focus of care shifts to a combination of improvement in the patient's quality of life (QOL) and secondary prevention of complications via lifestyle modifications and long-term medical therapy.(3,4,8) Optimal medical therapy (OMT) after PCI includes Aspirin, P2Y12 Inhibitors, statins and β-blockers, unless there is a contraindication. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) and aldosterone antagonists have been shown to be beneficial in patients who have Left ventricular dysfunction (LVD) or accompanying comorbidities.(9,10)

Although significant efforts have been made to discover the most appropriate approaches in prevention and management of CAD, it still continues to be a leading killer worldwide, and many patients suffer from poor QOL. Therefore, yet much work has to be done to reveal more effective and safe strategies that are urgently needed in order to reduce the burden of CVD. (11)

This poses a serious challenge in medicine, not only to improve functional results of treatment but also to improve patient's QOL, because there has been a shift in medicine from relying on objective findings or biomarkers to including patient reported outcome (PRO) measures since PROs have the opportunity to integrate patients' experiences, thereby resulting in patient-centeredness of care.(12) As a result, currently, PROs are growingly utilized as end point assessments in clinical practice and trials.

Angina and dyspnea are the most critical markers for underlying CAD and patients' perception of their disease-specific health status; thus, their management is of great importance. The Seattle Angina Questionnaire (SAQ) has emerged as the most frequently used measure of angina symptoms and their impact on physical functioning and QOL due to its approved validity, reliability and sensitivity to clinical change.(13) Moreover, there is a wide variability across physicians in recognizing and recording angina, and as a result there is a chance of over- or under-estimation of patient's angina.(14) But the use of a standard questionnaire could prevent this.

In terms of dyspnea level evaluation in patients with CAD, the Rose Dyspnea Scale (RDS) has been extensively validated and demonstrated to be associated with QOL, rehospitalization and mortality.(15)

Co-enzyme Q10 (called Ubiquinone or CoQ10) is an essential vitamin-like, fat-soluble quinone compound in the human body that is biosynthesized in healthy individuals and is considered one of the most important lipid anti-oxidants.(16) It is present in all human tissues, but highly concentrated in organs exhibiting a high level of metabolic activity such as heart, liver, kidney, brain, and muscles due to its critical role in cellular energy production.(2) However, its physiological concentration decreases with aging, statin usage (17), and in some pathophysiologic states mainly in CVDs.(16)

Clinical evidence presents that CoQ10 administration can reduce death from cardiovascular causes and improve clinical outcomes.(2) Ubiquinol is the most advanced form of CoQ10 with the highest bioavailability, which is the active form and thus does not need enzymatic metabolism in body to be converted; this is critically important for patients above the age of 20 as the essential metabolic enzyme required for activation of CoQ10 starts to decrease.(18–21) Thus, ubiquinol may have a beneficial impact on improving CAD patients' health status through different mechanisms.

Therefore, the aim of this study was to investigate the influence of ubiquinol on angina severity and dyspnea level in patients who are receiving optimal long-term medical therapy after ACS. This could be an effective and safe therapeutic strategy in clinical practice for optimizing therapeutic outcome of CAD, secondary prevention of consequent ischemic events and improving patient's quality of life.

METHODS AND PATIENTS

Study design

This was a prospective, randomized, controlled clinical trial of ubiquinol in patients with ACS after administration of PCI on changes in angina severity and dyspnea level. Patients were enrolled from across Iraqi cities in the Erbil Cardiac Center. This study was performed in 2022 and was approved by the Ethics Committee of the Ministry of Higher Education and Scientific Research/ Hawler Medical University (HMU-PE 213-180921).

In this study, 123 patients were screened, of whom 50 were eligible for enrollment in the study according to the inclusion criteria. The patients were randomly assigned to the control group (n = 25) or the ubiquinol group (n = 25), and written informed consent has been taken from all patients. Intervention was administered for 8 weeks.

The control group received only optimal long-term medical therapy (OMT), while the second group also received a ubiquinol daily dose of 200 mg (100 mg × 2) in addition to the OMT. Angina severity and dyspnea level were evaluated at baseline and after 8 weeks of intervention via utilization of the below mentioned questionaries.

Inclusion and exclusion criteria

Patients were eligible for enrollment (between 35 and 75 years of age) if they had ACS and undergone PCI, were prescribed optimal long-term medical therapy, and had not taken CoQ10 for at least the past 12 months.

Exclusion criteria were: known allergy to CoQ10, dyspnea due to other causes, congenital heart disease, severe non-cardiac diseases including malignancy, psychosocial instability or anticipated problems with compliance, women of childbearing potential and lactating female patients, and supplemental CoQ10 intake within the last 12 months before run-in.

Questionaries

Measurement of the patients' angina and dyspnea severity was carried out at baseline and at 2 months post PCI via the use of the Seattle Angina Questionnaire-7 (SAQ) and the Rose Dyspnea Scale (RDS), respectively. The questionnaires were administered via direct interview with the patients.

Statistics

All statistical analyses were performed using version 26 of IBM SPSS statistical software. Data are presented as mean ± SD and the Shapiro-Wilk test was utilized to identify the distribution pattern of the data. Categorical variables are demonstrated as frequencies and percentages (%). Additionally, comparison of continuous variables was made utilizing the Student's t-test (or Mann-Whitney U tests as appropriate), while comparison of categorical variables was made using the chi-square or Fisher exact test as appropriate. Finally, a p value of <0.05 was considered significant.

RESULTS

Baseline characteristics

Both groups were similar with respect to a range of baseline characteristics, and there were no significant differences between them in baseline health-status measures (table 1).

To predict patients' angina-related health status, the patients were examined at baseline for demographic characteristics (age, gender, BMI, smoking status and alcohol), existence of hypertension, existence of DM, baseline SAQ scores and baseline RDS grades. There was no statistically significant difference between the groups.

TABLE 1. Comparison of baseline patient characteristics between the control and Ubiquinol groups

Character	Control Group (Only OMT) Mean ± SD or n (%)	Ubiquinol Group (OMT + Ubiquinol) Mean ± SD or n (%)	P value
Age, years (Mean ± SD)	56.36 ± 8.65	55.92 ±8.00	0.85
Gender (male, n (%))	13 (52)	17 (68)	0.25
BMI (Mean ± SD)	28.30 ± 5.170.78	27.82 ± 4.58	0.73
Smoking status (smoker, n (%))	5 (20)	11 (44)	0.069
Alcohol status (alcoholic, n (%))	2 (8)	2 (8)	1.00
Hypertension (hypertensive, n (%))	10 (40)	11 (44)	0.77
Diabetes mellitus (diabetic, n (%))	13 (52)	12 (48)	0.78
SAQ-7 PL PRE (Mean ± SD)	27.67 ± 22.79	35.00 ± 24.53	0.28
SAQ-7 AF PRE (Mean ± SD)	50.80 ± 15.25	49.20 ± 14.98	0.71
SAQ-7 QOL PRE (Mean ± SD)	23.50 ± 21.75	19.00 ± 27.75	0.53
SAQ-7 Summary PRE (Mean ± SD)	33.99 ± 16.28	34.40 ± 20.02	0.94
RDS (n (%))			
0 (No dyspnea)	1 (4)	0 (0)	0.24
1 (Grade 1 dyspnea)	4 (16)	4(16)	
2 (Grade 2 dyspnea)	4 (16)	9 (36)	
3 (Grade 3 dyspnea)	5 (20)	7 (28)	
4 (Grade 4 dyspnea)	11 (44)	5 (20)	

BMI = Body Mass Index, OMT = Optimal Medical Therapy, SD = Standard deviation, SAQ-7 PL = Seattle Angina Questionnaire-7 Physical Limitation domain, SAQ-7 AF = Seattle Angina Questionnaire-7 Angina Frequency domain, SAQ-7 QOL= Seattle Angina Questionnaire-7 Quality of Life domain, RDS = Rose Dyspnea Scale

Effect of OMT on angina severity and dyspnea level in ACS patients (control group)

There was no significant improvement in dyspnea level after 8 weeks of intervention in the control group, and 20% of the patients were still suffering from grade 4 dyspnea (the most severe level) while none of them were completely dyspnea free (table 2).

TABLE 2. Comparison of RDS grades before and after intervention in the control group

Group Name	No dyspnea n (%)	Grade 1 dyspnea n (%)	Grade 2 dyspnea n (%)	Grade3 dyspnea n (%)	Grade 4 dyspnea n (%)	P value
Before intervention	1 (4)	4 (16)	4(16)	5 (20)	11 (44)	0.301
After intervention	0 (0)	5 (20)	7 (28)	8 (32)	5 (20)	

Nonetheless, the control group showed significant improvements in the SAQ domains of Angina Frequency, Quality of Life, and Summary score, with p values of 0.001, 0.014 and 0.009 respectively. However, no significant change was detected from the baseline value in the Physical Limitation domain (table 3).

TABLE 3. Comparison of SAQ scores before and after intervention in the control group

Character	Before intervention	After intervention	P value
SAQ-7 PL score	27.67 ± 22.79	34.67 ± 20.37	0.162
SAQ-7 AF score	50.80 ± 15.25	65.20 ± 13.88	0.001
SAQ-7 QOL score	23.50 ±21.75	36.50 ±19.07	0.014
SAQ-7 Summary score	33.99 ±16.28	45.45 ± 14.95	0.009

SAQ-7 PL = Seattle Angina Questionnaire-7 Physical Limitation domain, SAQ-7 AF = Seattle Angina Questionnaire-7 Angina Frequency domain, SAQ-7 QOL= Seattle Angina Questionnaire-7 Quality of Life domain

Effect of ubiquinol addition to OMT on angina severity and dyspnea level in ACS patients (Ubiquinol group)

After 8 weeks of 200 mg ubiquinol administration, there was a marked significant improvement in dyspnea level in the ubiquinol group with a p value of < 0.001, none of the patients had daily or weekly angina and 13 (52%) of the patients became dyspnea free (table 4).

TABLE 4. Comparison of RDS grades before and after intervention in the Ubiquinol group

Group Name	No dyspnea n (%)	Grade 1 dyspnea n (%)	Grade 2 dyspnea n (%)	Grade3 dyspnea n (%)	Grade 4 dyspnea n (%)	P value
Before intervention	0 (0)	4 (16)	9 (36)	7 (28)	5 (20)	0.001
After intervention	13 (52)	12 (48)	0 (0)	0 (0)	0 (0)	

In addition, there were substantial significant improvements in all three SAQ domains and its summary score, with p values of <0.001 (table 5).

TABLE 5. Comparison of SAQ scores before and after intervention in the ubiquinol group

Character	Before intervention	After intervention	P value
SAQ-7 PL score	35.00 ± 24.53	87.00 ± 18.49	0.001
SAQ-7 AF score	49.20 ± 14.98	94.00 ± 7.07	0.001
SAQ-7 QOL score	19.00 ± 27.75	90.00 ± 13.98	0.001
SAQ-7 Summary score	34.40 ± 20.02	90.33 ± 9.84	0.001

SAQ-7 PL = Seattle Angina Questionnaire-7 Physical Limitation domain, SAQ-7 AF = Seattle Angina Questionnaire-7 Angina Frequency domain, SAQ-7 QOL= Seattle Angina Questionnaire-7 Quality of Life domain

Comparison between improvements in both groups

There was a statistically significant difference in terms of RDS improvement between the groups after 8 weeks of intervention (p value < 0.001): 13 (52%) of patients in the ubiquinol group became completely dyspnea free and 12 (48%) experiencing only mild grade 1 dyspnea, however, residual dyspnea was still present in all patients of the control group and 5 (20%) of them were still suffering from grade 4 dyspnea (table 6).

TABLE 6. Post RDS grade comparison between both groups after intervention

Group Name	No dyspnea n (%)	Grade 1 dyspnea n (%)	Grade 2 dyspnea n (%)	Grade3 dyspnea n (%)	Grade 4 dyspnea n (%)	P value
Control	0 (0)	5 (20)	7 (28)	8 (32)	5 (20)	0.001
Ubiquinol	13 (52)	12 (48)	0 (0)	0 (0)	0 (0)	

A substantial difference between the groups was observed concerning the SAQ scores' improvement after 2 months of intervention from baseline, with much greater significant mean changes in the ubiquinol group compared to the control group (p value < 0.001 according to both SAQ numerical scores and SAQ categorical grades, tables 7 and 8). The mean change of SAQ-Summary score in the ubiquinol group was 55.93 ± 19.71 compared to 11.47 ± 16.47 in the control group and the mean change was 52.00 ± 25.15 vs 7.00 ± 18.74, respectively, in the domain of SAQ-Physical Limitation and 71.00 ± 28.35 vs 13.00 ± 18.92, respectively, in the domain of SAQ-Quality of Life.

Furthermore, patients in the ubiquinol group reported significantly larger reductions in angina episodes compared to the control group (mean change of 44.80 ± 13.88 vs 14.40 ± 15.57, p value < 0.001).

TABLE 7. Comparison between changes in SAQ categories of the control and Ubiquinol groups after 2 months of intervention

SAQ-7 Post Physical Limitation Grades					
Group Name	Grade 1 (Poor health) n (%)	Grade 2 (Fair health) n (%)	Grade3 (Good health) n (%)	Grade 4 (Excellent Health) n (%)	P value
Control	9 (36)	7 (28)	9 (36)	0 (0)	0.001
Ubiquinol	0 (0)	0 (0)	1 (4)	24 (96)	
SAQ-7 Post Anginal Frequency Grades					
Group Name	Grade 1 (Daily angina) n (%)	Grade 2 (Weekly angina) n (%)	Grade3 (Monthly angina) n (%)	Grade 4 (No angina) n (%)	P value
Control	0 (0)	12 (48)	13 (52)	0 (0)	0.001
Ubiquinol	0 (0)	0 (0)	13 (52)	12 (48)	
SAQ-7 Post Quality of Life Grades					
Group Name	Grade 1 (Poor health) n (%)	Grade 2 (Fair health) n (%)	Grade3 (Good health) n (%)	Grade 4 (Excellent Health) n (%)	P value
Control	5 (20)	11 (44)	8 (32)	1 (4)	0.001
Ubiquinol	0 (0)	1 (4)	0 (0)	24 (96)	
SAQ-7 Post Summary Grades					
Group Name	Grade 1 (Poor health) n (%)	Grade 2 (Fair health) n (%)	Grade3 (Good health) n (%)	Grade 4 (Excellent Health) n (%)	P value
Control	4 (16)	10 (40)	11 (44)	0 (0)	0.001
Ubiquinol	0 (0)	0 (0)	1 (4)	24 (96)	

TABLE 8. The net difference in SAQ scores' improvements before and after 8 weeks of intervention between both control and Ubiquinol groups

Character	Control Group	Ubiquinol Group	P value
SAQ-7 PL Score Change	7.00 ± 18.74	52.00 ± 25.15	0.001
SAQ-7 AF Score Change	14.40 ± 15.57	44.80 ± 13.88	0.001
SAQ-7 QOL Score Change	13.00 ± 18.92	71.00 ± 28.35	0.001
SAQ-7 Summary Score Change	11.47 ± 16.47	55.93 ± 19.71	0.001

SAQ-7 PL = Seattle Angina Questionnaire-7 Physical Limitation domain, SAQ-7 AF = Seattle Angina Questionnaire-7 Angina Frequency domain, SAQ-7 QOL= Seattle Angina Questionnaire-7 Quality of Life domain

DISCUSSION

The burden of CVDs is increasing every year. Although their management has greatly improved over the years, it is still far from perfect. Thus, new management approaches are required.(11,22) Increasing evidence attributes CoQ10 deficiency, an essential compound of the human body, to cardiovascular disorders and its supplementation might be beneficial in various cardiac diseases.(2,23) Furthermore, studies have found that ubiquinol, the active form of CoQ10, has 6–10 times higher bioavailability than ordinary CoQ10.(18,20) According to the best of our knowledge, there have not been any clinical trials on the effect of Ubiquinol on angina and dyspnea levels in CAD patients; therefore, we aimed to study this in ACS patients after PCI.

Patient-reported outcomes (PROs) are progressively utilized as standard assessment tools in clinical practice and trials, because their use has the opportunity to increase patient centered care by involving patient experiences.(24,25) For patients with CAD, the SAQ is the most frequently used tool for measurement of patient's health status in order to appraise severity of angina and the extent of its influence on their functioning and QOL. SAQ scores have shown to be highly valid, sensitive to clinical change and strongly associated with the risk of mortality, hospitalization, MI, and costs (according to prior work, a change of 8–10 points in any of the subscales or summary scores is considered to be clinically important).(25–28)

Among the SAQ domains, the Physical Limitation score is most predictive of mortality;

notably, scores of 50-74, 25-49, and 0-24 are associated at one year with 1.5, 2, and 4 fold higher odds of death, correspondingly, as opposed to scores of 75-100.(29) On the contrary, the SAQ-Angina Frequency score is most predictive of cardiovascular hospitalizations with daily, weekly and monthly angina attributed to a 2.2, 1.4 and 1.3 fold higher odds of cardiac rehospitalization at one year.(24) To get this into perspective, in current study on patients with similar risk of clinical events, 36% of the patients in the control group still had SAQ-Physical Limitation score <25 and 48% of them had yet experienced weekly angina after intervention, they are 4 times as likely to experience death and 1.4 times as likely to encounter hospital admission for an ACS in contrast to the ubiquinol group with none of the patients having such scores.

The SAQ is not able to assess if patients are experiencing dyspnea or other anginal equivalents. In order to defeat this limitation, the most common method is to supplement the SAQ with the Rose Dyspnea Scale.(26) The RDS has been validated and revealed to be associated with cardiovascular rehospitalization, QOL and morbidity in CAD patients.(27,30) A one-unit change in the RDS would be regarded as clinically significant because it is an ordinal scale.

Among the 50 patients who expressed dyspnea at baseline, in the control group; 11 (44%) had improvement in their dyspnea, 12 (48%) had an unchanged dyspnea level, and 2 (8%) had worsened dyspnea after the intervention. While in the Ubiquinol group, only one patient (4%) had no change and 24 (96%) had >= 1 unit improvement. On average, there was a 2.04 ± 0.79 unit improvement in RDS in the Ubiquinol group compared with a 0.32 ± 1.07 unit change in the control group (p value < 0.001). This difference is highly significant and has an extremely important clinical impact on patients' QOL. Noteworthy, as far as we know, there has not been any study conducted on the effect of even ordinary CoQ10 on dyspnea in CAD patients, but there are a few studies on CoQ10's effect on dyspnea in COPD and asthmatic patients. However, they cannot be compared since the causes and mechanism of dyspnea in CAD patients are totally different.

After 2 months of the intervention, this study has demonstrated a much higher SAQ-AF improvement in the ubiquinol group compared to the control group, an average of 44.8 ± 13.88 compared to 14.4 ± 15.57 score improvements, respectively (p value < 0.001). These results are relevant with a number of studies that have shown CoQ10 to be effective in the treatment of angina via reductions in both anginal frequency and use of nitroglycerin.(31,32) In contrast, Kamikawa and his colleagues could not obtain such significant results, this might be due to their use of low dose and ubiquinone form of CoQ10.(33)

Complications of acute MI involve LVD as a result of myocardial remodeling and functioning loss that are thought to be mainly because of reduced energy synthesis (deficit CoQ10) and lipoxidation.(34,35) The aforementioned ventricular remodeling in combination with CoQ10 deficiency may lead to an impaired prognosis and/or heart failure, which is the major cause of morbidity and mortality in patients with acute MI.(36)

Ubiquinol might be an important therapeutic aid for prevention of such complications because several clinical trials have revealed that treatment with CoQ10 could limit myocardial remodeling, restore myocardial tissue CoQ10 deficiency (34), increase post-ischemic recovery (37) and increase less ST-segment depression.(32) With end results of significant improvement in angina severity, arrhythmia and LVD.(38) Furthermore, circulating CoQ10 levels have also shown gradual reduction with time in patients with acute MI, but a higher CoQ10 plasma level at one month post angioplasty was correlated with favorable LV remodeling and systolic performance 6 months after ST- segment elevation MI. STEMI.(39)

Improvement of all of those factors would contribute to improvements in patients' health status, physical activity limitation and QOL, this was actually relevant in this study results, which demonstrate a highly significant difference between the groups in terms of improving these domains of SAQ scores with larger improvements in the ubiquinol group. On average, the SAQ-Physical Limitation score was improved by 52 ± 25.14 in the ubiquinol group compared to 7 ± 18.7 in the control group, and the most dominant improvement was in the SAQ-Quality of Life score which was increased by 71 ±28.35 in the ubiquinol group compared to 13 ±18.91 in the control group (p value < 0.001).

Worthy to mention about this study is the great difference between the groups also in SAQ-

Summary score improvement after 8 weeks of intervention, which was 55.93 ± 19.71 in the ubiquinol group but 11.47 ± 16.47 in the control group (p value < 0.001).

As a result, the better improvements of the ubiquinol group could be attributed to several reasons. First of all, CoQ10's plasma levels in patients with CAD were demonstrated to be much lower than in healthy ones, and its concentration also decreases with aging.(16,34) Secondly, statin use among them depletes the body of CoQ10 even more.(17) Thirdly, CoQ10 plays a fundamental role in the heart's bioenergetic requirements.(16) Fourthly, the protective effect of CoQ10 could be elucidated by its influence on coagulation. Zozina et al. have found reductions in plasma fibronectin, thromboxane B2, prostacyclin, and endothelin-1 after 200 mg of CoQ10 administration per day for 20 days.(23)

Furthermore, the better results revealed by our study might be due to the utilization of ubiquinol instead of ordinary CoQ10, since most researches to date have been limited to the use of low doses of ubiquinone rather than appropriate doses of ubiquinol.

Studies have shown that Ubiquinol has 6–10 times higher bioavailability than ordinary CoQ10; hence, higher ubiquinol plasma levels can be achieved with lower dosages.(18,20) Oxidized CoQ10 (ordinary CoQ10 or Ubiquinone) should first be converted to the ubiquinol form in order to completely exert its pharmacologic effect, but by the age of 20, the body's ability for this metabolization begins to decline. Hence, patients aged over 20 years old are recommended to take ubiquinol instead of ordinary CoQ10. (18,21,40)

A limitation of this study was the duration, because it was inadequate to enroll larger number of patients, and 2 months of intervention might not be enough to evaluate long-term outcomes. Nevertheless, the standard questionnaires used have been extensively investigated and their strong association with long-term end-points have been widely approved.

CONCLUSION

This study demonstrates that ubiquinol (200 mg/day) addition to OMT after ACS has a highly significant effect on improving clinical outcomes and patients' quality of life through greater reductions in anginal frequency, physical limitations and dyspnea severity. These findings suggest that Ubiquinol could be an effective and safe therapeutic strategy in clinical practice for optimizing the therapeutic outcome of CAD and secondary prevention of consequent cardiovascular events since larger improvements in SAQ scores and RDS have been approved to be strongly associated with greater reductions in morbidity and mortality and improved QOL.

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