



## ORIGINAL ARTICLE

# Effect of hydrosoluble coenzyme Q10 on blood pressures and insulin resistance in hypertensive patients with coronary artery disease

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In a randomised, double-blind trial among patients receiving antihypertensive medication, the effects of the oral treatment with coenzyme Q10 (60 mg twice daily) were compared for 8 weeks in 30 (coenzyme Q10: group A) and 29 (B vitamin complex: group B) patients known to have essential hypertension and presenting with coronary artery disease (CAD). After 8 weeks of follow-up, the following indices were reduced in the coenzyme Q10 group: systolic and diastolic blood pressure, fasting and 2-h plasma insulin, glucose, triglycerides, lipid per-

oxides, malondialdehyde and diene conjugates. The following indices were increased: HDL-cholesterol, vitamins A, C, E and beta-carotene (all changes  $P < 0.05$ ). The only changes in the group taking the B vitamin complex were increases in vitamin C and beta-carotene ( $P < 0.05$ ). These findings indicate that treatment with coenzyme Q10 decreases blood pressure possibly by decreasing oxidative stress and insulin response in patients with known hypertension receiving conventional antihypertensive drugs.

**Keywords:** hypertension; coronary disease; insulin resistant antioxidant vitamin; oxidant stress

## Introduction

Clinical and experimental studies indicate that coenzyme Q10 deficiency may be associated with hypertension, hyperlipidaemia, coronary artery disease (CAD) and congestive heart failure.<sup>1–7</sup> Coenzyme Q10 supplementation has been reported to be protective against cardiovascular disease.<sup>1–4</sup> Several investigators claim that coenzyme Q10 can decrease blood pressure in experimental models as well as in patients with hypertension.<sup>2,5–10</sup> No large scale, long-term placebo controlled studies have been published that demonstrates the hypotensive effect of coenzyme Q10.

Recent studies<sup>11–14</sup> indicate that free radical stress is an important mechanism for the development of hypertension which poses the possibility that antioxidants could be another line of management in the treatment of hypertension with oxidative stress. Digiesi *et al*<sup>8–10</sup> reported that the antihypertensive effect of coenzyme Q10 may be due to a decrease in peripheral vascular resistance as a result of improved metabolism of arteriolar smooth muscle cells.<sup>9</sup> Coenzyme Q10 in its reduced form is a potent antioxidant<sup>15</sup> and membrane stabilising agent and it

may also inhibit catecholamines and might improve insulin action and are important in the pathogenesis of hypertension.<sup>1,2,16,17</sup> Langsjoen *et al*<sup>2</sup> supplemented coenzyme Q10 to the presenting antihypertensive drug therapy in 190 patients who were known to have hypertension for several years and reported reduction in blood pressures, improvement in cardiac function and decreased requirement of antihypertensive drug therapy. However in this study, all the patients did not have CAD. No randomised study has examined the effect of coenzyme Q10 in known hypertensives with CAD. In the present study, we tested the hypothesis that treatment with coenzyme Q10 can decrease blood pressure and oxidative stress in patients with known hypertension and CAD.

## Subjects and methods

All patients who were receiving antihypertensive medication for more than 1 year and had coexisting CAD on admission to hospital were considered for inclusion to this substudy. This study is a part of the main trial of coenzyme Q10 in patients who present with acute CAD,<sup>18</sup> therefore sample size calculations were not done. In the earlier paper, only acute CAD and its outcome was discussed.

Angina pectoris ( $n = 8$ ) was diagnosed by a history of cardiac chest pain of <30-min duration and a positive electrocardiogram showing ST segment depression or more than 2 mm in chest leads and

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1 mm in the limb leads and/or T wave inversions with a positive response to sublingual nitrates. Myocardial infarction ( $n=45$ ) was considered<sup>19</sup> in the presence of any of the two criteria, a record showing a history of classical chest pain, electrocardiographic changes consistent with myocardial infarction and more than double the rise in cardiac enzymes, creatinine phosphokinase and serum glutamic oxalotransferase of normal values. Unstable angina ( $n=6$ ) was diagnosed if cardiac chest pain lasted for  $>30$  min without a significant increase in enzymes or absence of diagnostic electrocardiographic changes or a combination. The exclusion criteria were: if the patients had none of the above features and non-CAD diagnosis was considered ( $n=4$ ), death before randomisation ( $n=3$ ), patients lost to follow-up ( $n=5$ ), blood urea  $>40$  mg/dL ( $n=1$ ), diarrhoea or dysentery or persistent vomiting ( $n=1$ ), or known hypertension of  $<1$  year duration ( $n=2$ ). All patients presented within 3 days of the onset of chest pain and were hospitalised for 2–10 days. Out of a total of 59 patients who completed this study, 93.2% ( $n=55$ ) were receiving monotherapy for hypertension.

### Treatment

The subjects in both groups remain blinded to whether or not they were in the control or coenzyme Q10 group and both the groups met separately. The test products were provided to patients in identical containers in all respects. We used B-complex vitamin capsules in control group B patients which are not known to cause any decrease in blood pressure during a trial of 8 weeks. The test drug coenzyme Q10 is marketed under the trade name Q-gel<sup>20</sup> which is a hydrosoluble coenzyme Q10 softsules (Tishcon Corporation, USA). Each capsule of Q-gel contains 30 mg coenzyme Q10. All patients in the intervention group (group A) were administered two capsules twice daily (120 mg of coenzyme Q10/day) from the same lot of Q-gel. The control group capsules containing thiamine mononitrate IP 3 mg, riboflavin IP 3 mg, pyridoxine hydrochloride IP 1 mg and nicotinamide IP 25 mg (two capsules twice daily) were administered in the comparison group B. Drug compliance was monitored by counting the number of capsules returned by the patients on follow-up visits or each day during hospitalisation. Both groups received similar advice on diet and lifestyle factors through a printed sheet given to each patient.

### Study design

All patients with the clinical diagnosis of CAD who were receiving antihypertensive medication for at least 1 year and had a clear diagnosis of hypertension was asked to give a written, duly informed consent (approved by the review board of human studies in our centre) to participate in the study. Each was individually randomised by the pharmacist to receive either coenzyme Q10 or vitamin capsules supplied in identical containers by the Heart Research Laboratory blinded to physicians and tech-

nicians examining the blood.<sup>18</sup> Treatment group A received coenzyme Q10 and the control group B received B-complex vitamins for the follow-up period of 8 weeks while maintaining similar diet and lifestyle in both groups. All other treatments such as nitrate, aspirin, and antihypertensive drugs were given to both groups of patients. Baseline blood pressure and heart rates were recorded after the observation period of 24 h in basal resting condition in the hospital. At the end of study, blood pressures were recorded in similar basal conditions.

### Clinical data

Blood pressure was measured in the right arm with a mercury manometer after a 5-min rest with the patient resting comfortably in a supine position. Phase V Korotkoff sounds were recorded for diastolic blood pressure. Blood pressure  $>140/90$  mm Hg was considered as hypertension. Alcohol intake was considered in the presence of alcohol consumption (60 ml or above of whisky or 740 ml or beer) at least once in a week. Smoking was considered to be the smoking of one or more cigarettes or beedies per day. A 12-lead electrocardiograph recorded in all the patients at entry to the study and whenever indicated in all the patients. Clinical data, angina pectoris, complications, drug intake and their adverse effects were recorded for 8 weeks with the help of a questionnaire unaware of treatment groups. All patients were followed at weekly intervals. Drug intake was reduced if the systolic blood pressure decreased  $<120$  mm Hg and angina did not occur in last 48 hours.

### Laboratory data

Blood samples were drawn at entry and later in a fasting state in the morning. Blood was analysed for blood counts, haemoglobin, urea, glucose, cardiac enzymes, lipid peroxides (thiobarbituric acid reactive substances, TBARS), malondialdehyde, and diene conjugates as well as vitamin A, E and C and beta-carotene in all the patients.<sup>20–25</sup> Serum or heparin plasma was stored in a refrigerator after centrifugation. All the reagents were made in our laboratory. Laboratory personnel analysing the blood were blind to the two treatment groups. An increase in plasma levels of TBARS, malondialdehyde and diene conjugates are indicators of free radical stress.

The coefficient of variation for vitamin A, E and C and beta-carotene were 4.1%, 3.4%, 4.5% and 2.2% respectively.

Fasting and 2-h plasma insulin<sup>26</sup> and glucose levels after taking 75 g oral glucose mixed with 200 ml water, were obtained in all the patients. Plasma levels of vitamin A, E and C and beta-carotene were obtained by colorimetric methods.<sup>24,25</sup> Enzymatic methods were used to determine total cholesterol. High density lipoprotein (HDL) cholesterol was estimated after precipitation of non-HDL cholesterol with manganese heparin substrate.

## Statistical analysis

Statistical comparisons were done by Friedman's two-way (repeated measures) analysis of variance for ordinal variables. Chi square test (Z score) for proportion were used to obtain the statistical significance among the intervention and control group. A *P* value <0.05 and two-tailed *t*-test were considered significant. Those patients who were not available during the follow-up were excluded from the analysis. Blood pressure recorded after 24 h of observation period was considered as baseline blood pressure. Data is shown as mean and standard deviation, number of subjects, or per cent incidence.

## Results

Of 64 hypertensive patients with CAD who were randomised to either coenzyme Q10 group A (*n* = 32) or control group B (*n* = 32), two patients in group A and three in group B were not available for follow-up during the period of 8 weeks. Mean age, body weight, and body mass index were comparable between the two groups (Table 1). Current smokers were slightly more frequent in the intervention group, but male sex alcohol intake, myocardial infarction, unstable angina and angina pectoris were comparable. In the prior drug therapy, nifedipine intake was slightly higher and enalapril maleate intake lower in the coenzyme Q10 group than the control group. Drug therapy at entry to the study showed that nitrate intake was significantly lower in the coenzyme Q10 group but antihypertensive drugs diltiazem, metoprolol and enalapril maleate intakes

were comparable between the two groups. Drug intake at completion of study revealed that the consumption of diltiazem, metoprolol, enalapril maleate and nitrate were significantly lower in the coenzyme Q10 group than placebo group (Table 1).

Table 2 shows that systolic and diastolic blood pressure, heart rate and waist-hip ratio in men showed significant decline in the coenzyme Q10 group than control group. Fasting and 2-h plasma insulin and glucose levels and fasting triglyceride levels showed significant reduction whereas HDL cholesterol showed significant increase in the coenzyme Q10 group compared to the control group. Fasting plasma insulin/fasting glucose ratio also showed greater decline in the intervention group compared to control group. The net reductions in systolic and diastolic blood pressures, heart rate, waist-hip ratio, fasting and 2-h plasma insulin and glucose levels and triglycerides levels and net increase in HDL-cholesterol were also significantly greater in the coenzyme Q10 group compared to the control group (Table 2). Body weights which were comparable at entry to study showed only non-significant minor decrease at 8 weeks of follow-up in coenzyme Q10 and placebo groups respectively ( $65.0 \pm 5.7$  vs  $64.6 \pm 5.3$  kg).

After 4 weeks of follow-up, systolic blood pressure, fasting plasma insulin and blood glucose levels respectively showed significantly a decline in the coenzyme Q10 group than control group (Table 2).

Mean levels of antioxidant vitamin A, E, C and vitamin E/cholesterol ratio and beta-carotene showed significant greater rise in the coenzyme Q10 group than the control group. However, TBARS, malondialdehyde and diene conjugates (which are indicators of free radical stress and were comparable at entry), showed significant reduction both at 4 and 8 weeks in the intervention group A compared to the B vitamin group control group (Table 3). At 4 weeks, vitamin E, C and beta-carotene showed a significant rise in the coenzyme Q10 group whereas only vitamin C and beta-carotene were significantly increased in the control group.

Angina pectoris assessed by questionnaire (6.6 vs 44.8%, *P* < 0.05) and sublingual trinitrate consumption (6.5 vs 20.6 mg/day, *P* < 0.02) were also significantly less in the coenzyme Q10 group compared to the control group. Adverse effects of test medications such as nausea (6 vs 3) vomiting (2 vs 1) and headache (1 vs 1), and abdominal discomfort (2 vs 1) were slightly more in the coenzyme Q10 group than the control group.

## Discussion

This study shows that treatment of blood pressure in patients with known hypertension and CAD with coenzyme Q10 (60 mg twice daily) administration may be associated with a significant reduction in systolic and diastolic blood pressure in the coenzyme Q10 group compared to control group during a follow-up period of 8 weeks. Fasting plasma insulin and glucose levels and 2-h plasma insulin and glucose concentrations also showed a significant decline in the intervention group compared to

**Table 1** Characteristics of randomised subjects at entry to study

	Coenzyme Q10 ( <i>n</i> = 30)	Placebo ( <i>n</i> = 29)
Men	26 (86.6)	26 (89.6)
Mean age (years)	48.3 ± 7.2	48.0 ± 7.0
Body weight (kg/m <sup>2</sup> )	65.1 ± 5.7	64.8 ± 5.3
Body mass index (kg/m <sup>2</sup> )	23.9 ± 1.2	23.8 ± 1.1
Current smokers	17 (56.6)	13 (44.8)
Alcohol intake	6 (20.0)	6 (20.7)
Coronary artery disease		
Myocardial infarction	24 (80.0)	21 (72.4)
Unstable angina	2 (6.6)	4 (13.8)
Angina pectoris	4 (13.3)	4 (13.8)
Prior drug therapy		
Diltiazem	10 (33.3)	11 (37.9)
Nifedipine	16 (53.3)	10 (34.5)
Enalapril maleate	4 (13.3)	8 (27.6)
Nitrate	4 (13.3)	3 (10.4)
Aspirin	3 (10.0)	3 (10.4)
Drug therapy given on admission		
Diltiazem (60–180 mg/day)	162 ± 16	156 ± 17
Metoprolol (40–120 mg/day)	100 ± 6	105 ± 7
Enalapril maleate (5–10 mg/day)	7.5 ± 1.2	8.1 ± 1.5
Aspirin (75–150 mg/day)	92 ± 8	105 ± 10
Nitrates (20–10 mg/day)	65 ± 5*	90 ± 8
Drug therapy at the end of the study		
Diltiazem (60–180 mg/day)	110 ± 10*	160 ± 18
Metoprolol (40–120 mg/day)	76 ± 5*	108 ± 9
Enalapril maleate (5–10 mg/day)	4.2 ± 0.8*	8.2 ± 1.3
Aspirin (75–150 mg/day)	97 ± 8	102 ± 8
Nitrates (20–10 mg/day)	56 ± 4*	85 ± 7

\**P* < 0.05.

**Table 2** Clinical and biochemical data at baseline and during follow-up

	Coenzyme Q10 (n = 30)			Placebo (n = 28)			Differences in two groups at 8 weeks (95% CI)
	Baseline	4 weeks	8 weeks	Baseline	4 weeks	8 weeks	
Heart rate per minute	112 ± 7.8	102 ± 6.5	85 ± 4.8*	115 ± 8.2	112 ± 6.7	105 ± 6.7	20* (9.6–31.6)
Blood pressure (mm Hg)							
Systolic	168 ± 9.6	160 ± 8.5*	152 ± 8.2*	166 ± 8.5	167 ± 8.6	164 ± 8.2	-11.6* (5.2–23.2)
Diastolic	106 ± 4.6	104 ± 4.2	97 ± 4.1*	105 ± 4.8	106 ± 4.8	103 ± 4.6	-95.7* (28.2–202.5)
Waist-hip ratio							
Male	0.94 ± 0.15	0.93 ± 0.12	0.92 ± 0.13*	0.94 ± 0.14	0.94 ± 0.14	0.94 ± 0.14	-0.2* (0.005–0.0046)
Female	0.89 ± 0.12	0.88 ± 0.11*	0.87 ± 0.11*	0.88 ± 0.12	0.89 ± 0.12	0.89 ± 0.12	-0.2* (90.006–0.047)
Fasting plasma insulin (pmol/L)	465 ± 57	362 ± 42*	257 ± 45*	460 ± 52	441 ± 44	421 ± 48	-164* (78.4–336)
2-hour plasma insulin (mmol/L)	618 ± 68	502 ± 55*	398 ± 45*	609 ± 65	590 ± 60	567 ± 63	169* (75.6–345)
Fasting blood glucose (mmol/L)	7.86 ± 1.1	6.52 ± 1.0*	5.26 ± 1.1*	7.78 ± 1.0	7.56 ± 1.1	7.18 ± 0.8	-1.92* (0.82–3.76)
2-hour blood glucose (mmol/L)	9.12 ± 1.5	7.62 ± 1.2	6.25 ± 1.3*	8.92 ± 1.3	8.61 ± 1.3	8.22 ± 1.2	1.97* (0.91–11.4)
Fasting plasma insulin/fasting blood glucose ratio	59.1 ± 5.7	55.5 ± 5.6	48.8 ± 5.2*	59.1 ± 5.6	58.3 ± 5.4	54.5 ± 5.4	-5.7* (2.3–11.4)
Fasting triglycerides (mmol/L)	1.8 ± 0.58	1.78 ± 0.55	1.62 ± 0.53*	1.78 ± 0.52	1.76 ± 0.53	1.75 ± 0.51	-0.31* (0.05–0.27)
High density lipoprotein cholesterol (mmol)	1.14 ± 0.20	1.18 ± 0.19	1.024 ± 0.18*	1.15 ± 0.21	1.14 ± 0.19	1.14 ± 0.19	+0.1* (0.04–0.22)

Values are expressed as mean ± ISD. CI = confidence interval. \* $P < 0.05$ , \*\* $P < 0.01$ .

**Table 3** Plasma concentrations of antioxidants and oxidative stress at baseline and during follow-up

	Coenzyme Q10 (n = 30)			Placebo (n = 28)			Differences in two groups at 8 weeks (95% CI)
	Baseline	4 weeks	8 weeks	Baseline	4 weeks	8 weeks	
Vitamin A ( $\mu\text{mol/L}$ )	1.91 ± 0.11	2.18 ± 0.12	2.52 ± 0.13*	1.94 ± 0.12	2.06 ± 0.13	2.11 ± 0.13	0.41* (0.18–0.92)
Vitamin E ( $\mu\text{mol/L}$ )	15.6 ± 2.6	25.6 ± 3.0*	34.4 ± 4.5**	14.6 ± 2.4	16.8 ± 2.3	17.8 ± 2.2	16.6** (6.7–3.2)
Vitamin E/Cholesterol	2.76 ± 0.32	3.1 ± 0.30	4.57 ± 0.57/*	2.63 ± 0.53	2.8 ± 0.58	3.01 ± 0.65	1.56* (0.71–3.5)
Vitamin C ( $\mu\text{mol/L}$ )	3.71 ± 1.1	20.0 ± 3.2*	26.3 ± 4.1**	4.0 ± 1.2	9.8 ± 2.5*	13.6 ± 3.2*	12.7* (5.5–25.1)
Beta-carotene ( $\mu\text{mol/L}$ )	0.15 ± 0.03	0.38 ± 0.07*	0.6 ± 0.11**	0.17 ± 0.03	0.26 ± 0.04*	0.3 ± 0.06*	0.3* (0.12–0.62)
TBARS (pmol/L)	1.66 ± 0.27	0.84 ± 0.16*	0.78 ± 0.12*	1.67 ± 0.26	1.65 ± 0.24	1.6 ± 0.23	-0.82* (0.35–1.7)
Malondialdehyde (pmol/L)	1.77 ± 0.28	0.90 ± 0.18*	0.900.15*	1.68 ± 0.27	1.66 ± 0.25	1.6 ± 0.22	-0.7** (0.32–1.52)
Diene conjugates (OD Units)	29.8 ± 3.4	24.6 ± 3.1*	23.1 ± 3.0*	30.2 ± 3.6	28.8 ± 3.4	28.6 ± 3.5	- 5.5* (2.4–10.6)

Values are expressed as mean ± ISD. CI = confidence interval. \* $P < 0.05$ , \*\* $P < 0.01$ . TBARS = thiobarbituric acid reactive substance.

the control group. While HDL-cholesterol showed a significant increase, triglycerides revealed a significant decline in the coenzyme Q10 group compared to the control group. Fasting plasma insulin/fasting glucose ratio which is an indicator of impaired insulin action showed a significant reduction in the coenzyme Q10 group than the placebo group. These results indicate that treatment with coenzyme Q10 reduces hypertension, hyperinsulinaemia, hyperglycaemia, hypertriglyceridaemia and increases HDL-cholesterol which are indicators of insulin resist-

ance syndrome.<sup>27</sup> There was a significant decrease in antihypertensive drugs in the active treatment group which also indicated that the reduction in blood pressures and drug intake may be due to coenzyme Q10 on account of a decrease in insulin resistance.

Apart from the above finding, there was a significant marked rise in the plasma levels of antioxidant vitamins A, E and C and beta-carotene from the initial low levels and a reduction in the TBARS, malondialdehyde and diene conjugates in the coenzyme Q10 group than the control group. Control

group B also showed a significant rise in the plasma levels of vitamin C and beta-carotene at 4 and 8 weeks. These biochemical parameters are indicators of free radical stress in patients with hypertension and CAD.<sup>11-14</sup> Low concentrations of vitamin C and decrease in vitamin A and E and beta-carotene initially after acute myocardial infarction with a spontaneous increase in the next few weeks of follow-up have also been reported in other studies.<sup>28-31</sup> It seems that treatment with coenzyme Q10 has a sparing effect on other antioxidants due to its protective effects on myocardium in high risk patients with acute myocardial stress and free radical stress. Although the free radical stress is maximum during the first few hours of ischaemia and reperfusion, reactive oxygen species continue to produce free radicals during several weeks of follow-up in patients with chronic CAD and hypertension.<sup>11-14</sup> It is possible that acute myocardial stress in acute myocardial infarction (AMI) may be associated with increased consumption of antioxidant reserve to fight against free radicals resulting in a marked decrease in vitamins and coenzyme Q10 status which recovers gradually with a decrease in myocardial stress.<sup>28-31</sup> Therefore a part of the increase in vitamin levels in both the groups may be due to spontaneous decrease in free radical stress and increased intake through dietary supplementation. No other study has examined the effect of coenzyme Q10 on vitamin levels in patients with AMI. It is possible that a part of the decrease in blood pressure may be due to a decrease in oxidative stress,<sup>11-13</sup> which may be a cause of hypertension. However, there are a large number of data comparisons indicating multiple causes of hypertension in the coenzyme Q10 and placebo-treated groups. It is also not clear how many of these results are false-positive indicating further study.

The exact mechanisms how coenzyme Q10 decreases blood pressure and how oxidative stress causes hypertension and hyperinsulinaemia are not known.<sup>11-13</sup> Beta cells of the pancreas are highly susceptible to damage because of the poor endogenous antioxidant enzyme system. Coenzyme Q10 is also a normal constituent of beta cells and liver.<sup>16</sup> The beta function and glucose and fatty acid metabolism in the liver may worsen in the presence of a deficiency of coenzyme Q10, vitamin A, E and C and beta-carotene resulting in impaired insulin action and hyperinsulinaemia.<sup>11-14,27</sup> Oxidative stress also impairs the metabolism of arterial smooth muscle cells and endothelial function which may cause increased peripheral vascular resistance.<sup>11</sup> It is also possible that oxidative stress and hyperinsulinaemia may be associated with higher catecholamine levels and may predispose vascular resistance and hypertension.<sup>27,32</sup> There is evidence that hyperinsulinaemia can predispose hypertension.<sup>33,34</sup>

Treatment with coenzyme Q10 may provide protection to beta cells of the pancreas, liver cells and arterial smooth muscles and endothelial cells resulting in improved cell metabolism and insulin action<sup>16,27,32</sup> and decrease in peripheral vascular resistance and hypertension. Coenzyme Q10 is a potent antioxidant which is known to protect

against genetic damage and prevent human vitronection receptor expression.<sup>35</sup> This poses the possibility that coenzyme Q10 might also down-regulate insulin receptors and improve leptin expression and insulin action.<sup>36</sup> Leptin concentration is positively associated with insulin resistance which is secreted by a gene in obese and non-obese subjects.<sup>26,32,36</sup> It is also possible that insulin resistance syndrome observed in south Asians may, at least in part, be due to oxidative stress as a result of a poor antioxidant system.<sup>32-34</sup> Insulin is also known<sup>27</sup> to have adverse effects on proliferation of smooth muscle cells and possibly endothelial cells either directly or by potentiating growth factors.

Experimental studies indicate that coenzyme Q10 deficiency may be associated with hypertension and treatment with coenzyme Q10 can decrease blood pressures.<sup>5-7</sup> In one double-blind trial, Yamagami reported<sup>37</sup> a significant decrease in blood pressure in the intervention group. Digiesi *et al*<sup>8-10</sup> showed that coenzyme Q10 had an independent antihypertensive effect without any influence on plasma renin activity, urinary aldosterone or serum and urinary sodium and potassium. In a more recent study,<sup>2</sup> treatment with coenzyme Q10 (225 mg/day) in 109 patients with hypertension caused a substantial reduction in mean systolic (from 159 to 147 mm Hg) and diastolic (94 to 85 mm Hg) blood pressures with concomitant improvement in functional class, blood pressure and myocardial function. Our study also showed a significant decrease in angina pectoris and nitrate consumption indicating that coenzyme Q10 supplementation may be a drug of choice for hypertensive patients with CAD.

In conclusion, the findings of our study indicate that coenzyme Q10 administration can decrease blood pressure and a need for classical antihypertensive drugs in patients with known hypertension. Treatment with coenzyme Q10 may also decrease oxidative stress and hyperinsulinaemia which are important in the pathogenesis of hypertension and CAD in Indians.<sup>34</sup> Long-term intervention trials would be necessary to confirm whether treatment with coenzyme Q10 can decrease insulin resistance syndrome.

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## References

- 1 Enster L, Dallner G. Biochemical, physiological and medical aspects of ubiquinone function. *Biochimica Biophys Acta* 1995; **1271**: 195-204.
- 2 Langsjoen P, Langsjoen P, Willis R, Folkers R. Treatment of essential hypertension with coenzyme Q10. *Mol Aspects Med* 1994; **15** (Suppl): 265-272.
- 3 Kontush A *et al* Plasma ubiquinol is decreased in patients with hyperlipidemia. *Atherosclerosis* 1997; **129**: 119-126.
- 4 Yokoyama H *et al* Coenzyme Q10 protects coronary endothelial function from ischemia reperfusion injury via an antioxidant effect. *Surgery* 1996; **120**: 189-196.

- 5 Iwamoto Y, Yamagami T, Folkers K, Bloomquist CG. Deficiency of coenzyme Q10 in hypertensive rats and reduction of deficiency by treatment with coenzyme Q10. *Biochem Biophys Res Comm* 1974; **58**: 743–748.
- 6 Yamagami T, Iwanoto Y, Folkers K, Bloomquist CG. Reduction by coenzyme Q10 of hypertension induced by deoxycorticosterone and saline in rats. *Int J Vit Nutr Res* 1974; **44**: 487–496.
- 7 Okamoto H, Kawaguchi H, Togashi H. Effect of coenzyme Q10 on structural alterations in the renal membrane of stroke-prone spontaneously hypertensive rats. *Biochem Metab Biol* 1991; **45**: 216–226.
- 8 Digiesi V, Cantini F, Brodbeck B. Effect of coenzyme Q10 on essential arterial hypertension. *Curr Ther Res* 1990; **47**: 841–845.
- 9 Digiesi V *et al* Coenzyme Q10 in essential hypertension. *Mol Aspects Med* 1994; **15** (Suppl): 275–283.
- 10 Digiesi V *et al* Mechanism of action of coenzyme Q10 in essential hypertension. *Curr Ther Res* 1992; **51**: 668–672.
- 11 Sagar S *et al* Oxygen free radicals in essential hypertension. *Mol Cell Biochem* 1992; **110**: 103–108.
- 12 Vijaya Kumar K, Das UN. Are free radicals involved in pathobiology of human essential hypertension. *Free Rad Res Comm* 1993; **19**: 59–66.
- 13 Singh RB *et al* Plasma levels of antioxidant vitamins and oxidative stress in health and disease. A hospital based case control study. *J Nutr Environ Med* 1995; **5**: 235–242.
- 14 Ceriello A, Giugliano D, Quattraro A. Antioxidant show an anti-hypertensive effect in diabetic and hypertensive subjects. *Clin Sci* 1991; **81**: 739–749.
- 15 Stocker R, Bowry WV, Frei B. Ubiquinol-10 protects human low density lipoproteins more efficiently against lipid peroxidation than does alpha-tocopherol. *Proc Natl Acad Sci, USA* 1991; **88**: 1646–1650.
- 16 Caballero B. Vitamin E improves the action of insulin. *Nutr Review* 1993; **51**: 339–340.
- 17 Ursini F, Gambini C, Paciaroni E, Littarru GP. Coenzyme Q10 treatment of heart failure in the Elderly: preliminary results. In: Folkers K, Littarru GP, Yamagami T (eds). *Biomedical and clinical aspects of coenzyme Q10*. Vol 6. Elsevier Amsterdam, 1991; pp 473–480.
- 18 Singh RB *et al* Randomised, double blind, placebo controlled trial of coenzyme Q10 in patients with acute myocardial infarction. *Cardiovasc Drug Ther* 1998; **12**: 347–353.
- 19 Rose GA, Blackburn H, Gilburn RF, Prineas RJ. *Cardiovascular Survey Methods* World Health Organisation: Geneva, 1982.
- 20 Chopra RK, Goldman R, Sinatra ST, Bhagvan HN. Relative bioavailability of coenzyme Q10 formulations in human subjects. *Int J Nutr Vit Res* 1998; **68**: 109–113.
- 21 Niato C, Kawamura M, Yamamoto Y. Lipid peroxides as the initiating factor of atherosclerosis. *Ann NY Acad Sci* 1993; **676**: 27–45.
- 22 Lunec J, Hallován SP, White AG, Dormandy TL. Free radical oxidation (peroxidation) products in serum and synovial fluids in rheumatoid arthritis. *J Rheumatol* 1981; **8**: 233–245.
- 23 Esterbauer H, Cheeseman KH. Determination of aldehyde peroxidation in products malondialdehyde and 4 hydroxynonenal. *Method Enzymol* 1990; **186**: 407–421.
- 24 Brubacker G, Vuilleumier JP. Vitamin C. In: Curtis HC, Roth M (eds). *Clinical Biochemistry, Principles and Methods*. Vol 2. Berlin de Gruyter, 1974, pp 989–997.
- 25 Vuilleumier JP, Keller HE, Gysel D, Hunziker F. Clinical chemical methods for the routine assessment of the Vitamin status in human population. Part 1. The fat soluble vitamins A, E and beta-carotene. *Int J Nutr Vit Res* 1983; **58**: 265–272.
- 26 Yalow RS, Berson SA. Immunoassay of endogenous plasma insulin in man. *J Clin Invest* 1960; **39**: 1157–1175.
- 27 Krentz AJ. Insulin resistance. *BMJ* 1996; **313**: 1385–1389.
- 28 Singh RB *et al* Plasma levels of antioxidant vitamins and oxidative stress in patients with acute myocardial infarction. *Acta Cardiol* 1994; **49**: 441–452.
- 29 Machtey I, Syrkis I, Fried M. Studies of blood ascorbic acid levels in acute myocardial infarction. *Clin Chim Acta* 1975; **62**: 149–151.
- 30 Labodarios D, Brink PA, Wiesch HSH. Plasma vitamins A, E, C and B<sub>6</sub> levels in myocardial infarction. *S Afr Med J* 1987; **71**: 561–563.
- 31 Ramirej J, Flowers NC. Leucocyte ascorbic acid and its relationship to coronary artery disease in man. *Am J Clin Nutr* 1980; **33**: 2077–2087.
- 32 Loven DP, Oberley LW. Free radicals, insulin action and diabetes. In: Oberley LW (ed). *Superoxide-dismutase* Vol III. CRC Press: Ecce Raton Florida, 1985.
- 33 Ferrannini E, Halfner SM, Mitchell BD, Stern MP. Hyperinsulinemia the key features of a cardiovascular and metabolic syndrome. *Diabetologia* 1991; **34**: 416–422.
- 34 Singh RB *et al* Blood pressure trends, plasma insulin levels and risk factors in rural urban elderly populations of north India. *Coronary Art Dis* 1997; **8**: 463–468.
- 35 Serbruany VL *et al* Dietary coenzyme Q10 supplementation alters platelet size and inhibits human vitronectin (CDSI/CD61) receptor expression. *J Cardiovasc Pharmacol* 1997; **29**: 16–22.
- 36 Auwerx J, Staels B. Leptin: review article. *Lancet* 1998; **351**: 737–742.
- 37 Yamagami T *et al* Effect of coenzyme Q10 on essential hypertension, a double blind, controlled study. In: Folkers K, Littarru GP, Yamamura Y (eds). *Biomedical and clinical aspects of coenzyme Q*. Vol 5. Elsevier: Amsterdam, 1986; pp 337–343.