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Beneficial effects of aged garlic extract and coenzyme Q10 on vascular elasticity and endothelial function: The FAITH randomized clinical trial

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ABSTRACT

Objective: Aged garlic extract (AGE) is associated with a significant decrease in atherosclerotic plaque progression and endothelial function improvement. Similarly, coenzyme Q10 (CoQ10) has significant beneficial effects on endothelial function. A stressful lifestyle is a well-known risk factor for the presence and progression of atherosclerosis. This study investigated the effect of AGE plus CoQ10 on vascular elasticity measured by pulse-wave velocity (PWV) and endothelial function measured by digital thermal monitoring (DTM) in firefighters.

Methods: Sixty-five Los-Angeles County firefighters who met the eligibility criteria were enrolled in this placebo-controlled, double-blinded randomized trial. The firefighters were randomized to four tablets of AGE (300 mg/tablet) plus CoQ10 (30 mg/tablet) or placebo. The participants underwent quarterly visits and 1-year follow-up. PWV and DTM were measured at baseline and at the 1-year follow-up.

Results: There were no significant differences in age, cardiovascular risk factors, PWV, and DTM between the AGE/CoQ10 and placebo groups at baseline ($P > 0.5$). At 1-y, PWV and DTM significantly improved in the AGE/CoQ10 compared with the placebo group ($P < 0.05$). After an adjustment for cardiovascular risk factors and statin therapy, the mean decrease in vascular stiffness (PWV) was 1.21 m/s in the AGE/CoQ10 compared with the placebo group ($P = 0.005$). Similarly, the mean increase in the area under the temperature curve, the DTM index of endothelial function, was 31.3 in the AGE/CoQ10 compared with the placebo group ($P = 0.01$).

Conclusion: The combination of AGE and CoQ10 was independently associated with significant beneficial effects on vascular elasticity and endothelial function in firefighters with high occupational stress, highlighting the important role of AGE and CoQ10 in atherosclerotic prevention of such individuals.

Introduction

The risk of major adverse cardiovascular events is three-fold higher in firefighters compared with the general population [1]. The leading cause of line-of-duty death in firefighters is sudden cardiac death, accounting for approximately 45% of duty deaths [2]. Studies have shown that self-perceived psychological stresses and occupational stressors such as fire-fighting are independent risk factors for coronary artery disease (CAD) and major cardiac adverse events such as myocardial infarction [3,4].

A growing body of literature supports the linkage of endothelial dysfunction, inflammation, and immunologic factors to the acceleration of the atherosclerotic process from the early subclinical phase to overt clinical CAD with complications [5]. Our group previously reported that aged garlic extract (AGE) has cardiovascular protective effects by decreasing the progression of the coronary atherosclerotic burden, oxidative biomarkers, and blood cholesterol levels in intermediate-risk individuals [6].

A primary prevention method to retard the progression of atherosclerosis at the earliest subclinical stages in individuals with highly stressful occupational or environmental lifestyles has not been well validated. The Firefighter Aged Garlic Extract Investigation with Coenzyme (CoQ10) as a Treatment for Heart

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Disease (FAITH), a randomized, placebo-controlled trial, was designed to assess the effects of AGE plus CoQ10 on vascular elasticity and endothelial function in firefighters.

Materials and methods

Sixty-five asymptomatic Los Angeles County firefighters who met the eligibility criteria (Table 1) signed a written informed consent that has been approved by the institutional review board of the Los Angeles Biomedical Research Institute and were enrolled in the placebo-controlled, double-blinded randomized FAITH clinical trial (Clinicaltrials.gov identifier, NCT00860847). Demographic and cardiovascular risk factors and serum lipid profiles were obtained using standard techniques at baseline and during the 1-y course of the trial. Pulse-wave velocity (PWV) and digital thermal monitoring (DTM) tests were measured at baseline and after the 1-y follow up.

Firefighters were randomized to four identical tablets of AGE/CoQ10 or placebo at a 1:1 ratio using a computer-generated randomization method. The AGE/CoQ10 tablets contained AGE 300 mg and CoQ10 30 mg, which were provided by Wakanuga Inc. of America (Mission Viejo, CA, USA). The participants underwent quarterly visits for compliance assessment, drug refills, and diet and nutritional consultations.

Pulse-wave velocity

Carotid and radial PWVs were measured by the SphygmoCor device (AtCor Medical, Sydney, Australia) based on the tonometry in two steps. The first step is used to simultaneously record carotid pulse waves and the electrocardiogram; the second step is the recording of the radial pulse wave and the electrocardiogram. The electrocardiographic recording during the measurements was used for the synchronization of the carotid and radial pulse-wave times. The transit time between the carotid and radial pressure waves was calculated using the wave foot-to-foot method. Wave "foots" are identified using intersecting tangent algorithms. The PWV is calculated as the ratio of the pulse-wave travel distance from the carotid to the radial artery to its transit time (meters per second) [7].

Digital thermal monitoring

The DTM measurements were performed in a quiet, dimmed room at a controlled ambient temperature of 23.5°C to 25.0°C. The DTM of both hands was obtained during a 5-min stabilization, a 2-min cuff inflation to 50 mmHg greater than systolic blood pressure, and a 3-min deflation using an automated, operator-independent protocol (VENDYS, Endothelix Inc., Houston, TX, USA). Thermal changes during a 5-min arm cuff-induced reactive hyperemia test were monitored continuously in the fingertips of the occluded and non-occluded arms using VENDYS software. The device consists of a computer-based thermometric system (0.005°C thermal resolution) with two fingertip, resistance temperature detector, fast-response probes, designed to minimize the skin–probe contact area and fingertip pressure, attached to the pulp of the index finger on each hand. The system includes a common automated sphygmomanometric cuff, a cuff-inflation pump, and a release valve to permit the non-invasive measurement of arterial pressure and the control of occlusive hyperemia. Dual-channel temperature data are simultaneously acquired at a 1-Hz sampling rate. The area under the temperature curve (TMP-AUC), a DTM index of endothelial function, was used to assess the difference in response in endothelial function between the AGE/CoQ10 and placebo groups [8].

Statistical analysis

Mean ± standard deviation and proportions were used to summarize the characteristics of the study sample. Continuous variables were compared by *t* test, and categorical variables were compared by the chi-square test. Multivariate logistic regression analyses were employed to assess the relation of vascular elasticity and endothelial function to the AGE/CoQ10 versus placebo treatment before and after an adjustment for conventional cardiovascular risk factors. All statistical analyses were performed with SAS 9.1 (SAS Institute, Cary, NC, USA; http://www.sas.com). The level of significance was set at $P < 0.05$ (two-tailed). The study protocol and consent form were approved by the institutional review board committee of the Los Angles Biomedical Research Institute at Harbor UCLA Medical Center (Torrance, CA, USA).

Results

Table 2 lists the baseline and 1-y measurements of the studied markers between the AGE/CoQ10 and placebo groups. There was no significant difference between the placebo and AGE/CoQ10 groups in age, systolic and diastolic blood pressures, triacylglycerols, low-density lipoprotein cholesterol level, prevalence of hypertension, diabetes mellitus and family history of premature CAD at baseline ($P > 0.05$). The baseline PWV was no different in the AGE/CoQ10 group than in the placebo group (8.11 ± 0.91 versus 8.26 ± 1.15 m/s, $P = 0.6$). Similarly, there was no difference between the AGE/CoQ10 and placebo groups in baseline TMP-AUC (61.4 ± 8.3 versus 47.3 ± 7.3, $P = 0.3$). After 1 y of the study, the mean decrease in PWV was 1.21 m/s in the AGE/CoQ10 group compared with the placebo group ($P = 0.005$), and the mean increase in TMP-AUC was 31.28 in the AGE/CoQ10 group compared with the placebo group ($P = 0.01$) after an adjustment for all risk factors (Table 2, Fig. 1A). An increase in TMP-AUC, which corresponds to faster temperature rebound response after induced ischemia, is a marker of improved endothelial function. Because blood traveling through more elastic vessels takes a longer time, a decrease in PWV also corresponds with an improvement in vascular elasticity.

Compared with the placebo treatment, the relative risk of the AGE/CoQ10 treatment in decreasing the PWV was 1.21 (95% confidence limit −2.1 to −0.32, $P = 0.005$), and a relative risk of 31.3 (95% confidence limit 1.67–60.91, $P = 0.01$), increased the TMP-AUC, providing strong evidence of an improvement in vascular elasticity and endothelial functions, respectively. Based on these two different methods of vascular function evaluation,

Table 1
Inclusion and exclusion criteria for asymptomatic Los Angeles County firefighters ($n = 65$)

Inclusion criteria	Exclusion criteria
Age 35–84 y	known hypersensitivity to AGE
Agree to refrain from supplemental garlic or significant dietary garlic	current tobacco use
Agatston CAC score >20	current intake of garlic supplements
Willing to sign informed consent	current use of anticoagulants (except for antiplatelet agents)
	chronic renal failure
	weight ≥325 lbs.
	diabetic subjects with HbA1c >12%
	serum creatinine >1.4 mg/dL
	triacylglycerols >400 at visit 1
	NYHA class III or IV heart failure
	known bleeding disorder
	history of myocardial infarction stroke or life-threatening arrhythmia
	presence of metal clips (i.e., patients with bypass) or intracoronary stenting precluding accurate measurement of coronary calcification
	partial ileal bypass or known gastrointestinal disease limiting drug absorption

AGE, aged garlic extract; CAC, coronary artery calcium; HbA1c, hemoglobin A1c; NYHA, New York Heart Association