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Original article

Cardiovascular risk and benefits from antioxidant dietary intervention with red wine in asymptomatic hypercholesterolemics

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SUMMARY

Background & aims: The role of red wine in cardiovascular risk prevention has been documented by several epidemiological studies in patients and normocholesterolemic healthy individuals. However, it is unclear whether hypercholesterolemic individuals free of cardiovascular disease would equally benefit from moderate red wine consumption to prevent atherosclerosis and the development of cardiovascular disease.

Methods: Forty (40) healthy male and female volunteers were recruited, divided into 2 age-adjusted groups according to their total cholesterol levels; in asymptomatic hypercholesterolemics (AHC), and normocholesterolemics (NC). Total Antioxidant Capacity (TAC), Lipid profile, Vitamin E, and cardiovascular risk indexes (Low Density Lipoproteins (LDL)/High Density Lipoproteins (HDL) and Vitamin E/Total Cholesterol (TC) were evaluated in the blood serum of all subjects prior to and 1 month after once daily red wine consumption as well as prior to and after being given a placebo drink following a 1 month wash out period.

Results: TAC significantly increased after the intervention in all subjects in AHC and NC group with a mean difference (post-pre) 1.78 mmol/l and 0.87 mmol/l, respectively. Vitamin E significantly increased especially in AHC group (13.1% increase) compared to NC group (5.41%) after red wine consumption, with higher increase in the AHC group. There was marginal significant treatment effect (decrease) on fasting LDL/HDL ratio ($p = 0.05$) and a statistically significant increase on Vitamin E/TC ratio relative to drinking placebo for NC ($p < 0.005$) and AHC group ($p < 0.002$).

Conclusions: Asymptomatic hypercholesterolemic (AHC) individuals are more likely to develop cardiovascular disease as presented by high cholesterol levels in addition to the presence of low baseline serum α-tocopherol (vitamin E) concentrations, leading to atherosclerosis. AHC individuals following an early dietary intervention, seem likely to reduce the risk factors for cardiovascular disease by increasing circulating concentrations of TAC and α-tocopherol (vitamin E) so as vitamin E/TC ratio increases.

1. Introduction

Cardiovascular disease (CVD) remains the main cause of mortality today, and it is essential to detect the early stage parameters that lead to atherosclerosis and to prevent the disease using natural dietary interventions. According to the World Heart Organization, there are many risk factors associated with cardiovascular

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disease. Some risk factors, such as family history, ethnicity and age, cannot be changed. Other risk factors, such as tobacco exposure, high blood pressure (hypertension), high cholesterol, obesity, physical inactivity, diabetes, unhealthy diets, and harmful use of alcohol, can be changed by interventions [1]. Among them high cholesterol level was selected for the study, a factor that is not usually given appropriate importance, although it can be treated or changed with dietary measures before vascular injuries and cardiovascular disease develops and before pharmaceutical interventions are needed.

Evidence-based epidemiological studies have revealed an association between the lower risk of CVD and moderate red wine consumption [2]. Many studies have indicated that alcohol (ethanol) consumption is the most obvious cause and is mediated through HDL [3]. Furthermore, recent studies have suggested that another ingredient in red wine, possibly polyphenol, may contribute to the improvement of micro vessel function and, consequently, cardioprotection [4]. Recent studies attributed the decrease in the incidence of cardiovascular disease to a diet rich in plant polyphenols [5–7]. Red wine affects cholesterol by several mechanisms through polyphenols by affecting the hepatic cholesterol and lipoprotein metabolism. This mechanism works by reducing cholesterol absorption and decreasing delivery of cholesterol to the liver, which reduces plasma cholesterol. Additionally, polyphenols affect apolipoprotein B secretion rates, modify Very Low Density Lipoproteins (VLDL) particles and reduce plasma Triglycerides (TG) due to possible increased Lipoprotein Lipase (LPL) activity, which leads to decreased LDL in circulation [8].

Oxidative stress is a unifying characteristic of almost all cardiovascular risk factors and is known to drive the atherosclerotic process, including hypercholesterolemia. The role of oxidative stress in the pathophysiology of CVD is well established [9]. Red wine, with its polyphenolic compounds, plays a protective role in cardiovascular disease due to their antioxidant, antithrombotic, anti-ischemic, vasorelaxant and antihypertensive properties [8]. Synergy and the added value of several antioxidants provide more protection in combination against free radicals than any single ingredient. Therefore, the assessment of the combined antioxidant status would provide more relevant biological information compared to that obtained by the measurement of individual compounds [10]. Accordingly, Total Antioxidant Capacity (TAC) was selected to evaluate oxidative stress as a potential predictor of cardiovascular risk. Although low to moderate alcohol consumption has been found to be beneficial for the cardiovascular system, chronic heavy drinking has detrimental effects [11]. Therefore, heavy drinking in all forms should be discouraged.

It has been demonstrated that the quality of grapes and the amount of flavonoids in grapes determines the antioxidant activity of red wine [12] and, more specifically, the grape variety, cultivation area, sun exposure, wine-making technique and wine age. Therefore, we chose the Northern Greece “tannat” variety, because of its high level of phenolic compounds [13].

This study was designed to determine whether AHC individuals with established risk factor of cardiovascular or coronary disease would benefit from red wine consumption and reduce the risk for the development of the disease.

2. Materials and methods

2.1. Subjects

A total of 40 healthy volunteers, including 21 males and 19 females (age range 20–70), were recruited for the study in the outpatient clinic of our institution from December 2012 to December 2013 and were divided into two age-adjusted groups according to their blood cholesterol levels: AHC (healthy individuals with elevated cholesterol level (cholesterol > 200 mg/dl) with no established cardiovascular disease and under no treatment) and NC (normal cholesterol level (cholesterol $\leq$ 200 mg/dl)). Subjects enrolled in the study had no pathological underlying condition besides elevated cholesterol levels, and they were not taking any medications. If their cholesterol status is not higher than AHC's baseline level, they are not a sign of disease but are merely a risk factor.

With the term asymptomatic hypercholesterolemic individuals we describe individuals who did not appear from the health status questionnaire and general examination to have any cardiovascular symptoms due to hypercholesterolemia with significant narrowing of the arteries leading to their hearts or brains so far as follows: No chest pain (angina) or other symptoms of coronary artery disease, as well as no symptoms of decreased blood supply to the brain (transient ischemic attacks or stroke), no cholesterol deposits, no hypertension (blood pressure was measured) and they did not take any medications for cardiovascular disease. Doppler was only performed in individuals with higher levels of cholesterol and none of them had more than 20% of both carotid arteries obstruction.

Exclusion criteria included documented dyslipidemia (abnormal level of fat or cholesterol very high or very low), chronic liver disease, malnutrition, neoplastic or acute infectious diseases and habitual use of vitamin and antioxidant supplements as well as uncommon dietary habits (e.g. vegetarianism) and alcoholism.

Of the 40 subjects recruited for the study, 3 withdrew for the following reasons: respiratory infection (n = 1), need to travel (n = 1), and refusal to drink wine after tasting it (n = 1). Thirty-seven (37) subjects completed the study. The somatometric characteristics of participants are presented in Table 1. All subjects gave a full medical history as well as their smoking habits, which were expressed in pack years (number of cigarette packs/day/years); alcohol consumption (units/day); and exercise activity level as degrees from 1 to 10.

The Institutional Review Board of Aristotle University of Thessaloniki, School of Engineering, Faculty of Chemical Engineering, Division of Technology, Laboratory of Food and Processing engineering, approved the study protocol, and all participants signed an informed consent form.

Table 1
Demographic, Somatometric and Lifestyle Characteristics of participants in both groups at baseline.

Characteristics	NC (n = 17) Mean (±SD)	AHC (n = 20) Mean (±SD)
Age (years)	38.2 (13.1)	50.4 (14.1)
Height (cm)	171 (8.4)	174 (9.2)
Weight (kg)	74 (16.7)	77 (14.4)
BMI (kg/m^2)	25.0 (5.1)	25.2 (3.1)
Waist circumference (cm)	80.76 (15.78)	88.25 (13.07)
Hip circumference (cm)	100.06 (13.71)	101.50 (7.00)
Waist/Hip ratio	0.80 (0.08)	0.87 (0.10)
Smoking (pack years)	3.29 (5.22)	1.95 (3.24)
Physical exercise (deg. 1–10)	2.59 (3.30)	3.65 (3.41)
Alcohol consumption (unit/day)	0.87 (0.54)	1.05 (1.04)

Body Mass Index (BMI) is calculated as body weight (Kg) divided by height^2 (m^2), one unit of alcohol: 22.9 g alcohol.
Pack years: number of cigarette packs/day/years smoked, deg. 1–10: low to high exercise activity level.