Nutrition 31 (2015) 678–685

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Effect of pistachio nut consumption on endothelial function and arterial stiffness

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ARTICLE INFO

Article history:
Received 19 June 2014
Accepted 30 October 2014

Keywords:
Cardiovascular disease
Hypertension
Arterial stiffness
Pulse wave velocity
Augmentation index

ABSTRACT

Objectives: Previous studies have demonstrated beneficial effects of regular consumption of pistachio nuts on glycemic, lipid, and oxidative stress parameters. The aim of this study was to determine its effect on vascular health, which has not been adequately studied so far.
Methods: In this open label, randomized parallel-group study, 60 adults with mild dyslipidemia were randomized to lifestyle modification (LSM) alone or LSM with consumption of 80 g (in-shell) pistachios (equivalent to 40 g or 1.5 oz shelled pistachios) daily for 3 mo. Biochemical parameters, brachial artery flow-mediated vasodilation (BAFMD), and carotid-femoral and brachial-ankle pulse wave velocity (cfPWV and baPWV, respectively) were measured before and after the intervention.
Results: At 3 mo, there was no change in any of the clinical or biochemical parameters in the LSM group. However, the patients in the pistachio group had a significant increase in high-density lipoprotein cholesterol (HDL-C; 35.7 ± 8.8 mg/dL versus 37.8 ± 10.1 mg/dL; $P = 0.04$) and a reduction in low-density lipoprotein cholesterol (137.2 ± 32.6 mg/dL versus 127.6 ± 34.0 mg/dL; $P = 0.02$), total cholesterol (TC)-to-HDL-C ratio (5.8 ± 1.3 mg/dL versus 5.3 ± 1.1 mg/dL; $P = 0.001$), and fasting blood sugar (88.8 ± 7.1 mg/dL versus 86.6 ± 6.3 mg/dL; $P = 0.05$). Additionally, whereas LSM alone was associated with no improvement in BAFMD or PWV, individuals in the pistachio group had significant reduction in left baPWV (1261.7 ± 187.5 cm/sec versus 1192.4 ± 152.5 cm/sec; $P = 0.02$) and statistically nonsignificant improvement in most other parameters, including BAFMD. As a result, at 3 mo the patients in the pistachio group had lower cfPWV (770.9 ± 96.5 cm/sec versus 846.4 ± 162.0 cm/sec; $P = 0.08$), lower left baPWV (1192.4 ± 152.5 cm/sec versus 1326.3 ± 253.7 cm/sec; $P = 0.05$), and lower average baPWV (1208.2 ± 118.4 cm/sec versus 1295.8 ± 194.1 cm/sec; $P = 0.08$) compared with the LSM group. Two-way analysis of variance revealed significant treatment effect of pistachio consumption on cfPWV, left baPWV, average baPWV, and BAFMD ($P = 0.037$, 0.01, 0.07, and 0.046, respectively).
Conclusions: The present study demonstrates that regular consumption of pistachio nuts not only improves glycemic and lipid parameters, but also results in improvements in vascular stiffness and endothelial function. Importantly, these improvements were seen in apparently healthy individuals and with a diet (including pistachios) and exercise regimen that every adult individual is expected to follow.

This study was fully supported by a grant from the Paramount Farms Inc., in California. However, the funding agency had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the article for publication. RRK was responsible for the study design, patient enrollment, overall administrative support, and supervision of the study execution. MB participated in the study design and execution, data analysis, and manuscript preparation. RM conducted the clinical assessment of patients, offered general lifestyle advice, and assisted with manuscript preparation. KPY planned the diet and counseled the participants. NT was involved in patient enrollment and overall administrative support.

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http://dx.doi.org/10.1016/j.nut.2014.10.019
0899-9007/

Introduction

Cardiovascular disease (CVD) is currently among the leading causes of death and a source of considerable morbidity worldwide. CVD has usually been looked at as a disease of developed nations and affluent societies. However, recent evidence suggests that even in developing nations there has been a progressive shift in the disease prevalence patterns from infectious diseases to noncommunicable diseases, driven predominantly by the increase in the prevalence of CVD [1]. Consequently, prevention of CVD has become one of the most important goals of health care delivery worldwide.

Although the advancements in pharmacotherapy, such as the advent of cardioprotective drugs like aspirin, statins, and angiotensin-converting enzyme inhibitors, have resulted in substantial reduction in the incidence of CVD over the past few decades, lifestyle modifications (LSMs) also have contributed in good measure to this reduction [2]. It has been estimated that nearly half of the decline in the deaths related to coronary artery disease in the United States from 1980 to 2000 could be attributed to reduction in major CV risk factors achieved through a combination of LSM and pharmacotherapies [3].

Dietary changes are an integral component of LSM aimed at prevention of CVD. Reduction in the consumption of fats and refined carbohydrates along with increased consumption of fiber, nuts, fruits, and vegetables are associated with improvements in glycemic indices; lipid parameters; weight reduction; reduced risk for diabetes and hypertension; and a lower CV mortality [2,4–11]. Of all these different food components, nuts, particularly pistachios, almonds, and walnuts, are known to have numerous health benefits [12–14]. They are rich in proteins, fiber, phytosterols, antioxidants, and several minerals and vitamins. They have a favorable fat composition (higher concentration of monounsaturated fatty acids [MUFAs], low saturated fat content, zero cholesterol, etc.), which makes them an attractive health food option. Compared with other edible nuts, pistachios have higher MUFA content (67%), lower ratio of polyunsaturated to saturated fat and a lower glycemic index, which provides incremental health benefits [15–18]. Consistent with these observations, numerous studies have documented lipid-lowering and antioxidant properties of pistachios [16–24]. However, only limited data is available to assess whether these beneficial properties of regular consumption of pistachios actually translate into improved vascular health [25,26]. The present study was therefore conducted to assess the effects of pistachio consumption on brachial artery flow-mediated vasodilation (BAFMD) and arterial pulse-wave velocity (PWV)—the two noninvasive markers of endothelial function and arterial stiffness, respectively.

Methods

This was an open-label, randomized parallel-group study (Fig. 1) conducted at a tertiary care center in India (Medanta-The Medicity, Gurgaon). Sixty adults between the ages of 25 to 60 y with dyslipidemia, defined as low-density lipoprotein cholesterol (LDL-C) 131 to 190 mg/dL or high-density lipoprotein cholesterol (HDL-C) <40 mg/dL in men and <50 mg/dL in women, or both were included in this study from December 2010 to February 2013. The patients who were already on lipid-lowering drug therapy or those who had lipid abnormalities that mandated initiation of pharmacotherapy during the first visit itself (serum triglycerides >500 mg/dL or LDL-C >190 mg/dL) were excluded from the study. Additionally, patients with diabetes mellitus, uncontrolled hypertension requiring modification of antihypertensive treatment, known CVD, pregnant women, and those who were not willing to participate in the study were also excluded.

Once enrolled, all participants underwent baseline evaluation, after which they were randomized to either LSM alone or LSM with daily pistachio consumption. The dietary intervention was continued for 3 mo, at the end of which a repeat evaluation was performed (Fig. 1).

The study was approved by the Institutional Review Board and the Medanta Independent Ethics Committee (ref. no MICR-003/2010). All participants provided written informed consent.

Baseline evaluation

At baseline, all participants were subjected to clinical evaluation, biochemical investigations, and measurements of BAFMD and PWV. Clinical evaluation included detailed history regarding the presence or absence of CV risk factors, duration of CV risk factors, use of statins, and so on. Physical examination included measurement of height, weight, waist circumference, blood pressure (BP), and examination of the CV system. BP was measured in the right arm, with the participant in supine position, using a standard sphygmomanometer. Biochemical investigations included fasting and 2-h postprandial blood glucose, fasting lipid profile including estimation of apolipoprotein A1 (Apo-A1), apolipoprotein B (Apo-B), and measurement of high-sensitivity C-reactive protein (hs-CRP).

BAFMD

Brachial artery flow-mediated dilation measurement is a noninvasive ultrasound-based test. It was performed using a 7.5 MHz linear array transducer attached to a commercially available ultrasound system. The test was done after overnight fasting. Smoking was prohibited for ≥4 h before the test and all the vasoactive drugs, such as nitrates, were withheld for a period of 48 h preceding the test. For the test, the patient was laid in supine position and a standard sphygmomanometer cuff was tied on the right arm. The right brachial artery was then imaged in the antecubital fossa and its diameter measured at end-diastole using electrocardiographic (ECG) gating. This was followed by occlusion of the brachial artery by inflating the sphygmomanometer cuff to at least 50 mm Hg above systolic BP and the occlusion was sustained for 5 min. At the end of 5 min, the cuff was suddenly deflated to allow rapid inflow of the blood in to the forearm. The brachial artery diameter was measured again at 1 min after the relief of occlusion and flow-mediated dilation (FMD) was calculated as percentage increase in the diameter of the brachial artery from the baseline. These measurements were performed off-line from the movie clips of the brachial artery recorded at baseline and at 1 min after the release of occlusion. A lower BAFMD value indicated worse endothelial function.

The reproducibility of BAFMD measurement in our laboratory has been reported previously [27].

PWV measurement

The measurement of arterial PWV was performed using a noninvasive device—the PeriScope® (Genesis Medical Systems Pvt Ltd, Hyderabad, India)—which has been shown to have high degree of reproducibility for this purpose [28]. The device is based on oscillometric method and records arterial pressure waveforms noninvasively. ECG-gated pressure waveforms are recorded simultaneously from both arms and both ankles. From these pressure waveforms, in-built software automatically calculates PWV for different vascular segments [29].

The procedure was performed in the morning, after 10 h of overnight fast. Participants were asked to refrain from smoking for ≥4 h before the procedure. Ongoing medications were not discontinued, but morning doses were delayed until completion of the test. The procedure was performed in supine position. After 10 min of rest in supine position, four BP cuffs, which were connected to the PeriScope® device, were tied around both arms and both ankles. These BP cuffs carried oscillometric sensors to record pressure waveforms from the underlying arteries. ECG electrodes were applied on wrists and ankles to allow for ECG gating. The machine then automatically inflated and deflated all the cuffs simultaneously, while recording pressure waveforms from all four sites. From these pressure waveforms, carotid-femoral PWV (cfPWV) and right and left brachial-ankle PWV (baPWV) were calculated and used for analysis. A higher value of PWV indicated greater arterial stiffness in the corresponding vascular segment (Fig. 2).

Therapeutic intervention and follow-up

All study participants were given exercise and diet counseling, which was similar in both groups, except for the inclusion of pistachios in the pistachio group.

The participants were encouraged to participate in regular physical activity defined as a ≥30-to 45-min brisk walk, or equivalent, daily for at least 5 d/wk. The dietary advice was primarily based on the "therapeutic lifestyle change" diet recommended by the American Heart Association but was individualized according to height, weight, and physical activity level of the study participants. In the LSM group, the composition of recommended diet was aimed at providing 50% to 55% of total calories from carbohydrates, 15% to 18% from proteins, and 25% to 30% from fats. Participants in the LSM group were requested to refrain from regular consumption of pistachios and other nuts during the study period. In the pistachio group, 80 g in-shell, roasted, and salted pistachio nuts daily (equivalent