



Evaluation of The Effects of Raisins and Hazelnuts Added To the Diet on Lipid Profiles and Anthropometric Measurements in Women with Hyperlipidemia

Hiperlipidemili Kadınlarda Diyete Fındık ve Kuru Üzüm Eklenmesinin Lipid Profili ve Antropometrik Ölçümler Üzerine Etkisinin Değerlendirilmesi

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ABSTRACT

Objective: The positive effects of nuts and grape products on lipid profiles have been proved by epidemiological and clinical studies. However, studies investigating the effect of raisins on lipid profiles are limited. The aim of this study was to compare the effects of consuming a cardioprotective control diet, and the cardioprotective diet containing either raisins, hazelnuts, or a combination of raisins and hazelnuts in hyperlipidemic obese women in terms of lipid profiles and anthropometric measurements.

Methods: Thirty-seven hyperlipidemic obese women were involved in a parallel controlled randomized clinical trial. Participants were randomly divided into four groups. The control group consumed a cardioprotective diet for six weeks while the other participants consumed 50 g/day hazelnut, 50 g/day raisins or 50 g/day hazelnut +50 g/day raisins in a cardioprotective diet. Blood lipids, blood glucose levels, blood pressure, and anthropometric measurements were measured at the beginning and at the end of the study.

Results: There was not any significant difference between groups in terms of lipid profiles, blood glucose, blood pressure and anthropometric measurements (all $p>0.05$). Compared with initial measurements, total cholesterol, low density lipoprotein cholesterol, and body mass index levels decreased statistically significantly (all $p<0.05$) in all groups at the end of the study.

ÖZ

Amaç: Yağlı tohumlar ve üzümünden elde edilen ürünlerin lipid profili üzerine olumlu etki gösterdiği epidemiyolojik ve klinik araştırmalarla kanıtlanmıştır. Bununla beraber kuru üzümün lipid profili üzerine etkisini araştıran çalışmalar sınırlıdır. Bu araştırmada hiperlipidemili obez kadınlarda fındık, kuru üzüm veya fındık ile birlikte kuru üzüm içeren kardiyoprotektif diyetlerin tüketilmesi ile kardiyoprotektif kontrol diyeti tüketilmesinin lipid profili ve antropometrik ölçümler açısından karşılaştırılması amaçlanmıştır.

Yöntemler: Paralel kontrollü randomize klinik araştırmaya 37 hiperlipidemili obez kadın katılmıştır. Katılımcılar randomizasyonla dört gruba ayrılmıştır. Altı hafta boyunca kontrol grubu kardiyoprotektif diyet, diğer gruplardaki katılımcılar bulundukları gruba göre 50 g/gün fındık, 50 g/gün kuru üzüm ve 50 g/gün fındık+ kuru üzüm içeren kardiyoprotektif diyetleri tüketmişlerdir. Araştırmanın başında ve sonunda katılımcıların kan lipidleri, kan glikozu düzeyleri ve kan basıncı ölçümleri yapılmış, antropometrik ölçümleri alınmıştır.

Bulgular: Gruplar arasında lipid profilleri, kan glikozu, kan basıncı ve antropometrik ölçümler bakımından anlamlı fark bulunmamıştır (tüm $p>0,05$). Başlangıç ölçümleri ile karşılaştırıldığında, araştırmanın sonunda tüm gruplarda toplam kolesterol, düşük yoğunluklu lipoprotein kolesterol ve beden kütle indeksi düzeyleri istatistiksel olarak anlamlı düzeyde azalmıştır (tüm $p<0,05$).

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Conclusion: Because of the improvement on lipid profile and anthropometric measurements in four groups at the end of the study, it was concluded that consumption of hazelnut, raisins or combination of hazelnut and raisins can be recommended to hyperlipidemic individuals in addition to an appropriate diet program.

Keywords: Hazelnut, raisins, cardioprotective diet, hyperlipidemia, lipid profile, anthropometric measurements

Sonuç: Araştırmanın sonunda dört grubun lipid profilleri ve antropometrik ölçümlerinde meydana gelen olumlu değişiklikler nedeniyle hiperlipidemili bireylere uygun bir diyet programına ek olarak fındık, kuru üzüm ve fındıkla beraber kuru üzüm tüketiminin önerilebileceği sonucuna varılmıştır.

Anahtar Sözcükler: Fındık, kuru üzüm, kardiyoprotektif diyet, hiperlipidemi, lipid profili, antropometrik ölçümler

Introduction

Among chronic diseases, cardiovascular diseases (CVD) play an important role with high mortality and morbidity rates (1,2). For CVD, the most important risk factors are high level of blood lipids and high blood pressure, unhealthy eating habits, physical inactivity and tobacco use (2). The total cholesterol level of 200-239 mg/dL and the LDL cholesterol level of 130-160 mg/dL are defined as borderline high values regarding hyperlipidemia and therapeutic lifestyle changes are recommended. These changes include; regulation of diet content, weight control, and increased physical activity (3). Only a single diet pattern is insufficient to regulate the diet content. Studies using the Mediterranean diet as a cardioprotective and healthy diet have shown that it reduces CVD risk. There is not a single type of Mediterranean diet. The common characteristics of Mediterranean diets are as follows: High consumption of vegetables, fruits, whole grain products, nuts, legumes, fish, olive oil; low consumption of red meat, moderate consumption of wine, dairy products, poultry, and eggs (4).

Nuts are high-energy foods which are rich in monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA). Besides the appropriate fatty acid composition, nuts contain a variety of bioactive substances: Plant protein, minerals, alpha-tocopherol, phenolic compounds and fiber (5). In many clinical and epidemiological studies, it has been shown that all nuts have cholesterol-lowering efficacy due to their appropriate fatty acid composition and bioactive components, and frequent consumption of them reduces the incidence of CVD (6,7). Hazelnut has the highest unsaturated/saturated fatty acid ratio among nuts. Its oil pattern consists of 83.2% MUFA, 9% PUFA, while saturated fatty acid content is lower than 8% (8,9). MUFA are mainly oleic acid (82.7%) and PUFA are omega-6 (8.9%) and omega-3 (0.1%) (8). In addition to its fatty acid content, hazelnut is a cardioprotective food (9-11) which involves nutrients such as soluble fiber, arginine, β -sitosterol, vitamin E, folate, vitamin B6, potassium, and magnesium (10,11). Clinical studies with hazelnuts have proven positive effects on lipid profiles (9,12-14).

Raisins, containing fructose and glucose equally are also rich in vitamins, minerals, fiber, and antioxidants (15). The results of several studies have provided that the consumption of grape and grape products has protective effects against chronic diseases. This effect is attributed to the antioxidant compounds in the

grape (16,17). Studies on the effect of grape-based products on lipid profiles in humans or animals have used products made from grapes (grape seed extract, grape juice, and wine) (18-24). Studies using raisins have generally been carried out on the glycemic index and blood glucose (15,25). Raisin has a high antioxidant capacity but the studies investigating its effect on lipid profile in humans are limited. According to our research hypothesis, a cardioprotective diet containing raisins is expected to lower blood lipids more than just a cardioprotective diet and raisins with hazelnuts more than just a hazelnut containing diet. The aim of this study was to compare the effects of consuming a cardioprotective control diet, and the cardioprotective diet containing either raisins, hazelnuts, or a combination of raisins and hazelnuts in hyperlipidemic obese women in terms of lipid profile, and anthropometric measurements.

Methods

Subjects

The study was carried out according to the principles of the Helsinki Declaration. All the research related procedures were approved by the Istanbul No 6 Ethics Committee of Clinical investigations in Bakırköy Dr. Sadi Konuk Training and Research Hospital with the decision dated 29.04.2013 and numbered 2013/05/01. A protocol was signed with the approval of the Istanbul Public Health Directorate for the research conducted in a Family Health Centre, located in the Pendik Community Health Centre area.

The research was carried out with volunteer participants who registered to a family health center, attended for routine health check-ups between 11.11.2013-01.03.2014 and met the inclusion criteria of the survey. Non-pregnant women aged 40 years or older who had no accompanying chronic disease and did not use medication due to hyperlipidemia with body mass index (BMI) >30 kg/m² with total cholesterol >200 mg/dL, LDL cholesterol level >130 mg/dL, fasting blood glucose <110 mg/dL and systolic/diastolic blood pressure $<140/90$ mmHg were included in the study. The exclusion criteria were having a chronic illness (diabetes, hypertension, cancer, chronic kidney failure), using drugs due to hyperlipidemia and having allergies to specific foods (nuts, raisins). The health information of the participants was approved by the family physicians. The research was conducted with only women to prevent sex differences affecting the results of the research. According to the results of

a study of cardiovascular disease and risk factors in Turkey (26), mean cholesterol concentrations in women aged 40-59 years were found to be 204 mg/dL in the research area. Because this result was above the hyperlipidemia limit value of 200 mg/dL, the age of the participants was determined to be over 40 years.

For the study, 138 women who attended the Family Health Center for routine check-ups between 11.11.2013 and 01.03.2014, and who were over 40 years old, had BMI >30 kg/m² and had no accompanying chronic disease, were informed about the study and then blood lipids were examined from capillary blood after 12 hours of fasting. Ninety-four women were not included because their lipid profiles were normal (total cholesterol <200 mg/dL, LDL cholesterol level <130 mg/dL). Only 44 of these individuals fit the inclusion criteria of the survey. The participants were informed about the research and the experimental period was started after signing the informed consent form.

Sample Size

The sample size was determined to be 9 per group. In power analysis, when the probability of Type 1 error is 0.05, the power of test is 82%, Type 2 error is 17%, SD of means is 15.16, SD is 25.00, and effect size is 0.61. It was found that at least 9 individuals should be in each group in order to compare four groups (27,28). The study was started with 11 individuals per group.

Study Design

For this parallel controlled randomized clinical trial, participants who fit the inclusion criteria were divided randomly into four groups according to registration number respectively: 1 hazelnut group (HG), 2 raisin group (RG), 3 hazelnut+RG (HRG), and 4 control group (CG).

At the beginning of the study, some socio-demographic information (age, marital status, working status, education status) and health condition (chronic diseases diagnosed by a doctor, drug and supplement usage, food allergy) of the participants were investigated with a questionnaire prepared by the researcher. The accuracy of health information was confirmed by the participants' family physicians.

Blood lipids are known to stabilize within 3 weeks (29). Clinical studies researching the effect of nuts on blood lipids lasted 4-8 weeks (11). Therefore, the experimental period of the research lasted 6 weeks.

HG consumed a cardioprotective diet with 50 g of hazelnuts added to their diet (HD), RG consumed a cardioprotective diet with 50 g of raisins added to their diet (RD), HRG consumed a cardioprotective diet with 50 g of hazelnuts and 50 g of raisins added to their diet (HRD) and the CG consumed a cardioprotective controlled diet. The American Food and Drug Administration recommend consuming 42.8 g/day of nuts to reduce the risk of CVD due to their positive effects on blood lipids (30). In clinical trials, 40-100 g of nuts were used daily to investigate the effects on blood lipids (11). In our study, 50

g of hazelnuts and the same amount of raisins were given to the participants per day.

According to the cardioprotective diet recommended in the context of lifestyle changes in the prevention of CVD, daily energy should be adjusted to maintain ideal body weight. The energy distribution taken from macronutrients should be as follows: 50-60% carbohydrates, 15% proteins, and 25-35% fats (3,31-33). In addition to these recommendations, whole grains, vegetables, fruits, fish, legumes, nuts are important nutrients to be consumed in terms of cardiovascular disease control (32). The diets of the research groups were prepared in accordance with this information. Daily diet menus designed by the researcher and consumed by the participants during the research are given in Table 1. Energy and nutritional values of the diets were calculated using the BeBIS7.2 program (Entwickeltan der Universität Hohenheim, Stuttgart Copyright 2010 Dr. J. Erhardt, Stuttgart, Germany). Energy and nutritional values of the diets and the percentage of Recommended Dietary Allowance coverage (34) are given in Table 2. When diets are designed, it is aimed to be as equal as possible regarding energy and nutrients for all four groups. As shown in Table 2, diets are very close to each other in terms of energy, carbohydrate, protein, total fat and fiber content. Because hazelnuts are rich in total fat and MUFA, the diets of other groups are designed to be equal in terms of fat. Due to the differences in eating habits of the groups (such as using sunflower oil while cooking), the diets had differences in their PUFA and MUFA contents. For this reason, PUFA was higher in diets of the CG and RG, and MUFA was higher in diets containing hazelnut.

At the beginning of the study, the researcher gave the nutrition guide and daily diet menu to the participants according to their group; and explained the diet. Participants consumed the diets which were recommended to them according to their group. Only hazelnuts and raisins were provided by the researcher. In order to prevent cross-contamination between the groups, the participants were told not to consume the products of the other groups (the CG was told not to consume hazelnuts and raisins to; the HG was told not to consume raisins; and the RG was told not to consume hazelnuts) and they were followed up weekly. Any change in physical activity was not recommended for the participants so as not to influence the result of the diet.

During the research, subjects were followed up weekly and their weekly required hazelnuts and raisins were provided by the researcher in daily 50 g packages, free of charge. Individuals were asked to fill out weekly product consumption schedules. In weekly checks, the researcher investigated product consumptions and dietary compliance. If the participants did not comply with the diets, they reported that to the researcher. Instructions about product consumption and diets were repeated in weekly checks.

Biochemical Measurements

At the beginning and at the end of the 6-week experimental period, after 12 hours of fasting and 10 minutes of rest, capillary blood was taken by the family physician from the participants' fingertips to analyze total cholesterol, LDL, HDL

Table 1. Daily diet menus designed by the researcher and consumed by the participants during the research

Daily HD menu	Daily RD menu	Daily HRD menu	Daily CD menu
Breakfast	Breakfast	Breakfast	Breakfast
Tea 2 slice low fat white cheese (60 g) 3 slices whole grain bread (75 g) Tomatoes (100 g) Cucumber (100 g)	Tea 2 slice low fat white cheese (60 g) 3 slices whole grain bread (75 g) Tomatoes (100 g) Cucumber (100 g)	Tea 2 slice low fat white cheese (60 g) 3 slices whole grain bread (75 g) Tomatoes (100 g) Cucumber (100 g)	Tea 1 slice low fat white cheese (30 g) 2 slices whole grain bread (50 g) Tomatoes (100 g) Cucumber (100 g)
Snack	Snack	Snack	Snack
Apple (120 g)	Apple (120 g)	Apple (120 g)	Apple (120 g)
Lunch	Lunch	Lunch	Lunch
4 tablespoons vegetable (200 g) 4 tablespoon bulgur or pasta (40 g) (oil not added) Salad (oil not added) Half cup of yogurt (100 g) 2 slices whole grain bread (50 g)	1 cup of soup (200 g) 4 tablespoons vegetable (200 g) 2 tablespoon bulgur or pasta (20 g) Salad (with olive oil) Half cup of yogurt (100 g) 2 slices whole grain bread (50 g)	4 tablespoons vegetable (200 g) 4 tablespoon bulgur or pasta (40 g) (oil not added) Salad (oil not added) Half cup of yogurt (100 g) 2 slices whole grain bread (50 g)	1 cup of soup (200 g) 4 tablespoons vegetable (200 g) 2 tablespoon bulgur or pasta (20 g) Salad (with olive oil) Half cup of yogurt (100 g) 2 slices whole grain bread (50 g)
Snack	Snack	Snack	Snack
1 packet of hazelnut (50 g)	1 packet of raisin (50 g)	1 packet of hazelnut (50 g) and 1 packet of raisin (50 g)	1 slice low fat white cheese (30 g) 2 slices whole grain bread (50 g) Mandarin (125 g)
Dinner	Dinner	Dinner	Dinner
Chicken or fish (60 g) 4 tablespoons vegetable (200 g) Salad (oil not added) Half cup of yogurt (100 g) 3 slices whole grain bread (75 g)	Chicken or fish (60 g) 4 tablespoons vegetable (200 g) 4 tablespoon bulgur or pasta (40 g) Salad (oil not added) Half cup of yogurt (100 g) 2 slices whole grain bread (50 g)	Chicken or fish (60 g) 4 tablespoons vegetable (200 g) Salad (oil not added) Half cup of yogurt (100 g) 3 slices whole grain bread (75 g)	Chicken or fish (60 g) 4 tablespoons vegetable (200 g) 2 tablespoon bulgur or pasta (20 g) Salad (with olive oil) Half cup of yogurt (100 g) 2 slices whole grain bread (50 g)
Snack	Snack	Snack	Snack
Apple (120 g) Orange (200 g) Half cup of milk (100 g)	Orange (200 g) Half cup of milk (100 g)	Orange (200 g) Half cup of milk (100 g)	Orange (200 g) Half cup of milk (100 g)

HD: Hazelnut diet, RD: Raisin diet, HRD: Hazelnut + raisins diet, CD: Control diet

and triglyceride with refractometric photometric measuring system using CardioChek® P. Analyzer (PTS Diagnostics, Indianapolis, USA) portable whole blood test system. The use of capillary blood for the measurement of blood lipids is valid and reliable (35). CardioCheck PA system uses a single reagent strip to measure the lipid profile. It separates plasma from red

blood cells, then some of the plasma is directed to analyte-specific reaction pads and lipid concentrations are determined by reflectance photometry. HDL is initially separated from LDL and VLDL fractions following precipitation by phosphotungstic acid. Total cholesterol and HDL cholesterol are both converted enzymatically to cholest-4-en-3-one and hydrogen peroxide.

Table 2. The energy and nutrients of the diets designed by the researcher and consumed by the participants during the research

	HD	HD RDA%	RD	RD RDA%	HRD	HRD RDA%	CD	CD RDA%	RDA
Energy (kcal)	1996.5	103	2015.2	104	1998.7	103	2013.5	104	1934.1
Protein (g)	70.1 g	123	65.8	115	69.8	122	68.0	119	57.1
Protein (%)	14	-	13	-	14	-	14	-	-
CHO (g)	255.8	93	266.7	97	256.9	93	264.4	96	276.1
CHO (%)	51	-	53	-	52	-	53	-	-
Total fat (g)	78.7 g	120	77.5	118	78.1	119	77.7	118	65.6
Total fat (%)	34	-	34	-	34	-	34	-	-
Total SFA (g)	22.4	-	24.1	-	22.4	-	24.0	-	-
Total SFA (%)	10.1	-	10.7	-	10.1	-	10.7	-	-
Total MUFA (g)	40.0	-	30.1	-	40.0	-	30.2	-	-
Total MUFA (%)	18.0	-	13.5	-	18.0	-	13.5	-	-
Total PUFA (g)	11.0	110	18.1	181	10.6	106	18.3	183	10.0
Total PUFA (%)	4.9	-	8.1	-	4.8	-	8.2	-	-
Omega 3 (g)	1.2	109	1.2	109	1.1	100	1.3	118	1.1
Omega 6 (g)	9.8	89	16.9	153	9.5	86	17.0	154	11.0
Cholesterol (mg)	117.6	-	117.6	-	117.6	-	117.6	-	-
Fiber (g)	39.8	133	31.0	103	34.1	114	34.9	116	30.0
Vitamin A (µg)	1034.1	129	929.1	116	907.5	113	1095.2	137	801.0
Vitamin E (mg)	26.9	224	24.0	200	25.9	216	24.2	202	12.0
Vitamin K (µg)	150.3	251	153.2	255	147.2	245	151.9	252	60.0
Thiamine (mg)	1.4	139	1.2	115	1.3	131	1.3	125	1.0
Riboflavin (mg)	1.9	156	1.7	143	1.8	149	1.8	150	1.2
Niacin (mg)	25.7	197	23.4	180	24.8	191	24.6	189	13.0
Pantothenic acid (mg)	6.5	109	5.6	92	6.0	100	6.2	103	6.0
Vitamin B6 (mg)	2.0	167	1.7	144	1.9	154	1.8	151	1.2
Biotin (µg)	79.9	178	55.2	123	73.8	164	59.6	133	45.0
Folic acid (µg)	360.1	90	318.5	80	339.6	85	354.4	86	400.0
Vitamin B12 (µg)	5.3	176	5.3	176	5.3	176	5.3	176	3.0
Vitamin C (mg)	154.0	154	122.0	122	123.5	123	154.9	155	100.1
Sodium (mg)	2193.6	110	2316.5	116	2182.2	109	2456.4	123	2001.0
Potassium (mg)	3999.9	114	3460.5	99	3740.4	107	3637.5	104	3500.0
Calcium (mg)	1259.9	126	1106.6	111	1213.4	121	1176.4	118	1001.0
Magnesium (mg)	438.3	146	331.6	111	405.0	135	364.8	122	300.0
Phosphor (mg)	1504.2	215	1330.2	190	1466.2	209	1394.4	199	701.0
Iron (mg)	13.8	92	11.6	77	13.0	87	11.9	79	15.0
Zinc (mg)	12.9	184	11.7	167	12.3	176	12.4	177	7.0
Copper (mg)	2.0	158	1.3	106	1.9	152	1.3	106	1.3
Manganese (mg)	9.1	260	5.8	166	8.5	242	6.5	186	3.5
Iodine (µg)	66.4	33	62.2	31	61.7	31	64.5	32	200.1

HD: Hazelnut diet, RD: Raisin diet, HRD: Hazelnut + raisins diet, CD: Control diet, SFA: Saturated fatty acids, MUFA: Mono-unsaturated fatty acids, PUFA: Poly-unsaturated fatty acids, RDA: Recommended dietary allowance, %: Ratio of energy from nutrients

Table 3. The baseline characteristics of the four groups

	HG (n=9)		RG (n=9)		HRG (n=9)		CG (n=10)		p-value
	X	SD	X	SD	X	SD	X	SD	
Baseline characteristics									
Age (years)†	52.0	6.4	49.7	7.8	48.1	6.4	52.0	3.5	0.500
Total cholesterol (mg/dL)†	238.7	26.7	232.6	31.0	229.3	19.7	232.5	25.9	0.804
LDL cholesterol (mg/dL)†	158.2	15.7	153.6	17.2	142.7	17.9	155.4	19.1	0.059
HDL cholesterol (mg/dL)‡	49.9	9.4	51.4	11.4	51.3	9.7	49.3	4.9	0.942
Triglyceride (mg/dL)‡	151.8	78.1	137.6	76.9	176.3	76.7	140.5	49.8	0.641
Glucose (mg/dL)‡	94.2	7.8	92.9	6.6	96.1	8.3	94.7	9.8	0.872
Systolic blood pressure (mmHg)†	121.7	6.1	123.3	6.6	123.6	4.5	126.0	4.6	0.402
Diastolic blood pressure (mmHg)†	77.2	7.5	76.7	5.0	79.7	4.4	80.5	1.6	0.331
Weight (kg)‡	78.5	12.5	83.7	13.7	80.0	9.9	81.9	12.8	0.821
BMI (kg/m²)‡	35.7	4.7	35.8	6.4	34.6	4.3	36.0	6.1	0.945
Waist circumference (cm)‡	104.1	11.2	106.1	9.4	98.3	10.7	108.1	16.5	0.376
Waist/Hip ratio‡	0.88	0.07	0.89	0.05	0.85	0.05	0.91	0.07	0.196
Fat mass (kg)‡	34.0	6.7	35.4	7.9	33.3	6.5	35.7	7.0	0.868
Fat mass (%)‡	43.1	2.6	41.9	2.6	41.4	3.6	43.4	2.8	0.407

HG: Hazelnut group, RG: Raisin group, HRG: Hazelnut-raisin group, CG: Control group, BMI: Body mass index, X: Mean, SD: Standard deviation, †p-values were assessed using the Kruskal-Wallis tests, ‡p-values were assessed using the OnewayAnova tests

The peroxide then reacts with disubstituted aniline to form quinoneimine dyes. Triglyceride also undergoes enzymatic conversion to dihydroxyacetone phosphate and hydrogen peroxide. Its concentration is determined using the same color reaction as cholesterol and HDL. LDL is calculated using the Friedewald formula for samples with triglyceride concentrations. Fasting blood glucose is analyzed with GlukoDr (AGM-2100, China) blood glucose test meter. The GlucoDR reference device is the YSI 2300 Analyzer. Measurements were done five minutes after the blood was taken.

Blood Pressure Measurements

Individuals systolic and diastolic blood pressure were measured by the family nurse at the beginning and at the end of the 6 weeks after 10-minute rest with Omron Q142 Hem-1040-e Full Automatic Blood Pressure Monitor from each arm. Blood pressure measured in duplicate, the higher value was recorded.

Anthropometric Measurements

At the beginning and at the end of the 6-week experimental period weight, height, waist and hip circumference and skinfold thickness measurements were taken by the researcher. Measurements were repeated 3 times, mean values were recorded. Tanita BC 601 body analysis scale for weight measurement, Holtain Skinfold Caliper for skinfold thickness, and standard tape measure for waist and hip circumference were used. Weight and height measurements were used for calculating BMI, waist and hip measurements were used for calculating waist/hip ratio. Body fat mass and fat-free tissue mass were calculated

by measuring the skinfold thicknesses from 4 regions (triceps, biceps, subscapular and suprailiac).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS version 16.0, Chicago, IL) program was used to statistically evaluate the data obtained from questionnaires, biochemical tests, and anthropometric measurements. Obtained continuous variables were expressed as mean (X) and standard deviation (SD). Normality distribution of variables was analyzed with Kolmogorov-Smirnov. Oneway-ANOVA was used for the data with normal distribution and Kruskal-Wallis test was used for the data without normal distribution. The General Linear Model-Repeated Measures analysis was used for the evaluation of repeated measurements between the groups. For the evaluation of changes in measurement over time within groups (changes occurring in itself), General Linear Model-Repeated Measures analysis was used for data with normal distribution and the Wilcoxon test was used for data without normal distribution. To determine the significance of the study, statistical analyzes focused on comparing the changes that occurred in biochemical and anthropometric measurements between the four groups at the end of 6 weeks and comparing the self-generated changes in the groups compared with baseline measurements. The statistical significance level in the tests was evaluated as $p < 0.05$.

Results

Forty-four hyperlipidemic women participated in the study. The research was completed with a total of 37 individuals. Data from

9 individuals in the HG, 9 individuals in the RG, 9 individuals in the HRG and 10 individuals in the CG were finally analyzed (see CONSORT flow-diagram in Figure 1).

Generally, the compliance rate was high. All of hazelnuts and raisins were consumed during the study in requested groups. No serious complications were reported during the study.

According to surveys conducted at the beginning of the research, it was determined that 94.6% (n=35) of the participants were educated for five years or less, 91.9% (n=34) did not work and 89.2% (n=33) were married. None of the participants had chronic illness, used a drug, a supportive product such as vitamin-mineral usage, or had food allergy. The baseline characteristics (age, blood lipids, blood glucose, blood pressure, and anthropometric measurements) of the four groups are given in Table 3.

At the end of the study, changes in blood lipids, blood glucose, blood pressure and anthropometric measurements between groups were compared with general linear model repeated measures analysis. As shown in Table 4, there was no statistically significant difference between groups regarding the changes in blood lipids, blood glucose, blood pressure and anthropometric measurements at the end of the study (all $p>0.05$).

The evaluation of initial and final blood lipids, blood glucose, blood pressure levels and anthropometric measurements by groups are given in Table 5. At the end of the study, total cholesterol and LDL cholesterol values were found to be statistically significantly

(all $p<0.05$) lower in all groups compared to the baseline measurements. The decrease in total cholesterol was -21.8 ± 13.9 mg/dL for the HG, -22.6 ± 27.7 mg/dL for the RG, -24.7 ± 20.4 mg/dL for the HRG, and -15.7 ± 10.9 mg/dL for the CG. There was an increase in HDL cholesterol values in HG and HRG (2.7 ± 3.8 mg/dL, 1.1 ± 11.3 mg/dL respectively), and a decrease in RG and CG ($-1.86.5$ mg/dL, -1.9 ± 7.3 mg/dL respectively). Triglycerides decreased in HG, RG and HRG (-27.9 ± 48.7 mg/dL, 9.4 ± 43.5 mg/dL, -30.6 ± 55.3 mg/dl respectively) and triglycerides increased in CG (24.9 ± 54.1 mg/dL).

As shown in Table 4, at the end of the study there was no statistically significant difference between groups regarding the changes in weight, BMI, waist circumference, waist/hip ratio, and fat mass (all $p>0.05$). As shown in Table 5, there was a statistically significant decrease in the BMI levels and fat masses (kg) of all groups ($p<0.05$) at the end of the study. While there was a statistically significant decrease in terms of waist circumference in CG, HG and RG ($p<0.05$) compared to baseline measurements, there was not found a significant difference in HRG ($p>0.05$) (Table 5).

Discussion

The aim of the study was to evaluate the effects of raisin consumption in hyperlipidemic obese women regarding lipid profile and anthropometric measurements and compare it with hazelnut consumption and cardioprotective diet which are known to have beneficial effects on the lipid profile. As a result of the research, no significant difference was found between the four groups regarding blood lipids and anthropometric measurements (Table 4).

Nuts are rich in unsaturated fatty acids and most nuts include high MUFA. Because of having healthy fats, frequent nut intake lowers cholesterol, increases LDL resistance to oxidation, improves endothelial function and prevents CVD (36). Besides having appropriate fatty acid composition, nuts contain a variety of bioactive substances: plant protein, minerals, alpha-tocopherol, phenolic compounds and fiber (5). These bioactive components reduce oxidation, have anti-inflammatory effect, and improve endothelial function (6). More than 40 interventional studies on healthy or moderately hyperlipidemic subjects have shown that nuts raise HDL, lowers total cholesterol and LDL (37). An important result of the studies conducted on nuts is that the cholesterol-lowering effects of these products depend on the amount of consumption and they are especially effective in patients with high baseline LDL levels (7).

Among nuts, hazelnut is important for nutrition and health because of its MUFA content. Besides MUFA, other components including PUFA, phytosterols, and soluble dietary fiber, present in hazelnut, decrease plasma total cholesterol, and LDL. Hazelnut also contains fat-soluble bioactive components (tocopherols and phytosterols), minerals (magnesium, selenium), amino acids, antioxidants, and phytochemicals (8,9). Moreover, vitamin E, found in hazelnut, has a cardioprotective effect (by inhibition of LDL oxidation) (9).

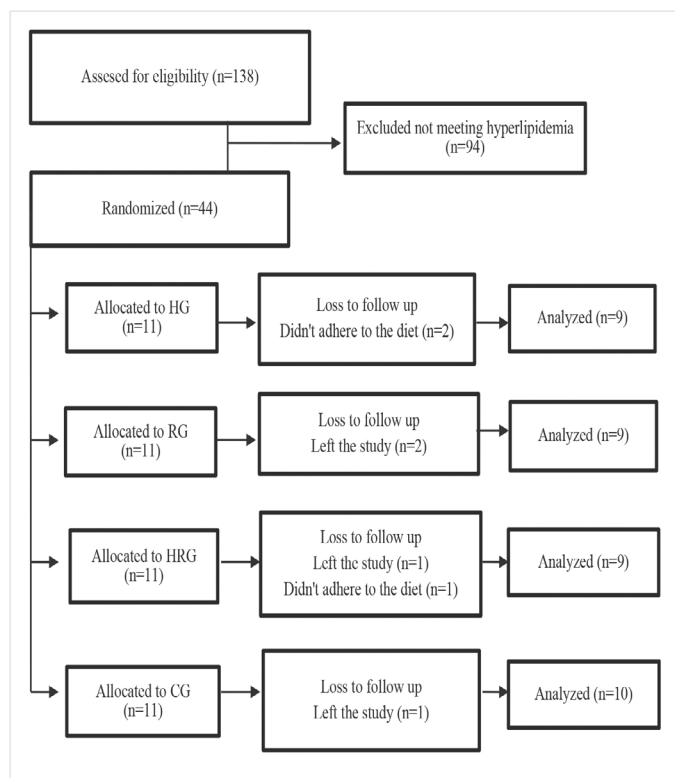


Figure 1. CONSORT 2010 flow diagram for the randomized controlled clinical trial

HG: Hazelnut group, RG: Raisin group, HRG: Hazelnut-raisin group, CG: Control group

Table 4. Evaluation of changes in biochemical measurements, blood pressure and anthropometric measurements among groups

	HG (n=9)		RG (n=9)		HRG (n=9)		CG (n=10)		F	P value*
	X	SD	X	SD	X	SD	X	SD		
Biochemical indicate										
Total cholesterol (mg/dL)										
Baseline	238.7	26.7	232.6	31.1	229.3	19.7	232.5	25.9	0.391	0.760
After intervention	216.9	29.7	210.0	18.5	204.7	34.4	216.8	35.1		
LDL cholesterol (mg/dL)										
Baseline	158.2	15.7	153.6	17.2	142.7	17.9	155.4	19.1	0,007	0.999
After intervention	139.7	27.2	134.8	16.2	123.0	22.3	136.4	31.2		
HDL cholesterol (mg/dL)										
Baseline	49.9	9.4	51.4	11.4	51.3	9.7	49.3	4.9	0.784	0.511
After intervention	52.6	11.3	49.7	8.9	52.4	11.3	47.4	6.6		
Triglycerides (mg/dL)										
Baseline	151.8	78.1	137.6	76.9	176.3	76.7	140.5	49.8	2.442	0.082
After intervention	123.9	42.1	128.1	55.6	145.8	53.8	165.4	79.9		
Glucose (mg/dL)										
Baseline	94.2	7.8	92.9	6.6	96.1	8.3	94.7	9.8	2.427	0.083
After intervention	93.3	11.7	101.6	6.9	93.1	10.4	98.5	8.2		
Blood pressure										
Systolic										
Baseline	121.7	6.1	123.3	6.6	123.6	4.5	126.0	4.6	1.236	0.312
After intervention	121.1	5.5	119.4	7.3	115.6	8.5	122.0	7.9		
Diastolic										
Baseline	77.2	7.5	76.7	5.0	79.7	4.4	80.5	1.6	0.663	0.581
After intervention	75.6	5.3	76.7	5.6	75.6	7.3	77.5	5.4		
Anthropometric measurements										
Weight (kg)										
Baseline	78.5	12.5	83.7	13.7	80.0	9.9	81.9	12.8	0.558	0.647
After intervention	76.0	12.5	82.2	13.5	77.9	9.6	79.6	12.3		
BMI (kg/m²)										
Baseline	35.7	4.7	35.8	6.4	34.6	4.3	36.0	6.1	0.560	0.645
After intervention	34.5	4.7	35.1	6.2	33.6	4.0	34.9	5.7		
Waist circumference (cm)										
Baseline	104.1	11.2	106.1	9.4	98.3	10.7	108.1	16.5	1.714	0.183
After intervention	98.3	10.9	101.2	9.9	95.1	9.0	99.9	13.9		
Waist/Hip ratio										
Baseline	0.88	0.07	0.89	0.05	0.85	0.05	0.91	0.07	1.852	0.157
After intervention	0.85	0.04	0.86	0.04	0.85	0.05	0.87	0.04		
Fat mass (kg)										
Baseline	34.0	6.7	35.4	7.9	33.3	6.5	35.7	7.0	1.232	0.314
After intervention	31.8	6.2	34.1	7.9	31.1	6.0	33.5	6.6		
Fat mass (%)										
Baseline	43.1	2.6	41.9	2.6	41.4	3.6	43.4	2.8	1.036	0.389
After intervention	41.7	2.5	41.1	3.3	39.6	3.7	41.9	2.9		

HG: Hazelnut group, RG: Raisin group, HRG: Hazelnut-raisin group, CG: Control group, BMI: Body mass index, X: Mean, SD: Standard deviation, *p values were assessed using the general linear model of variance for repeated measures

Table 5. Effect of 6 weeks of diet intervention on biochemical indices, blood pressure and anthropometric measurements based on groups

	Baseline		After intervention		Δ		p value
Biochemical indicate	X	SD	X	SD	X	SD	
Total cholesterol (mg/dL)							
HG (n=9)†	238.7	26.7	216.9	29.7	-21.8	13.9	0.008
RG (n=9)†	232.6	31.1	210.0	18.5	-22.6	27.7	0.021
HRG (n=9)‡	229.3	19.7	204.7	34.4	-24.7	20.4	0.020
CG (n=10)‡	232.5	25.9	216.8	35.1	-15.7	10.9	0.004
LDL cholesterol (mg/dL)							
HG (n=9)†	158.2	15.7	139.7	27.2	-18.6	14.9	0.008
RG (n=9)†	153.6	17.2	134.8	16.2	-18.8	19.6	0.008
HRG (n=9)†	142.7	17.9	123.0	22.3	-19.7	16.3	0.008
CG (n=10)†	155.4	19.1	136.4	31.2	-19.0	17.2	0.019
HDL cholesterol (mg/dL)							
HG (n=9)‡	49.9	9.4	52.6	11.3	2.7	3.8	0.207
RG (n=9)‡	51.4	11.4	49.7	8.9	-1.8	6.5	1.000
HRG (n=9)‡	51.3	9.7	52.4	11.3	1.1	11.3	1.000
CG (n=10)‡	49.3	4.9	47.4	6.6	-1.9	7.3	1.000
Triglycerides (mg/dL)							
HG (n=9)‡	151.8	78.1	123.9	42.1	-27.9	48.7	0.373
RG (n=9)‡	137.6	76.9	128.1	55.6	-9.4	43.5	1.000
HRG (n=9)‡	176.3	76.7	145.8	53.8	-30.6	55.3	0.408
CG (n=10)†	140.5	49.8	165.4	79.9	24.9	54.1	0.202
Glucose (mg/dL)							
HG (n=9)‡	94.2	7.8	93.3	11.7	-0.9	12.2	1.000
RG (n=9)‡	92.9	6.6	101.6	6.9	8.7	9.2	0.068
HRG (n=9)‡	96.1	8.3	93.1	10.4	-3.0	9.1	1.000
CG (n=10)‡	94.7	9.8	98.5	8.2	3.8	9.3	0.683
Blood pressure							
Systolic (mmHg)							
HG (n=9)†	121.7	6.1	121.1	5.5	-0.6	6.3	0.705
RG (n=9)‡	123.3	6.6	119.4	7.3	-3.9	8.2	0.579
HRG (n=9)†	123.6	4.5	115.6	8.5	-8.0	9.2	0.040
CG (n=10)†	126.0	4.6	122.0	7.9	-4.0	8.8	0.168
Diastolic (mmHg)							
HG (n=9)†	77.2	7.5	75.6	5.3	-1.7	6.1	0.450
RG (n=9)†	76.7	5.0	76.7	5.6	0.0	7.5	1.000
HRG (n=9)†	79.7	4.4	75.6	7.3	-4.1	7.1	0.078
CG (n=10)†	80.5	1.6	77.5	5.4	-3.0	5.4	0.098
Anthropometric measurements							
Weight (kg)							
HG (n=9)‡	78.5	12.5	76.0	12.5	-2.5	2.3	0.030
RG (n=9)‡	83.7	13.7	82.2	13.5	-1.5	1.6	0.074
HRG (n=9)‡	80.0	9.9	77.9	9.6	-2.1	1.2	0.002
CG (n=10)‡	81.9	12.8	79.6	12.3	-2.4	2.1	0.017
BMI (ka/m²)							

Table 5 continued

HG (n=9)‡	35.7	4.7	34.5	4.7	-1.2	1.1	0.031
RG (n=9)‡	35.8	6.4	35.1	6.2	-0.7	0.7	0.046
HRG (n=9)‡	34.6	4.3	33.6	4.0	-0.9	0.6	0.004
CG (n=10)‡	36.0	6.1	34.9	5.7	-1.1	0.9	0.020
Waist circumference (cm)							
HG (n=9)‡	104.1	11.2	98.3	10.9	-5.7	6.9	0.113
RG (n=9)‡	106.1	9.4	101.2	9.9	-4.9	1.4	0.0001
HRG (n=9)‡	98.3	10.7	95.1	9.0	-3.2	3.9	0.122
CG (n=10)‡	108.1	16.5	99.9	13.9	-8.2	5.2	0.002
Waist/Hip ratio							
HG (n=9)‡	0.88	0.07	0.85	0.04	-0.03	0.06	0.650
RG (n=9)‡	0.89	0.05	0.86	0.04	-0.03	0.02	0.009
HRG (n=9)‡	0.85	0.05	0.85	0.05	-0.01	0.03	1.000
CG (n=10)†	0.91	0.07	0.87	0.04	-0.05	0.04	0.009
Fat mass (kg)							
HG (n=9)‡	34.0	6.7	31.8	6.2	-2.21	1.42	0.005
RG (n=9)‡	35.4	7.9	34.1	7.9	-1.32	1.10	0.021
HRG (n=9)‡	33.3	6.5	31.1	6.0	-2.26	0.96	0.0001
CG (n=10)‡	35.7	7.0	33.5	6.6	-2.17	1.31	0.002
Fat mass (%)							
HG (n=9)‡	43.1	2.6	41.7	2.5	-1.41	0.68	0.001
RG (n=9)‡	41.9	2.6	41.1	3.3	-0.90	1.35	0.241
HRG (n=9)‡	41.4	3.6	39.6	3.7	-1.72	0.94	0.002
CG (n=10)‡	43.4	2.8	41.9	2.9	-1.42	0.95	0.003

HG: Hazelnut group, RG: Raisin group, HRG: Hazelnut-raisin group, CG: Control group, BMI: Body mass index, X: Mean, SD: Standard deviation, Δ: Difference after intervention-baseline, p values show the general differences among baseline and diet periods for each group, †p-values were assessed using the Wilcoxon tests, ‡p-values were assessed using the general linear model of variance for repeated measures

In a study, moderately hyperlipidemic subjects consumed daily 30 g hazelnut, 5 days a week for 4 weeks. Compared to baseline measurements, total cholesterol and LDL statistically significantly reduced, and HDL raised after hazelnut consumption (38). In this study, similar to study, daily 50 g hazelnut consumption in HG statistically significantly decreased total cholesterol and LDL compared to initial measurements. Despite the increase in HDL and a decrease in triglyceride compared to baseline measurements, there was no statistically significant difference (Table 5).

The results of various studies have determined that the consumption of grape and grape products has a protective effect against CVD (15,16,18-21). This effect is attributed to the antioxidant compounds found in the grape (17). Anthocyanin is an important component of raisin. A study comparing the effect of anthocyanin supplementation with the placebo in hyperlipidemic subjects revealed that the anthocyanin supplements reduced LDL cholesterol levels statistically significantly ($p<0.001$) compared to baseline measurements. LDL cholesterol reduced in a much more extent in the anthocyanin group ($p=0.001$). Supplementation of anthocyanin increased HDL cholesterol levels compared to baseline measurements. HDL raised in a much more extent

in the anthocyanin group compared with the placebo group after the intervention ($p=0.001$) (39). Without changing the daily diet of healthy individuals, the effect of 6-week raisin consumption and walking on blood lipids was investigated in a study and at the end, the total cholesterol and LDL statistically significantly decreased compared to initial measurements and no difference was found between the groups (40). In this study, similar to the study by Puglisi et al. (40), a statistically significant reduction was detected in the total cholesterol and LDL levels of the RG compared to the baseline measurements and there was no statistically significant difference in terms of blood lipids between groups.

Studies using nut and grape products have shown that these products have beneficial effects on lipid profiles and reduce CVD risk (6,7,10,19,38,41). As a result of these positive results, it was expected that the consumption of hazelnut and raisins together would decrease the risk of CVD. As a result of this research, positive changes in blood lipids were determined in HRG compared to initial measurements. As shown in Table 5, the total cholesterol and triglyceride levels of HRG decreased more than those of CG and the increase in HDL levels was found to be higher. However, when compared with the CG, the changes in

the HRG were not statistically significant ($p>0.05$). Nevertheless, these results are thought to be important in decreasing CVD risk.

As a result of the research, positive changes were found compared to the initial measurements in lipid profiles and anthropometric measurements of the four groups, which consumed cardioprotective diets with similar energy content, containing either raisins, hazelnuts, or a combination of raisins and hazelnuts. The difference in blood lipids between dietary groups was not statistically significant. This may be due to the cardioprotective diet consumption in all groups.

Epidemiological studies have shown a negative relation between regular nut consumption and type 2 diabetes in women (42). Raisin is rich in fiber and fructose, and it belongs to the low-middle glycemic index nutrient class (15). It has been shown in some clinical trials that the consumption of raisins does not have any adverse effect on blood glucose (15,43,44). As a result of this study, there was no statistically significant difference in fasting blood glucose compared to initial measurements. This result is also supporting previous studies.

Epidemiological and clinical studies have found a negative relation between the consumption of nuts (5,45), dry fruits (15,44), and blood pressure. There was no statistically significant change in systolic/diastolic blood pressures measured at baseline compared to the values measured after 6 weeks on the diet. Therefore, it was concluded that hazelnuts and raisins have no adverse effect on blood pressure.

At the end of our study, positive changes were found in the anthropometric measurements of all four groups. Long-term epidemiological and clinical studies have shown that there is no significant relationship between consumption of nuts and weight gain (46). In some studies conducted by adding nuts such as hazelnuts (12,38), pistachios (47), and peanuts (48) to daily diets, no significant difference was found in anthropometric measurements compared to baseline. At the end of our study, there was a statistically significant decrease in weight, BMI levels, waist circumference and fat mass in all groups as expected because all the individuals were obese and their diet contained recommended daily energy values. The decrease in waist circumference, an important risk factor for CVD, was also observed in all groups, but there was no significant difference in terms of waist circumference between the groups.

As shown in Table 4, there were no statistically significant differences in weight, BMI, and body fat mass changes between groups. It was concluded that the reason for not finding any difference between groups regarding the anthropometric measurements was the isocaloric diet consumption of all groups during the study.

Study Limitations

The sample size was considered among the limitations of research. Reasons such as strict inclusion criteria for research, abandonment of research and individuals not complying with the diet limited the sample size negatively. There were some

limitations for diets in this research: Participants consumed diet menus given to them by the researcher for 6 weeks. The dietary assessment was made only with the participants' declaration. The dietary record was not received. Individual compliance with diets and consumption of nuts and grapes given to them were checked with the product consumption schedule given to them at weekly controls, and no individual observations were made. Another limitation was that the amount of MUFA in diets of hazelnut-consuming groups was higher than the amount of PUFA in other groups. In order to demonstrate the effects of the products on blood lipids and anthropometric measurements clinically, it is suggested to increase the amount of the products, to have a larger study group and to have a longer study period.

Conclusion

As a result of the research, there was no significant change in lipid profile and anthropometric measurements between the four groups. This may be due to consumption similar cardioprotective diet with similar energy content in all groups. Because of the improvement on lipid profile and anthropometric measurements of four groups at the end of the study, it was concluded that hazelnut and raisins consumption can be recommended in addition to an appropriate diet program to hyperlipidemic individuals.

Ethics

Ethics Committee Approval: All the research related procedures were approved by the Istanbul No 6 Ethics Committee of Clinical investigations in Bakırköy Dr. Sadi Konuk Education and Research Hospital with the decision dated 29.04.2013 and numbered 2013/05/01.

Informed Consent: The participants were informed about the research and the experimental period was started after signing the informed consent form.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.Ö.Y., B.Ö., Design: H.Ö.Y., B.Ö., Data Collection or Processing: H.Ö.Y., Analysis or Interpretation: H.Ö.Y., Literature Search: H.Ö.Y., Writing: H.Ö.Y., B.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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