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OLIVE LEAVES HERBAL TEA EFFECT IN TYPE 2 DIABETIC PATIENTS WITH PREHYPERTENSION

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ABSTRACT

Olive tree leaves have been widely used in traditional medicine for its antioxidant, antihypertensive, hypoglycemic, hypocholesterolemic and cardioprotective activity. A clinical study was conducted to evaluate the anti-hypertensive effect of olive leaves herbal tea (50 g of dried and ground leaves in 250 ml of warm water/twice daily for 28 weeks) in type 2 diabetic patients (n=31, 13 women and 18 men) diagnosed with prehypertension. The primary efficacy in reducing of SBP and DPB was seen after only 4 weeks of the study. At the end of the study, blood pressure dropped to normal values in of 53% women and 61.11% of men (-11.2 mm Hg and -6.7 mm Hg for SBP and DBP respectively in women subjects; and -8.3 mm Hg and -6.7 mm Hg for SBP and DBP respectively in men subjects). Olive leaves herbal tea, at the dosage regimen of 500 mg twice daily, may represent an effective diet regimen that lowers blood pressures in type 2 diabetic subjects diagnosed with prehypertension as the JNC 7 report.

KEYWORDS: Olive leaves herbal tea; prehypertension; type 2 diabetic patients.

INTRODUCTION

Type 2 diabetes (T2DM) is one of the fastest growing public health problems in developing countries and is associated with a 70% to 80% chance of premature death from cardiovascular disease (CVD) and stroke.[1] It is estimated that the number of diabetic patients will double in 2030 to reach about 366 million and this increase has been highly linked to the westernized dietary patterns, physical inactivity and increasing rates of obesity and metabolic syndrome.[2] Type 2 diabetes patients generally carry a number of risk factors for CVD, including hyperglycemia, hypertension, dyslipidemia, alterations in inflammatory mediators and coagulation parameters, as well as other risk factors which are closely associated with insulin resistance.[3]

Epidemiological studies have indicated that hypertension and type 2 diabetes are frequently associated conditions and their concordance is increased in populations. Hypertension affects more than 40% of diabetic patients and cardiovascular disease risk doubles for each increment of 20/10 mm Hg.[4-6] The JNC 7 report has introduced a new classification that includes the term "prehypertension" for those with blood pressure ranging from 120 to 139 mm Hg systolic (SBP) and/or 80 to 89 mm Hg diastolic blood pressure (DBP). This new designation is intended to identify those individuals at high risk of developing hypertension and who are not candidate for drug therapy. They are unambiguously advised to adopt healthy lifestyles which could reduce blood pressure, decrease the rate of progression of blood pressure to hypertensive levels with age, or prevent hypertension entirely.[4] Except for individuals with prehypertension who also have diabetes, those patients should be considered candidates for appropriate drug therapy if a trial of lifestyle modification fails to reduce their BP to 130/80 mm Hg or less.[5] The United Kingdom Prospective Diabetes Study (UKPDS)[7] demonstrated that each 10 mm Hg decrease in SBP was associated with average reductions in rates of diabetes-related mortality of 15%; myocardial infarction, 11%; and the microvascular complications of retinopathy or nephropathy, 13%.

Non-pharmacologic interventions such as healthy diet and exercise are first-line therapies and are used with pharmacologic therapy when necessary. The American Diabetes Association (ADA) does not recommend a specific diet over another for the diabetic patients. On the other hand, the ADA lists three different types of diets either low-carbohydrate, low-fat calorie-restricted or Mediterranean diet as a mean for weight loss for individuals who have or are at risk of having diabetes and it was proven to be associated with 52% reduction of

diabetes mellitus incidence.[8,9] Mediterranean diet is known for its health benefits, especially given to the large amount of polyphenols found in fruits, vegetables, bread, cereals and olive oil.[10]

There are five groups of identified phenolic compounds in olive tree and oleuropein is the most abundant phenolic compound in olive leaves, followed by hydroxytyrosol, luteolin-7-glucosides, apigenin-7-glucosides and verbascoside.[11] These polyphenols have numerous beneficial effects to human health, such as antioxidant capacity, anti-hypertensive, hypoglycemic, hypo-cholesterolemic, cardio protective, anti-inflammatory efficacy.[12-16]

As a successful management of CVD associated with diabetes represents a major challenge to the clinicians. The present study sought to confirm the hypertensive lowering efficacy of the olive leaves herbal tea in type 2 diabetic adults.

MATERIALS AND METHODS

Preparation of olive leaves herbal tea

Olive leaves were collected from Safita area, a coastal region in Tartous/Syria. They were scientifically approved in the Department of Botany, Al-Andalus University for Medical Sciences. The plant was cleaned and shed dried at 25°C, then ground with a blender. A tea was prepared by soaking 5 g of dried and ground leaves in 250 ml of warm water for about 5 min. Finally, the tea was filtered.

Study design

The present study is a clinical trial of 28 weeks duration. The study group (n = 31, 13 women and 18 men) was recruited from a convenience sample of consecutive patients treated at the diabetic clinic in Tartous between November 2015 and May 2016. The eligible patients had been diagnosed with type 2 diabetes, were 25–69 years of age, had a body mass index < 40 kg/m^2, were on oral (metformin or sulfonylureas) and/or diet therapy for T2DM and were diagnosed to have prehypertension s described by the JNC 7 report. The excluded patients were on insulin therapy; had hepatic or renal dysfunction; pregnancy or breastfeeding during the trial period.

All patients were asked to complete validated activity and dietary behaviors questionnaires at baseline and were encouraged to perform moderate physical activity daily and to follow general healthy dietary patterns as described by the American Dietary Guidelines 2010.

A written consent was obtained from the participants, expressing their willingness to participate in the study. Ethical approval was obtained from Al-Andalus University for Medical Sciences prior to commencement of the study.

Participants received the olive leaves' tea two times per day during the whole 28 weeks of the study. During the follow up period all patients were given a monthly checklist form to confirm adherence to herbal tea use. SBP and DBP were measured every 4 weeks.

Measures

BMI was calculated by measuring weight in light clothing and no shoes, and measuring height to a wall mounted ruler. Blood pressure (BP) was measured with a special precaution to reduce the variation of BP value with resting values; individuals were requested to take 10 minutes rest prior to measuring the BP with a standard electronic BP measuring instrument (Table 1).

Table 1. Baseline measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP).

	Women	Men
Number of patients	13	18
Age (years)	25-56	29-69
BMI (kg/m^2)	31.56±2.26	36.23±3.19
Fasting glucose level (mg/dL)	193±36.11	162.38±42.64
Antidiabetic drugs	Metformin 76.92% Sulfonylureas 23.07%	Metformin 66.66% Sulfonylureas 33.33%
SBP (mm Hg)	133.84±6.81	133.88±5.66
DBP (mm Hg)	83.84±5.82	84.44±6.43

Fasting blood samples were collected in EDTA vial and plasma was separated by centrifuging the blood samples at 8000 rpm for 10–15 minutes following which glucose was determined by the glucose oxidase method (Table 1).

Statistical analysis

Baseline descriptive data are presented as mean ± standard deviation (SD). ANOVA test with repeated measures was used to compare each parameter in each group before and after the treatment. In addition, $p<0.05$ was considered statistically significant.

RESULTS

Effects on blood pressures

At the beginning of the study the mean blood pressure in women subjects was 133.84±6.81 mm Hg for SBP and 83.84±5.82 mm Hg for DBP, while it was 133.88±5.66 mm Hg for SBP and 84.44±6.43 mm Hg for DBP in men subjects (Fig. 1).

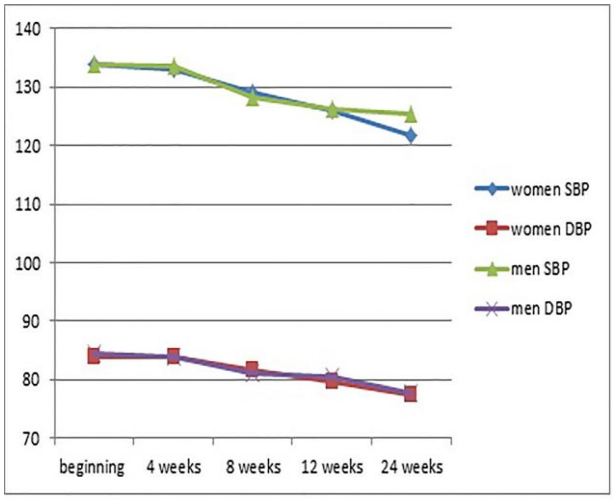

Fig. 1. Blood pressure levels throughout the study in both women and men subjects with baseline SBP level of > 120 mm Hg and DBP level of > 80 mm Hg. The number of subjects was 13 women and 18 men.

After 4 weeks of study, a small statistically significant decrease ($p < 0.05$) in SBP and DBP in both subject groups was seen (-0.8 mm Hg and -0.2 mm Hg for SBP and DBP respectively in women subjects; and -0.2 mm Hg and -0.6 mm Hg for SBP and DBP respectively in men subjects). The Olive leaves herbal tea demonstrated a significant lowering blood pressure effect at 8 weeks of the study with -4.6 mm Hg and -2.5 mm Hg decrease for SBP and DBP respectively in women subjects; and -5.5 mm Hg and -2.8 mm Hg decrease for SBP and DBP respectively in men subjects. At the end of the study and as presented in Table 2, the SBP and SBP dropped to normal values in 53% of women and 61.11% of men (-11.2 mm Hg and -6.7 mm Hg for SBP and DBP respectively in women subjects; and -8.3 mm Hg and -6.7 mm Hg for SBP and DBP respectively in men subjects).

Table 2. Measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) after 28 weeks of the study.

	Women	Men
Number of patients	13	18
BMI (kg/m^2)	29.92±4.15	37.01±5.12
Fasting glucose level (mg/dL)	122.46±21.89	117.77±30.28
SBP (mm Hg)	122.69±8.90	125.55±10.25
DBP (mm Hg)	77.30±4.64	77.77±6.06

DISCUSSION

A prophylactic blood pressure lowering action of the olive leaf extract has been shown in a preclinical study with rats rendered hypertensive by daily oral doses of L-NAME (NG-nitro-L-arginine methyl ester, 50 mg/kg) for a period of 8 weeks.[17] The same extract was tested for 8 weeks as a food supplement at 500 or 1000 mg/day dose in an open study including 40 borderline hypertensive monozygotic twins with mild hypertension (systolic BP of 120–160mmHg and diastolic BP of 80–95mmHg). Systolic and diastolic blood pressure changed significantly within pairs, depending on the dose.[18] Susalit et al. (2011) also found a beneficial effect of the extract (500 mg twice daily) in subjects with stage-1 hypertension (SBP between 140 and 160 mm Hg) compared with the effect of Captopril (12.5-25 mg twice daily) for a period of 8 weeks.[12] Means of SBP reduction from baseline to the end of study were −11.5±8.5 and −13.7±7.6 mm Hg in olive leaf extract and captopril groups, respectively; and those of DBP were −4.8±5.5 and −6.4±5.2 mmHg, respectively.[12] Consistent with the previous study's result, in the current study we also found a beneficial effect of the olive leaves herbal tea in type 2 diabetic subjects with prehypertension (with baseline systolic blood pressure higher than 120 but lower than 139 mm Hg, and a diastolic blood pressure higher than 80 but lower than 89 mm Hg) as shown in table 2.

The mechanism of action by which olive leaf extract exerts its anti-hypertensive effects is continuously being studied. Oleuropein, the most abundant polyphenol in olive leaf extract is suggested to be the main constituent that exerts this anti-hypertensive effect. It enhances in a dose-dependent manner the production of nitrite in LPS-challenged mouse macrophages. This effect was blocked by the iNOS inhibitor L-NAME, indicating increased iNOS activity. Also, Western blot analysis of cell homogenates shows that oleuropein increases iNOS expression in such cells. Taken together, these data suggest that, during endotoxin challenge, oleuropein potentiates the macrophage-mediated response, resulting in higher NO production, currently believed to be beneficial for the cardiovascular system due to vasorelaxant activities.[19] It was also proved that oleuropein could be cleaved by β-glucosidase to derivatives with high ACE inhibitor activity and direct L-type Calcium channel antagonistic activity directly and reversibly.[20.21] These results could explain the decrease in SBP and DBP observed in our study as oleuropein concentration in seven Syrian olive leaves varieties ranged from 4.3±0.5 to 9.2±0.3 mg/g as reported by Tayoub et al.[22] Whether, its concentration in herbal tea ranged varied from 0.103±3.7 mg/g of dried powder soaked at 70°C for 5 minutes[23] and reaches 13.0±9.1 mg/g prepared by soaking dried powder gathered from various cultivars of Iran at 60°C for 1 hour.[24]

CONCLUSION

Prevention and treatment by dietary means is of special relevance, as recommended by WHO. The effect of olive leaves herbal tea in reducing blood pressure is advantageous since lower levels are a target for reducing the risk for cardiovascular diseases associated with diabetes.

All persons with type 2 diabetes must be started on primary prevention by encouraging healthy lifestyle diets so as to reduce the risk of CVD. The use of this intervention should be further investigated in a clinical trial large enough to evaluate extract-drug interactions and to come to an in-depth understanding on the ultimate therapeutic potential of olive polyphenols.

REFERENCES

1. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med, 1998; 339: 229–234.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care, 2004; 27: 1047–1053.
3. Kalofoutis C, Piperi C, Kalofoutis A, Harris F, Phoenix D, Singh J. Type 2 diabetes mellitus and cardiovascular risk factors: Current therapeutic approaches. Exp Clin Cardiol, 2007; 12(1): 17–28.
4. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green A, Izzo JL et *al.* and the National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA, 2003; 289: 2560-72.
5. American Diabetes Association. Treatment of hypertension in adults with diabetes. Diabetes Care, 2003; 26(1): S80-2.
6. Hu G, Jousilahti P, Barengo NC, Qiao Q, Lakka TA, Tuomilehto J. Physical activity, cardiovascular risk factors, and mortality among Finnish adults with diabetes. Diabetes Care, 2005; 28: 799-805.
7. Adler AI, Stratton IM, Neil HA, Yudkin JS, Matthews DR, Cull CA et *al.* Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. BMJ, 2000; 321: 412–419.
8. Franz MJ, Boucher JL, Green-Pastors J, Powers MA. Evidence-based nutrition practice guidelines for diabetes and scope and standards of practice. J Am Diet Assoc, 2008; 108(4): S52-8.
9. Salas-Salvadó J, Bulló M, Babio N, Martínez-González MÁ, Ibarrola-Jurado N, Basora J et *al.* and PREDIMED Study Investigators. Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes Care, 2011; 34(1): 14-9.
10. Keys A. Mediterranean diet and public health: personal reflections. Am J Clin Nutr, 1995; 61(6): 1321S-1323S.
11. Benavente-García O, Castillo J, Lorente J, Ortuño A, Del Río JA. Antioxidant activity of phenolics extracted from Olea europea L. leaves. Food Chem, 2000; 68(4): 457-62.
12. Susalit E, Agus N, Effendi I, Tjandrawinata RR, Nofiarny D, Perrinjaquet-Moccetti T et *al.* Olive (Olea europaea) leaf extract effective in patients with stage-1 hypertension: Comparison with Captopril. Phytomedicine, 2011; 18: 251-8.
13. Kontogianni VG, Charisiadis P, Margianni E, Lamari FN, Gerothanassis IP, Tzakos AG. Olive Leaf Extracts Are a Natural Source of Advanced Glycation End Product Inhibitors. J Med Food, 2013; 16(9): 817–22.
14. Jemai H, El Feki A, Sayadi S. Antidiabetic and antioxidant effects of hydroxytyrosol and oleuropein from olive leaves in alloxan-diabetic rats. J Agric Food Chem, 2009; 57(19): 8798- 804.
15. Nekooeian AA, Khalili A, Khosravi MB. Oleuropein offers cardioprotection in rats with simultaneous type 2 diabetes and renal hypertension. Indian J Pharmacol, 2014; 46(4): 398-403.
16. Khalatbary AR, Zarrinjoei GR. Anti-Inflammatory Effect of Oleuropein in Experimental Rat Spinal Cord Trauma. Iran Red Crescent Med J, 2012; 14(4): 229-34.
17. Khayyal MT, El-Ghazaly MA, Abdallah DM, Nassar NN, Okpanyi SN, Kreuter MH. Blood pressure lowering effect of an olive leaf extract (Olea europaea) in L-NAME induced hypertension in rats. Arzneimittelforschung, 2002; 52(11): 797-802.
18. Perrinjaquet-Moccetti T, Busjahn A, Schmidlin C, Schmidt A, Brad B, Aydogan C. Food supplementation with an olive (*Olea europaea* L.) leaf extract reduces blood pressure in borderline hypertensive monozygotic twins. Phytother Res, 2008; 22: 1239-42.
19. Visiolil F, Bellosta S, Galli C. Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages. Life Sciences, 1998; 62(6): 541-546.
20. Gilani AH, Khan AU, Shah AJ, Connor J, Jabeen Q. Blood pressure lowering effect of olive is mediated through calcium channel blockade. Int J Food Sci Nutr, 2005; 56(8): 613-20.
21. Scheffler A, Rauwald HW, Kampa B, Mann U, Mohr FW, Dhein S. Olea europaea leaf extract exerts L-type Ca(2+) channel antagonistic effects. J Ethnopharmacol, 2008; 120: 233–240.
22. Tayoub G, Sulaiman H, Hassan AH, Alrofi M. Determination of Oleuropein in leaves and fruits of some Syrian olive varieties. Int J Med Arom Plant, 2012; 2(3): 428-433.

23. Lalas S, Athanasiadis V, Gortzi O, Bounitsi M, Giovanoudis I, Tsaknis J et *al*. Enrichment of table olives with polyphenols extracted from olive leaves. Food Chemistry, 2011; 127: 1521–1525.
24. Ansaria M, Kazemipourb M, Fathi S. Development of a Simple Green Extraction Procedure and HPLC Method for Determination of Oleuropein in Olive Leaf Extract Applied to a Multi-Source Comparative Study. J Iran Chem Soc, 2011; 8(1): 38-47.