

THE EFFECT OF WALNUT OIL CONSUMPTION ON BLOOD SUGAR CONTROL IN PATIENTS WITH TYPE TWO DIABETES

Kamran Aghasadeghi, Mohammad Javad Zibae Nezhad, Hossein Hakimi, Hajar Khazraei

Cardiovascular Research Centre, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Pielęgniarstwo Chirurgiczne i Angiologiczne 2019; 2: 78–82

Praca wpłynęła: 5.01.2019; przyjęto do druku: 6.05.2019

Adres do korespondencji:

Mohammad Javad Zibae Nezhad, Cardiovascular Research Centre, Faculty of Medicine, Shiraz University of Medical Sciences, Zand St., 71348-44119 Shiraz, Iran, e-mail: yasaman_kh1981@yahoo.co.in

Summary

Introduction: Various epidemiological studies have shown the relationship between increased risk of atherosclerosis and cardiovascular diseases (CAD) on the one hand and poor control of blood sugar and lipid profile on the other hand. Furthermore, it has been shown that substitution of saturated fatty acids with polyunsaturated fatty acids (PUFAs) and α linolenic acid (ALA) would improve glucose homeostasis.

Material and methods: One hundred diabetic patients were assigned to the experiment and control groups randomly. For the experiment group, walnut oil (15 g/day for three months) was added to the diet, while the control group did not undergo any interventions. Before initiation of the experiment and after the end of the experiment, the systolic and diastolic blood pressure (SBP and DBP) levels of the patients were measured and recorded. Also, weight and height of the patients were recorded, and a blood sample was taken for measurement of fasting blood sugar (FBS) and HbA1c and using paired *t*-test and *t*-test for analysis.

Results: The results demonstrated that HbA1c and FBS levels decreased significantly in the experiment group ($p = 0.032$ and $p = 0.029$, respectively). However, the two groups were not significantly different in terms of SBP ($p = 0.103$), DBP ($p = 0.687$), body weight ($p = 0.202$), and BMI ($p = 0.416$).

Conclusions: Consumption of walnut oil (15 g/day for three months) improved blood glucose homeostasis in type 2 diabetic patients. Because no changes in the bodyweight and blood pressure of the patients were seen, it could be used in hypertensive or obese patients.

Key words: type 2 diabetes, FBS, glycosylated haemoglobin.

Introduction

Prevalence of type 2 diabetes mellitus (DM) is increasing globally and in the USA. The health and economic burden of the disease is very large and will increase in future. It is estimated that in western countries, the prevalence of DM will increase by 40–45%, and the number of patients will grow from 51 million cases in 1995 to 72 million in 2025 [1].

Diabetes is one of the major causes of blindness and kidney transplantation. The disease increases the risk of cardiovascular diseases (CAD), especially in women (by 2–5 fold) [2, 3]. Researchers believe that the disease prevalence has rapid growth in India, China, Central and South America, Africa, and the Middle East [4].

Hyperglycaemia caused by impaired insulin secretion or insulin resistance or both are known as the characteristics of type 2 DM [5].

A higher share of fats and proteins of plant origin in the diet is associated with reduced risk of CAD and DM [6]. Studies have demonstrated that increased intake of mono- and polyunsaturated fatty acids (MUFAs and PU-

FAs) and lower intake of saturated and trans-fatty acids are associated with lower risk of type 2 DM [7]. Furthermore, replacement of carbohydrates with MUFAs and PUFAs in the daily diet is known as a therapeutic strategy in DM [8]. In this regard, MUFA intake in the daily diet of diabetic patients restores HDL levels and improves blood sugar control [9].

Among foods that contain a desirable fatty acid composition, nuts have received attention because of the epidemiological relationship found between their regular intake and a protective role against CAD [10, 11]. Accordingly, in prospective studies, reduced risk for CAD development and the mortality caused by CAD has been reported with increased consumption of the nuts [12, 13]. The risk of progression of type 2 DM is reduced by consuming nuts such as walnuts. In this regard, because of the lower mortality caused by CAD and cancers in the Mediterranean population, the Mediterranean diet is considered favourable [14]. A diet rich in walnuts has a positive effect on the endothelial function and endothelium-dependent vasodilation in type 2 DM. This consequently reduces the overall risk of CAD [15].

According to the reports of the US Department of Agriculture (USDA), 100 g of walnut contains 15.2 g of protein, 65 g of fat, and 6.7 g of fibre. Moreover, it contains higher amounts of PUFA (47%) when compared with other nuts, of which 38% is n6 PUFA (linoleic acid) and 9% is n3 PUFA (α linolenic acid – ALA) [16].

Considering the high prevalence of diabetes and the complications caused by the disease, diet modification by adding oils such as walnut oil containing PUFAs and ALA would improve glucose homeostasis and prevent cardiovascular complications of diabetes.

Considering the potential role of PUFAs in the prevention of DM and lipid profile improvement, some studies have been carried out on walnut. However, there are no studies on the control of blood sugar in DM patients using a diet containing walnut. Thus, the current study was carried out to evaluate the effect of walnut oil on blood sugar control in type 2 DM patients.

Material and methods

This controlled clinical trial (without placebo medication) was performed on type 2 DM patients referred to the Shiraz Healthy Heart Home, affiliated with the Shiraz Cardiovascular Research Centre. The project was approved by the Ethics Committee of Shiraz University of Medical Sciences in advance by the number CT.P.92.5670. The study was registered in the Iranian Registry of Clinical Trials (IRCT) with the code IRCT2014022216682N1.

The sample size for the experiment group was determined to be 45 patients with regard to 5% level of significance, power level of 95%, and the results obtained from similar studies. Moreover, 45 patients were considered as the control group. The research methodology was firstly explained to the participants, and then all the participants signed a written consent form. Moreover, they were assured of the confidentiality of their data and their right to withdraw from the study if they were not willing to continue. The study was carried out on 100 male and female type 2 DM patients, who were regularly monitored in the Shiraz Healthy Heart Home for at least two years. The inclusion criteria were having type 2 DM according to the definition of the American Diabetes Association (ADA), taking a maximum of two oral hypoglycaemic agents, having diabetes diagnosis for at least two years, being in the age range of 20-80 years, and lacking other chronic metabolic diseases. These patients had received nutritional education about a low-fat diabetic diet and were familiar with appropriate administration of hypoglycaemic medications. The participants did not have chronic metabolic disorders, including liver, kidney, and thyroid diseases. All the patients received oral hypoglycaemic agents and did not have a history of receiving insulin. They took

a maximum of two oral hypoglycaemic agents, and during the previous three months their medications had been kept unchanged and they had eaten a low-fat diet. The patients were randomly assigned to the experiment and control groups. Before initiation of the experiment, the systolic and diastolic blood pressure (SBP and DBP) levels of the patients were measured by a standard sphygmomanometer (ALPK2, Japan) and recorded. Blood pressure was measured when the patient had at least 10 min rest and did not drink coffee or tea, had or smoked in the past 30 minutes. Also, the weight and height of the patients were measured by a digital measure (Sahand, Iran). A blood sample was taken for measurement of fasting blood sugar (FBS) and HbA1c, and the values were determined using enzymatic assay kits (Pars Azmoon, Iran). The control group did not receive any intervention. The experiment group received walnut oil (15 g/day for three months). Before initiation of the experiment, the walnut oil used (prepared according to the cold-press method) was analysed in the Faculty of Pharmacy, Shiraz University of Medical Sciences.

According to the results obtained, the oil contained 72.5% PUFAs (64% linoleic acid, 8.5% ALA), 13.1% MUFA (oleic acid), 13.1% palmitic acid, and 1.3% stearic acid. All the participants were examined by a physician and a nutritionist at the beginning of the study and then on a monthly basis. Moreover, the patients had weekly follow-up telephone calls. Nutritional recommendations, evaluation of adherence to the food and medication regimen, and check for maintaining unchanged diet, medications, and physical activity were done for all the patients. At the end of a three-month period, blood sampling was performed to measure the FBS and HbA1c levels. Moreover, weight, SBP, and DBP were measured and recorded. The patients in the control group did not undergo any intervention. The data obtained were analysed using SPSS version 16. Normal distribution of the data was measured using the Kolmogorov-Smirnov test. Comparison of pre- and post-test means of the variables was carried out using paired t-test, and the mean comparison between the groups was performed by the *t*-test; *p* values < 0.05 were considered statistically significant.

Results

In the study, 100 diabetic patients were evaluated – 50 in the experiment group and 50 in the control group. Among the participants in the experiment group, two patients had GI intolerance of the oil and three of them did not cooperate in following the diet and medication regimen, so they were excluded from the study (24 women and 21 men).

In the control group, one was excluded because of lack of cooperation in the diet control and four were

Table 1. Comparison of distribution of the variables studied for the experiment and control groups before the experiment

| Variable | Experiment group | Control group | p-value |
|--------------------------|------------------|---------------|---------|
| Age (year) | 55.5 ±10.75 | 54 ±11.37 | 0.507 |
| Body weight (kg) | 75.9 ±8.56 | 73.81 ±7.15 | 0.212 |
| BMI (m ² /kg) | 27.60 ±2.47 | 27.21 ±2.27 | 0.435 |
| SBP (mm Hg) | 137.75 ±14.5 | 132.57 ±17.01 | 0.124 |
| DBP (mm Hg) | 81.62 ±7.65 | 81.13 ±7.01 | 0.753 |
| FBS (mg/dl) | 158.37 ±48.1 | 153.88 ±54.76 | 0.681 |
| HbA1c (%) | 7.003 ±1.08 | 6.97 ±1.208 | 0.894 |

BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, FBS – fasting blood sugar, ± indicates standard deviation

Table 2. Comparison of the mean values of the variables before and after the experiment for the experiment group using t-test

| Variables | Before intervention | After intervention | p-value |
|--------------------------|---------------------|--------------------|---------|
| Body weight (kg) | 75.90 ±8.56 | 75.75 ±8.25 | 0.225 |
| BMI (m ² /kg) | 27.60 ±2.47 | 27.55 ±2.34 | 0.233 |
| SBP (mm Hg) | 137.75 ±14.5 | 137.51 ±12.27 | 0.688 |
| DBP (mm Hg) | 81.62 ±7.65 | 81.42 ±7.21 | 0.692 |
| FBS (mg/dl) | 158.37 ±48.16 | 137.91 ±23.24 | 0.005 |
| HbA1c (%) | 7.00 ±1.08 | 6.37 ±1.29 | 0.001 |

BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, FBS – fasting blood sugar, ± indicates standard deviation

Table 3. Comparison of the mean values of the variables before and after the experiment for the control group using t-test

| Variables | Before intervention | After intervention | p-value |
|--------------------------|---------------------|--------------------|---------|
| Body weight (kg) | 73.81 ±7.15 | 73.65 ±7.22 | 0.504 |
| BMI (m ² /kg) | 27.21 ±2.27 | 27.15 ±2.30 | 0.500 |
| SBP (mm Hg) | 132.57 ±17.01 | 132.42 ±16.70 | 0.707 |
| DBP (mm Hg) | 81.73 ±7.01 | 80.84 ±6.83 | 0.605 |
| FBS (mg/dl) | 153.88 ±54.76 | 153.93 ±42.06 | 0.995 |
| HbA1c (%) | 6.97 ±1.21 | 6.98 ±1.33 | 0.941 |

BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, FBS – fasting blood sugar, ± indicates standard deviation

excluded because of lack of final evaluation of the experiment (23 women and 22 men).

Normal distribution of all variables was confirmed by the Kolmogorov-Smirnov test.

According to the results obtained, the two groups were not significantly different with regard to distribution of age, height, weight, BMI, SBP, DBP, FBS level, and HbA1c (Table 1).

Three months after the beginning of the experiment, the patients were re-evaluated for the variables evaluat-

ed at the beginning of the study. According to the analysis, the two groups were not significantly different with regard to the weight, BMI, SBP, and DBP. A statistically significant decrease was observed in the FBS level of the experiment group. Such finding was not observed for the control group, and the FBS level remained relatively unchanged. Comparing the two groups after the experiment indicated that the FBS level decreased significantly in the experiment group ($p < 0.05$).

This was true for the HbA1c level, so that a statistically significant decrease was observed in the experiment group, while the value did not change significantly in the control group. Comparison of the two groups after the intervention indicated that the HbA1c level significantly decreased in the experiment group ($p < 0.05$).

The values related to the variables before and after the experiment were compared using the t-test. The results are shown in Table 2.

Considering the data provided in Table 2 and Table 3, and comparison of the values obtained for each parameter before and after the experiment in each group, it can be observed that none of the variables changed significantly in the control group.

However, this is not the case with the experiment group; weight, BMI, SBP, and DBP did not change significantly when compared with the values obtained before the experiment, while FBS ($p < 0.05$) and HbA1c ($p < 0.05$) decreased significantly after the intervention.

Discussion

The prevalence of DM is increasing around the world, and the health and economic burden caused by the disease is very large and is set to increase in the future [1]. Several epidemiological studies have confirmed the relationship between increased risk of atherosclerosis and CAD on the one hand and poor control of blood sugar and lipid profile, on the other hand. The studies performed on the role of diet in blood sugar control in DM patients emphasise the replacement of conventional oils with the oils containing PUFAs.

In the current study, the effect of consumption of walnut oil (which contains high levels of PUFAs [72.5%] and ALA [8.5%]) on blood sugar control in type 2 DM patients was investigated. According to the results obtained, consumption of walnut oil for three months (15 g daily) could significantly reduce the FBS and HbA1c levels. However, no obvious changes were observed in the weight, BMI, and blood pressure levels. This is in agreement with the results of some previous studies.

In human and animal physiological studies, it has been demonstrated that the oils containing PUFAs could exert their antidiabetic effect by reducing the resistance and enhancement of sensitivity to insulin via the mechanism of overexpression of glucose trans-

porter GLUT4 and insulin receptors on the adipocyte membrane while also reducing the inflammatory effect on the adipose tissue by decreasing the inflammatory markers in this tissue [17].

In the study performed by Moloney *et al.* in 2007, on mice receiving a cis 9, trans 11-conjugated linoleic acid (CLA)-enriched diet for six weeks, it was demonstrated that this CLA isomer can reduce insulin resistance and decrease FBS and serum insulin levels by increasing the adipose tissue plasma membrane GLUT4. Moreover, this type of CLA can reduce inflammation in the adipose tissue via a 50% decrease in the TNF- level. Therefore, it was suggested that this CLA isomer attenuates insulin resistance by having anti-inflammatory effects in the adipose tissue [17].

Previous studies have shown that diabetes is potentially associated with increased oxidative stress [18]. Furthermore, oxidative stress could be associated with activation of stress-sensitive signalling pathways or insulin resistance [19]. Thus, based on the idea that oxidative stress can act as an activator in the initiation and progression of DM, antioxidants have been suggested as a part of DM treatment [20].

Moreover, it has been shown that the high level of antioxidants in nuts could be a protective mechanism against oxidative injury [21]. It has been reported that walnut has a higher antioxidant capacity when compared with other nuts [22]. These antioxidants are possibly of the phenolic compounds [23] including hydrolysed tannins, tocopherol [24], and melatonin, all of which have a high antioxidant capacity [25].

In the study by Ansar *et al.* performed in Shiraz in 2011, the effect of daily consumption of α lipoic acid, as an antioxidant, for two months was compared with a placebo in type 2 DM patients. It was observed that in the group receiving α lipoic acid, the FBS and insulin resistance homeostasis model assessment (IR-HOMA) decreased significantly but body weight remained unchanged. In this regard, it was concluded that α lipoic acid could be employed as an antioxidant in the treatment and improvement of glucose homeostasis in diabetic patients [26].

In the current study, the FBS level significantly decreased in the group receiving walnut oil ($p < 0.05$), while no significant change was observed in weight, SBP, and DBP. Lack of change in blood pressure was also reported by Jenkins *et al.* [9].

In the study conducted by Rahimi *et al.* it was reported that diabetic rats receiving walnut oil had a statistically significant decrease in the HbA1c level, similar to receiving glibenclamide. Thus, it was suggested that walnut oil can have an antidiabetic effect [27].

In a study performed by Tapsell *et al.*, the effects of walnut oil on PUFAs were evaluated on the metabolic parameters of the DM patients. They reported that dietary fat change in DM patients (increase in the PUFA/

saturated fatty acid ratio) could effectively decrease the FBS, HbA1c, and serum insulin levels during the six months of intervention [28].

In general, the results obtained indicate that a change in the dietary oil composition consumed by type 2 DM patients, and shifting from oils containing saturated fatty acids to oils containing PUFAs and ALA, such as walnut oil (15 g/day for three months) led to statistically significant decreases in the FBS and HbA1c levels. This eventually improved blood glucose homeostasis without changing the weight or blood pressure.

Acknowledgements

The authors would like to thank the kind cooperation of the staff of Shiraz Cardiovascular Research Centre and Shiraz Healthy Heart House. This paper was extracted from the thesis of Dr. Hossein Hakimi (No. 5670) carried out in Shiraz University of Medical Sciences.

The authors declare no conflict of interest.

References

- King H, Aubert RE, Herman WH. Global burden of diabetes prevalence, numerical estimates and projections. *Diabetes Care* 1998; 21: 1414-1431.
- Pan WH, Cedres LB, Liu K, et al. Relationship of clinical diabetes and asymptomatic hyperglycemia to risk of coronary heart disease mortality in men and women. *Am J Epidemiol* 1986; 123: 504-516.
- Barrett-Connor E, Wingard DL. Sex differential in ischemic heart disease mortality in diabetics: a prospective population-based study. *Am J Epidemiol* 1983; 118: 489-496.
- Adeghate E, Schattner P, Dunn E. An update on the etiology and epidemiology of diabetes mellitus. *Ann N Y Acad Sci* 2006; 1084: 1-29.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2004; 27 (Suppl 1): S5-S10.
- Sabaté J, Oda K, Ros E. Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials. *Arch Intern Med* 2010; 170: 821-827.
- Risérus U, Willett WC, Hu FB. Dietary fats and prevention of type 2 diabetes. *Prog Lipid Res* 2009; 48: 44-51.
- Franz MJ, Bantle JP, Beebe CA, et al. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. *Diabetes Care* 2002; 25: 148-198.
- Jenkins DJ, Kendall CW, Banach MS, et al. Nuts as a Replacement for Carbohydrates in the Diabetic Diet. *Diabetes Care* 2011; 34: 1706-1711.
- Fraser GE, Sabate J, Beeson WL, et al. A possible protective effect of nut consumption on risk of coronary heart disease: the Adventist Health Study. *Arch Intern Med* 1992; 152: 1416-1424.
- Kushi LH, Folsom AR, Prineas RJ, et al. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. *N Engl J Med* 1996; 334: 1156-1162.
- Kris-Etherton PM, Zhao G, Binkoski AE, et al. The effects of nuts on coronary heart disease risk. *Nutr Rev* 2001; 59: 103-111.
- Hu FB, Stampfer MJ. Nut consumption and risk of coronary heart disease: a review of epidemiologic evidence. *Curr Atheroscler Rep* 1999; 1: 204-209.
- Yochum LA, Folsom AR, Kushi LH. Intake of antioxidant vitamins and risk of death from stroke in post-menopausal women. *Am J Clin Nutr* 2000; 72: 476-483.

15. Ma Y, Njike VY, Millet J, et al. Effects of Walnut Consumption on Endothelial Function in Type 2 Diabetic Subjects. *Diabetes Care* 2010; 33: 227-232.
16. Pan A, Sun Q, Manson JE, et al. Walnut Consumption Is Associated with Lower Risk of Type 2 Diabetes in Women. *J Nutr* 2013; 143: 512-518.
17. Moloney FI, Toomey SI, Noone EN, et al. Anti-diabetic Effects of cis-9, trans-11-Conjugated Linoleic Acid May Be Mediated via Anti-inflammatory Effects in White Adipose Tissue. *Diabetes J* 2007; 56: 574-582.
18. Hannon-Fletcher MP, O'Kane MJ, Moles KW, et al. Levels of peripheral blood cell DNA damage in insulin dependent diabetes mellitus human subjects. *Mutat Res* 2000; 460: 53-60.
19. Evans JL, Maddux B, Goldfine ID. Antioxidant in diabetic complications and insulin resistance. In: *From Research to Diagnosis and Treatment*, Raz I, Skyler J, Shafir E (eds.). Informa Healthcare, London (UK) 2003; 479-496.
20. Rosen P, Tritschler HJ. Vascular complications in diabetes Mechanisms and the influence of antioxidants. In: *Handbook of antioxidants* (2nd ed.), Packer L, Cadenas E (eds.). CRC, California 2000; 511-533.
21. Dreher ML, Maher CV, Kearney P. The traditional and emerging role of nuts in healthful diets. *Nutr Rev* 1996; 54: 241-245.
22. Wu X, Beecher GR, Holden JM, et al. Lipophilic and hydrophilic antioxidant capacities of common foods in the United States. *J Agric Food Chem* 2004; 52: 4026-4037.
23. Fukuda T, Ito H, Yoshida T. Antioxidative polyphenols from walnuts (*Juglans regia* L.). *Phytochemistry* 2003; 63: 795-801.
24. Anderson KJ, Teuber SS, Gobeille A, et al. Walnut polyphenolics inhibit in vitro human plasma and LDL oxidation. *J Nutr* 2001; 131: 2837-2842.
25. Reiter RJ, Manchester LC, Tan DX. Melatonin in walnuts: influence on levels of melatonin and total antioxidant capacity of blood. *Nutrition* 2005; 21: 920-924.
26. Ansar HA, Mazloom ZO, Kazemi FA, et al. Effect of alpha-lipoic acid on blood glucose, insulin resistance, and glutathione peroxidase of type 2 diabetic patients. *Saudi Med J* 2011; 32: 584-588.
27. Rahimi P, Kabiri N, Asgary S, et al. Anti-diabetic effects of walnut oil on alloxan-induced diabetic rats. *J Pharm Pharmacol* 2011; 5: 2655-2661.
28. Tapsell LC, Batterham MJ, Teuss G, et al. Long-term effects of increased dietary polyunsaturated fat from walnuts on metabolic parameters in type II diabetes. *Eur J Clin Nutr* 2009; 63: 1008-1015.