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WALNUT INCLUSION IN THE DIET OF YOUNG MALE PATIENTS WITH ESSENTIAL HYPERTENSION

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ABSTRACT
Nuts have been shown to have beneficial effects on human health due to the healthy fat content. Among naturally occurring foods, walnuts are one of the highest sources of the n-3 fatty acid alpha-linolenic acid so we aimed the present study to assess the effect of inclusion of walnut in the diet of male patients of Stage I essential hypertension without secondary complications, on lipid profile, blood pressure. 27 patients of stage I essential hypertension were selected and were assigned the two types of diet in which one is control and other is study diet incorporated with the walnut diet for six weeks. All measurements like anthropometry (Body mass index was calculated, Waist circumference and Hip circumference was measured and the ratio is derived), blood pressure and lipid profile are done at the beginning and after completion of intake of control diet and study diet. Results are tabulated. The serum lipid profiles shows the mean total cholesterol level decreased, LDL cholesterol decreased, HDL/LDL ratio decreased by 28.94 which is statistically more significant and increase HDL cholesterol p value 0.02 is significant. The systolic blood pressure is reduced P value < 0.001 and diastolic blood pressure reduced P value < 0.001 are also Very Significant, the Waist circumference and Waist Hip ratio were significant due to walnut diet as compared to control diet. Nut consumption improves blood lipid levels, blood pressure and waist-to-hip ratio as compared to control diet.

KEYWORDS: *Walnuts, Waist circumference, lipid profile, blood pressure.*

INTRODUCTION
Nuts are a rich source of unsaturated fatty acids, vitamin E (which may function as an antioxidant), fiber, magnesium, potassium, and arginine[1]. Unsaturated fatty acids and fiber may improve plasma lipids (by decreasing triacylglycerol and cholesterol concentrations)[2–4], decrease platelet aggregation[5–7], and prevent arrhythmias[8]. Cations, such as magnesium and potassium, may improve blood pressure[9], and arginine may lower blood pressure by promoting the production of nitrous oxide and causing vasodilation[10]. A unique aspect of walnuts is that they are a rich source of both n-6 and n-3 PUFAs [11], they contain approximately 9 gm of alpha-linolenic acid per 100 g of edible matter. Studies of dietary intervention with walnut in the humans show beneficial effect on serum lipid profile and blood pressure [12-15].

Inclusion of walnut in the diet increases the polyunsaturated to saturated fatty acid ratio (P: S) which has been reported to reduce blood pressure in humans to a significant extent [16]. In a controlled feeding trial by Sabaté and colleagues, a diet in which walnuts represented 55% of the energy from fat reduced blood cholesterol levels in normal young men when compared with a standard low-fat diet. Animal studies indicate that polyunsaturated fatty acids coordinately regulate the expression of several enzymes that leads to negative energy balance [17] and reduced central obesity [18,19]. So we aimed this study is to evaluate the effects of walnut consumption on various parameters.

MATERIALS AND METHOD
The study was approved by Ethical Committee.

27 newly diagnosed male patients of Stage I Essential hypertension with no other risk factors (Classification based on the European Society of hypertension [20], age between 34 to 42 years and having body mass index above 28 are selected from Medicine outpatient department

Mallareddy institute of medical sciences, Jeedimatla, Hyderabad. Exclusion criteria includes known food allergy to nuts, Familial hypercholesterolemia, diabetes mellitus, secondary hypertension, liver, kidney, thyroid or other endocrine diseases assessed by medical history, a complete physical examination and laboratory tests were done, intake of medications known to affect lipid metabolism including hypolipidemic agents for the previous 8 weeks. Patients were assigned the two types of diet in which one is control and other is study diet incorporated with walnut. Individually all the patients were given in detail written and oral instructions of the diet to be followed. The experimental diets were individually prescribed and were based on estimated energy requirements. The patients followed control diet for four weeks and then the walnut diet for six weeks as lipoprotein changes due to dietary intervention stabilize in less than 4 weeks [21]. The experimental diets were individually prescribed and were based on estimated energy requirements. Diets were calculated in increments of 200 kcal to cover the range from 1600 to 2200 kcal. Prepacked shelled walnuts were provided daily in amounts varying from 30 g to 45 g (the equivalent of 6 to 8 walnuts); according to the participants' total energy intake. In the study diet, walnuts contributed approximately 18% of the total energy and 35% of the total fat.

Height and weight of the subjects was measured on a pre-standardized weighing scale (Weight height machine, L.C.S. Control PVT. LTD., Chennai). Body mass index (BMI) was calculated using the formula weight (in kg) divided by square of height (in m^2).

Waist circumference and Hip circumference was measured and the ratio is derived.

Blood pressure was measured by a standard mercury sphygmomanometer (Industrial Electronic and Allied Products, Pune, India).

Venous blood were obtained after a 14 hours of overnight fast and Total cholesterol (TC), High Density Lipoprotein- Cholesterol (HDL-C) and Triglycerides (TG) in plasma were measured by enzymatic methods using auto analyzer in the central clinical laboratory (De Behring Dimension RXL Max with HM). Low-Density Lipoprotein-Cholesterol (LDL-C) was calculated by Friedewald's [22] formula.

All measurements like anthropometry, blood pressure and lipid profile are done at the beginning and after completion of intake of control diet and study diet.

The two measurements obtained at baseline and at the end of each dietary period were averaged. Means and SDs are presented for each measurement. With methods described by Fleiss [23], two-tailed *t*-tests and the percentage difference were used to compare changes in outcome variables in response to dietary treatment at the end of control diet (4 weeks).

RESULTS:

Table I: Changes in the lipid Profile

Sr. No	Variable	Start	After Control Diet	After Walnut Diet	P value
		0 weeks	4 Weeks	6 Weeks	
		Mean ± SD	Mean ± SD	Mean ± SD	
1	Total Cholesterol	193.9 SD ± 37.2	191.9 SD ± 38.2	173.4 SD ± 14.3	< 0.01 More significant
2	Triglycerides	164.14 SD ± 63.9	160.3 SD ± 67.4	139.12 SD ± 36.9	< 0.01 More Significant
3	HDL-cholesterol	45.36 SD ± 4.83	43.30 SD ± 4.05	48.67 SD ± 3.02	0.02 significant
4	LDL-Cholesterol	110.89 SD ± 22.98	113.89 SD ± 27.28	98.35 SD ± 10.38	< 0.01 More significant
6	HDL/LDL ratio	0.41	0.38	0.49	<0.001 Very Significant

Table II: Changes in Blood pressure

Sr. N	Parameter	Before start of the study	After control Diet (4weeks)	After walnut Diet (6 weeks)	P value
		Mean +/- SD	Mean +/- SD	Mean +/- SD	
1	Systolic Blood pressure	148.61 SD 9.89	147.61 SD +/-7.89	130.53 SD 8.09	<0.001 Very Significant
2	Diastolic Blood pressure	94.48 SD 4.16	95.76 SD +/- 5.16	86.3 SD +/-5.32	<0.001 Very Significant

Table III : Changes in the various parameters of Anthropometry

Sr. No.	Parameter	Baseline	After Control Diet (4 weeks)	After Study Diet (6 weeks)	P value
		Mean +/- SD	Mean +/- SD	Mean +/- SD	
1	Weight (Kg)	82.11 SD +/-4.17	82.14 SD +/-4.81	80.157 SD +/-4.92	Not significant
2	BMI (Kg/m2)	28.12 SD +/-2.32	28.13 SD +/-2.79	27.73 SD +/-2.56	Not significant
3	Waist (cm)	92.1 SD +/-7.315	91.48 SD +/-7.90	87.25 SD +/-7.18	P value <0.05 Significant
4	Hip (cm)	98.39 SD +/-8.36	98.36 SD +/-7.17	97.38 SD +/-7.29	P value > 0.05 Not significant
5	WHR	0.929 SD +/-0.102	0.931 SD +/-0.107	0.89 SD +/-0.112	P value < 0.05 Significant

DISCUSSION

In our study "the effect of inclusion of walnut in the diet of male patients of Stage I essential hypertension without secondary complications", we found that substituting walnuts for approximately 33% of the energy from fat decreased total cholesterol and LDL cholesterol levels and increased HDL cholesterol and lowered the HDL / LDL ratio significantly, associated with decreased systolic and diastolic blood pressure significantly. Our findings are consistent with those of an earlier study by Sabaté J [4].

The serum lipid profiles are presented in **Table I**. The mean total cholesterol level decreased P value is < 0.01 more significant, LDL cholesterol decreased P value is < 0.01 more significant, HDL/LDL ratio decreased < 0.001 which is statistically more significant and increase HDL cholesterol p value 0.02 is significant due to walnut diet as compared to control diet.

Nuts are rich in plant sterols, natural compounds that might contribute to cholesterol lowering by interfering with cholesterol absorption, [24] and this effect would be blunted when cholesterol absorption rates are low.

Changes in Blood pressure are presented in **Table II**. The systolic blood pressure is reduced P value < 0.001 and diastolic blood pressure reduced P value < 0.001.

Essential hypertension is associated with an abnormal level of antioxidant status compared to normal response to oxidative stress or both [25]. An increase in production of Reactive oxygen species (ROS) like superoxide anion and hydrogen peroxide, reduction of nitric oxide synthesis, and a decrease in bioavailability of antioxidants have been demonstrated in human hypertension[26]. Findings suggest a strong association between blood pressure and some oxidative stress-related parameters and an abnormal level of antioxidant status as compared to normal response in development of the pathophysiology of essential hypertension [27]. (**Table III**)

Walnut intake improves endothelial function by virtue of its anti-inflammatory potential of polyphenolic-rich component ellagic acid on endothelial cells. Evaluation of the effect of walnuts extracts shows that expression of CAMs (cell adhesion molecules) on endothelial cells is reduced which prevents binding and recruitment of circulating monocytes which is the first step of atherosclerosis and as well as modulation of endothelial function and receptor mediated LDL clearance [28,29] that attenuates the process of atherosclerosis. Walnut is rich in the amino acid arginine, releases NO which delays endothelial cell senescence [30].

Reiter RJ et al suggests melatonin is present in walnuts and, when eaten increase blood melatonin concentrations[31]. It also contains vitamin E (as γ-tocopherol) and several non-flavonoid polyphenols (e.g., ellagic acid monomers and polymeric ellagitannins) are known to have the antioxidant capacity. So Walnut consumption increases the blood Melatonin and polyphenol correlates with an increased antioxidative capacity of serum which scavenges the free radicals and increases the bio-availability of nitric oxide (NO) leads to increase in the vasodilatation, and leads to decreased blood pressure [32].

Walnuts rich in n-3 pufa and melatonin solves both problems of sleep disturbance and high arterial blood pressure and betters circadian rhythm of blood pressure which involves night time dip in the blood pressure. Omega 3 fatty acids are also known to enhance parasympathetic activity and to increase the secretion of anti-inflammatory cytokines as well as acetylcholine in the hippocampus and helps to decrease the blood pressure and autonomic imbalance in patient of essential hypertension [33, 34].

An animal study indicates (n-3) polyunsaturated fatty acids (PUFA)-deficient diet lessens the melatonin rhythm, weakens endogenous functioning of the circadian clock, and plays a role in nocturnal sleep disturbances, increases sympathetic nervous system activity and leads to higher setting of arterial blood pressure [35].

We observed that due to walnut consumption there is statistically significant reduction in the waist circumference P value < 0.05 Significant and waist to hip ratio P value < 0.05 Significant as there is reduction in the central obesity. In centrally obese persons the chronic hyperleptinemia [36] as a result of excess secretion of leptin from adipocytes increases blood pressure because these acute depressor effects are impaired and/or additional sympathetic nervous system-independent pressor effects appear, such as oxidative stress, NO deficiency, enhanced renal sodium reabsorption and overproduction of endothelin 1, a potent vasoconstrictor from endothelial cells. Reduced central obesity results in decreased blood pressure due to reduced leptin and endothelin 1 level [37].

Visceral form of obesity is reduced to some extent by Melatonin in walnut which reduces sleep disturbance as it reduces the appetite because of reduction in ghrelin: leptin through a complex neuroendocrine regulation pattern [38]. A clinical trial involving humans shows long term supplementation of L-Arginine results in decrease in fat mass and waist circumference due to reduction in central obesity [39]. Walnut is rich in the L-arginine plays important role in reduction in visceral obesity.

An animal study indicates that polyunsaturated fatty acids coordinately regulate the expression of several enzymes involved in carbohydrate and lipid metabolism which are effective at suppressing the level of mRNAs encoding genes specific for glycolytic and lipogenic enzymes that leads to negative energy balance[40]. The alterations in gene expression in the liver associated with up-regulation[41] of beta-oxidation activity and in adipose tissue fat accumulation[42] in rats which might explain the reduced central obesity in humans. Further advance study is recommended to evaluate the change in the gene expression level of metabolic enzymes stated above to reaffirm the findings in the humans which leads reduced central obesity due to consumption n-3 PUFA.

In conclusion, although nut intake may affect human health significantly, mechanisms underlying these effects are not completely known. The present study suggests that the walnuts nut consumption improves blood lipid levels, blood pressure and waist-to-hip ratio as compared to control diet, the potential antiatherogenic effects of nuts and their possible adverse effects necessitate further research.

REFERENCES:

1. Dreher ML, Maher CV, Kearney P. The traditional and emerging role of nuts in healthful diets. Nutr Rev 1996;54:241–5.

2. Berry EM, Eisenberg S, Harahtz D, et al. Effects of diets rich in monounsaturated fatty acids on plasma lipoproteins—the Jerusalem Nutrition Study: high MUFAs vs high PUFAs. Am J Clin Nutr 1991;53:899–907.
3. Chan JK, Bruce VM, McDonald BE. Dietary 1-linolenic acid is as effective as oleic acid and linoleic acid in lowering blood cholesterol in normolipidemic men. Am J Clin Nutr 1991;53:1230–4.
4. Sabate J, Fraser GE, Burke K, Knetsen SF, Bennett H, Linsted KD. Effects of walnuts on serum lipid levels and blood pressure in normal men. N Engl J Med 1993;328:603–7.
5. Chan JK, McDonald BE, Gerrard JM, Bruce VM, Weaver BJ, Holub BJ. Effect of dietary acid and its ratio to LA on platelet and plasma fatty acids and thrombogenesis. Lipids 1993;28:811–7.
6. Mest HJ, Beitz J, Heinroth I, Block HU, Forster W. The influence of linseed oil diet on fatty acid pattern in phospholipids and thromboxane formation in platelets in man. Klin Wochenschr 1983;61:187–91.
7. Kinsella JE. Effects of polyunsaturated fatty acids on factors related to cardiovascular disease. Am J Cardiol 1987;60:23G–32G.
8. Hu FB, Stampfer MJ, Manson JE, et al. Dietary intake of _-linoleic acid and risk of fatal ischemic heart disease among women. Am J Clin Nutr 1999;69:890–7.
9. Elin RJ. Is the magnesium content of nuts a factor for coronary heart disease? Arch Intern Med 1993;153:779–80.
10. Fraser GE. Nut consumption, lipids, and risk of a coronary event. Clin Cardiol 1999;22(suppl):III11–5.
11. Greve LC, McGranahan G, Hasey J, et al. Variation in polyunsaturated fatty acids composition of Persian walnuts. J Am Soc Hort Sci 1992;117:518–22.
12. Daniel Zambón, MD; Joan Sabaté, MD, DrPH; Sonia Muñoz, PhD; Betina Campero, RD;Elena Casals, MD; Manuel Merlos, PhD; Juan C. Laguna, PhD; and Emilio Ros, MD. Substituting Walnuts for Monounsaturated Fat Improves the Serum Lipid Profile of Hypercholesterolemic Men and Women. Ann Intern Med. 2000 Apr 4;132(7):538-46.
13. Iwamoto M, Imaizumi K, Sato M, Hirooka Y, Sakai K, Takeshita A, Kono M. Serum lipid profiles in Japanese women and men during consumption of walnuts. Eur J Clin Nutr. 2002 Jul;56(7):629-37.
14. Zibaeenezhad MJ, Rezaiezadeh M, Mowla A, Ayatollahi SM,Panjehshahin MR. Antihypertriglyceridemic effect of walnut oil. Angiology. 2003 Jul-Aug;54(4):411-4.
15. Iwamoto M, Imaizumi K, Sato M, Hirooka Y, Sakai K, Takeshita A, Kono M. Serum lipid profiles in Japanese women and men during consumption of walnuts. Eur J Clin Nutr. 2002 Jul;56(7):629-37.
16. Strazzullo P, Ferro-Luzzi A, Siani A, Scaccini C, Sette S, Catasta G,Mancini M. Changing the Mediterranean diet: effects on blood pressure. J Hypertens. 1986 Aug;4(4):407-12.
17. Jump DB, Clarke SD, Thelen A, Liimatta M. Coordinate regulation of glycolytic and lipogenic gene expression by polyunsaturated fatty acids.J Lipid Res. 1994 Jun;35(6):1076-84.
18. Takahashi Y, Ide T. Dietary n-3 fatty acids affect mRNA level of brown adipose tissue uncoupling protein 1, and white adipose tissue leptin and glucose transporter 4 in the rat.Br J Nutr. 2000 Aug;84(2):175-84.
19. Murase T, Aoki M, Tokimitsu I. Supplementation with alpha-linolenic acid-rich diacylglycerol suppresses fatty liver formation accompanied by an up-regulation of beta-oxidation in Zucker fatty rats. Biochim Biophys Acta. 2005 Apr 15;1733(2-3):224-31. Epub 2005 Jan 13.
20. Summary of the 2007 European Society of Hypertension (ESH) and European Society of Cardiology (ESC) Guidelines for the Management of Arterial Hypertension.
21. Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL.Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. N Engl J Med. 1989; 320:915-24.
22. Freidwald WT, Levy RI, Frederickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of preoperative ultracentrifuge. Clin Chem 1972;18:499-502.
23. Fleiss JL. The Design and Analysis of Clinical Experiments. New York: J Wiley; 1986.
24. Segura R, Javierre C, Lizarraga MA, Ros E. Other relevant components of nuts: phytosterols, folates and minerals. *Br J Nutr*. 2006;96(2)(suppl 2):S36-S44.
25. Kashyap MK, Yadav V, Sherawat BS, Jain S, Kumari S, Khullar M, Sharma PC, Nath R. Different antioxidants status, total antioxidant power and free radicals in essential hypertension.Mol Cell Biochem. 2005 Sep;277(1-2):89-99.
26. Saito Y, Nakamura T, Kurabayashi M. Oxidative stress and mild hypertension. Nippon Rinsho. 2008 Aug;66(8):1525-9.
27. Rodrigo R, Prat H, Passalacqua W, Araya J, Guichard C, Bächler JP. Relationship between oxidative stress and essential hypertension. Hypertens Res. 2007 Dec;30(12):1159-67.
28. Almario RU, Vonghavaravat V, Wong R, Kasim-Karakas SE. Effects of walnut consumption on plasma fatty acids and lipoproteins in combined hyperlipidemia. Am J Clin Nutr. 2001 Jul;74(1):72-9.
29. Anderson KJ, Teuber SS, Gobeille A, Cremin P, Waterhouse AL,Steinberg FM.Walnut polyphenolics inhibit in vitro human plasma and LDL oxidation. J Nutr. 2001 Nov;131(11):2837-42.
30. Hayashi T, Matsui-Hirai H, Miyazaki-Akita A, Fukatsu A, Funami J, Ding QF, Kamalanathan S,Hattori Y, Ignarro LJ, Iguchi A. Endothelial cellular senescence is inhibited by nitric oxide: implications in atherosclerosis associated with menopause and diabetes.Proc Natl Acad Sci U S A. 2006 Nov 7;103(45):17018-23. Epub 2006 Oct 30.
31. Reiter RJ, Manchester LC, Tan DX.Melatonin in walnuts: influence on levels of melatonin and total antioxidant capacity of blood.Nutrition. 2005 Sep;21(9):920-4.
32. Torabian S, Haddad E, Rajaram S, Banta J, Sabaté J. Acute effect of nut consumption on plasma total polyphenols, antioxidant capacity and lipid peroxidation. J Hum Nutr Diet. 2009 Feb;22(1):64-71.
33. Singh RB, Pella D, Mechirova V, Otsuka K.Can brain dysfunction be a predisposing factor for metabolic

syndrome?Biomed Pharmacother. 2004 Oct;58 Suppl 1:S56-68.

34. Maser RE, Lenhard MJ.An overview of the effect of weight loss on cardiovascular autonomic function.Curr Diabetes Rev. 2007 Aug;3(3):204-11.
35. Lavialle M, Champeil-Potokar G, Alessandri JM, Balasse L, Guesnet P, Papillon C, Pévet P, Vancassel S, Vivien-Roels B, Denis I.An (n-3) polyunsaturated fatty acid-deficient diet disturbs daily locomotor activity, melatonin rhythm, and striatal dopamine in Syrian hamsters.Biomed Pharmacother. 2004 Oct;58 Suppl 1:S56-68.
36. Bełtowski J.Role of leptin in blood pressure regulation and arterial hypertension.J Hypertens. 2006 May;24(5):789-801.
37. Quehenberger P, Exner M, Sunder-Plassmann R, Ruzicka K, Bieglmayer C, Endler G,Muellner C, Speiser W, Wagner O. Leptin induces endothelin-1 in endothelial cells in vitro. Circ Res. 2002 Apr 5;90(6):711-8.
38. Copinschi G.Sleep and vascular disorders.Metabolism. 2006 Oct;55(10 Suppl 2):S45-9.
39. Lucotti P, Setola E, Monti LD, Galluccio E, Costa S, Sandoli EP, Fermo I, Rabaiotti G, Gatti R,Piatti P. Beneficial effects of a long-term oral L-arginine treatment added to a hypocaloric diet and exercise training program in obese, insulin-resistant type 2 diabetic patients. Am J Physiol Endocrinol Metab. 2006 Nov;291(5):E906-12. Epub 2006 Jun 13.
40. Jump DB, Clarke SD, Thelen A, Liimatta M. Coordinate regulation of glycolytic and lipogenic gene expression by polyunsaturated fatty acids.J Lipid Res. 1994 Jun;35(6):1076-84.
41. Murase T, Aoki M, Tokimitsu I. Supplementation with alpha-linolenic acid-rich diacylglycerol suppresses fatty liver formation accompanied by an up-regulation of beta-oxidation in Zucker fatty rats. Biochim Biophys Acta. 2005 Apr 15; 1733(2-3):224-31. Epub 2005 Jan 13.
42. Takahashi Y, Ide T. Dietary n-3 fatty acids affect mRNA level of brown adipose tissue uncoupling protein 1, and white adipose tissue leptin and glucose transporter 4 in the rat.Br J Nutr. 2000 Aug; 84(2):175-84.

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