Effects of dietary saturated, monounsaturated, and n−3 fatty acids on blood pressure in healthy subjects[1–3]

Birthe M Rasmussen, Bengt Vessby, Matti Uusitupa, Lars Berglund, Eva Pedersen, Gabrielle Riccardi, Angela A Rivellese, Linda Tapsell, and Kjeld Hermansen for The KANWU Study Group

ABSTRACT

Background: The quantity and quality of fats consumed in the diet influence the risk of cardiovascular disease (CVD). Although the effect of diet on plasma lipids and lipoproteins is well documented, less information exists on the role of fats on blood pressure (BP).

Objective: The objective was to evaluate the effects of different types of dietary fat on BP in healthy subjects.

Design: Healthy subjects ($n = 162$) were randomly assigned for 3 mo to follow 1 of 2 isoenergetic diets: 1 rich in monounsaturated fatty acids (MUFA diet) and the other rich in saturated fatty acids (SFA diet). Each group was further randomly assigned to receive supplementation with fish oil (3.6 g n−3 fatty acids/d) or placebo.

Results: Systolic BP (SBP) and diastolic BP (DBP) decreased with the MUFA diet [−2.2% ($P = 0.009$) and −3.8% ($P = 0.0001$), respectively] but did not change with the SFA diet [−1.0% ($P = 0.2084$) and −1.1% ($P = 0.2116$)]. The MUFA diet caused a significantly lower DBP than did the SFA diet ($P = 0.0475$). Interestingly, the favorable effects of MUFA on DBP disappeared at a total fat intake above the median (>37% of energy). The addition of n−3 fatty acids influenced neither SBP nor DBP.

Conclusions: Changing the proportions of dietary fat by decreasing SFAs and increasing MUFAs decreased diastolic BP. Interestingly, the beneficial effect on BP induced by fat quality was negated by the consumption of a high total fat intake. The addition of n−3 fatty acids to the diet had no significant effect on BP. *Am J Clin Nutr* 2006;83:221–6.

KEY WORDS Diet, saturated fatty acids, monounsaturated fatty acids, n−3 fatty acids, blood pressure

INTRODUCTION

The quantity and quality of fats consumed in the diet are important features that influence the risk of cardiovascular disease (CVD) (1). The paradigm that dietary fats act exclusively via effects on serum lipids and lipoproteins has been challenged (2–6). Evidence suggesting the beneficial health effects of the Mediterranean diet has emerged from the classic studies of Keys (7), which indicate that the consumption of diets enriched in monounsaturated fat (MUFA) relates to a lower incidence of coronary heart disease. The Lyon Diet Heart Study (3) showed that a Mediterranean-type diet reduces the rate of recurrence after a first myocardial infarction. The replacement of saturated fat (SFA) with MUFA and α-linolenic acids (n−3 fatty acids) seems to induce beneficial effects in persons with CVD without changing plasma lipid concentrations. The Diet and Reinfarction Trial (DART; 5) supported the ability of diets rich in eicosapentaenoic acid (EPA) to lower ischemic complications of arteriosclerosis. The study by Trichopoulou et al (8) corroborated the Lyon Diet Heart Study (3) and showed that strict adherence to a Mediterranean diet is associated with a significant reduction in total mortality.

Studies focusing on surrogate risk markers for CVD other than plasma lipids and lipoproteins are needed to clarify the effects of dietary fat on CVD. In this regard, it seems prudent to evaluate the effect of dietary fat on CVD risk factors such as blood pressure (BP), insulin sensitivity, endothelial function, hemostatic factors, and microalbuminuria.

Genetic factors seem to be responsible for as much as 20–40% of BP variations in the general population (9). However, epidemiologic data implicate that lifestyle factors (eg, dietary habits) are a major contributor to the high prevalence of hypertension (10). Nevertheless, our knowledge of the influence of macronutrients such as fat on BP is limited. Data suggest that both the fat quantity and quality of the diet could be important for the development of insulin resistance (11). In the KANWU study (12, 13) we showed that MUFA, in contrast with SFA, improved the insulin sensitivity in healthy subjects (12) and concomitantly

[1] From the Department of Clinical Endocrinology and Metabolism C, Aarhus University Hospital, Aarhus, Denmark (BMR, EP, and KH); the Unit for Clinical Nutrition Research, Department of Public Health and Caring Sciences/Geriatrics, University of Uppsala, Uppsala, Sweden (BV); the Department of Clinical Nutrition, University of Kuopio, Kuopio, Finland (MU); the Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden (LB); the Department of Clinical and Experimental Medicine, School of Medicine, Federico II University, Naples, Italy (GR and AAR); and the Department of Biomedical Sciences and Smarts Food Centre, University of Wollongong, Wollongong, Australia (LT).

[2] Supported by the Danish Medical Research Council, the Swedish Council for Forestry and Agricultural Research, Health Research Council Academy of Finland, Helga and Peter Kornings Foundation, and International Council of Olive Oil. The food for the study was generously supplied by MD Foods (ARLA), Denmark; Carlshamn Mejeri AB, Svenska Nestlé AB, and Van den Bergh Foods AB, Sweden; Eridania Beghin-Say, Belgium; and Meadow Lea Foods, Australia. The Pikasol capsules were supplied by Lube Ltd, Hadsund, Denmark.

[3] Reprints not available. Address correspondence to K Hermansen, Department of Clinical Endocrinology and Metabolism C, Aarhus University Hospital, Aarhus Sygehus, Tage-Hansens Gade 2, DK 8000 Aarhus C, Denmark. E-mail: kjeld.hermansen@as.aaa.dk.

Received May 23, 2005.

Accepted for publication October 24, 2005.

reduced plasma cholesterol and triacylglycerol concentrations (13). More recently, it was shown that insulin sensitivity improved when dietary SFA was substituted for polyunsaturated fat (PUFA) (14). An important question is whether the quantity or quality of fat also affects BP and thereby the risk of hypertension. The aim of this study was to investigate whether dietary MUFA, compared with SFA, affects BP in healthy subjects. Second, we investigated whether the addition of long-chain n−3 fatty acids had a modifying effect.

SUBJECTS AND METHODS

Design

The study was a 3-mo controlled, parallel, multicenter study, performed at 5 different centers (Kuopio, Finland; Aarhus, Denmark; Naples, Italy; Wollongong, Australia; and Uppsala, Sweden). The design was reported in detail previously (12).

Healthy subjects were randomly assigned to a diet containing either a high proportion of SFAs (SFA diet) or a high proportion of MUFAs (MUFA diet). Within each of these 2 groups, the subjects were randomly assigned to receive supplementary capsules containing fish oil [3.6 g n−3 fatty acids/d providing 2.4 g EPA and docosahexaenoic fatty acids (DHA); Pikasol, Lube Ltd, Hadsund, Denmark] or placebo capsules containing the same amount of olive oil.

The test period was preceded by a 2-wk run-in period during which the subjects consumed their habitual diets supplemented with placebo capsules. Routine clinical tests, including an oral-glucose-tolerance test (15), were carried out during this period. The subjects kept a 3-d dietary record (2 weekdays and 1 weekend day) to document pretrial dietary habits. Two additional 3-d dietary records were kept at the beginning of the second and third months of the test period. Tests and laboratory analyses were carried out at baseline and at the end of the study. Blood pressure was measured at baseline and at the end of study.

Subjects

A total of 162 healthy white subjects (n = 95 men and 67 women) aged 30–65 y and with normal or moderately increased body weight [BMI (in kg/m^2) = 22–32] were included. Health status was screened via medical history and routine laboratory examinations. Subjects with impaired glucose tolerance (15) but without diabetes were included. Other reasons for exclusion were specific eating habits due to cultural or religious beliefs, high habitual physical activity, high alcohol intake (ie, binge drinking or a regular alcohol intake >40 g/d), and hepatic, cardiac, thyroid, and disabling diseases. Body weight during the past 3 mo should not have changed >4 kg. Subjects taking acetyl salicylic acid, thiazide diuretics, β-blockers, lipid-lowering drugs, and corticosteroids were also excluded. If a subject was taking any other medication, the dose had to remain constant during the test period. Alcohol consumption, weight, and the degree of physical activity were kept stable during the study. Smoking was allowed, but smoking habits had to remain unchanged during the study. Premenopausal women had all tests made during the same period of their menstrual cycle.

All subjects were fully informed of the experimental nature of the investigation, which had been approved by the local ethics committees. Informed consent was obtained before the study began, and all subjects complied fully with the protocol.

Diets

All subjects were instructed to eat isoenergetic diets containing the same amount of macronutrients: 37% of energy as fat with a high proportion of SFAs (SFA diet) or MUFAs (MUFA diet). The SFA diet contained 17% of energy as SFAs, 14% of energy as MUFAs, and 6% of energy as PUFAs, whereas the MUFA diet contained 8% of energy as SFAs, 23% of energy as MUFAs, and 6% of energy as PUFAs, respectively. Trained dietitians instructed all subjects on the preparation of their diets. To ensure good adherence to the diets, the subjects met the dietitians at least every second week until the end of the study. The participants were supplied with edible fats to be used as spreads on bread, for cooking, and in dressings. Core foods such as margarine, oils, and a range of other staple items were provided. Butter, margarines, and oils to be used in the diets were prepared centrally and distributed to the different European centers. The SFA diet included butter and table margarine containing a relatively high proportion of SFAs. The MUFA diet included spread and margarine with a high proportion of oleic acid, derived from high–oleic acid sunflower oil and negligible amounts of *trans* fatty acids, n−3 fatty acids, and olive oil. The study center in Australia obtained similar oil from local suppliers. The intake during the test period was calculated as the mean values from the dietary records provided during the second and third months of the study. The dietary records were estimated, not weighed. Local nutrient analysis software programs containing country-specific food databases were used in the analyses. Data on margarine and other specially prepared foods were entered into these databases for inclusion in the analyses. The adherence to the test fats was verified by analyses of the phospholipid fatty acid composition of serum (12).

Blood pressure and body weight

Blood pressure was measured at baseline and at the end of the study to the nearest 5 mm Hg with a sphygmomanometer. Systolic and diastolic BP was defined as phase I and V Korotkoff sounds, respectively. Blood pressure was measured from the same arm, with subjects in a sitting position, after 10 min of rest from the time the cuff had been placed on the arm. Measurements were made 3 times at 2-min intervals in each case. The data analyzed were the means of the 3 BP values. Body weight was measured at each visit to ensure that the participants were weight stable.

Statistical methods

Results are presented as mean ± SD. The study was an intention to treat study, ie all randomized subjects, with at least one measurement during treatment were included in the analyses. The treatment effects were estimated from a statistical model in which treatment categories (SFA or MUFA diet with or without n−3 fatty acids) and their interaction were analyzed factors, whereas center, age, sex, and baseline value of the outcome variable were covariates. The difference between groups for adjusted mean treatment effects are presented with P values and 95% CIs.

A post hoc subgroup analysis was made according to the relative intake of total fat during treatment (above or below the median of 37% of energy). The abovementioned model was used with the addition of an interaction term between treatment and relative fat intake (above or below the median).

TABLE 1
Clinical characteristics of the healthy subjects at entry[1]

	SFA diet ($n = 83$)		MUFA diet ($n = 79$)	
	Placebo ($n = 42$)	n−3 FA ($n = 41$)	Placebo ($n = 40$)	n−3 FA ($n = 39$)
Age (y)	49.3 ± 7.1	48.5 ± 8.0	47.0 ± 8.8	49.5 ± 7.3
BMI (kg/m^2)	26.3 ± 2.7	26.9 ± 3.0	26.1 ± 3.2	26.5 ± 3.1
SBP (mm Hg)	121.6 ± 11.5	122.7 ± 11.4	123.1 ± 16.6	122.4 ± 12.9
DBP (mm Hg)	77.2 ± 7.6	77.1 ± 9.0	77.8 ± 9.9	74.6 ± 9.1

[1] All values are $\bar{x}$ ± SD. SFA, saturated fatty acid; MUFA, monounsaturated fatty acid. No statistically significant differences in the clinical characteristics were observed between the groups (Student's unpaired *t* tests).

Of the 83 subjects assigned to the SFA diet, 42 subjects were in the SFA + placebo group (1 dropout) and 41 subjects were in the SFA + n−3 fatty acid group (1 dropout). Of the 79 subjects assigned to the MUFA diet, 40 subjects were in the MUFA + placebo group (no dropouts) and 39 subjects were in the MUFA + n−3 fatty acid group (1 dropout).

RESULTS

The clinical characteristics of the 162 subjects ($n = 76$ women and 86 men) assigned randomly to the SFA and MUFA diets did not differ significantly (**Table 1**). Mean (±SD) body mass index (BMI; in kg/m^2) and body weight remained unchanged during the study. BMIs at baseline and at end of the SFA diet period were 26.6 ± 2.9 and 26.7 ± 2.9 and at the end of the MUFA diet were 26.6 ± 3.1 and 26.3 ± 3.2, respectively.

Dietary records

The average nutrient composition before the study, as calculated from the dietary records (**Table 2**), was not different between the SFA and MUFA diet groups, respectively. During the test period there was a slight increase in the proportion of dietary fat in both groups. The recorded mean intake of fat and fatty acids during the study was similar to the target values. During the study the amount of fiber was significantly higher ($P = 0.0444$), and the amount of cholesterol was significantly lower ($P = 0.0006$), in the MUFA than in the SFA diet. The estimated proportions of *trans* fatty acids were low and not different between the diets. Adherence to the diets was not different between the SFA and MUFA diet groups. These data were reported previously (12).

Effects on blood pressure

A significant decrease in SBP (−2.2%; $P = 0.009$) and DBP (−3.8%; $P = 0.0001$) was observed during the MUFA diet, whereas no significant changes were seen during the SFA diet. The MUFA diet caused a significantly lower DBP than did the SFA diet ($P = 0.0475$) (data not shown). We also looked at the effects of a low compared with a high fat intake, ie, a fat intake below or above the median fat intake of 37% of energy (**Table 3**). In subjects with a total fat intake below the median, the MUFA diet reduced the SBP ($P = 0.0408$) and the DBP ($P = 0.0023$) significantly. Interestingly, the differences in SBP and in DBP disappeared with a total fat intake above the median. Addition of n−3 fatty acids did not influence SBP or DBP. Thus, the mean (±SD) changes in DBP in response to n−3 fatty acids and to placebo were −2.2 ± 0.7 and −1.6 ± 0.7 mm Hg ($P = 0.5700$), respectively, and the corresponding changes in SBP were −2.2 ± 1.1 and −1.8 ± 1.1 mm Hg ($P = 0.7567$), respectively

TABLE 2
Dietary nutrient composition in the healthy subjects before and during the study[1]

	SFA diet ($n = 83$)		MUFA diet ($n = 79$)		*P* for adjusted mean differences in treatment effects (SFA versus MUFA diet period)	Target values for fat composition during the study	
	Before[2]	During	Before[2]	During		SFA diet	MUFA diet
Energy (kcal)	2250 ± 550[3]	2140 ± 390	2120 ± 500	2150 ± 450	0.0768	—	—
Protein (% of energy)	15.6 ± 3.0	15.2 ± 2.5	15.8 ± 2.8	14.8 ± 2.3	0.1005	—	—
Carbohydrate (% of energy)	45.8 ± 6.7	44.1 ± 5.2	47.3 ± 7.0	45.9 ± 4.2	0.0519	—	—
Fat (% of energy)	33.7 ± 6.5	37.1 ± 4.1	33.3 ± 6.1	37.1 ± 4.2	0.7975	37	37
SFA	13.5 ± 3.6	17.6 ± 2.5	13.3 ± 3.7	9.6 ± 1.8	< 0.0001	17	8
MUFA	13.0 ± 3.7	13.1 ± 2.5	13.1 ± 3.2	21.1 ± 4.0	< 0.0001	14	23
PUFA	4.8 ± 1.6	4.7 ± 1.5	4.7 ± 1.5	4.6 ± 0.8	0.1768	6	6
Fiber (g/d)	23.8 ± 7.7	22.4 ± 6.6	23.0 ± 8.4	23.0 ± 8.4	0.0444	—	—
Cholesterol (mg/d)	316 ± 126	322 ± 91	310 ± 139	254 ± 80	0.0006	—	—

[1] PUFA, polyunsaturated fat; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid. Statistical method: intention-to-treat study in which the categories (SFA or MUFA diet with or without n−3 fatty acids) and their interactions were analyzed; center, age, sex, and the baseline value of the outcome variables were covariates.

[2] The average nutrient composition before the study was not significantly different in the subjects randomly assigned to the SFA and MUFA diets.

[3] $\bar{x}$ ± SD (all such values).

TABLE 3
Effect of a 12-wk dietary intervention and n−3 fatty acids on diastolic (DBP) and systolic (SBP) blood pressure in the healthy subjects[1]

	SFA diet ($n = 83$)				MUFA diet ($n = 79$)				Differences in treatment effects (SFA versus MUFA diet period)		
	Baseline[2]	Change[3]	Percentage change	P	Baseline[2]	Change[3]	Percentage change	P	$\bar{x}$ Difference	95% CI	P
DBP (mm Hg)											
Placebo											
<37 % of energy	76.2 ± 6.8[4]	1.9 ± 8.2	2.5	0.0663	78.3 ± 11.8[5]	−4.8 ± 8.5	−6.1	0.0160	6.4	2.3, 10.5	0.0023
>37 % of energy	78.2 ± 8.4[4]	−2.7 ± 5.3	−3.5	0.0144	77.3 ± 8.1[4]	−2.1 ± 7.8	−2.7	0.1789	−1.7	−5.6, 2.2	0.3973
n−3 Fatty acids											
<37 % of energy	74.4 ± 8.7[6]	−1.0 ± 6.4	−1.3	0.6059	74.2 ± 9.0[4]	−2.3 ± 6.3	−3.1	0.0897	1.7	−2.3, 5.7	0.4107
>37 % of energy	79.7 ± 8.6[4]	−1.3 ± 6.1	−1.6	0.2030	74.9 ± 9.6[2]	−3.4 ± 5.1	−4.5	0.0224	1.8	−2.4, 5.9	0.3940
SBP (mm Hg)											
Placebo											
<37 % of energy	122.4 ± 10.3[4]	3.5 ± 11.6	2.9	0.1568	125.8 ± 16.8[5]	−4.8 ± 8.2	−3.8	0.1520	6.6	0.3, 12.9	0.0408
>37 % of energy	120.8 ± 12.8[4]	−3.2 ± 5.7	−2.7	0.0524	120.7 ± 16.4[4]	−2.4 ± 11.6	−2.0	0.2642	−1.9	−7.9, 4.1	0.5286
n−3 Fatty acids											
<37 % of energy	121.1 ± 11.1[6]	−2.1 ± 13.2	−1.7	0.2940	125.0 ± 10.1[4]	−2.3 ± 10.9	−1.8	0.2865	−0.1	−6.3, 6.0	0.9691
>37 % of energy	124.1 ± 11.7[4]	−1.4 ± 7.1	−1.1	0.5575	119.5 ± 15.4[7]	−3.2 ± 11.9	−2.7	0.2793	1.3	−5.0, 7.7	0.6802

[1] SFA, saturated fatty acid; MUFA, monounsaturated fatty acid. Statistical method: intention-to-treat study in which the categories (SFA or MUFA diet with or without n−3 fatty acids) and their interactions were analyzed; center, age, sex, and the baseline value of the outcome variables were covariates. Post hoc analysis: a subgroup analysis was made according to the relative intake of total fat during the treatment (above or below the median of 37% of energy). The model was used with the addition of an interaction term between treatment and relative fat intake (above or below the median). A significant 3-factor interaction between SFA or MUFA diet, n−3 fatty acids, and % of energy (above or below the median) for the change in DBP ($P = 0.048$) was found. There were no significant interactions with SBP.

[2] All values are $\bar{x} \pm$ SD.

[3] All values are least-squares $\bar{x} \pm$ SD.

[4] $n = 21$.

[5] $n = 19$.

[6] $n = 20$.

[7] $n = 18$.

(data not shown). As seen in Table 3, the addition of n−3 fatty acids had no influence on SBP or DBP. In the main model (without % of energy as fat), no interactions were found between SFA and MUFA and n−3 fatty acids. In the post hoc analysis, however, the 3-factor interaction between SFA or MUFA, n−3 fatty acids, and % of energy as fat (above or below the median) was significant for the change in DBP ($P = 0.048$). There were no significant interactions with SBP.

DISCUSSION

Comparison of the effects of MUFA and SFA on blood pressure

In the present study we found that a MUFA-rich diet, in contrast with an SFA-rich diet, reduced the DBP in healthy, normotensive subjects. Although the type of fat, rather than the amount of fat, in the diet may be more important in terms of determining health outcomes, it is noteworthy that a MUFA-rich diet causes a reduction in both SBP and DBP at a fat intake below 37% of energy, whereas the positive effect of MUFA on BP seems to be lost at a high total fat intake. Whether the slightly higher dietary fiber content and the lower cholesterol content may have contributed to the positive effect of MUFA on BP cannot be ruled out. The calculated dietary intakes of calcium, sodium, potassium, and alcohol did not differ significantly between the MUFA and SFA diet groups; this finding supports the suggestion that the difference in health outcomes was related to the quality of dietary fat. Body weight was stable in both diet groups.

In the Multiple Risk Factor Intervention Trial (MRFIT; 16, 17), the main findings in the multivariate analysis of the 6-y observational data were significant, independent, positive relations between dietary SFA and DBP and between dietary cholesterol and SBP and DBP and an inverse relation of the PUFA-SFA ratio to DBP. A BP-lowering effect of MUFA has been suggested in some epidemiologic studies among populations with a high intake of MUFA (7, 18–20). Although limited in number, intervention studies also suggest a BP-lowering effect when MUFA is substituted for SFA (21, 22). In a small group of hypertensive women, a diet rich in MUFA from olive oil showed beneficial effects on BP (23). However, other trials in normotensive subjects showed no evidence of a BP-reducing effect of MUFA (16). Interestingly, substituting dietary PUFA with MUFA lowered both systolic and diastolic BP in 16 type 2 diabetic subjects (24), whereas only a minor lowering in DBP could be detected in healthy subjects (25). A diet rich in olive oil lowered the SBP and DBP by 4–5 and 3 mm Hg, respectively, as compared with a carbohydrate-rich diet in normotensive type 2 diabetic subjects (26), whereas such an effect was not detected in a small group of insulin-treated type 2 diabetic subjects with microalbuminuria (27). Finally, a slight reduction in SFA intake along with a supplement of olive oil markedly lowered the daily dose of antihypertensive drugs needed by hypertensive subjects

(28). We showed that the present change in the proportion of dietary fatty acids, ie, a decrease in SFAs and an increase in MUFAs, improves insulin sensitivity (12). Prolonged insulin resistance has been shown to be associated with structural alterations of arterial vascular smooth muscle, which may provide the anatomic substrate for the propagation of hypertension (29). Insulin is a growth factor that stimulates the synthesis of vascular smooth muscle cells and results in proliferative changes in the arteries. Elevated circulating concentrations of insulin are associated with activation of the sympathetic nervous system and increased peripheral resistance and sodium retention (10, 30). The beneficial effect on BP of MUFA, in contrast with SFA, may thus, at least in part, be mediated via an improvement in insulin sensitivity. Interestingly, the beneficial effect of the MUFA diet on insulin sensitivity was not seen when the absolute fat intake was high (>37% of energy) (12). In line with this, the effect of MUFA on BP faded away at a high fat intake (>37% of energy). Another possibility could be that the olive oil phenolics, which are powerful antioxidants, partially accounted for the BP-lowering effect (30).

Some of the discrepancies among studies investigating similar dietary changes may be due to differences in populations (eg, an effect of dietary factors may be easier to find in hypertensive than in normotensive individuals) or in methods of measuring BP. Thus, ambulatory BP monitoring with repeated measurements over 24 h much more accurately detects small changes in BP than do clinical BP measurements. Interestingly, we previously found that the diurnal BP was unaffected by a change in the quality of SFAs, ie, between the 2 most important SFAs, stearic and palmitic acids, in type 2 diabetic subjects (31). Mediterranean diets are associated with a reduced risk of CVD, and additional research on the effects of MUFA on BP is warranted to elucidate the potential of MUFA-rich diets to lower BP via diurnal BP measurements, sufficient population samples, and different populations.

n−3 Fatty acids and blood pressure

In the present study we found that the addition of 3.6 g n−3 fatty acids/d did not affect DBP or SBP in normotensive subjects, regardless of whether they were consuming a high-fat (>37% of energy) or a low-fat diet. In a meta-analysis (32), relatively high doses of n−3 PUFAs, typically >3 g/d, reduced BP but only in hypertensive subjects. Weighted pooled estimates of SBP and DBP changes (mm Hg) and 95% CIs were −1.0 (−2.0, 0.0) and −0.5 (−1.2, 0.2) in normotensive subjects and were −5.5 (−8.1, −2.9) and −3.5 (−5.0, −2.1) in the trials of untreated hypertensive subjects. The magnitude of BP reduction was greatest at a high BP but was not significantly associated with dose of n−3 fatty acids. In contrast, another meta-analysis showed a dose-response effect of fish oil on BP with an amount of n−3 fatty acids of >3.3 g/d needed to be associated with an effect on BP (33). However, the effect of n−3 fatty acids on BP occurred only in subjects with hypertension, hypercholesterolemia, and atherosclerosis and not in healthy normotensive subjects. In subjects with peripheral arterial disease, a recent Cochrane analysis (34) found that n−3 fatty acid supplementation reduced DBP but not SBP. Interestingly, the Lugalawa Study (35) found that a daily fish consumption of 300–600 g increased plasma n−3 fatty acids and decreased BP. The effect of n−3 fatty acids on BP in normotensive subjects is not convincing. Thus, in a 9-mo intervention study the addition of n−3 fatty acids lowered SBP and DBP in normotensive subjects (36). However, a 12-mo study of the addition of n−3 fatty acids in normotensive subjects found no effect on SBP or DBP (37).

Dietary fats may modulate BP through different mechanisms. Also, n−3 and n−6 PUFAs are converted to prostaglandins, which reduce BP by affecting arterial vasodilation, electrolyte balance, and renal release of renin or pressor hormones. The incorporation of unsaturated fatty acids into cell membranes increases membrane permeability, thus stimulating the transport of sodium and cations across the membrane. In summary, n−3 fatty acids seem to have a small dose-dependent, hypotensive effect, the extent of which seems to be dependent on the degree of hypertension. In view of the high dose required to lower BP, an increased intake of n−3 fatty acids has a limited role in the management of hypertension.

Conclusions

Changing the proportions of dietary fat by decreasing SFAs and increasing MUFAs decreased diastolic BP. Interestingly, the beneficial effect on BP induced by fat quality was negated by the consumption of a high total fat intake (>37% of energy). The addition of n−3 fatty acids did not alter the BP.

BMR, BV, MU, GR, AAR, LT, and KH were the daily project leaders, were involved in the study scheme and data interpretation, and wrote the manuscript. LB was involved in the study scheme and data interpretation and provided significant advice. EP was involved in carrying out the study and provided significant advice. The KANWU Study Group consists of B Vessby, M Uusitupa, K Hermansen, G Riccardi, AA Rivellese, LC Tapsell, L Berglund, BM Rasmussen, and E Pedersen. None of the authors had a conflict of interest.

REFERENCES

1. Willett WC. Diet and coronary heart disease. In: Willett WC, ed. Nutritional epidemiology. 2nd ed. New York, NY: Oxford University Press, 1998:414–466.
2. Singh RB, Rastogi SS, Niaz MA, Ghosh S, Singh R, Gupta S. Effect of fat-modified and fruit- and vegetable-enriched diets on blood lipids in the Indian Diet Heart Study. Am J Cardiol 1992;70:869–74.
3. deLorgeril M, Renaud S, Mamelle N, et al. Mediterranean alpha-linoleic acid rich diet in secondary prevention of coronary heart disease. Lancet 1994;343:1454–9.
4. deLorgeril M, Salen P, Martin J, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors and the rate of cardiovascular complications after myocardial infarction. Final report of the Lyon Diet Heart Study. Circulation 1999;99:779–85.
5. Burr ML, Fehily AM, Gilbert JF, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (DART). Lancet 1989;2:757–61.
6. Dietary supplementation with n−3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 1999;354:447–55.
7. Keys AB. Seven countries: a multivariate analysis of death and coronary heart disease. Cambridge, MA: Harvard University Press, 1980.
8. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med 2003;348:2599–608.
9. Ward R. Familial aggregation and genetic epidemiology of blood pressure. In: Laragh JH, Brenner BM, eds. Hypertension, pathophysiology, diagnosis and management. New York, NY: Raven Press, 1990:81–100.
10. Hermansen K. Diet, blood pressure and hypertension. Br J Nutr 2000; 83(suppl):113–9.
11. Storlien LH, Baur LA, Kriketos AD, et al. Dietary fats and insulin action. Review Diabetologia 1996;39:621–31.
12. Vessby B, Uusitupa M, Hermansen K, et al. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU study. Diabetologia 2001;44:312–9.

13. Rivellese AA, Maffetone A, Vessby B, et al. Effects of dietary saturated, monounsaturated and n−3 fatty acids on fasting lipoproteins, LDL size and postprandial lipid metabolism in healthy subjects. Atherosclerosis 2003;167:149–58.
14. Summers LK, Fielding BA, Bradshaw HA, et al. Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity. Diabetologia 2002;45:369–77.
15. World Health Organization Expert Committee on Diabetes Mellitus. World Health Organ Tech Rep Ser 1985;742.
16. Stamler J, Caggiula A, Grandits GA, Kjelsberg M, Cutler JA, for the MRFIT Research Group. Relationship to blood pressure of combinations of dietary macronutrients. Findings of the Multiple Risk Factor Intervention Trial (MRFIT). Circulation 1996;94:2417–23.
17. Stamler J, Caggiula AW, Grandits GA. Relation of body mass and alcohol, nutrient, fiber, and caffeine intakes to blood pressure in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr 1997;65(suppl):338S–65S.
18. Williams PT, Fortmann SP, Terry RB, et al. Associations of dietary fat, regional adiposity, and blood pressure in men. JAMA 1987;257:3251–6.
19. Rubba P, Mancini M, Fidanza F, et al. Adipose tissue, fatty acids and blood pressure in middle-aged men from southern Italy. Int J Epidemiol 1987;16:528–31.
20. Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study. Am J Clin Nutr 2004;80:1012–8.
21. Mensink RP, Janssen M-C, Katan MB. Effect on blood pressure of two diets differing in total fat but not in saturated and polyunsaturated fatty acids in healthy volunteers. Am J Clin Nutr 1988;47:976–80.
22. Lahoz C, Alonso R, Ordovas JM, Lopez-Farre A, de Oya M, Mata P. Effects of dietary fat saturation on eicosanoid production, platelet aggregation and blood pressure. Eur J Clin Invest 1997;27:780–7.
23. Ruitz-Gutierrez V, Muriana FJ, Guerrero A, Cert AM, Villar J. Plasma lipids, erythrocyte membrane lipids and blood pressure of hypertensive women after ingestion of dietary oleic acid from two different sources. J Hypertens 1996;14:1483–90.
24. Thomsen C, Rasmussen OW, Hansen KW, Vesterlund M, Hermansen K. Comparison of the effects on the diurnal blood pressure, glucose, and lipid levels of a diet rich in monounsaturated fatty acids with a diet rich in polyunsaturated fatty acids in type 2 diabetic subjects. Diabet Med 1995;12:600–6.
25. Mutanen M, Kleemola P, Valsta LM, Mensink RP, Rasanen L. Lack of effect on blood pressure by polyunsaturated and monounsaturated fat diets. Eur J Clin Nutr 1992;46:1–6.
26. Rasmussen OW, Thomsen C, Hansen KW, Vesterlund M, Winther E, Hermansen K. Effects on blood pressure, glucose, and lipid levels of a high-monounsaturated fat diet compared with a high-carbohydrate diet in NIDDM subjects. Diabetes Care 1993;16:1565–71.
27. Nielsen S, Hermansen K, Rasmussen OW, Thomsen C, Mogensen CE. Urinary albumin excretion rate and 24-h ambulatory blood pressure in NIDDM with microalbuminuria: effects of a monounsaturated-enriched diet. Diabetologia 1995;38:1069–75.
28. Ferrara LA, Raimondi S, d′Episcopo L, Guida L, Dello Russo A, Marotta T. Olive oil and reduced need for antihypertensive medications. Arch Intern Med 2000;160:837–42.
29. Farmer JA. Hypertension and the metabolic syndrome. Curr Cardiol Rep 2004;6:427–33.
30. Visioli F, Galli C. Biological properties of olive oil phytochemicals. Crit Rev Food Sci Nutr 2002;42:209–21.
31. Storm H, Thomsen C, Pedersen E, Rasmussen O, Christiansen C, Hermansen K. Comparison of a carbohydrate rich diet and diets rich in stearic or palmitic acid in NIDDM patients: effects on lipids, glycemic control and diurnal blood pressure. Diabetes Care 1997;20:1807–13.
32. Appel LJ, Miller ER III, Seidler AJ, Whelton PK. Does supplementation of diet with ‘fish oil’ reduce blood pressure? A meta-analysis of controlled clinical trials. Arch Intern Med 1993;153:1429–38.
33. Morris MC, Sacks F, Rosner B. Does fish oil lower blood pressure? A meta-analysis of controlled trials. Circulation 1993;88:523–33.
34. Sommerfield T, Hiatt WR. Omega-3 fatty acids for intermittent claudication. Cochrane Database Syst Rev 2004;3:CD003833.
35. Pauletto P, Puato M, Caroli MG, et al. Blood pressure and atherogenic lipoprotein profiles of fish-diet and vegetarian villagers in Tanzania: the Lugalawa study. Lancet 1996;348:784–8.
36. Schmidt EB, Lervang HH, Varming K, Madsen P, Dyerberg J. Long-term supplementation with n−3 fatty acids. I: Effect on blood lipids, haemostasis and blood pressure. Scand J Clin Lab Invest 1992;51:221–8.
37. Deslypere JP. Influence of supplementation with n−3 fatty acids on different coronary risk factors in men—a placebo controlled study. Verh K Acad Geneeskd Belg 1992;54:189–216.