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Effects of dietary trans fatty acids on blood pressure in normotensive subjects

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Consumption of essential fatty acids of the (n-6) series may affect blood pressure in man. Trans fatty acids in the diet interfere with the metabolism of essential fatty acids in rats. We therefore measured the effect of dietary trans fatty acids on blood pressure in 25 men and 34 women. Each subject consumed, in random order, three mixed natural diets, each for three weeks. The composition of the three diets was similar, except for 10.4 per cent of energy, which was provided by either oleic acid, trans fatty acids, or saturated fatty acids. The intake from polyunsaturated fatty acids was 3.4 per cent on the saturated-fat diet and 4.6 per cent on the other two diets.

On the oleic-acid diet systolic blood pressure was 113 ± 12.8 mmHg and diastolic blood pressure 66 ± 8.3 mmHg, on the trans-fatty-acid diet 112 ± 12.2 mmHg and 67 ± 8.1 mmHg, and on the saturated-fat diet 112 ± 12.6 mmHg and 67 ± 8.1 mmHg. No significant differences were observed in blood pressure levels between the three diets.

We conclude that neither trans nor saturated fatty acids influence blood pressure levels in normotensive subjects relative to oleic acid.

Introduction

Trans fatty acids can be formed during hydrogenation or hardening of oils rich in unsaturated fatty acids. Hydrogenation is a widely used process to make fats which can be used for production of certain types of margarines and shortenings. In addition, trans fatty acids are also present in small amounts in fat from ruminants (Senti, 1988). High intakes of trans fatty acids have been claimed to interfere with the metabolism of polyunsaturated fatty acids in rat (Hill, Johnson & Holman, 1979). In man, there is some evidence that the intake of these essential fatty acids of the (n-6) and (n-3) series influences blood pressure levels (Stern, *et al.*, 1980; Knapp & FitzGerald, 1989), possibly through their effects on prostaglandin formation (Heinemann & Lee, 1976). It is doubtful whether an interaction between trans fatty acids and polyunsaturated fatty acids also exists in man. However, our controlled trial on the effects of trans fatty acids on serum lipids and lipoproteins (Mensink & Katan, 1990) has also given us the opportunity to examine the effects of trans fatty acids on blood pressure. Trans fatty acids in the diet were replaced by either oleic acid, a monounsaturated fatty acid with the cis configuration, or by saturated fatty acids. Thus, this study also allowed us to examine whether saturated fatty acids affect blood pressure relative to oleic acid. The intake of other nutrients and minerals was similar on all three diets.

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Methods

Subjects

Subjects were 34 female and 25 male volunteers, who participated in an experiment to study the effects of trans fatty acids on serum lipids (Mensink & Katan, 1990). Most of them were students at the Agricultural University. All subjects were healthy, as indicated by a medical questionnaire and by the absence of protein and glucose in the urine. One woman used a β-adrenergic blocking agent throughout the experiment, without any change in dosage. Eight women used oral contraceptives. Two of the women and none of the men were smokers. Baseline characteristics are shown in Table 1.

The protocol and aim of the study were fully explained, and subjects gave their informed consent. Prior approval for the study was obtained from the ethics committee of the Department of Human Nutrition.

Design and diets

All subjects consumed three different diets during three consecutive periods. One diet was high in oleic acid, another high in trans isomers of oleic acid, and the third diet was high in saturated fatty acids. Before the study, subjects were categorized according to sex, and females also according to use of oral contraceptives. From each category about one sixth of the subjects were randomly allocated to one of the six possible diet sequences. Each dietary period lasted three weeks. All subjects were studied simultaneously for 63 days from 26 September to 28 November 1988.

Diets used during the study consisted of conventional solid foods, and menus were changed daily in a cycle of 21 days. The composition of the three diets was similar, except for 10.4 per cent of total energy, which was provided by either oleic acid, trans fatty acids, or saturated fatty acids (Table 2). For the oleic acid group a margarine was made from a sunflower oil high in oleic acid (TRISUN; SVO Enterprises, Wickliffe, Ohio). This margarine contained 71 g of oleic acid per 100 g of fatty acids. To prepare a margarine and a shortening high in trans fatty acids (43 g per 100 g of fatty acid), the same high-oleic-acid sunflower oil was hydrogenated under conditions that promoted the formation of trans monounsaturated fatty acids rather than that of saturated fatty acids. For the diet high in saturated fat a margarine and a shortening were produced with a high level of lauric (14 g per 100 g of fatty acid) and palmitic acid (15 g per 100 g of fatty acid) (Mensink & Katan, 1990). Special fats and margarines were prepared by the Unilever Research Laboratory, Vlaardingen, The Netherlands. The intakes of protein, fat, polyunsaturated fatty acids, carbohydrates, fibre, sodium, potassium, calcium and magnesium were similar on the three diets.

Diets were formulated at 28 levels of energy intake, ranging from 5.5 to 20.0 MJ per day. The amount of food necessary to meet each individual's energy requirement was weighed out. Body weights were checked by us twice weekly, and energy intake was adjusted when necessary. All food was provided, except for free-choice items, free of fat and cholesterol. Free-choice items were listed and accorded points corresponding to their energy value, with one point equalling 41.8 kJ (10 kcal). Each subject was required to consume a constant number of points per day, which varied with total energy intake and corresponded with 7 to 11 per cent of the total energy intake. Typical choices were an apple (6 points), orange juice (6 points) or a glass of beer (9 points). In our experience, the free-choice system helps subjects to reconcile the rigid requirements of participation in a trial with their social life and personal preferences. The importance of not changing one's selection of free-choice items between periods was repeatedly explained and stressed. Subjects recorded in diaries their free-choice items, the amount of coffee used, and any deviations from the protocol.

Subjects were asked not to change their smoking habits, use of oral contraceptive, or their physical activity pattern during the study.

For each of the three diets, duplicate portions for one imaginary participant with an energy intake of 10 MJ (2390 kcal) per day were collected daily and stored at −20°C for later analysis.

Other details have been published (Mensink & Katan, 1990).

Measurements

Baseline data were obtained in August and/ or September 1988. Standing height was measured without shoes, and weight without shoes or heavy clothing was recorded to the nearest 0.1 kg. During this period subjects were also asked to weigh and record their food intake on three separate days, two working days and one weekend day. Foods were coded and the composition of the diets calculated using the 1985 edition of the *Netherlands Nutrient Data Bank* (Commissie UCV, 1985). From our previous studies it was known that such records tend to underestimate actual energy needs by some 10 to 15 per cent (Mensink, Janssen & Katan, 1988; Mensink, Stolwijk & Katan, 1990). The calculated energy content was therefore increased by 10 per cent and this value was used as starting level of energy intake at the start of the experiment.

Blood pressure was measured during the morning hours with an automatic sphygmomanometer with recorder (Takeda Medical UA-751, Adquipment Medical BV, Rotterdam, The Netherlands) on one occasion before and once a week during the experiment. The cuff used was 14 cm wide and had a greatest length of 40 cm. Systolic pressure was recorded at Korotkoff phase I and diastolic pressure at Korotkoff phase V. Subjects were asked not to perform physical activity or eat or smoke for 1 h prior to the blood pressure measurements. At each session four measurements were made on the left arm, in a quiet room, after approximately 5 min of rest, with the subject sitting upright. Subjects wore loosely fitting sleeves. During the measurement they rested their left forearm on a table. One trained investigator (MdL), who was blind to each subject's diet, performed all the measurements, using the same sphygmomanometer throughout. All measurements on a particular subject were generally made at the same time of the day to eliminate effects of diurnal variations in blood pressure. Subjects were never told their blood pressure readings during the experiment.

The fatty-acid composition of erythrocyte membranes on the last day of each dietary period was determined to estimate dietary adherence.

The duplicate portions of each diet period were mixed thoroughly, and then freeze-dried. The ash content and the moisture level (Osborne & Voogt, 1978) were determined and then the material was stored at −20°C. Aliquots were analysed for protein (Williams, 1984), total fat (Folch, Leese & Stanley, 1957), the proportions of individual fatty acids (Metcalfe, Schmitz & Pelka, 1966), dietary fibre (Prosky *et al.*, 1984), and cholesterol (van de Bovenkamp & Katan, 1981). Available carbohydrate was calculated by difference. Sodium, potassium, calcium and magnesium were determined by atomic absorption spectrophotometry (Perkin-Elmer Corporation, 1976) in the freeze-dried material after it had been wet ashed and neutralized. The mean composition of the diets was calculated from the duplicate portion analysis plus the calculated contribution of the free-choice items.

Statistical methods

The first blood pressure measurement of each session was discarded and the remaining three measurements were averaged per subject. Body weights were averaged per week. To compare the effects of the three different diets, an analysis of variance was carried out using the General Linear Model (GLM) procedure of the Statistical Analysis System (SAS) (SAS Institute Inc., 1985). The design of the study made it possible to eliminate variation due to time effects or residual effects of the previous diet (Snedecor & Cochran, 1980). All P values are two-tailed.

Results

Subjects

The volunteers were between 19 and 57 years of age. The body mass indexes ranged between 18.4 and 25.4 kg/m^2 for men and between 17.4 and 29.7 kg/m^2 for women. Systolic blood pressure, as measured four weeks before the study, ranged from 90 to 156 mmHg and diastolic blood pressure from 47 to 90 mmHg (Table 1).

Table 1. Baseline characteristics of the subjects.

	Men (n = 25)			*Women (n = 34)*		
	Mean	*s.d.*	*Range*	*Mean*	*s.d.*	*Range*
Age (years)	24.7	8.3	19–52	25.6	9.9	19–57
Height (cm)	185	6.2	175–200	170	6.8	157–187
Weight (kg)	75	6.2	65–87	64	8.3	54–90
Body mass index (kg/m^2)	22.0	1.9	18.4–25.4	22.0	2.5	17.4–29.7
Blood pressure (mmHg)						
Diastolic	74	7.9	58–90	70	9.6	47–88
Systolic	129	12.2	115–157	109	10.4	90–129

Body weights were on average 69.1 ± 9.3 kg on the oleic-acid diet, 69.3 ± 9.4 kg on the trans-fatty-acid diet, and 69.0 ± 9.4 kg on the saturated-fat diet. Over the nine weeks of the study average body weight decreased by 0.3 ± 1.2 kg (range, −3.1 to 2.4 kg).

Nutrient intake

The mean daily intake of energy and the composition of the diets before and during the study are shown in Table 2. Compared with the diet high in oleic acid the intake from saturated fatty acids did not change on the trans-fatty-acid diet, but the intake increased from 9.5 to 19.4 per cent of energy on the saturated-fat diet. The total energy derived from polyunsaturated fatty acids was 4.6 per cent on the oleic-acid and trans-fatty-acid diet and 3.4 per cent on the saturated-fat diet. The ratio of polyunsaturated to saturated fatty acids was 0.48

Table 2. Mean daily intake of energy and nutrients of subjects before the experiment, and during the oleic-acid diet period, the trans-fatty-acid diet period, and the saturated-fat diet period.

		Diet		
	Habitual[a]	*Oleic-acid*[b]	*Trans-fatty-acid*[b]	*Saturated-fat*[b]
Energy				
(MJ/day)	10.3 ± 3.4	11.6	11.5	11.4
(kcal/day)	2464 ± 813	2780	2751	2734
Protein (% of energy)	14.3 ± 1.9	13.1	13.3	14.0
Fat (% of energy)	34.7 ± 5.6	39.6	40.2	38.8
Saturated fatty acids	13.9 ± 2.7	9.5	10.0	19.4
Monounsaturated fatty acids	12.3 ± 2.3	24.1	24.2	14.7
cis-C18:1		23.0	12.6	12.8
trans-C18:1		0.0	10.9	1.8
Polyunsaturated fatty acids	6.4 ± 2.3	4.6	4.6	3.4
Linoleic acid	5.4 ± 2.2	4.0	4.2	2.9
Carbohydrates (% of energy)	49.7 ± 6.5	46.3	45.6	46.1
Mono- and disaccharides	24.7 ± 5.6	26.2	25.3	24.0
Polysaccharides	24.9 ± 4.7	19.9	20.2	22.0
Alcohol (% of energy)	1.6 ± 2.1	1.1	0.9	1.3
Dietary fibre (g/MJ)	3.2 ± 0.8	4.1	4.1	4.3
Sodium (mmol/MJ)	11.5 ± 2.3	11.9	12.1	11.8
Potassium (mmol/MJ)	10.1 ± 2.0	11.4	11.0	11.1
Calcium (mmol/MJ)	3.2 ± 0.9	3.0	3.3	3.7
Magnesium (mmol/MJ)		1.5	1.6	1.6

[a] No values for magnesium and cis- and trans-isomers are available in the food composition table used.
[b] Each value represents the mean of the three different periods, during which each diet was consumed by a different third of the subjects. Standard deviations for the amounts of energy needed to maintain body weight were 2.8 MJ on the oleic-acid diet, 2.7 MJ on the trans-fatty-acid diet, and 2.9 MJ on the saturated-fat diet. Differences in diet composition between periods and between subjects were negligible and standard deviations are therefore not given.

on the oleic-acid diet, 0.46 on the trans-fatty-acid diet, and 0.18 on the saturated-fat diet. The consumption of alcohol on the three test diets was similar. The intake of dietary fibre, sodium, potassium, calcium and magnesium was similar on all three diets. Coffee intake averaged 2.2 cups per day during consumption of the oleic-acid and saturated-fat diet, and 2.3 cups per day during consumption of the trans-fatty-acid diet.

Dietary adherence was confirmed by the fatty-acid composition of erythrocyte membranes. The ratio of *cis*-C18:1 to *trans*-C18:1 was 17.1 ± 6.3 on the oleic-acid diet, 4.6 ± 1.2 on the trans-fatty-acid diet, and 14.5 ± 4.9 on the saturated-fat diet.

Inspection of the diaries did not reveal any deviations from the study protocol.

Blood pressure

Time courses of blood pressure values are shown in Figure 1.

In the third week on the oleic-acid diet, the mean systolic blood pressure was 113 ± 12.8 mmHg and the mean diastolic blood pressure was 66 ± 8.3 mmHg. On the trans-fatty-acid diet these values were 112 ± 13.3 (95 per cent confidence interval for difference with the oleic-acid diet, −2.9 to 1.5 mmHg) and 67 ± 8.1 mmHg (95 per cent confidence interval, −0.9 to 2.7 mmHg), and on the diet high in saturated fat 112 ± 12.6 (95 per cent confidence interval, −2.9 to 1.5 mmHg) and 67 ± 8.1 mmHg (95% confidence interval, −1.0 to 2.5 mmHg) (Table 3). The blood pressure values on the three test diets were not significantly different from each other. In the 30 subjects with the highest diastolic blood pressures at the start of the study, levels were 78 ± 5.4 mmHg on their habitual diet, 70 ± 5.4 mmHg on the oleic-acid diet, 72 ± 6.6 mmHg on the trans-fatty-acid diet, and 71 ± 8.0 mmHg on the saturated-fat diet. The values on the three test diets were not significantly different from each other. The mean systolic blood pressure of the 30 subjects with the highest systolic blood pressure levels was 129 ± 10.8 mmHg on their habitual diet, 120 ± 12.1 mmHg on the oleic-acid diet, 121 ± 11.6 mmHg on

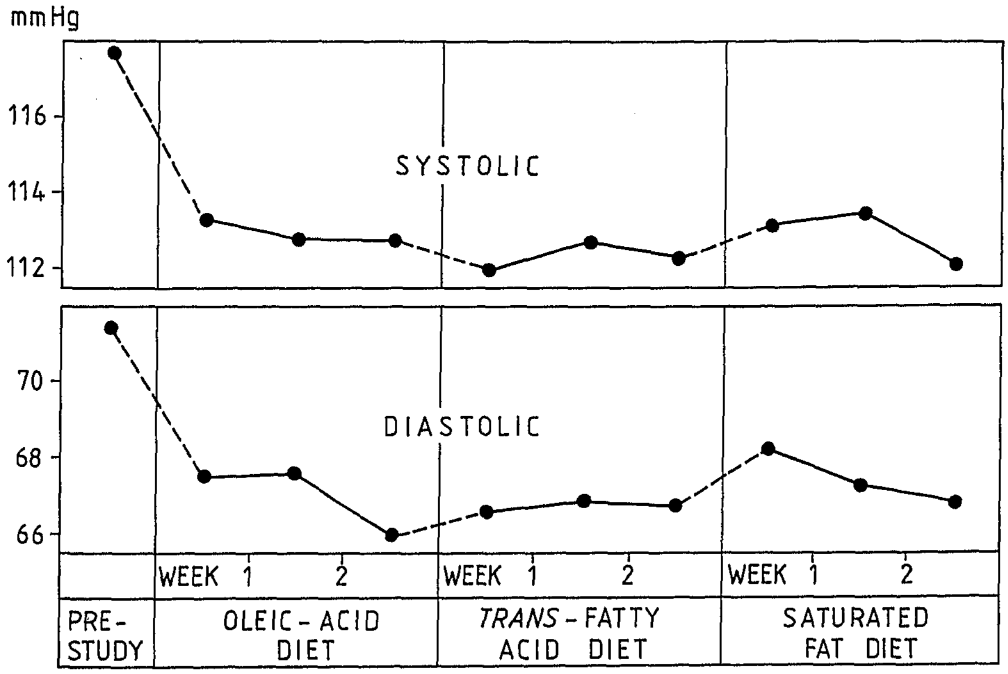

Fig. 1. Mean systolic and diastolic blood pressure before and during the experiment. During the study 25 men and 34 women consumed each diet in random order for three weeks.

Table 3. Systolic and diastolic blood pressure during consumption of diets high in oleic acid, in trans monounsaturated fatty acids, or in saturated fatty acids.[a]

	Oleic-acid diet	*Trans-fatty-acid diet*	*Saturated-fat diet*
Systolic (mmHg)			
Men	121 ± 11.8	122 ± 12.2	122 ± 8.7
Women	106 ± 9.6	105 ± 9.3	105 ± 10.2
All	113 ± 12.8	112 ± 13.3	112 ± 12.6
Diastolic (mmHg)			
Men	66 ± 8.3	69 ± 8.5	68 ± 7.6
Women	66 ± 8.5	65 ± 7.7	65 ± 8.3
All	66 ± 8.3	67 ± 8.1	67 ± 8.1

[a] Values are means ± s.d. Each diet was fed for three weeks to each of the 25 men and 34 women, in random order.

the trans-fatty-acid diet, and 119 ± 10.4 mmHg on the saturated-fat diet. Again, no significant differences were found between the three test diets.

Discussion

Animal studies have shown that high levels of trans fatty acids in the diet require an increased intake from the essential fatty acid linoleic acid (Hill *et al.*, 1979). In man linoleic acid might lower blood pressure (Stern *et al.*, 1980). In theory, diets high in trans fatty acids may thus increase blood pressure. In the present study no effects of trans fatty acids on blood pressure levels in normotensive subjects could be demonstrated relative to *cis* monounsaturated or saturated fatty acids. Linoleic acid provided 3 to 5 per cent of energy intake and total fat 39 to 40 per cent in all three diets. The power in this experiment for detecting a true difference of 3 mmHg between two diets was over the 90 per cent. Thus, it is not likely that we have missed a biologically significant change in blood pressure purely by chance. We conclude that trans fatty acids have no effects on blood pressure at the levels of linoleic acid intake that are common in most populations.

Our study also showed that saturated fatty acids have the same effect on blood pressure as *cis* monounsaturated fatty acids. Few studies have examined the effect of an increased intake of saturated fatty acids on blood pressure at a nearly constant intake of polyunsaturated fatty acids. Two groups of investigators (Iacona *et al.*, 1981; Sacks *et al.*, 1984) did not observe an effect on blood pressure when the intake of saturated fat plus monounsaturated fat was decreased and replaced by carbohydrates. In contrast, slight effects on systolic (Sacks *et al.*, 1981) or on systolic and diastolic blood pressure have also been reported (Strazzullo *et al.*, 1986). Thus, studies in normotensive subjects have not produced consistent results. It should be noted that in some of these studies saturated fatty acids were replaced by monounsaturated fatty acids (Sacks *et al.*, 1981) but in others by carbohydrates (Iacona *et al.*, 1981; Sacks *et al.*, 1984; Strazzullo *et al.*, 1986). However, we have earlier shown that monounsaturated fatty acids and carbohydrates have similar effects on blood pressure (Mensink *et al.*, 1988).

It is known that the extent of changes in blood pressure levels caused by diet is related to initial blood pressure values. Puska *et al.* (1983) found a greater decrease in both systolic and diastolic blood pressure after dietary fat modification in subjects with mild hypertension than in normotensive subjects. However, it is not likely that the level of blood pressure in our study was too low to allow changes to be seen. Blood pressure levels of the subjects in the two studies where effects of decreasing saturated fat intake were reported (Sacks *et al.*, 1981; Strazzullo *et al.*, 1986) were even lower than of our subjects. In addition, we could not demonstrate differences in responses between subjects from the upper and the lower half of the blood pressure distribution.

The experimental diets in our study were consumed for three weeks. It could be argued that this period might have been too short to induce a change in blood pressure. However, other diet studies suggested that blood pressure levels were already stabilized after three weeks (Iacona *et al.*, 1981, 1983).

Results in our study were not confounded by other factors which may affect blood pressure: body weights were kept constant, and the intake of dietary fibre, alcohol, sodium, potassium, calcium and magnesium was similar on all three diets. The exchange of trans monounsaturated for either cis monounsaturated or saturated fatty acids was the only dietary intervention. We conclude that at intake levels of linoleic acid higher than 3 per cent of energy, trans monounsaturated fatty acids cis monounsaturated fatty acids and saturated fatty acids have the same effect on blood pressure in normotensive subjects.

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