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The Tromsø heart study: coffee consumption and serum lipid concentrations in men with hypercholesterolaemia: a randomised intervention study

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Abstract

In a 10 week trial to assess the effects of coffee consumption and coffee brewing methods on serum cholesterol concentrations 33 men with hypercholesterolaemia were randomly assigned to: continue with their usual coffee intake; stop drinking coffee altogether; or stop drinking coffee for five weeks, thereafter drinking either boiled or filter coffee.

Cholesterol concentrations fell significantly in all subjects abstaining for the first five weeks compared with subjects not giving up and continued to fall in those abstaining for 10 weeks. Cholesterol concentrations rose

again in subjects returning to boiled coffee but remained the same in those returning to filter coffee.

Abstention from heavy coffee drinking is an efficient way of reducing serum cholesterol concentrations in men with hypercholesterolaemia. The extent to which the brewing method affects this relation requires further study.

Introduction

Two recent reports have linked coffee consumption with serum cholesterol concentration.^{1 2} Findings in both studies were based on consumption of black, boiled coffee. The only other study of this relation in man of which we are aware confirms these findings.³ Here we report a study to assess the effect on blood lipid concentrations of: (1) abstention from coffee in men with hypercholesterolaemia and (2) brewing coffee in two different ways.

Subjects and methods

The participants originated from a multifactorial intervention study of 1373 men at high risk of heart disease, aged 35-54, initiated during

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the second Tromsø heart study in 1979-80. Eligible were coffee drinking men from the intervention group who, after three years of intervention, still had a total cholesterol concentration exceeding 8.3 mmol/l (321 mg/100 ml). Forty eight men fulfilled the criteria, and 33 volunteered to take part in the experiment.

During the week before the trial the participants recorded their daily intake of coffee. They were then randomly allocated to one of four 10 week regimens for coffee drinking: participants in the first group continued their habitual coffee intake; those in the second group abstained from coffee during all 10 weeks; and those in the third and fourth groups abstained from coffee for the first five weeks and then returned to their usual amount of coffee, boiled and filtered respectively. The boiled coffee was brewed in the following way: 50 g coarsely ground coffee was added to 1 l boiling water; the pot was then removed from the heat for at least 10 minutes before serving. The filter coffee was brewed on a coffee filter machine (Moccamaster, Technivorm type 70), the amount of coffee per litre of water being the same as for the boiled coffee, and drunk within 30 minutes.

During the study period the participants recorded the number of cups of coffee or tea they drank each day and the amount of sugar and cream they added. The size of the cups was not standardised. One participant in the third group missed giving the last serum sample because of a traffic accident. Coffee and tea (tea was suggested as a substitute for coffee in the periods without coffee) were provided free of charge. The participants were urged not to change their dietary or other habits during the trial.

Non-fasting blood samples for lipid analysis were drawn at the start of the trial and every two and a half weeks thereafter. The serum samples were kept frozen at -20°C until after the trial and then analysed blind for total cholesterol, high density lipoprotein (HDL) cholesterol, and triglyceride concentrations at the University Teaching Hospital of Tromsø. Details of methods are given elsewhere.¹ Difference between the groups were tested by paired *t* test.

Results

The table shows the mean total serum cholesterol concentration at screening and follow up, baseline values, and mean change in concentration during the trial for the four groups. The figure also shows the mean changes from baseline values.

Mean (SD) cholesterol concentrations (mmol/l) at screening and follow up, baseline concentrations, and mean (SD) changes (mmol/l) from baseline values in subjects drinking coffee as usual for 10 weeks (group 1), subjects abstaining from coffee for 10 weeks (group 2), and subjects abstaining for five weeks and then drinking boiled (group 3) or filter (group 4) coffee

	Group 1 (n = 8)	Group 2 (n = 9)	Group 3 (n = 8)	Group 4 (n = 8)
Total cholesterol:				
At screening	8.64 (0.46)	8.87 (0.87)	8.58 (1.06)	8.94 (0.41)
At follow up	8.89 (0.25)	8.97 (0.42)	8.76 (0.19)	8.93 (0.45)
Baseline	8.48 (0.78)	8.72 (0.75)	8.45 (1.17)	9.10 (0.71)
Change from baseline:				
After 2.5 weeks	0.32 (1.04)	-0.36 (0.60)	-0.52 (0.35)	-0.51 (0.89)
After 5 weeks	0.67 (1.43)	-0.90 (0.85)	-0.88 (0.68)	-0.91 (0.47)
After 7.5 weeks	0.34 (1.25)	-1.01 (0.95)	-0.55 (0.97)	-0.70 (0.95)
After 10 weeks	0.35 (1.35)	-1.16 (0.73)	-0.36 (0.45)*	-0.91 (1.14)

*n = 7.

Conversion: SI to traditional units—Cholesterol: 1 mmol/l $\approx$ 39 mg/100 ml.

Concentrations in the control group (habitual coffee consumption) showed a non-significant increase during the first five weeks but approached baseline values in the last five weeks. Subjects in the other three groups (no coffee for 10 weeks, no coffee followed by boiled coffee, and no coffee followed by filter coffee), starting with five weeks of abstinence from coffee, showed almost identical mean falls in cholesterol concentration from baseline values of 0.90, 0.88, and 0.91 mmol/l (35, 34, and 35 mg/100 ml) and falls compared with the control group of 1.57 mmol/l (61 mg/100 ml) ($p < 0.02$), 1.55 mmol/l (60 mg/100 ml) ($p < 0.02$), and 1.58 mmol/l (61 mg/100 ml) ($p < 0.01$) respectively. For all 25 subjects in the three groups eliminating coffee together this represented a mean fall in cholesterol concentration of 10.2% from baseline, ranging from a decrease of 24.4% to an increase of 2.6%. Only three of the 25 subjects showed an increase. Mean coffee intake in these three groups the week before the trial was 7.3 cups a day, and mean tea intake during the first five weeks was 4.8 cups a day, with a mean sugar intake of 6.1 teaspoons a day.

In subjects who abstained from coffee for the full 10 weeks the cholesterol concentration continued to fall, to 1.16 mmol/l (45 mg/100 ml) below the baseline value—that is, a mean (range) decrease of 13.0% (3.3-25.5%). Compared with the control group the fall was 1.51 mmol/l (58 mg/100 ml) ($p < 0.02$).

In subjects consuming boiled coffee during the second five weeks an increase in total cholesterol concentration of 0.36 (SD 0.45) mmol/l (14 (SD 17) mg/100 ml) was observed. This increase was significant compared with concentrations in those abstaining throughout ($p < 0.02$) but not compared with concentrations in those drinking filter coffee, who showed no rise in cholesterol concentration during the second five week period.

Changes in HDL cholesterol and triglyceride concentrations during the trial were inconsistent and unrelated to coffee regimen.

Mean changes in total cholesterol concentration from baseline values over 10 weeks in men with hypercholesterolaemia, of whom eight continued their habitual intake of coffee (●—●), nine gave up drinking coffee altogether (○—○), and 16 gave up for only five weeks, thereafter drinking boiled (▼—▼) or filter (△—△) coffee.

Conversion: SI to traditional units—Cholesterol: 1 mmol/l $\approx$ 39 mg/100 ml.

Discussion

The observed reduction in total cholesterol during abstinence from coffee was considerable, uniform, and independent of concomitant use of sugar and cream, cigarette smoking, or tea drinking. Otherwise the diet was not monitored. The participants were, however, chosen from a group of hypercholesterolaemic men who, for the previous three years, had been trying without much success to reduce their cholesterol concentration by dietary means. The possibility that any sudden, unconscious dietary change could lead to a fall in cholesterol concentration of the magnitude seen here was therefore unlikely.

Our trial failed to give conclusive answers on the extent to which the coffee cholesterol relation is dependent on the method of brewing the coffee. The composition of coffee solids in the ultimate brew depends on: the blend, degree of roast, duration of contact between water and coffee, the temperature of the water, the composition of the water, and the method of coffee extraction.¹ The predominant way of brewing coffee locally—boiling coarsely ground coffee—was compared with a filter method brewing at a lower temperature and with a shorter contact time. The results suggest that the difference in method might be important, but the power of the trial on this point was too low to give conclusive answers.

The prerequisites for claiming a direct relation between coffee consumption and serum cholesterol concentration have not been completely fulfilled in this case. Firstly, a biological description of the possible mechanism is lacking. Secondly, a dose related response has so far not been shown, even though the cross sectional data have suggested a linear increase in total cholesterol concentration with increasing coffee consumption.¹ The present trial was not designed to show a dose related response as the size

of the cups was not standardised and the intake of coffee was not graded within each subject. Even so, the conclusion from this experiment must be that abstinence from coffee in hypercholesterolaemic men is followed by a substantial reduction in total cholesterol concentration. The implication of this relation is not clear yet, but the reduction in total cholesterol concentration in the present subjects was comparable with that observed in the Oslo study in which the traditional low fat, low cholesterol diet was used and a considerable reduction in coronary morbidity and mortality was observed.⁵

On the basis of these and our earlier findings we thought it safe to advise hypercholesterolaemic subjects in our population to reduce their coffee consumption. We are, however, reluctant to advise people generally to do this because of the lack of prospective data and the possibility of singling out and eliminating the active substance from coffee.

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SHORT REPORTS

Rapid development and progression of proliferative retinopathy after strict diabetic control

There have been some reports of deterioration in pre-existent diabetic retinopathy after the institution of adequate diabetic control.^{1,2} This paper reports a patient with diabetes mellitus in whom the institution of tight metabolic control was followed by the development of rapidly progressive retinopathy.

Case report

A 31 year old diabetic woman in collapse was admitted to hospital with diabetic ketoacidosis. A neurological cause was excluded by the clinical absence of focal neurological signs, normal cerebrospinal fluid, and normal computed tomographic appearances of the brain. Her fundi were normal. She had been diabetic for nine years and had been treated erratically with insulin or dietary restriction with and without glibenclamide. After rehydration and treatment with insulin she recovered completely and was started on twice daily injections of insulin. Blood glucose concentrations varied from 3 to 10 mmol/l (54-180 mg/100 ml) before and after her discharge from hospital. Her HbA_{1c} concentration fell to 8% (reference range 5.5-8.5%) in eight weeks. She now complained of visual blurring. Examination of the fundi showed extensive soft exudates, haemorrhages, and macular oedema; the visual acuity was reduced to 6/18 in each eye. Fluorescein angiography showed early neovascularisation of both discs, profuse leakage of the dye, multiple microaneurysms, and extensive areas of capillary closure (see figure). Panretinal Argon laser burns were carried out bilaterally. Nevertheless, appreciable progression of the neovascularisation of both discs continued and the right sided vision deteriorated to 6/24. The left eye was treated with xenon laser, but the patient developed a serous detachment at the posterior pole. Before the right eye could be treated, the disc vessels bled.

Platelet studies at the time of the discovery of proliferative retinopathy showed appreciable hyperaggregability; the release of thromboxane A₂ during platelet aggregation was also appreciably increased. Platelet aggregation after challenge with 0.2, 0.5, and 5.0 µmol/l of adrenaline was 65%, 68%, and 69% compared with 7%, 24%, and 70% respectively in 20 controls. Thromboxane B₂ release after 0.2, 0.5, and 5 µmol/l of adrenaline was 27.0, 36.2, and 40.3 ng/10⁸ platelets in the patient compared with <2.0, <2.0, and 10.2 ng/10⁸ platelets in the controls; that after 1.0 µg/ml collagen was 38.0 ng/10⁸ platelets in the patient compared with 16.7 in the controls; and that after 10 µM adenosine diphosphate was 12.2 ng/10⁸ platelets in the patient compared with 1.8 in the controls. β Thromboglobulin concentration was 0.7 pmol/l (normal) and platelet factor 4 was not detectable.

Her diabetic control continued to be excellent, with her HbA_{1c} concentration being maintained at 7.5%.

Comment

This case shows that rapidly progressive diabetic retinopathy may develop within weeks. Very tight control of diabetes after years of inadequate treatment and control of hyperglycaemia may have precipitated the development of retinopathy, but we cannot be certain of a direct causal relation.

Rapid falls in blood glucose concentrations may induce diminutions in retinal blood flow, since high blood glucose concentrations are associated with increased retinal perfusion.³ Diminished perfusion and ischaemia trigger new vessel formation in the retina. The considerable hyperaggregability of her platelets may also have contributed to retinal ischaemia. We have not found such hyperaggregability in other patients with proliferative retinopathy without concomitant macrovascular disease.⁴ The release of serotonin, thromboxane A₂, adenosine diphosphate, and calcium during platelet aggregation may all have contributed to retinal vasospasm. Platelet hyperaggregability persisted despite the maintenance of excellent diabetic control. β Thromboglobulin and platelet factor 4 concentrations were, however, not raised. Similar dissociation has been described in diabetic patients with hyperaggregable platelets.⁵

In conclusion, this patient developed de novo a severe progressive retinopathy after the institution of near perfect control of her diabetes. Combined with other recent similar data from patients with pre-existent retinopathy who deteriorated after the institution of strict

Rapidly progressive retinopathy: (a) microaneurysms, exudates, and haemorrhages; (b) neovascularisation of retina, including leashes of new vessels on the optic disc; (c) haemorrhage from new vessels on the optic disc; (d) fluorescein angiogram showing multiple microaneurysms, diffuse fluorescein leakage, ischaemic zones, and haemorrhages.