connective tissue matrix. The infiltration of fissured plaque caps by foam cells has been noted previously.[2] There thus may be three-dimensional anomalies in the tissue not readily visible in two-dimensional histology sections that create stress levels sufficient to determine localisation of fracture.

Intimal tears can also occur when there is no lipid pool within the intima; such tears may be less important clinically than those occurring in the presence of a pool of lipid because a large intraintimal thrombus cannot form in the absence of a potential space within the intima. Several pathological circumstances can intensify local stress to the point of intimal tearing in the absence of non-load-bearing lipid pool—for instance, where there is a calcified plate within the intima, adjacent areas will be subject to high shear stress, as confirmed by necropsy findings of some tears at such sites. Although this mechanism of tearing was not often found, it may be more common in the ectatic calcified arteries of old people. Similar concentrations of shear stress will occur when there are circumferential layers with varying mechanical properties. Such concentric layers of fibrosis are not uncommon in atherosclerotic lesions and may also predispose to intimal tearing in the absence of a lipid pool.

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Correspondence should be addressed to M. J. D., Cardiovascular Pathology Unit, St George's Hospital, London SW17 0RE.

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FISH INTAKE AND ARTERIAL WALL CHARACTERISTICS IN HEALTHY PEOPLE AND DIABETIC PATIENTS

MARK L. WAHLQVIST CHE SAM LO
KENNETH A. MYERS

Departments of Medicine and Surgery, Monash University, Prince Henry's Hospital, Melbourne, Victoria, Australia 3004

Summary The relation between fish consumption and indices of arterial wall pathology was investigated in 31 healthy subjects and in 22 patients with non-insulin-dependent diabetes mellitus (NIDDM). Arterial compliance in non-fish eaters, as measured by doppler ultrasonography, was significantly lower than that in fish eaters in the healthy group, in the NIDDM group, and in the two groups combined. In non-fish eaters an increase in proximal resistance at the common femoral artery and in the posterior tibial artery was significant only in the combined groups and in healthy subjects, respectively. The results support the hypothesis that fish consumption may be important for better arterial wall characteristics.

Introduction

EPIDEMIOLOGICAL comparisons of Greenland Eskimos and mainland Danes indicate that diets rich in fish or marine oil may reduce the incidence of occlusive vascular disease.[1,2] In Eskimo, Japanese, and Caucasian populations, a diet rich in fish oil or ω-3 fatty acids significantly reduces plasma cholesterol and triglyceride concentrations, improves fat tolerance, prolongs bleeding time, reduces platelet count, and decreases platelet adhesiveness.[3] We have investigated the relation between fish consumption and indices both of arterial compliances and of proximal resistance in non-insulin-dependent diabetic patients and healthy controls.

Subjects and Methods

Subjects

The study was approved by the Ethics Committee at Prince Henry's Hospital according to the statement on human experimentation by the National Health and Medical Research Council of Australia. Informed consent was obtained.

31 healthy people (group A) and 22 patients with non-insulin-dependent diabetes mellitus (NIDDM) managed by diet alone (group B) were included in the study. Healthy subjects were recruited from community groups in the vicinity of the hospital, whereas diabetic patients were recruited sequentially from the hospital's diabetic clinic. Subjects were divided into fish eaters or non-fish eaters and matched for age, body mass index (BMI), and blood pressure (table I). None of the subjects smoked and all were normotensive (diastolic pressure < 95 mm Hg). No subject had any symptoms or history of arterial disease. None of the diabetic patients had evidence of retinopathy, nephropathy, or neuropathy. All had normal ankle pressure indices at rest and after exercise, as judged by doppler ultrasonography.[4,5]

Analysis

Food intake.—All subjects completed a seven-day dietary record, with reference to household measures, in the week after the doppler studies. A clinical nutritionist then reviewed the diet record with each subject and clarified information necessary for data coding. Food models were used to check quantities and types of food eaten. Neither the subjects nor the nutritionist knew the results of the arterial wall studies. From the dietary records we divided subjects into fish eaters and non-fish eaters. Fish eaters were defined as those who ate one serving (100 g) or more of fish in a week. Non-fish eaters ate no fish in a week. 'Nutritionist III' (4·0; N-squared Computing, Oregon, USA) modified with Australian food analyses for dietary fibre was used for nutrient analysis of the food records.

disease in both European and North American populations.[10]

Dietary n-3 polyunsaturated fatty acids (n-3PUFAs), abundant in marine organisms, may retard the development of arteriosclerotic cardiovascular disease: in men who needed coronary angioplasty, treatment with fish oil reduced the incidence of restenosis.[11] Weiner et al[12] found that pigs fed with cod-liver oil had significantly less arterial disease; the mean lesion area, mean luminal encroachment, and mean maximal luminal encroachment per vessel were lower in animals that were fed cod-liver oil compared with controls. They concluded that in their animal model cod-liver oil retarded the development of coronary artery disease, possibly through changes in prostaglandin metabolism. The data from laboratory animals and volunteers are similar in indices such as serum lipoproteins and platelet functions.

Recently, Hamazaki et al[13] reported that the PWV and the incidence of ischaemic heart disease were significantly lower in residents of Japanese coastal fishing villages than in mountainous farming villages. They suggest that a long-term fish diet is likely to slow arteriosclerotic change. We have shown that non-fish eaters have a significantly lower arterial compliance than fish eaters. That we could only show a significant difference for the proximal resistance at the posterior tibial artery in the apparently normal subjects and not for the NIDDM patients may indicate that for assessment of arterial wall characteristics measurements of proximal resistance are not as sensitive as compliance measurements.[4,14] The differences between fish eaters and non-fish eaters lend support to the potential importance of fish consumption for better arterial wall characteristics when there is no apparent clinical evidence of macrovascular disease.

Correspondence should be addressed to M. L. W.

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RESPONSES TO HUMAN AND PORCINE INSULIN IN HEALTHY SUBJECTS

R. J. HEINE E. A. P. VAN DER HEYDEN
E. A. VAN DER VEEN

Departments of Internal Medicine and Endocrinology, Free University Hospital, PO Box 7057, 1007 MB Amsterdam, The Netherlands

Summary In a double-blind randomised study, eight healthy men received equimolar amounts of human or porcine insulin by infusion (50 mU/kg per hour). Insulin potencies, in terms of the amount of glucose infused to maintain euglycaemia, were almost identical. Hypoglycaemia (blood glucose concentration 2 mmol/l or below) was then induced and the symptoms and hormonal counter-regulatory responses were recorded. The number of sympathoadrenergic (but not neuroglycopenic) symptoms was significantly greater with porcine than with human insulin, as was the integrated noradrenaline response. Glucagon, growth hormone, cortisol, and adrenaline responses were similar for the two insulins.

Introduction

UNAWARENESS of hypoglycaemia ("hypoglycaemia unawareness"), a hazard in insulin-treated diabetic patients, is said to arise more frequently with human insulin than with animal insulins.[1-4] Consequently, there have been calls for the continued manufacture of porcine insulin. These have generated controversy because no consistent differences are reported between the counter-regulatory hormone responses to the different types of insulin.[5] Controlled trials comparing human and animal insulin have failed to demonstrate the differences in the frequency of hypoglycaemia requiring treatment.[3,5-8] One study[3] showed fewer sympathoadrenergic symptoms in patients transferred from porcine to human insulin. We have investigated the matter in healthy, rather than diabetic, volunteers to exclude the influences of autonomic neuropathy and variations in metabolic control on catecholamine responses.

Subjects and Methods

Eight healthy male volunteers with a mean age of 23 years (range 20–30 years) and mean body mass index of 22·9 kg/m² (range 19·1–25·2) took part. They had never before received insulin injections and had no family history of diabetes. The Free University Hospital ethical committee gave permission for the experiments.

The insulins (40 IU/ml) were provided by Nordisk. The semisynthetic human short-acting insulin was manufactured by chemical conversion of porcine to human insulin. The measured protein contents of the highly purified semisynthetic human and highly purified porcine insulins were 1·41 mg/ml (batch 6843) and 1·43 mg/ml (batch 6929), respectively.

Study Design

Each subject was studied on two occasions separated by one week. Subjects fasted from 2200 h the evening before and were admitted to the metabolic ward at 0800 h. After insertion of one cannula in a dorsal hand vein, for sampling of arterialised venous blood, and a second cannula in the antecubital fossa of the contralateral arm, for infusions, the subjects rested in a supine position for at least 1 hour. Samples were taken for basal values of glucose and hormone levels.[9] The subjects were randomised to receive human or porcine insulin and administration was double blind. Then, at time t = 0 min, intravenous administration of the insulins, at an infusion rate of 50 mU/kg per hour, for 150 min was

TABLE I—SUBJECT CHARACTERISTICS

Subjects	Age (yr)	BMI (kg/m²)	$\overline{BP}$ (mm Hg)
Healthy			
Fish* (n = 19)	69·1 (1·6)	26·4 (1·0)	97 (1·9)
Non-fish† (n = 12)	67·1 (3·2)	29·0 (1·3)	96 (1·4)
NIDDM patients			
Fish (n = 13)	65·1 (2·8)	28·0 (1·0)	97 (1·8)
Non-fish (n = 9)	68·0 (2·4)	27·6 (1·8)	100 (2·4)
Combined			
Fish (n = 32)	67·5 (1·5)	27·1 (0·7)	97 (1·3)
Non-fish (n = 21)	67·6 (2·1)	28·4 (1·0)	98 (1·4)

Values are means (SEM).
*Fish eaters: fish intake 1–5 servings/week per person (about 100–500g/week).
†Non-fish eaters: no fish intake in a week.
BMI = body mass index.
$\overline{BP}$ = geometric mean blood pressure: (systolic + [2 × diastolic]) ÷ 3.

Doppler ultrasonography.—Each subject rested supine for at least 10 min and the examination began when the blood pressure was stable. Mean compliance between the left subclavian artery and each femoral artery at the inguinal ligament was calculated from pulse wave velocity (PWV) recorded by two 4-MHz doppler ultrasound probes (Sonicaid Medical, Virginia) through a 'Spectrum Analyser' (Medishield, London), as previously described.[4-6] The PWV down the aorto-iliac segment was measured from the ratio of the time delay (T) to the distance between the probes (L)—ie, PWV = L ÷ T m/s. The compliance (C) was calculated as $C = 66{\cdot}7 \div PWV^2$. Each measurement consisted of the mean of ten pulse-wave calculations on each side. Pulse-wave damping (PWD) at the common femoral arteries and at the posterior tibial arteries was measured with an 8-MHz vascular doppler ultrasound probe through the spectrum analyser. A Fourier analysis of the pulse wave at each site was done to calculate the Laplace damping factor or PWD, which is related to proximal resistance.[4,7,8]

Statistical analysis.—We compared fish eaters with non-fish eaters for differences in arterial wall indices using Student's *t* test.

Results

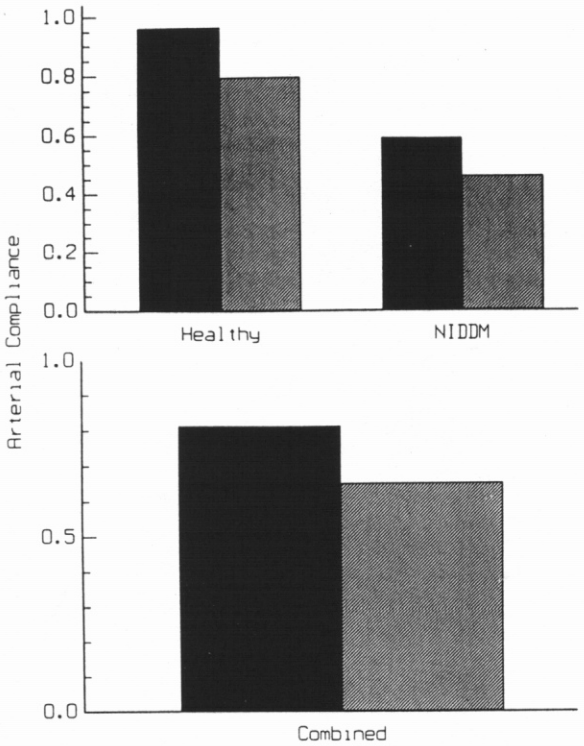
Food Intake and Biochemical Indices

Of the 31 group A subjects, 19 were fish eaters; and of the 22 group B subjects, 13 were fish eaters. There were no significant differences in total energy intake or macronutrient intake (protein, fat, carbohydrates, alcohol, fibre, and saturated, mono-unsaturated, and polyunsaturated fatty acid composition) or in biochemical indices (serum cholesterol, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, triglyceride, glucose, free fatty acid, insulin, and glycosylated haemoglobin) between fish eaters and non-fish eaters of either group A or group B subjects.

TABLE II—ARTERIAL INDICES OF FISH EATERS AND NON-FISH EATERS

Group	Arterial compliance	Proximal resistance	
		Common femoral artery	Posteror tibial artery
Healthy subjects			
Fish (n = 19)	0·96 (0·03)*	0·32 (0·02)	0·35 (0·01)*
Non-fish (n = 12)	0·79 (0·07)	0·40 (0·04)	0·44 (0·04)
NIDDM patients			
Fish (n = 13)	0·59 (0·03)*	0·44 (0·04)	0·51 (0·04)
Non-fish (n = 9)	0·46 (0·04)	0·49 (0·06)	0·54 (0·06)
Combined			
Fish (n = 32)	0·81 (0·04)*	0·37 (0·02)*	0·42 (0·02)
Non-fish (n = 21)	0·65 (0·06)	0·44 (0·03)	0·48 (0·03)

Values are means (SEM).
*$p < 0{\cdot}05$ for comparison of fish eaters with non-fish eaters.



Arterial compliance in fish-eaters (black) and in non-fish eaters (grey) in healthy people and NIDDM patients (top) and in the combined categories (bottom).

$p < 0{\cdot}05$ for comparison between fish-eaters and non-fish eaters in all categories.

Arterial Compliance (Table II, Figure)

Arterial compliance in non-fish eaters was significantly lower than that in fish eaters in group A ($p < 0{\cdot}025$), in group B ($p < 0{\cdot}05$), and in the two groups combined ($p < 0{\cdot}05$).

Proximal Resistance (Table II)

Common femoral artery.—When the two groups were considered, the mean proximal resistance at the common femoral artery in non-fish eaters was significantly higher than that in fish eaters ($p < 0{\cdot}05$). However, this increase was not significant for either group considered separately.

Posterior tibial artery.—Proximal resistance was higher in non-fish eaters than in fish eaters but only in group A subjects was this increase significant ($p < 0{\cdot}025$).

Discussion

The consumption of as little as one or two fish dishes per week may prevent coronary heart disease. Kromhout et al[1] reported that mortality from coronary heart disease among those who ate at least 30 g of fish per day was more than 50% lower than that among those who did not eat fish; moreover, populations with a diet rich in marine lipids may have a lower risk of atherosclerotic vascular disease.[9] Studies based on dietary history have suggested that even a small intake of fish may have reduced the incidence of coronary vascular