1004

INFLUENCE OF DIETARY FISH ON PLATELET FUNCTION AND THROMBOXANE FORMATION. A.C. v. Houwelingen (1), A. Hennissen (1), F. Verbeek-Schippers (2), T. Simonson (3), S. Fischer (4) and G. Hornstra (5). Department of Human Biology (1) and Department of Biochemistry (5), University of Limburg, Maastricht, The Netherlands, TNO-CIVO, Zeist, The Netherlands (2), University of Tromsø, Norway (3), University of Munich, FRG (4).

Many studies have been performed with respect to the effects of fish (products) on the possible prevention of ischemic cardiovascular disease in man. Most of the trials, however, were poorly designed without a proper control group, and their results are equivocal. We, therefore, performed a well-controlled intervention trial to investigate the effect of a reasonable amount of dietary fish on certain risk indicators of arterial thrombogenesis. In Tromsø, Maastricht and Zeist, healthy male volunteers were given a dietary supplement consisting of 135 g of canned mackerel (n=40) or meat paste (control, n=42) per day for a period of 6 weeks. Compliance was monitored on the basis of the urinary excretion of lithium, added to the supplements. Average compliance was about 80% and decreased slightly with time. Bleeding time was significantly prolonged and platelet number decreased in the mackerel group. Platelet aggregation in PRP induced by thrombin decreased only at a low dose. Collagen-induced platelet aggregation in PRP decreased significantly. This was associated with a 50% reduction of the collagen-induced TxB2 formation in PRP ($P < 0.001$). TxB3 synthesis increased significantly in the mackerel group from 0.9 to 7.8% of the TxB2 production (GC/MS). Collagen-induced platelet aggregation and ATP release in whole blood were measured with the Chrono-log whole blood lumi-aggregometer (Maastricht only). In the same samples TxB2 formtion was measured (RIA) and although a significant reduction was seen in the mackerel group, platelet functions were not significantly altered. However, platelet release (but not aggregration) was significantly related to the compliance and a decreasing effect of the mackerel supplement was observed in those 50% of the volunteers having the highest compliance. This demonstrates the necessity of monitoring compliance by objective means.

Acknowledgements: Financial support was obtained from the Dutch Heart Foundation. The International Association of Fish Meal Manufactures (Potters Bar, Herts, England) provided the mackerel.

1005

THE ANTITHROMBOTIC EFFECT OF PALM OIL IS CORRELATED WITH ITS CONTENTS OF VITAMIN E. G. Hornstra (1), A.H. Hennissen (2), R. Kalafusz (1) and D.T.S. Tan (3), Departments of Biochemistry (1) and Human Biology (2), Limburg University, Maastricht, the Netherlands, and Palm Oil Research Institute of Malaysia, Kuala Lumpur, Malaysia (3).

Dietary saturated fatty acids are known to increase platelet aggregation and arterial thrombogenesis. We recently demonstrated, however, that palm oil, rich in saturated palmitic acid, has a distinct antithrombotic affect, which is associated with a decrease of the thromboxane-prostacyclin ratio in activated whole blood. To identify the antithrombotic component(s) of palm oil, seven palm oil fractions were prepared with comparable fatty acid compositions of the triglycerides but containing various amounts of non-triglyceride material with different compositions. These fractions were fed to rats in amounts of 50 energy% for a period of 8 weeks, after which arterial thrombosis tendency was measured upon insertion of an aortic prosthesis, the aorta-loop. During loop insertion, 1 ml blood was collected in citrate for measuring platelet aggregation and ATP release in response to collagen, using the Chronolog whole blood lumi-aggregometer. Arterial thrombosis tendency was found to be negatively related to the total amount of non-triglyceride material in the various fractions ($r = 0.78$; $p < 0.05$). No significant relationship was observed between arterial thrombus formation and the various sterols, present in the non-triglyceride material. A significant negative correlation was found, however, with α-tocopherol ($r = 0.86$; $p < 0.02$). Collagen-induced platelet aggregation and ATP release in whole blood were not correlated to total amounts or α-tocopherol content of the non-triglyceride material. However, significant positive relationships were found between these platelet functions and the amounts of the various sterols (Campesterol: $r = 0.70$; $P < 0.10$. β-sitosterol : $r = 0.69$; $P < 0.10$. Cholesterol : $r = 0.81$; $P < 0.05$).

These findings demonstrate that effects of edible oils on platelet function and arterial thrombogenesis are not only mediated by the fatty acid compostion of the triglycerides, but can also be determined by 'minor components', present in the non-triglyceride part of the oils.

1006

DECREASE OF PLATELET AGGREGATION AFTER INTAKE OF SMALL AMOUNTS OF PURIFIED EICOSAPENTAENOIC ACID IN ELDERLY PEOPLE. POSSIBLE ROLE OF VITAMIN E. M.Croset, E.Vericel, M.Rigaud*, Ph.Coupron, M.Dechavanne and M.Lagarde. INSERM U.63, Roussel UCLAF, Lyon University and * Limoges University, France.

Platelet hyperactivity is believed to be involved in the thrombotic complications of elderly people. Since it has been proposed that eicosapentaenoic acid (EPA) can reduce platelet functions in normal humans, we have investigated its effect in elderly people. The daily intake (100 mg EPA) was at least 20 fold lower than usually tested. In a randomized, double blind study, eight people ingested EPA given as a pure triglyceride (1,3-didecanoyl,2-eicosapentaenoyl-glycerol) for 2 months and eight people ingested a placebo containing the same amount of vitamin E than in EPA preparation. Platelet aggregation, the oxygenated metabolism of arachidonic acid (AA), and vitamin E content of both plasma and platelets were investigated. Ingestion of EPA resulted in a slight but significant reduction of platelet-rich plasma aggregation in response to epinephrine and AA. The same decrease was observed with washed platelets when triggered by thrombin or collagen. EPA intake failed to affect the oxygenated metabolism of AA, measured by the formation of TXB2, HHT and 12-HETE from either exogenous or endogenous (thrombin stimulation) AA. Formation of AA oxygenated products including 6-keto-PGF1α in clotted blood was unaffected. Excretion of urinary TXB2, 6-keto-PGF1α and their 2,3-dinor metabolites was left unchanged by ingestion of EPA. Platelet, but not plasma α- and γ-tocopherols were significantly increased by EPA intake. We conclude that, in our experiment, the reduction of platelet aggregation could not be explained by modification of AA metabolism. Since vitamin E has been associated with a decrease of platelet aggregation, at least in vitamin E deficiency, and platelet vitamin E being reduced with age, we speculate that the decreased platelet aggregation after EPA intake might be related to the increased platelet tocopherols.

1007

CORNARY HEART DISEASE, DIET, SERUM LIPIDS, PLATELET FUNCTION AND PLATELET FATTY ACIDS IN TWO POPULATIONS WITH A HIGH AND A LOW INTAKE OF DIETARY FISH. T. Simonsen, Å. Vårtun, V. Lyngmo and A. Nordøy. Dept. of Medicine, University Hospital, Tromsø, Norway.

In the coastal areas of Northern Norway the intake of fish is by tradition high whereas in the inland area it is low. We have examined the mortality of CHD in the period 1975-84 in a coastal community (C) and an inland community (I). In addition we have examined 30 healthy male subjects aged 30-60 year, selected by random in the two communities. The examination included a dietary survey based on registration and weighing of all dietary items for one week, blood pressure, serum lipids, primary bleeding time, platelet aggregation induced by collagen and fatty acid composition of platelet total phospholipids.

The age-adjusted mortality of CHD was significantly higher for age groups 30-70 year in C whereas the opposite was found above 70 years of age. The mean intake of fish per day was 132 g (0.9 g eicosapentaenoic acid-EPA) in C and 53 g (0.25 g EPA) in I. Serum triglycerides was higher in C ($p<0.05$) whereas total cholesterol was similar. The primary bleeding time was not different in the two areas. Significantly lower concentrations of collagen was needed to induce 30 and 60% aggregation in platelet rich plasma in C than in I. No significant differences in the content of eicosapentaenoic acid (EPA) was observed in platelet total phospholipid fatty acids. This study has not confirmed that a high intake of fish as a single dietary variant, is associated with a low mortality of CHD. The lack of changes in plasma lipids, platelet fatty acid composition between representative groups from the two populations indicate that other factors mask the possible beneficial effects of a high fish diet. Furthermore, the daily intake of large amounts of lean fish give only a very moderate increase in dietary intake of EPA.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.