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Prevention of coronary heart disease by nutritional interventions. impact of nutritional education in groups and supplementation with alpha-linolenic acid.

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Summary

Cardiovascular diseases accounted for 35% of total mortality in The Netherlands in 1999. Coronary heart disease (CHD) is a subgroup of cardiovascular diseases, and atherosclerosis is the disorder underlying CHD. Modifiable biological and lifestyle factors that increase the risk of CHD are, among others, raised serum total cholesterol concentration, hypertension, smoking, and being overweight. For preventing CHD, the risk factors have to be beneficially modified by interventions in order to decrease future prevalence of CHD. Behaviours that increase the risk of developing CHD are a lack of physical activity and an unhealthy diet.

This thesis presents the results of the so-called MARGARIN project, an acronym of 'Mediterranean Alpha-linolenic en Riched Groningen dietARY INtervention project'. The study investigated the impact on CHD risk factors of two specific preventive strategies:

- 1) Nutritional group education taught by a dietician (intervention) as compared to a posted leaflet summarizing the standard Dutch nutritional guidelines (control) (3 years).

The nutritional group education was based on an (adapted) Mediterranean type of diet. Specifically, the guidelines advised the daily consumption of 5-7 slices of bread, 200-400 grams of vegetables, 2 pieces of fruit, 0-2 alcoholic beverages (only for regular consumers), 2-3 lean dairy products, fish at dinner twice per week, less red meat and more poultry, less fat cheese and eggs.

- 2) Providing margarine enriched with alpha-linolenic acid (ALA) as compared to a linoleic acid (LA) rich margarine (2 years; double blind). Both margarines contained an equally high amount of polyunsaturated fat (55%).

The dietary intake of ALA was on average 5.9 grams/day (2.3% of energy intake) among users of the ALA margarine, and 1.0 grams/day (0.4% of energy intake) among users of the LA margarine. The intake of LA was comparable between the users of the two types of margarines, i.e. around 10 % of energy intake.

The study population consisted of 282 men and women with moderate hypercholesterolaemia (6-8 mmol/l), and at least two of the aforementioned CHD risk factors (including a family history of early onset of CHD). The

baseline values were collected in November of 1997, and follow-up investigations were organised after 16, 52, 104, and 156 weeks.

—Chapter 1, the introduction, provides an overview of literature regarding the epidemiology of cardiovascular diseases, the role of nutrition in prevention, and the standard preventive primary care. The scientific background of the MARGARIN study is discussed, and an outline of the thesis is presented.

—Chapter 2 describes the methodology of the MARGARIN study and the several materials used.

—Chapter 3 describes the effects of the nutritional group education after 1 year. The nutritional education intervention (neI) group (n=103) decreased dietary intake of (saturated) fat, and increased their intake of fish, fruit, poultry, and bread more than the posted leaflet group (nutritional education control (neC) group) (n=163). Serum total cholesterol was 0.06 mmol/l lower (NS), and diastolic blood pressure was 3.5 mm Hg lower ($p<0.05$) in the neI group than in the neC group (chapter 9). After 16 weeks, body weight tended to decrease in the neI group, but after 1 year both the neI and neC groups had gained an equal amount of weight (+1%).

Because body weight increased in the neI group after 1 year, an educational meeting was organised during the second year that focused on weight control.

—Chapter 4 investigates the effects of this one time meeting, and describes psychological determinants of two behaviours relevant to weight loss. Predictive factors for the intention to dietary slimming behaviour were the attitude, subjective norm, and prior behaviour ($R^2=21\%$). Predictive factors for the intention to increase physical activity were prior behaviour, attitude, self-efficacy expectations (=perceived ability to execute the behaviour), and outcome efficacy ($R^2=34\%$). The one time educational meeting did not lead to a decrease in body weight.

—Chapter 5 describes, with respect to the second intervention of the MARGARIN study, baseline associations between intake of alpha-linolenic acid (ALA) and CHD risk factors. The content of ALA in the cholesteryl ester was positively associated with serum triglycerides ($r=0.13; p<0.05$), and

inversely with diastolic blood pressure ($r=-0.13$; $p<0.05$), when adjusted for confounding variables.

—*Chapter 6* investigates the effects of increased ALA intake on the carotid and femoral intima-media thickness (as indicative for progression of atherosclerosis), and on C-reactive protein (CRP), which is a marker for inflammation. After 2 years, the CRP level was lower among ALA users than among LA users (net difference -2.1 mg/dL; 95% CI $-4.3, 0$). The progression rate of carotid (ALA and LA: $+0.05$ mm) and femoral intima-media thickening (ALA: $+0.05$ mm; LA: $+0.04$ mm) was similar. Hence, ALA supplementation did not affect the intima-media thickness, despite a possible anti-inflammatory impact, when investigated against a background diet rich in LA.

—*Chapter 7* investigates predictive factors of intima-media thickening after 2 years. A decreased saturated fat intake was associated with less progression in intima-media thickness. Furthermore, decreased saturated fat intake was also associated with a lower level of soluble intercellular adhesion molecule-1 (sICAM-1) after 2 years. Among persons who reduced saturated fat intake the most (lowest quintile) the carotid IMT changed with $+0.03$ mm (SEM 0.03) and the femoral IMT with -0.09 mm (SEM 0.07). Among persons who increased saturated fat intake the most (top quintile) these changes were $+0.10$ mm (SEM 0.03) and $+0.17$ mm (SEM 0.07), respectively (p linear trend 0.07 (carotis), 0.02 (femorals)). The changes in sICAM-1 were -19.0 ng/mL (SEM 5.6) in the lowest quintile, versus $+8.6$ ng/mL (SEM 5.3) in the top quintile (p linear trend <0.001), when adjusted for confounding variables. These data suggest that persons at high cardiac risk should reduce their saturated fat intake. This may decrease progression of intima-media thickening, possibly by affecting the expression of sICAM-1.

—*Chapter 8* shows that after 2 years the neI group had a significantly lower intake of total and saturated fat intake and an increased fish intake, relative to the neC group. No significant differences in CHD risk factors existed between neI and neC groups. Regarding the second intervention, users of the ALA margarine ($n=96$) had a higher ratio of total/HDL cholesterol ($+0.34$; 95% CI 0.12, 0.56), a lower HDL cholesterol (-0.05 mmol/l; 95% CI $-0.10, 0$), higher serum triglycerides ($+0.24$ mmol/l; 95% CI 0.02, 0.46), and lower plasma fibrinogen (-0.18 g/l; 95% CI $-0.31, -0.04$; after 1 year) level than users of the LA margarine ($n=141$).

—Chapter 9 describes the results of the nutritional group education after 3 years. The neI group had a lower intake of total and saturated fat than the neC group (net differences -2.0 and -1.2 % of energy; $p < 0.05$), and a higher intake of fish (+11 g/d; $p < 0.01$). These beneficial dietary changes did not result in a more favourable cardiovascular risk profile, although serum total cholesterol level tended to decrease the most in neI women who attended at least two educational meetings (-7%; $n = 55$). After 3 years, the levels of serum total and LDL cholesterol decreased 4% and 7%, respectively, in the total study population. The calculated risk of developing CHD within 10 years, according to the Framingham function, decreased by 0.4 events/100.

—Chapter 10, the general discussion, discusses the results of the two preventive strategies and the role of nutritional education in standard health care for persons at high cardiac risk. The main conclusions regarding the effects of the two interventions are:

1) Nutritional group education established longterm dietary changes when compared to a posted leaflet (for 3 years). The additional effects on established CHD risk factors were moderate. Nevertheless, it is expected that the lower (saturated) fat intake and higher regular intake of (fatty) fish will eventually decrease CHD incidence, since the cardioprotective mechanisms of fish are not primarily mediated by an impact on established risk factors. The MARGARIN study population had a low mean educational level. This offers opportunities for lifestyle counseling in a broader context in groups with a low socioeconomic status.

2) The serum lipid profile was adversely affected among users of the ALA margarine. However, the adverse effects of ALA supplementation on the serum lipid profile (HDL cholesterol and triglycerides) may be counteracted by an anti-inflammatory impact, as suggested by the positive results regarding CRP and plasma fibrinogen. Hence, there is no contra-indication for using an ALA-rich margarine in prevention of CHD, although the present data do not strongly suggest the need to increase ALA intake for the purposes of primary prevention of CHD.