Effect of Fish Oil Concentrate on the Lipoprotein Profile in Patients Suffering from Diabetes mellitus Type II

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Unfavourable changes of the lipoprotein metabolism are reported in patients suffering from diabetes mellitus type II, which are partly responsible for the increased atherogenic risk in these patients [1, 6]. The endogenous synthesis of the very-low-density (VLDL)-triglycerides [13] and of the apolipoprotein B (apo B) [4] is increased and results in a pathological serum level of triglycerides. Low-density-lipoprotein (LDL)-apo B is also raised and linked with an unfavourable LDL-composition [5]. The overproduction of VLDL and LDL-apo B leads to premature coronary artery disease even in patients without hyperlipemia [6].

n-3 fatty acid rich fish oil diet results in a striking decrease of the triglyceride level in normolipemic and hypertriglyceridemic nondiabetics. This effect is probably reached by inhibition of the VLDL-triglyceride- and apo B-synthesis [3, 10]. In the case of a high dosage of fish oil, the LDL-apo B-turnover is reduced and the apo B-concentration in serum can also be reduced [8].

Beside the positive effects on the lipoprotein metabolism, n-3 fatty acid rich fish oil diet influences further atherogenic risk factors favourably. The eicosanoid balance is shifted towards the antiatherogenic and vasodilatoric side [3]. A reduction of the thrombocyte aggregation rate, a decrease of the blood pressure and an improvement of the blood or plasma viscosity are associated with it [3].

As diabetes mellitus type II is associated with increased serum levels of VLDL-triglycerides and VLDL-apo B, the intake of fish oil could be useful in lowering circulating VLDL in patients with diabetes mellitus type II. Therefore we studied the effect of n-3 fatty acid rich diet during 12 weeks of treatment in diabetics of type II who until now have not been treated by drugs but only by diet.

Patients and Methods

The study included 19 male patients suffering from diabetes mellitus type II (NIDDM) (age 47.8±9.4 years). The metabolic disorder had been known for about 4.1 years. All patients were treated by diet only and by medical advice. The metabolism was regularly controlled.

The investigations were carried out as an open study starting with a placebo-run-in-period for four weeks (phase I) (6 g rape seed oil capsules/d), fol-
lowing a twelve week verum period (phase II) (6 g fish oil concentrate capsules/d, FOURNIER PHARNMA GmbH), and concluding with a wash-out-period of four weeks (phase III) (6 g rape seed oil capsules/d).

The lipids, apolipoproteins, glucose, glucose tolerance, and insulin were checked at the beginning and at the end of each phase. The blood glucose was investigated in capillary blood by means of glucose sensitive electrode. The plasma insulin level (IRI) was determined by radioimmunological assay (Isocomerz), the apolipoproteins (apo) A-I and B by immunoturbidimetric test kit (SIFIN Berlin), and the enzyme activities (ALAT, GGT) by kinetic test kit combination (Boehringer). HDL-cholesterol and its subfractions as also LDL-cholesterol were quantified by precipitation techniques (Quantolip® A and B, Quantolip®-LDL, IMMUNO AG).

The patients were instructed to continue their life style recommended by their doctors. The patients practised their professions during the study. The body weight was constant during all test phases.

The statistical calculation was done by significance tests with the t-test by Student, after checking the variation with the F-test or the examination of normal distribution.

**Results**

The cholesterol level was relatively constant during all test phases. LDL-cholesterol increased during the verum phase by about 10%, but only the difference at the start was significant. In the wash-out-phase, LDL-cholesterol returned to the start level. Apo B increased slightly by about 5%. Only the difference at the beginning was statistically significant. During the wash-out period, apo B remained on the same level as before (Table 1).

HDL-cholesterol increased significantly by about 9%, especially HDL2-cholesterol. During the wash-out-period, HDL cholesterol showed no further change.

The fish oil treatment markedly lowered apo A-I by about 9%. During the wash-out-phase, apo A-I remained at the same low level.

Fish oil also caused a distinct fall in triglyceride concentration in serum by 29% followed by a strong increase during the wash-out-phase. The fasting blood glucose and the glucose tolerance test as well as the insulin level (fasting and after load test) did not change significantly at the end of the verum phase in comparison to the run-in-period.

**Discussion**

Our results support the hypothesis that fish oil inhibits the VLDL-and triglyceride-synthesis in the liver. The data profile is similar to that in normolipemics and hyperlipidemic patients after fish oil diet [3, 8–10]. The decrease in