

Summary

1 Statin therapy in patients with peripheral artery obstructive disease (PAOD)

1.1 Patients with lipid metabolism disorders

Simvastatin therapy with the dose titration adjusted to the effect led to the prolongation of claudication interval and to the elevation of ankle-brachial pressure index, which was statistically significant at the interval of 18 months after starting the therapy. At the same time we observed normalization of lipid levels and the lowest levels of oxidative stress markers. Statin use was also associated with lowering homocysteine level.

1.2 Patients without lipid metabolism disorders – the influence on laboratory parameters and functional capacity

In patients without lipid metabolism disorder, treated with simvastatin 20 mg daily, we noted an improvement, i.e. prolongation of claudication interval and elevation of ankle-brachial pressure index, while in the control group treated only with a diet we observed further deterioration of capacity. In the control group, the parameters of lipid metabolism were statistically significantly worse after six months and this trend remained even in further control visits with HDL cholesterol slightly lowering. In the simvastatin group, a statistically significant decrease of LDL occurred during several months as well as elevation of HDL cholesterol within normal range.

2 Pentoxifyllin therapy in patients with PAOD

Farmacodynamic and therapeutic effects of pentoxifyllin.

2.1 Oral and intravenous application of an individual dose.

After an oral application the mean fibrinogen level decreased ($p < 0.05$) and the activity of superoxidismutase ($p < 0.05$) as well as total antioxidant capacity increased. Similar results were obtained subsequently to intravenous pentoxifyllin therapy after 14 days of wash-out period. Pentoxifyllin probably keeps its efficacy even in the case of long term oral use.

2.2 Claudication interval before and after infusion therapy (lasting 8 days)

8 days of infusion therapy with pentoxifyllin together with intensive physical training in patients admitted for worsened symptoms of PAOD led to statistically significant prolongation of claudication interval ($p < 0.01$) and to the increase of ankle-brachial pressure index ($p < 0.001$).

3 Folate therapy in patients with PAOD

3.1 The prevalence of hyperhomocysteinaemia in patients with PAOD.

We found no association of lipid metabolism parameters and fibrinogen with homocysteine level. 64% of patients with PAOD had mild hyperhomocysteinaemia.

3.2 Methionine loading test.

6 hours after L- methionin ingestion the level of homocysteine raised approximately 2.5 fold, at the same time we observed a significant elevation of malondialdehyde ($p < 0.01$) as well as a nonsignificant shift of other markers towards prooxidant state.

3.3 Comparison of the effect of folic acid in PAOD patients and in a group of healthy seniors

Atherosclerotic disease of leg vessels was associated with higher homocysteine level. The level was lowered by folic acid use with simultaneous modification of procoagulant and prooxidant state in patients with PAOD as well as in healthy seniors with hyperhomocysteinaemia.

The dose of folic acid did not play a significant role in the effect; the modification of the parameters was comparable after higher and lower dose. In the followed groups, we found T/T mutation in MTHFR gene in 5 patients. These persons had the highest initial level of homocysteine. The initial level of fibrinogen showed statistically significant association with a genotype, with the highest value in T/T genotype.

4 Asymetric dimethylarginine (ADMA)

4.1 ADMA and conventional risk factors in a population sample MONICA

In the studied population we found higher lipid levels, the mean level of homocysteine was in normal range as well as ADMA. ADMA seems to be a parameter independent of conventional atherosclerotic risk factors. The level of ADMA increased significantly only with age.

4.2 ADMA in patients with premature coronary artery disease (CAD) and in a control group aged 45-55 years

In patients with CAD we found satisfactory values of blood pressure as well as in healthy persons, 90% of the CAD patients used antihypertensive therapy. Lipid parameters in CAD patients were above normal, 70% patients used hypolipidemic therapy. However, 20% of CAD patients did not quit smoking. In CAD patients we found statistically higher level of homocysteine, still in the normal range. The level of ADMA did not differ between these groups.