


Lipid-lowering with statins and fibrinolytic parameters

The interrelationship between lipoproteins and the fibrinolytic system is increasingly under scrutiny and it becomes apparent that it is not only the triglyceride-rich lipoproteins that can influence fibrinolysis, but that the apolipoprotein-B-containing very-low-density lipoproteins (VLDL), low-density lipoproteins (LDL) and possibly also intermediate-density lipoproteins (IDL) can all modulate endothelial synthesis and release of fibrinolytic enzymes. These enzymes are generally thought to be markers for an increased risk of myocardial infarction, but their role in the pathogenesis of atherosclerosis is not clarified yet. A better understanding of the relationship between lipoproteins and fibrinolysis may help to gain insight in the formation and evolution of the atherosclerotic plaque.

In the February issue Mitropoulos et al.[1] reported the results of a substudy of the Oxford Cholesterol Study which sought to elucidate the effect of simvastatin on haemostatic and fibrinolytic variables. A significantly lower LDL-, VLDL- and IDL-cholesterol concentration and a significantly higher plasminogen-activator-inhibitor (PAI)-1 activity was found in the patients assigned to simvastatin compared to the patients taking placebo, while other haemostatic parameters were not significantly different.

These results do not contradict the results of previously published studies with lovastatin (a compound related to simvastatin), since the authors of the cited study[2] determined PAI-1 concentration and not activity, two parameters that are not necessarily equivalent. Moreover, in a recently published paper[3], Bevilacqua et al. reported a significant decrease in LDL cholesterol accompanied by a significant increase of PAI-1 concentration and activity and by a significant decrease in tissue-type plasminogen activator (t-PA) in 24 patients with coronary artery disease treated with fluvastatin, another hydroxy-methylglutaryl-coenzyme (HMGCoA) reductase inhibitor. Interestingly, the increase in PAI-1 concentration and activity was also observed in the placebo group, while the decrease in t-PA was not.

In a study assessing the relationships between lipid metabolism and fibrinolytic parameters[4], significant correlations between apolipoprotein B and t-PA antigen as well as PAI-1 activity were found in 191 patients with hyperlipidaemia. Finally, Welty et al.[5] analysed the correlation between LDL-cholesterol and fibrinolytic parameters in 1878 members of the Framingham offspring population. Their data show a significant increase in the levels of t-PA and PAI-1 antigen with increasing LDL-cholesterol concentrations. This relationship was not altered by adjustment for several risk factors associated with coronary atherosclerosis.

The results of these studies indicate that there is an association between the LDL-cholesterol concentration and concentrations of the fibrinolytic enzymes, especially t-PA (which was not determined by Mitropoulos et al.). The somehow conflicting results concerning PAI-1 concentration and activity might be explained by its great variability and by the multitude of factors (such as time of day, activity, body mass index etc.) which influence its level in plasma.

Several large trials have shown that treatment with HMGCoA reductase inhibitors can dramatically reduce the incidence of myocardial infarction and the number of revascularization procedures in patients with hypercholesterolaemia and in patients with a history of coronary artery disease or myocardial infarction. This is thought to be due to the plaque stabilization and the improvement of endothelial dysfunction which accompanies the massive reduction in LDL-cholesterol brought about by these agents. Evidence is accumulating that the LDL-cholesterol reduction also exerts a favourable influence on fibrinolysis which may also contribute to the observed clinical benefits.

I. S. JOVIN
K. HEIDINGER
U. TABORSKI
G. MULLER-BERGAUS

Max-Planck Institut für physiologische und klinische Forschung
Bad Nauheim, Germany

References


