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Letter to the Editor

Short-term effects of atorvastatin on hemorheologic parameters and endothelial dysfunction in patients with hypercholesterolemia. Lower is better?

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We have read with interest the paper published recently by Uyuklu et al. in *Clinical Hemorheology and Microcirculation* [5]. It provides important experimental information on the effect of high dose atorvastatin on erythrocyte mechanical properties.

Numerous randomized trials confirmed the benefit of cholesterol-lowering therapy in patients with atherosclerotic cardiovascular diseases (ASCVD). In high-risk persons, the recommended LDL-C goal now is $<$100 mg/dl, but a question raised by HPS and PROVE IT studies is whether this goal is sufficiently low in very high-risk patients who already have relatively low LDL cholesterol at baseline. In HPS the subgroup whose LDL-C levels at baseline were $<$100 mg/dl exhibited significant risk reduction when statin therapy was introduced [3]. In PROVE IT, intensive LDL-C-lowering therapy with high dose atorvastatin reduced major cardiovascular events as compared with standard-dose pravastatin [1]. Based on the available clinical trial evidence, an LDL-C goal of $<$70 mg/dl is a reasonable clinical strategy when risk is very high [2].

Since cholesterol is one of the basic elements of the cell membranes, Uyuklu et al. addressed the question, whether lowering of cholesterol beyond a certain level – with supra-pharmacological dose of atorvastatin – may cause significant alterations in red blood cell (RBC) deformability. In their study they found no adverse rheological change, despite significant structural and functional alterations of the RBC membrane.

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In our previous study we investigated the effect of atorvastatin therapy on several hemorheological parameters, platelet aggregation and von Willebrand factor activity (vWf) (as a marker of endothelium dysfunction) in patients with hyperlipidemia and chronic cerebrovascular diseases [4]. 27 patients (mean age: 51 $\pm$ 8 years) were included and treated with low dose (10 mg/day) atorvastatin for 3 months. Besides routine laboratory parameters, hemorheological measurements (plasma fibrinogen, plasma and whole blood viscosity, RBC aggregation and filterability), collagen induced platelet aggregation and vWf activity were determined at baseline and after 3 months of treatment.

Cholesterol, LDL-cholesterol and triglyceride levels were lowered significantly ($p < 0.001$ for cholesterol and LDL-cholesterol, $p < 0.01$ for triglyceride), while HDL-cholesterol level did not change. Whole blood viscosity ($p < 0.05$) and RBC deformability ($p < 0.05$) showed a significant improvement after the three-month treatment. Collagen induced platelet aggregation also decreased significantly ($p < 0.001$) in spite of unaltered antiplatelet therapy. vWf activity provided a significant ($p < 0.05$) reduction compared to that of the baseline values. Both plasma fibrinogen and CRP showed a decreasing tendency.

Our findings indicate that besides lipid and inflammation marker reduction low dose atorvastatin improves also hemorheological parameters, another group of risk factors of cardiovascular diseases. The reduction in vWf activity implies that this drug can improve endothelium dysfunction and decrease high shear induced platelet aggregation. The possible direct antiplatelet property of atorvastatin and the decrease of high shear induced platelet aggregation may contribute to the effectiveness in the prevention of cardio- and cerebrovascular events.

Limited data exist about the rheological effects of aggressive lipid lowering therapy. Based on clinical trial evidences and our previous findings with low dose atorvastatin therapy, in our ongoing study we addressed the question, whether high dose statin therapy also exerts beneficial effect on the rheological properties, including RBC deformability, in patients with ASCVD.

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