Dear Sir,

It is still unclear whether antihypertensive therapy causes regression of arterial and arteriolar structural changes induced by essential hypertension and whether these effects are influenced by the type of drug treatment or by blood pressure decrement itself. Many reports suggest that hypertensive patients show clear endothelial dysfunction, an initial step of atherosclerosis, since the endothelium is involved in permeability, fibrinolysis, haemostasis and blood pressure control. The degree of endothelial damage can be detected by measuring microalbuminuria [1, 2] and circulating von Willebrand Factor (vWF), a glycoprotein released in greater concentration when endothelial cells are damaged [3]. This finding shows the essential role of vWF in the development of occlusive thrombosis. In addition, patients with cerebrovascular disease had increased vWF, and clinical trials stressed its importance as a risk factor for myocardial infarction and cardiovascular disease in hypertensive subjects [4]. When the damaged subendothelial matrix, which contains a large amount of vWF multimers, is exposed to flowing blood, platelets initially adhere through the interaction between vWF and platelet surface glycoprotein GPIb (receptor for vWF) and subsequently between vWF and glycoprotein GPIIb/IIIa (receptor for fibrinogen). In the prevention of atherosclerotic disease, the interaction of platelets and vWF is a logical target and such an approach has recently been introduced by blocking platelet glycoprotein GPIIb/IIIa with a monoclonal antibody [5]. This treatment showed a clinically meaningful reduction of restenosis after coronary angioplasty. Recent reports demonstrated the importance of glycoproteins GPIb and GPIIb/IIIa in the haemostatic balance and thrombotic phenomena, and their expression (reduced or increased) has been well correlated with clinical events in uraemic thrombocytopenia [6, 7], in erythropoietin-
induced hypertension and thrombosis [8,9] and in PUFA (ω-3 fish oil)-induced anti-aggregation [10]. A further contribution was given by the EPIC study [11], in which prevention of ischaemic complications in high-risk angioplasty by the monoclonal antibody c7E3 Fab against platelet GPIIb/IIIa receptor was clearly demonstrated. The aim of this study was to investigate whether hypertension itself and antihypertensive therapy could have an impact on the expression of platelet surface glycoproteins with clinical implications on atherosclerotic and thrombotic events in essential hypertension. Forty hypertensive patients treated with different drugs (10 with the β-blocker atenolol, 10 with the ACE inhibitor lisinopril, 10 with the Ca2+ antagonist amlodipine, 10 with the α-blocker doxazosin) were studied. Platelet surface glycoproteins GPIb (receptor for vWF) and GPIIb/IIIa (receptor for fibrinogen) were investigated with monoclonal antibodies CD42 and CD41 (Bryte, Italy) and a Bryte flowcytometer (Biorad, Italy) in the 40 hypertensive patients and in 10 healthy normotensive controls. Mean values of GPIb (mean flow ± SD) were: controls = 87.43 ± 6.09; patients treated with atenolol = 78.8 ± 15.34 (p < 0.05); lisinopril = 81.26 ± 16.1 (p = NS); amlodipine = 80.26 ± 9.30 (p < 0.05); doxazosin = 76.77 ± 4.48 (p < 0.025). Mean values of GPIIb/IIIa (mean flow ± SD) were: controls = 80.42 ± 5.07; patients treated with atenolol = 74.41 ± 17.49 (p = NS); lisinopril = 78.52 ± 13.91 (p = NS); amlodipine = 78.56 ± 9.26 (p = NS); doxazosin = 74.71 ± 4.71 (p < 0.05).

Many reports showed inhibition of platelet adhesion and aggregation by antihypertensive drugs like ACE inhibitors and calcium antagonists [12-14], but very few reports demonstrated a direct impact of therapy on platelet-endothelium interactions, a crucial step in atherosclerotic disease. Clinical and epidemiological studies suggest a favourable impact of new antihypertensive drugs on the progression of atherothrombotic hypertension (decrease in adverse events, reduction of carotid plaques studied by echo Doppler imaging) with a possible direct effect on the endothelium [15-17]. Our data support such a hypothesis, suggesting an ulterior mechanism of vascular protection by antihypertensive drugs: the reduction of expression of platelet surface receptors GPIb for vWF and GPIIb/IIIa for fibrinogen.

References


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