Vascular Endothelial Growth Factor in Plasma of Patients Undergoing Peripheral Angioplasty

Dear Sir,

Vascular endothelial growth factor (VEGF) is known to be upregulated in ischemic tissue and was demonstrated in the cytoplasm of vascular smooth muscle cells and cardiac myocytes (1). It is believed that VEGF production is an early adaptation of tissue to hypoxia, enhancing collateral blood vessel formation. Using VEGF DNA transfer this concept has been validated in animal experiments (2) and clinical investigations are under way (3). After percutaneous transluminal angioplasty (PTA) VEGF is believed to stimulate re-endothelialisation and thus plays a role in the control of restenosis (4). VEGF can not only be demonstrated locally in tissue but also systemically in plasma after the occurrence of ischemic events (5, 6). The probable source of plasmatic VEGF are platelets. No data are available on VEGF plasma levels in patients with peripheral arterial disease (PAD) in response to PTA and their impact on late clinical outcome.

We investigated VEGF levels in plasma of 30 patients (mean age 68 years; range, 54 to 86 years) with peripheral arterial disease (PAD) undergoing PTA of a single stenosis of the femoral or popliteal artery. All patients were pre-treated with aspirin, periinterventional thromboprophylaxis was either performed with unfractioned heparin (intravenously, aPTT adjusted for 48 h, n = 16) or low molecular weight heparin (subcutaneously 5000 IU b.i.d. for 48 h, n = 14). Aspirin treatment was resumed 48 h after intervention up to 6 months after PTA. Clinical success of angioplasty was documented by Colour Duplex Sonography performed before, 48 h and 6 months after PTA. Restenosis was defined as more than 50% luminal narrowing 6 months after successful angioplasty. Plasma samples were drawn before, 6, 24 and 48 h after PTA. Total plasma VEGF was determined using a commercially available immunoassay (R&D-Systems, Minneapolis, USA).

VEGF levels showed a large degree of variability. Higher levels were demonstrated in patients with advanced stage of PAD (Fig. 1; Fontain II: 53; range 0-361 pg/ml vs. Fontain IV: 157.5; range 36-247 pg/ml, p = 0.01) and diabetes mellitus (Fig. 2; diabetic patients: 148; non-diabetic patients: 100; p = 0.001).

Fig. 1. VEGF plasma levels before and after PTA in patients with PAD stage Fontain II (closed circles) and patients with critical limb ischemia (open triangles)

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range 23-247 pg/ml vs. non-diabetic patients: 51; range 0-361 pg/ml, p = 0.01). In comparison, an age matched control group had VEGF levels of 25; range 7-71 pg/ml. VEGF plasma levels did not change during the procedure of angioplasty within 48 h (median values for all patients: before PTA 67.5 pg/ml, after 6 h 63.5 pg/ml, after 24 h 80 pg/ml, after 48 h 73.5 pg/ml). Six months after PTA 33% (10/30) of the patients developed restenosis. VEGF plasma levels were similar in the groups of patients with or without restenosis (median before PTA 101.5 vs. 67.5 pg/ml; after 6 h 66.5 vs. 80 pg/ml; after 24 h 72 vs. 80 pg/ml; after 48 h 53.5 vs. 74 pg/ml). Throughout all timepoints patients with advanced stage of PAD (p = 0.06, Fig. 1) and diabetes (p = 0.03, Fig. 2) had increased VEGF levels.

As has been published previously, our results indicate that increased plasma VEGF levels can be demonstrated in most patients with PAD. VEGF levels were significantly higher in patients with advanced stage of disease and diabetes. The procedure of PTA had no impact on plasmatic VEGF levels, within 48 hours. VEGF plasma levels had no relation to eventual clinical outcome, restenosis versus patency.

Though it is very probable that VEGF plays an important role in re-endothelialization control of restenosis in loco (3, 4) plasmatic VEGF levels cannot be used to identify patients at risk for restenosis. They are a marker for hypoxia and metabolic disturbance and might reflect the endeavour of the organism to promote blood vessel growth into chronic ischemic tissue.

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References

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Fig. 2 VEGF plasma levels before and after PTA in patients with diabetes mellitus (open circles) and non-diabetic patients (closed triangles)

Dear Sir,

The FV Leiden mutation (FVL) and the 20210A mutation of prothrombin are known in Caucasians as risk factors for venous thrombosis. Recently new polymorphic markers of FV gene were described (1). A specific factor V gene haplotype (HR2) was defined by five restriction polymorphisms in exon 13 and a sequence variation of exon 16. The exon 13 markers included the Rsa I polymorphic site, the rare allele of which (R2) has been found to be associated with partial FV deficiency in the Italian population (2). Bernardi et al. (1) demonstrated, that the FV gene marked by the HR2 haplotype, is both able to contribute by itself to determine a mild APC resistance phenotype and to interact synergically with FVL to produce a severe APC resistance phenotype.

In this study we determined the prevalence of FVL and FVHR2 in two tribes of Indians: Chorotegas from Western Costa Rica and Bribri

High Prevalence of FVHR2 Polymorphism in Costarician Indians who Have no FVL

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