Vascular endothelial growth factor (VEGF) plasma concentrations in coronary artery disease

H F Alber, M Frick, J Dulak, J Dörler, R-H Zwick, W Dichtl, O Pachinger, F Weidinger

RESULTS

There was no difference in VEGF concentrations in patients without CAD (score 0) compared to those with CAD (score 1–3), when analysed in regard to the severity score (fig 1A). High density lipoprotein (HDL) cholesterol was lower, and triglycerides were higher in patients with triple vessel disease compared to patients with smooth coronaries (ANOVA, p < 0.03, post hoc p < 0.05) and both variables correlated with the severity score (r = −0.23, p = 0.008; r = 0.25, p < 0.05, respectively). Other laboratory parameters and risk factors were not different. As the severity and the modified Gensini score were correlated (r = 0.89, p < 0.001), the above mentioned results did not substantially change when VEGF was related to the latter. The adjustment to leucocyte and thrombocyte counts, which correlated weakly with VEGF (r = 0.17, p < 0.03 and r = 0.36, p < 0.001), did not change the results.

As statin treatment decreases VEGF, patients were divided into two groups according to prior statin use. Statin treated patients had lower VEGF (24.1 (20.2) v 46.2 (54.6) pg/ml; p < 0.05) (fig 1B) and lower low density lipoprotein (LDL) cholesterol (125.6 (40.0) v 144.7 (39.5) mg/dl; p < 0.02) concentrations than patients without statin treatment. There were more diabetic, hypertensive, and smoking patients in the untreated group.

Among 42 randomly selected patients, eight were undergoing statin treatment. The plasma from these patients induced the formation of 6.3 (3.1) tubes and the plasma from untreated patients stimulated 9.1 (4.9) tubes in the matrigel assay (p = 0.12) (fig 1C).

DISCUSSION

This study shows that VEGF plasma concentrations do not correlate with the severity and extent of CAD. Statin treated patients have lower VEGF concentrations compared to untreated patients.

Although VEGF has been considered for angiogenic gene therapy in patients with CAD, data on circulating and tissue VEGF concentrations in patients with documented CAD are scarce. In our data VEGF appears to be similar in CAD patients and patients without diseased coronaries. In fact, VEGF has recently been implicated to promote atherosclerosis by inducing plaque neovascularisation.

To our knowledge, this is the first study comparing VEGF concentrations with angiographically documented CAD in a large patient population. In accordance with our data, Fleisch and colleagues observed no substantial differences in VEGF in patients with various extents of CAD. In contrast, increased VEGF concentrations in CAD patients were reported by Blann and colleagues. This discrepancy is probably because of different patient populations. Firstly, CAD patients in the latter study had higher cholesterol concentrations.

Abbreviations: CAD, coronary artery disease; HUVEC, human umbilical vein endothelial cells; VEGF, vascular endothelial growth factor.
concentrations compared to controls. Cholesterol may stimulate VEGF production and hyperlipidaemic patients have higher VEGF concentrations compared to healthy subjects.5

Secondly, patients with recent acute myocardial infarction were excluded from our study, but were selectively included in the study by Blann and colleagues. Elevated VEGF concentrations were reported after acute myocardial infarction. Thirdly, our controls were referred for coronary angiography because of chest pain, whereas controls in the study by Blann and colleagues 3 consisted of healthy volunteers.

We confirmed our previous results5 demonstrating a VEGF lowering effect of statins in this larger patient population. Although there was no significant influence on tube formation in a matrigel assay, the observed inhibitory tendency of plasma from statin treated patients supports an anti-angiogenic effect of statins.

In conclusion, VEGF plasma concentrations do not correlate with the presence, severity, and extent of CAD. Statin treatment was associated with lower VEGF plasma concentrations. Further studies are required to examine the effects of statins on VEGF and on plaque neovascularisation in humans.

ACKNOWLEDGEMENTS

Dr J Dulak was the recipient of the fellowship of Austrian Society for Cardiology (1999–2001). The study was supported in part by the Polish-Austrian Collaboration Project. We thank Eva-Maria Mair for technical support.

Authors’ affiliations
H F Alber, M Frick, J Dulak, J Dörler, R-H Zwick, W Dichtl, O Pachinger, F Weidinger, Department of Cardiology, University of Innsbruck, Innsbruck, Austria

Correspondence to: Dr Franz Weidinger, Department of Cardiology, University of Innsbruck, A-6020 Innsbruck, Austria; f.weidinger@uibk.ac.at

Accepted 15 April 2004

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