

Abstract

Diabetes is a chronic disease with high prevalence and significant morbidity. Chronic changes in the wall of small and large vessels lead to main diabetes complications. Apart from long-term hyperglycemia, several factors are involved in the development of diabetes vasculopathy. The aim of this work was to describe new early biomarkers of these vascular changes, to identify risky patients. Alongside, gene polymorphisms involved in protective pathways of glucose metabolism were studied.

In three human studies with Type 1 (T1D) and Type 2 (T2D) diabetes patients special biochemical parameters of receptor for advanced glycation endproducts (RAGE) and its ligands, deglycation enzyme glyoxalase 1 (GLO1) and fructosamine 3-kinase (FN3K) gene polymorphisms were analyzed. Non-invasive measurement of glycation by skin autofluorescence (SAF) was assessed in all subjects.

Soluble RAGE, HMGB1 and endothelial dysfunction markers were increased in patients with diabetes as compared with controls, however the differences between T1D and T2D were not significant. For the first time, an association between FN3K (rs1056534) and (rs3848403) polymorphism and sRAGE concentration in diabetes was shown. GLO1 (rs4746) polymorphism was associated with changes in endothelial dysfunction. Patients with diabetes had higher skin autofluorescence reflecting increased glycation. Moreover, SAF was even higher if chronic vascular changes were present. Interestingly, SAF did not correlate enough with glycated hemoglobin, a common medium-term marker of glycation.

These results suggest heterogenous biochemical processes involved in the development of diabetic angiopathy. The role of sRAGE is still unclear – its previously suggested protective role seems unlikely. There could be some role of deglycation enzyme polymorphisms in the development of angiopathy, however it is not strong enough for prediction. On the contrary, skin autofluorescence seems to be a relevant tool for clinical purposes in risk prediction and early intensification of diabetes treatment.