Abstract

The main objective of this study was research on biomarkers used in both diagnosis and therapy of diabetic complications. The main focus of our work came to be on one of these biomarkers - glycemic variability (GV). High GV is linked with more frequent occurance of hypoglycemia. There are even indications it might contribute to development of diabetic complications. With modern technology - continuous glucose monitoring (CGM), we are now able to reliably describe, calculate and reduce GV.

So far it is unclear whether increased GV can contribute to the development of microvascular complications (MVC) in type 1 diabetes (T1D). Studies published so far have assessed GV primarily from routine self-monitoring of blood glucose (SMBG) using glucometers.

In the light of this uncertaity, the first part of this work compares GV calculated from CGM with the presence of MVC in T1D patients. GV calculated from CGM, but not from SMBG, proved to be significantly higher in T1D patients with MVC, even though there was no significant difference in glycated hemoglobin (HbA_{1c}). This finding supports the hypothesis that higher GV is related to higher risk of MVC and that HbA_{1c} does not describe diabetes control completely. Moreover, it was shown that GV calculated from SMBG is insufficient.

There is still no fully accepted standard method of assesing GV. Our results suggest that the more complex parameters (e.g. mean amplitude of glycemic excursions - MAGE) provide no additional information over simple parameters (eg. total standard deviation - SD_T). Furthermore, SD_T can be easily used in clinical practice.

Our work has also contributed to the introduction of novel research into GV in cell cultures. The new model is based on GV profiles of actual patients and thus reflects better real T1D situations. In this study high GV had, in comparison with continuous hyperglycemia, inceased or similar impact on the expression of various genes involved in the pathophysiology of MVC.

Our results suggest that decrease in GV could decrease the risk of MVC. However, the most effective tool for improving GV is unknown. Therefore, the next step was to compair four different treatment strategies for T1D based on different combinations of insulin delivery and monitoring systems. This further work showed that the most effective treatments are based on real-time CGM, irrespective of insulin delivery method.