Analyte Flux at a Biomaterial–Tissue Interface over Time: Implications for Sensors for Type 1 and 2 Diabetes Mellitus

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Abstract

Objective:
The very presence of an implanted sensor (a foreign body) causes changes in the adjacent tissue that may alter the analytes being sensed. The objective of this study was to investigate changes in glucose availability and local tissue metabolism at the sensor–tissue interface in patients with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM).

Method:
Microdialysis was used to model implanted sensors. Capillary glucose and subcutaneous (sc) microdialysate analytes were monitored in five T1DM and five T2DM patients. Analytes included glucose, glycolysis metabolites (lactate, pyruvate), a lipolysis metabolite (glycerol), and a protein degradation byproduct (urea). On eight consecutive days, four measurements were taken during a period of steady state blood glucose.

Results:
Microdialysate glucose and microdialysate-to-blood-glucose ratio increased over the first several days in all patients. Although glucose recovery eventually stabilized, the lactate levels continued to rise. These trends were explained by local inflammatory and microvascular changes observed in histological analysis of biopsy samples. Urea concentrations mirrored glucose trends. Urea is neither produced nor consumed in sc tissue, and so the initially increasing urea trend is explained by increased local capillary presence during the inflammatory process. Pyruvate in T2DM microdialysate was significantly higher than in T1DM, an observation that is possibly explained by mitochondrial dysfunction in T2DM. Glycerol in T2DM microdialysate (but not in T1DM) was higher than in healthy volunteers, which is likely explained by sc insulin resistance (insulin is a potent antilipolytic hormone). Urea was also higher in microdialysate of patients with diabetes mellitus compared to healthy volunteers. Urea is a byproduct of protein degradation, which is known to be inhibited by insulin. Therefore, insulin deficiency or resistance may explain the higher urea levels. To our knowledge, this is the first histological evaluation of a human tissue biopsy containing an implanted glucose monitoring device.

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Abstract cont.

Conclusions:
Monitoring metabolic changes at a material–tissue interface combined with biopsy histology helped to formulate an understanding of physiological changes adjacent to implanted glucose sensors. Microdialysate glucose trends were similar over 1-week in T1DM and T2DM; however, differences in other analytes indicated wound healing and metabolic activities in the two patient groups differ. We propose explanations for the specific observed differences based on differential insulin insufficiency/resistance and mitochondrial dysfunction in T1DM versus T2DM.