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Targeted CYP2E1 quantification: Research to clinical application

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The Cytochrome P450 enzymes are commonly known for the major role they in metabolism of endobiotics and xenobiotics. Besides its metabolic role, CYP2E1 gene expression in peripheral lymphocytes showed association with the onset of diabetic nephropathy. CYP2E1 protein elevation has also been reported to be responsible for the production of reactive oxygen species (ROS). The objective of this study is to investigate CYP2E1 protein expression in peripheral lymphocytes at various stages of diabetes.

This study is a cross sectional studies involving four groups of subjects (N=100): control (non-diabetes) pre-diabetes, early diabetes and established diabetes. We applied the targeted proteomic approach for absolute quantification of CYP2E1. YPEIEEK and GTVVVPTLYDNQEFPDPEK were the specific tryptic peptides selected for our analytical method. D3Ac-YPEIEEK and D3Ac-GTVVVPTLYDNQEFPDPEK were used as internal standards. Lymphocytes were isolated from whole blood, microsomes were prepared, followed by in-solution digestion for production of tryptic peptides. Quantification of YPEIEEK and GTVVVPTLYDNQEFPDPEK from patients' samples was calculated from a standard curve. HbA1c and ACR were analyzed at a hospital laboratory.

CYP2E1 protein levels in peripheral blood lymphocytes were not measureable in all control subjects. CYP2E1 proteins were measureable in pre-diabetes and higher elevations were observed in early diabetes and established diabetes. Elevations of CYP2E1 were observed even when gold standard clinical indicators for glycemic control (HbA1c) and kidney function (ACR) were still within normal reference limits.

The interim outcome of this study shows quantitation of CYP2E1 protein using proteomic approach is applicable in clinical practice. Quantitation of CYP2E1 may be useful as an additional tool for estimation of risks for diabetic complications.

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