Evaluation of important human CYP450 isoforms and P-glycoprotein phenotype changes and genotype in type 2 diabetic patients, before and after treatment, by using Geneva cocktail

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Abstract

The present study evaluates the influence of type 2 diabetes (T2D) on important CYP450 isoforms and P-glycoprotein (P-gp) transporter activities before and 3 months after intensifying treatment regimen of 40 patients. Results have been compared with 21 non-T2D healthy participants (control group). CYPs and P-gp activities were assessed after administration of Geneva cocktail. Mean metabolic ratios (MR) for CYP2B6 (1.81±0.93 vs. 2.68±0.87), CYP2C19 (0.420±0.360 vs. 0.687±0.558), and CYP3A4/5 (0.487±0.226 vs. 0.633±0.254) significantly decreased in T2D subjects compared to control group (p<0.05). CYP2C9 (0.089±0.037 vs. 0.069±0.017) activities slightly increased in diabetic subjects and no difference was observed for CYP1A2 (0.154±0.085 vs. 0.136±0.065), CYP2D6 (1.17±0.56 vs. 1.24±0.83) and P-gp activities in comparison with control group. Three months after intensifying treatment regimen, MRs of CYP2C9 (0.080±0.030) and CYP3A4/5 (0.592±0.268) have shown a significant improvement and were not statistically different compared to control group (P>0.05). Several covariables such as inflammatory markers (IL-1β and IL-6), genotypes, diabetes- and demographic-related factors were considered in our analyses. Our results indicate that low chronic inflammatory status associated with T2D modulates CYP450 activities in an isoform specific manner.

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