

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-1 β 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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