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Pharmacogenetic Study of Apo A5, Cetp and Mthfr Polymorphisms on Fenofibrate Therapy in Tunisians Type 2 Diabetic Patients

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Fibrates act to attenuate atherogenic dyslipidemia in type 2 diabetic patients. However an increase of serum homocysteine (tHcy) after fenofibrate treatment has been reported, compromising its cardiovascular benefit. Polymorphisms in candidate genes related to lipid, lipoprotein and tHcy metabolisms were suspected to influence this response. The association between polymorphisms in cholesteryl ester transfer protein (CETP), apolipoprotein A5 (apo A 5), and methylenetetrahydrofolate reductase (MTHFR) genes in response to fenofibrate treatment ((200 M) for 4 weeks was evaluated in twenty one type 2 diabetic patients.

After fenofibrate use a significant decrease of TG level (29%) and a decrease of total cholesterol ($p = 0.081$) and CETP activity ($p = 0.089$) were noted. However, the HDL-C concentration has increased ($p= 0.081$) while LDL-C levels did not vary. Moreover, the prevalence of hyperhomocysteinemia, rose to 100%.

Both apo A5 TT and TC carriers showed significant decrease of TG levels. Whereas the HDL-C variation is better in TT genotype (23.5% vs -1.3% for TT and TC respectively; $p = 0.062$). The decrease of TG levels after fenofibrate treatment is more important in B1B1 than in B2B2 genotype of CETP polymorphism. Only B1B1 homozygous showed a decrease of CETP activity and an increase of HDL-C. After fenofibrate use, the increase of tHcy levels was more important in MTHFR T carriers than in CC homozygous (39.97 ± 14.77 vs. 28.02 ± 8.59 µmol/l, respectively).

Pharmacogenomic studies have a great economic and health interest for a better treatment of type 2 diabetic patients.