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PGC-1A GLY482SER POLYMORPHISM INCREASES THE SUSCEPTIBILITY TO NAFLD IN TYPE 2 DIABETIC PATIENTS

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Background and aim The aim of this study is to investigate the relationship between peroxisome proliferators-activated receptor γ coactivator-1α (PGC-1α) Gly482Ser polymorphism and non-alcoholic fatty liver disease (NAFLD) with type 2 diabetes (T2DM), and to clarify the effect of this gene variant on the transcription of cytosolic phosphoenolpyruvate carboxykinase (PEPCK-C) gene.

Methods According to typical liver ultrasonographic findings, 70 NAFLD with newly-diagnosed T2DM patients, 74 NAFLD patients, 70 newly-diagnosed T2DM patients and 84 NGT subjects were recruited into this study. PCR-restriction fragment length polymorphism (PCR-RFLP) was used to analyse the genotype of each individual. Then wild-type and mutated plasmids of PGC-1α were transfected respectively into liver cells and the mRNA and protein levels of PEPCK-C and PEPCK-C promoter activity were detected after transfection.

Results We demonstrated that NAFLD patients were more obese and insulin resistant. PGC-1α Ser482Ser genotype frequency and Ser482 allele frequency were higher in NAFLD patients complicated with T2DM than NGT group ($p<0.05$). Objects possess this genotype had lower plasma HDL-C levels but higher LDL-C levels and had higher risk for NAFLD complicated with T2DM. And the PEPCK-C mRNA and protein levels in co-transfecting PGC-1α (G) and HNF4α plasmids group increased more than PGC-1α (S) plus HNF4α group ($p<0.05$). Moreover, PGC-1α (G) increased PEPCK-C promoter activity with 2.0-fold and 2.2-fold versus PGC-1α (S) in HepG2 and LO2 cells respectively ($p<0.05$).

Conclusion PGC-1α Gly482Ser variant contributed to the onset of NAFLD in type 2 diabetic patients probably through impairing PEPCK-C gene transcription and exacerbating fat deposition.