The association between vitamin D metabolites and the 7-dehydrocholesterol reductase (DHCR7) rs12785878 polymorphism in German type 2 diabetes

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Introduction

Hypercholesterolemia is frequently found in patients with type 2 diabetes (T2D) [1]. Cholesterol is metabolized from 7-dehydrocholesterol (7DHC) by 7-dehydrocholesterol reductase (DHCR7) from 7-dehydrocholesterol, a precursor of pre-vitamin D₃ [2]. Therefore single nucleotide polymorphisms (SNP) in the DHCR7 gene could regulate cholesterol [3] levels and concentrations of vitamin D metabolites (25(OH)D₃ or 1,25(OH)₂D₃). For this purpose we investigated the SNP rs12785878 located near the DHCR7 gene in German T2D patients and healthy controls (HC) as well as concentrations of vitamin D metabolites. Furthermore we investigated the cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol level and LDL/HDL ratio according to DHCR7 rs12785878 genotypes.

Methods: 527 T2D patients and 654 HC were genotyped for the DHCR7 SNP rs12785878 by a Taqman assay. Additionally, 25(OH)D₃ and 1,25(OH)₂D₃ plasma levels of 76 T2D patients and 281 HC were measured by radioimmunnoassay. The serum cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol levels were measured by ELISA. Statistical analyses were performed using allele-wise and genotype-wise chi(x2)-tests.

Results

The homozygous TT genotype of DHCR7 SNP rs12785878 was significantly more frequent in T2D patients compared to HC (TT: 54.9 vs. 50.2 %; GT: 38.4 vs. 37.8 %, GG: 6.6 vs. 12.1 %, p = 0.007), also the allele T (74.1 vs. 69.0% OR =1.22; 95% CI: 1.02-1.46) in contrast to allele G (25.9 vs. 31.0% OR =0.82; 95% CI: 0.68-0.98, p = 0.03). T2D patients had significantly lower 25(OH)D₃ (median 12.6 vs. 19.4 ng/ml p=0.0001) and 1,25(OH)₂D₃ levels (median 44.7 vs. 51 pg/ml p= 0.001) compared to HC. T2D patients with DHCR7 genotypes GG and GT had lower 25(OH)D₃ levels than those from HC with genotype GG and GT, and T2D patients with the TT genotype showed even lower 25(OH)D₃ (median 13.7 vs. 20.9 ng/ml p= 0.002) and 1,25(OH)₂D₃ levels (median 43.3 vs. 52.3 pg/ml p = 0.001) compared to HC with the same genotype. T2D patients with the GG had a lower LDL-cholesterol compared to GT and TT genotypes.

Conclusion

Our results reveal an association of the DHCR7 SNP rs12785878 with T2D in German patients. The allele T may predispose to the development of T2D. In addition, significantly lower 25(OH)D₃ and 1,25(OH)₂D₃ levels were observed in T2D patients with the TT genotype. GG genotype T2D patients had a lower LDL-cholesterol serum levels. The dysfunction of 7-dehydrocholesterol reductase may contribute to the complex pathophysiology of insulin action and or β-cell secretion independent from its effect on vitamin D deficiency being a risk factor for T2D development.

References and Acknowledgements:

2) Kuus V. BMC Evolutionary Biology (2013) 13:144-144

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