Investigating the association of rs2346061 (CNDP1), rs7555(CNDP2), and rs1801133 (MTHFR) variants and Homocysteine level with diabetic nephropathy in an Iranian population

Saeedeh Asgarbeik¹- Farideh Razi¹- Ensieh Nasli-Esfahani¹- Samaneh Enayati²- SeyedAbdolhamid Angaji³- Marzieh ArshadiMashkani⁴- Katayoon Forouzanfar¹ - Mahsa M.Amoli^{**5}

1- Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

2- Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

3- Department of Cellular and Molecular Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran

4- Department of Biology, School of Basic Science, Science and Research Branch, Islamic Azad University, Tehran, Iran

5- Metabolic Disorders Research Center, Endocrinology and Metabolism Molecular Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Background

The correlation between rs1801133 variant of the MTHFR gene and elevated homocysteine levels has been reported in diabetic nephropathy[1]. High levels of homocysteine contribute to the progression and exacerbation of diabetes complications[2]. Carnosine is a peptide that by antioxidant role can harness the toxic effect of homocysteine[3]. In addition, the CNDP1 and CNDP2 genes are involved in the degradation of carnosine. The purpose of this study was to investigate the correlation between the rs2346061 (CNDP1), rs7555(CNDP2), and rs1801133 (MTHFR) variants and diabetic nephropathy.

Methods and Materials

In this study 310 individuals in three groups including Diabetic Nephropathy (DN) (n=104), Type-2 Diabetes Mellitus without nephropathy (DM)(n=100), and Healthy Control (HC)(n=106) were recruited. The allele and genotype frequencies of rs2346061, rs7577 and rs1801133 were determined using PCR-RFLP technique .

Results

Mean serum homocysteine level was higher in patients with DN than individuals with DM or HC group. Plasma homocysteine level was positively associated with allele T of rs1801133 ($p<0.05$). Allele T of rs1801133 variant was significantly increased in DM group. The distribution of genotype and allele frequencies of rs2346061 and rs7577 variants were not significantly different in the studies groups ($p>0.05$). There was no relationship between rs2346061 and rs7555 polymorphisms and homocysteine level.

Conclusions

These results confirmed the effect of the rs1801133 polymorphism on DM and plasma homocysteine level. No association was observed between rs2346061 and rs7577 and diabetic nephropathy in our patients ($p>0.05$).

Key Words: MTHFR, CNDP1, CNDP2, Homocysteine, Type-2 Diabetes

Figure 2. Homocysteine level in DN, DM and HC groups.

*=($p<0.05$) DN vs. DM and DN vs. HC

1.Mtiraoui, N., et al., *MTHFR C677T and A1298C gene polymorphisms and hyperhomocysteinemia as risk factors of diabetic nephropathy in type 2 diabetes patients*. Diabetes research and clinical practice, 2007. **75**(1): p. 99-106.

2.Scullion, S., et al., *Enhancement of homocysteine toxicity to insulin-secreting BRIN-BD11 cells in combination with alloxan*. Journal of endocrinology, 2012. **214**(2): p. 233-238.

3.Boldyrev, A., *Carnosine: new concept for the function of an old molecule*. Biochemistry (Moscow), 2012. **77**(4): p. 313-326.