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IFCC-WorldLab
ISTANBUL 22-26 JUNE 2014

IFCC WORLDLAB ISTANBUL 2014

22nd International Congress of Clinical Chemistry and Laboratory Medicine
22nd Balkan Clinical Laboratory Federation Meeting (BCLF 2014)
26th National Congress of the Turkish Biochemical Society (TBS 2014)

22-26 June 2014, Istanbul, Turkey

Istanbul Congress Center

CLINICAL CHEMISTRY AND LABORATORY MEDICINE

Published in Association with the European Federation of Clinical Chemistry and Laboratory Medicine

CCLM is the official journal of the Association of Clinical Biochemists in Ireland (ACBI), the Austrian Society of Laboratory Medicine and Clinical Chemistry (ÖGLMKC), the Belgian Society of Clinical Chemistry (BVKC/SBCC), the German United Society for Clinical Chemistry and Laboratory Medicine (DGKL), the Hungarian Society of Laboratory Medicine (MLDT), the Italian Society of Clinical Biochemistry and Clinical Molecular Biology (SIBioC), the Korean Society of Clinical Chemistry (KSCC), the Slovenian Association for Clinical Chemistry (SZKK), and the Turkish Biochemical Society (TBD).

DE GRUYTER

Genetic testing

Cod: 0643

THE ROLE OF FUNCTIONAL POLYMORPHISMS INVOLVED IN HOMOCYSTEIN METABOLISM

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BACKGROUND: An increased plasma concentration of total homocysteine (tHcy) is not only an important risk factor for the development of cardiovascular diseases, but it is also has significant impact on development of neurodegenerative disorders, as well as estrogen-related hormonal cancers. Hyperhomocysteinemia is caused by both nutritional and genetic factors. Polymorphisms in the Methylenetetrahydrofolate reductase (MTHFR), Methionine synthase reductase (MTRR) genes are the important risk factors effecting tHcy level. In this study we investigated a relation between functional polymorphisms of MTHFR c.677 C>T (p.Ala222Val), c.1298 A>C (p.Glu429Val) and MTRR c.66 A>G (p.Ile22Met) with plasma homocystein level. Additionaly, Catechol-O-methyltransferase (COMT) variation at position c.472G>A (p.Val158Met) was included, which is important enzyme contributing to homocysteine formation via the methylation of endogenous catecholamines and catechol estrogens.

METHODS: MALDI-TOF based MassArray platform was used for genotyping of n=200 subjects. Multiple statistical analyses were performed to assess the influence of polymorphisms on tHcy.

RESULTS: Total Hcy was higher in males with MTHFR c.677T genotype (p=0.03), while any association were found in females. We unable to find relation between tHcy and variants of MTRR c.66 A>G and MTHFR c.1298 A>C. Significant relation was established with COMT c.472A (p.Met158) allele and tHcy level in females (p=0.01).

CONCLUSIONS: It is known that the c.472AA genotype is related with lower COMT activity in females and could promote a hypercatechol-estrogenic state, which might be implicated in the pathogenesis of mental disorders. The results of our study provides an evidence that the same COMT variant has gender depend influence on tHcy concentration and may be a risk factor for cardiovascular disorders in Turkish women. Our results will hopefully assist in the design of future studies that will investigate contribution of personal characteristics and nutritional factors to homocysteine level in Turkish population.