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The interaction of the C677T 5,10-methylenetetrahydrofolate reductase (MTHFR) polymorphism with serum B vitamins and homocysteine in pregnant women

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Hyperhomocysteinemia, a well-established independent risk factor for vascular diseases, is now being suggested as a possible cause for complications and adverse outcomes of pregnancy. Serum homocysteine(Hcy) level is known to be a product of an interaction between the MTHFR polymorphism and folate nutrition. The purpose of the present study was to investigate the relationship between serum vitamin B levels and Hcy with the 677 C-to-T mutation in the MTHFR genotypes in 177 pregnant women of 24~28 weeks of gestation. Serum vitamin B_2, vitamin B_6, and Hcy levels were measured by a HPLC-fluorescence detection method. Serum folate and vitamin B_{12} levels were analyzed by a radioimmunoassay. MTHFR gene mutation was investigated by the polymerase chain reaction of a genomic DNA fragment. Dietary intake of B-vitamins (vitamin B_2, B_6, B_{12} and folate) were estimated by a 24-hour recall method. The MTHFR allele frequencies for C/C, C/T, and T/T were 59 (33.3%), 87 (49.2%) and 31 (17.5%). Serum Hcy concentrations were significantly higher in women with the T/T genotype (9.3 ± 4.6 μmol/L) than the C/T (8.3 ± 2.9 μmol/L) or the C/C genotype (7.4 ± 2.6 μmol/L, $p<0.05$). More women with the T/T genotype (25%) were assessed as hyperhomocysteinemic ($\geq$ 14 μmol /L) than those with the C/T (4%) or the C/C genotype (0%). Serum folate concentrations were lower, but not significantly, among the carriers of a MTHFR mutant allele(T/T or C/T genotype) compared with those of no mutant allele (C/C genotype). Serum Hcy was negatively correlated with serum folate in all MTHFR genotypes, the correlation between two serum levels was stronger in the T/T type ($r=-0.569$, $p<0.001$) than in the C/T or C/C genotypes (C/T: $r=-0.373$, C/C: $r=-0.418$). Serum folate was positively correlated with serum vitamin B_{12} and pyridoxal-5-phosphate. Though dietary intake of B vitamin did not differ among the three genotypes, the negative correlation between dietary folate intake and the serum Hcy level was the strongest in the T/T type ($r=-0.266$) than in other genotypes (C/T: $r=-0.004$, C/C: $r=0.022$). Among the subject with the T/T type, the pregnant women who consumed folate less than 50% of the RDA had higher serum Hcy levels than those who consumed folate greater than 125% of the RDA (10.4 ± 5.9 vs 7.0 ± 1.5 μmol/L, $p<0.1$). Serum Hcy levels were higher in the women with micronutrient supplements than those with no supplements in the T/T type (7.2 ± 3.0 vs 10.6 ± 4.3 μmol /L, $p<0.1$), but such relation was not present in the C/C or the C/T type. In conclusion, the frequency for homozygotic C677→T mutation in MTHFR gene was as high as 17.5%. Serum Hcy levels were higher in women with homozygotes for the T677 allele in MTHFR gene than other genotypes, and their serum Hcy levels were influenced by serum folate levels or dietary folate intake.

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