Genetic polymorphisms in MTHFR 677 and 1298, GSTM1 and T1, and metabolism of arsenic

Streinmaus, Craig, Moore, Lee E., Shipp, Miriam, Kalman, Dave, Rey, Omar A., Biggs, Mary Lou, Hopenhayn, Claudia, Bates, Michael N., Zheng, Schichun, Wiencke, John and Smith, Allan H. (2007) *Genetic polymorphisms in MTHFR 677 and 1298, GSTM1 and T1, and metabolism of arsenic.* Journal of Toxicology and Environmental Health - Part A: Current Issues, 70 (2). pp. 159-170. ISSN 1087-2620

RESUMEN

Methylation is the primary route of metabolism of inorganic arsenic in humans, and previous studies showed that interindividual differences in arsenic methylation may have important impacts on susceptibility to arsenic-induced cancer. To date, the factors that regulate arsenic methylation in humans are mostly unknown. Urinary arsenic methylation patterns and genetic polymorphisms in methylenetetrahydrofolate reductase (MTHFR) and glutathione S-transferase (GST) were investigated in 170 subjects from an arsenic-exposed region in Argentina. Previous studies showed that subjects with the TT/AA polymorphisms at MTHFR 677 and 1298 have lower MTHFR activity than others. In this study, it was found that subjects with the TT/AA variant of MTHFR 677/1298 excreted a significantly higher proportion of ingested arsenic as inorganic arsenic and a lower proportion as dimethylarsinic acid. Women with the null genotype of GSTM1 excreted a significantly higher proportion of arsenic as monomethylarsonate than women with the active genotype. No associations were seen between polymorphisms in GSTT1 and arsenic methylation. This is the first study to report (1) associations between MTHFR and arsenic metabolism in humans, and (2) gender differences between genetic polymorphisms and urinary arsenic methylation patterns. Overall, this study provides evidence that MTHFR and GSTM1 are involved in arsenic metabolism in humans, and polymorphisms in the genes that encode these enzymes may play a role in susceptibility to arsenic-induced cancer.

TIPO DE DOCUMENTO: Artículo

DOI: https://doi.org/10.1080/15287390600755240

PALABRAS CLAVE: 5,10 methylenetetrahydrofolate reductase (FADH2). Arsenic. Cacodylic acid. Glutathione transferase. Methanearsonic acid.

TEMAS: R Medicina > R Medicina (General)

UNIDAD ACADÉMICA: Universidad Católica de Córdoba > Facultad de Ciencias de la Salud