Alcohol consumption and polymorphisms of cytochromes P4502E1 are high risks for ESCC

March 13 2008

Heavier alcohol consumption increases the risk of ESCC. There are synergetic interactions among alcohol drinking and ALDH2, ADH1B, CYP2E1 genotypes. The risk of ESCC in moderate-to-heavy drinkers, ALDH2 (1/2) combined with the ADH1B (1/1) genotype; ALDH2 (1/2) combined with the CYP2E1 (c1/c1) genotype; leads to synergetic interactions, higher than drinkers with ALDH2 (1/1) + ADH1B (1/2 + 2/2); ALDH2 (1/1) + CYP2E1 (c1/c2 + c2/c2).

This study, performed by a team led by Dr. Yan-Mei Guo, is described in a research article published in the March 7, 2008 issue of the *World Journal of Gastroenterology*.

ESCC is the seventh leading cause of cancer deaths worldwide. Epidemiologic studies have demonstrated that drinking alcoholic beverages is causally related to the development of ESCC. The genetic polymorphisms of Cytochromes P4502E1 (CYP2E1), aldehyde dehydrogenase-2 (ALDH2) and alcohol dehydrogenase-1B (ADH1B; previously called ADH2) affect the metabolism of alcohol. There were some other studies examining the roles of alcohol, CYP2E1, ALDH2 and ADH2 in ESCC. Their findings, however, were contradictory.

In the view of the authors, no clear explanation has, to date, existed to elucidate the susceptibility conferred by CYP2E1, ALDH2 and ADH1B genetic polymorphisms on ESCC. Neither have a definition and

evaluation been found to explain the individual and combined roles of these genes and alcohol consumption.

The innovative aspect of this study was the way it looked at the interaction between the CYP2E1, ALDH2 genotype and heavy alcohol drinking, with case-control designs. Previous studies have not examined this issue in detail and to our knowledge this is the first study to show a significant interaction between the CYP2E1, ALDH2 genotype and alcohol drinking. We found there was synergetic interaction with polymorphisms of CYP2E1, ALDH2 genotype and heavy alcohol drinking. Individuals with combined ALDH2 (1/2) and CYP2E1 (c1/c1) genotype showed a dramatically increased risk of ESCC, which is higher than that due to the respective genotypes.

The susceptibility of alcohol and aldehyde dehydrogenase genotypes on ESCC became evident in 2003 when it became widely accepted that alcoholic beverages are causally related to cancer of the esophagus. A review of case-control studies of the effects of ALDH2 and ADH2 genotypes shows consistently positive associations between inactive heterozygous ALDH2 and the risk for esophageal cancer in East Asian heavy drinkers. Only the ALDH2 genotype has been demonstrated to have a critical role in the development of ESCC.

Using an elegant study design, including 80 male patients with esophageal cancer and 480 controls (age and sex matched), the consumption of alcohol and the genetic polymorphism of enzymes involved in the metabolism of ethanol was examined. This research was performed by doctors from the Laboratory of Gansu College of Traditional Chinese Medicine, Lanzhou, China and from the Laboratory of First hospital of Lanzhou University, Lanzhou, China.

Source: World Journal of Gastroenterology