Abstracts

Session: 8 Paper Number: 85

NAT2 Slow Acetylation and Bladder Cancer in Workers Exposed to Benzidine

T. Carreón (1,2), A.M. Ruder (1), P.A. Schulte (1), R. B. Hayes (3), N. Rothman (3), G.K. LeMasters (2), M.A. Waters (1), D.J. Grant (4), R. Boissy (4), D.A. Bell (4), F.F. Kadlubar (5), G.P. Hemstreet (6), S. Yin (7)

(1) National Institute for Occupational Safety and Health, (2) University of Cincinnati, (3) National Cancer Institute, (4) National Institute of Environmental Health Sciences, (5) National Center for Toxicological Research, (6) University of Oklahoma, (7) Chinese Academy of Preventive Medicine

The slow NAT2 N-acetylation genotype inhibits detoxification of a range of monoarylamines and has been associated with increased risk for bladder cancer in cigarette smokers and workers in arylamine dye production. The diarylamine, benzidine, is also a strong bladder carcinogen, however, NAT2 N-acetylation is not key to its detoxification. This study expands a previous study that evaluated the impact of NAT2 polymorphisms on bladder cancer in male subjects occupationally exposed only to benzidine.
The combined analysis of 68 cases and 107 controls from a cohort of production workers in China occupationally exposed to benzidine, included 30 new cases and 67 controls not previously studied. NAT2 enzymatic activity phenotype was characterized by measuring urinary caffeine metabolite ratios. PCR-based methods identified genotypes for NAT2, NAT1 and GSTM1. NAT2 phenotype results were consistent with NAT2 genotype data. A protective association was observed for the slow NAT2 genotype (bladder cancer odds ratio = 0.3, 95% confidence interval 0.1-1.0) after adjustment for cumulative benzidine exposure and lifetime smoking. Individuals carrying NAT1*10, a low activity allele, showed a higher risk of bladder cancer (OR=2.3, 95% CI 0.8-7.0). No association was found between GSTM1 null and bladder cancer. The results of this study were compared with the results of a meta-analysis of case-control studies of NAT2 acetylation and bladder cancer conducted in general Asian populations not exposed occupationally to arylamines. The lower limit of the 95% CI of the risk estimate in the general Asian populations (OR=1.7, 95% CI 1.0-2.7) does not overlap the upper 95% CI for the estimate obtained in the current analysis.

Study findings demonstrate that slow acetylators are not at increased risk of developing benzidine-induced bladder cancer, in contrast to slow acetylators who smoke cigarettes or are exposed to monoarylamine dyes, who are at increased risk. Some evidence was found of the existence of an interaction between NAT2 acetylation and benzidine exposure. The data actually suggest decreased risk, although the mechanism for risk reduction needs further delineation.

NORA Symposium 2003

Working Partnerships: Applying Research To Practice

June 23-24, 2003

Hilton Crystal City Hotel
Arlington, VA

CDC Workplace Safety and Health

NIOSH

APHA