THE INFLUENCE OF GENETIC POLYMORPHISMS ON THE RISK OF DEVELOPING ASBESTOSIS

Alenka Franko, Clinical Institute of Occupational Medicine, University Medical Center, Ljubljana, Slovenia
Vita Dolzan, Institute of Biochemistry, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia
Niko Arneric, Clinical Institute of Occupational Medicine, University Medical Center, Ljubljana, Slovenia
Metoda Dodic-Fikfak, Clinical Institute of Occupational Medicine, University Medical Center, Ljubljana, Slovenia

Background and Aims: Relatively little is known about the genetic factors that may influence the development of asbestosis. The aim of this study was to investigate whether common functional polymorphisms in GSTT1, GSTM1, GSTP1, MnSOD, ECSOD, CAT and iNOS genes represent risk factors for developing asbestosis in workers occupationally exposed to asbestos.

Methods: The study included 262 cases with asbestosis and 265 controls with no asbestos-related disease. Data on cumulative asbestos exposure were available for all subjects. PCR based methods were used to genotype GSTM1-null, GSTT1-null, GSTP1 Ile105Val and Ala114Val, MnSOD Ala–9Val, ECSOD Arg213Gly, CAT –262C>T and iNOS (CCTTT)n polymorphisms. Logistic regression analysis was used to assess asbestosis risk.

Results: The OR of asbestosis was 3.21 (95% CI 2.43–4.23) for cumulative asbestos exposure, 1.01 (95% CI 0.71–1.43) for GSTM1-null; 0.61 (95% CI 0.40–0.94) for GSTT1-null; 1.52 (95% CI 1.08–2.15) for GSTP1 105Ile/Ile versus 105Ile/Val and 105Val/Val; 0.97 (95% CI 0.64–1.48) for GSTP1 114Ala/Ala versus 114Ala/Val and 114Val/Val; 1.50 (95% CI 1.01–2.24) for MnSOD –9Ala/Ala versus Ala/Val and Val/Val; 1.63 (95% CI 0.62–4.27) for ECSOD 213Arg/Gly versus Arg/Arg; 1.36 (95% CI 0.70–2.62) for CAT –262TT versus CT and CC; and 1.20 (95% CI 0.85–1.69) for iNOS LL versus SL and SS. The associations between MnSOD Ala–9Val polymorphism and asbestosis risk and between iNOS (CCTTT)n and asbestosis were modified by CAT –262C>T polymorphism (p=0.038; p=0.031, respectively).

Conclusions: Our study showed that GSTP1 105Ile/Ile and MnSOD –9Ala/Ala genotypes significantly increase the risk of developing asbestosis, whereas a protective effect was found for GSTT1-null genotype. A strong interaction was observed between MnSOD Ala–9Val and CAT –262C>T, as well as between iNOS (CCTTT)n and CAT –262C>T polymorphisms. The findings suggest that in addition to asbestos exposure, genetic factors may also have an important influence on developing asbestosis.