

The effect of multiple exposure to organic solvents on a single solvent biomarker

A.Pardo, A. Peretz, S. Umanski

Abstract

Organic solvents are used in almost all industrial sectors and in many cases appear in mixtures. Studies have demonstrated changes in the excretion levels of a solvent-specific biological marker in urine under circumstances of co-exposure to other solvents. Medical follow-up of workers exposed to organic solvents is based on exposure to the individual solvent. Thus additive effects of co-exposure to other solvents on a given biological site in the body are ignored, possibly leading to an underestimation of the health risk. The present study hypothesized that the level of a solvent-specific biological marker corresponding to exposure to an individual solvent may be higher or lower than the corresponding level resulting from exposure to that solvent when present in a mixture with other solvents. The goal of the study was to test the difference in the urinary excretion level of the markers of regulated solvents between the two exposure scenarios.

Databases of industrial hygiene monitoring results, and medical records of biological monitoring collected during 10 years as part of regulatory requirements were used to extract data pertaining to six regulated organic solvents (benzene, toluene, xylene, styrene, trichloroethylene, perchloroethylene), subject to inclusion and exclusion criteria. Data were collected with permission, in accordance with ethical conventions (Helsinki committee) to avoid ethical conflicts. The extracted data were divided into two groups, one referring to exposure to each individual solvent and the other referring to that solvent when present in a mixture with other solvents. Dependent variables included urinary levels of specific biological markers whereas occupational exposure levels comprised the independent variables. Each value of dependent variable was matched with a value of independent variable. Markers of liver and kidney functions as well as socio-demographics, habits and health condition were collected as control variables for the

reduction of confounding factors. Analysis of the data included descriptive statistics and statistical analysis on both groups employing t-test for testing the difference between interval variables, Fisher exact test for categorical variables and mixed models for fixed and random effects. Association between the levels of occupational exposure and the levels of the corresponding metabolic markers was assessed by linear regression, and slopes of the regression lines corresponding to the same solvents were compared between the two groups.

Exposure levels in most cases were within Threshold Limit Values (TLV). Workers exposed to benzene only and to benzene in mixtures of solvents (mainly aromatic mixtures) exhibited urinary trans-trans muconic acid values exceeding the BEI limit in 50% and 18% of cases, respectively. The mean levels of biological markers resulting from exposure to individual solvents differed significantly from those in solvent mixtures only in the case of styrene ($p = 0.029$). Worth noting, although not significant, was the difference in the mean levels for toluene ($p = 0.089$). Lack of significance in the difference between the biological marker means obtained for the other solvents may be partially due to small sample size. Linear regression performed for each solvent in both exposure scenarios to test the association between the occupational exposure level and the level of the corresponding biological marker indicated significant difference in slopes of the lines drawn for toluene, styrene and perchloroethylene (<0.001 , 0.005 , 0.034 , respectively). At exposure levels close to or higher than the TLV-TWA the vertical interval between the regression line of the individual aromatic solvent and the line of this solvent when present in solvent mixtures increased with increasing exposure level.

The results suggest possible changes in urinary excretion levels of a biological marker of a given solvent when the exposure to that solvent is combined with exposure to other solvents including those under regulations.