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Re: Genetic Polymorphism on Susceptibility to Nephrotoxic Properties of BTEXs Compounds

To the Editor:

The present study investigated the relationship between genetic polymorphisms and susceptibility of a group of petrochemical employees to nephrotoxic properties of benzene, toluene, ethyl-benzene and xylenes compounds. Cases and referent subjects were free from any preexisting medical conditions at the commencement of their employment. In addition, records of their preplacement medical and paraclinical examinations indicate that the parameters of kidney function of both groups were within normal range at the time. Furthermore, at present, no statistically significant differences are noted between both groups as far as their demographic variables, smoking habits, length of employment, and their exposure scenarios are concerned. However, at present, some employees have been found with abnormal kidney function tests (KFTs). To ascertain whether genetic polymorphism plays a role in the observed effects, this study, similar to a number of other investigations,[1–7] was undertaken. The results showed that the frequencies of GSTP1Ile-Val/Val-Val, null glutathione s-transferase theta 1 (GSTT1), and null GSTT1/glutathione s-transferase mu 1 (GSTM1) genotypes were significantly higher in the cases (individuals with abnormal KFTs) than in the referent subjects.

The Glutathione-S-transferase (GSTs) family includes phase 2 detoxifying enzymes. GSTs are involved in the detoxification of reactive oxygen species and play a crucial role in antioxidant defense mechanisms, by catalyzing detoxification of electrophilic xenobiotics and by inactivating a variety of endogenous by-products of oxidative stress.[8] Therefore, the null variants of these genes might result in reduced GST expression, leading to reduced antioxidant defense.[9] Increased reactive oxygen species levels have been considered as causative factors involved in various forms of chronic kidney diseases (CKDs).[10]

In addition, glutathione conjugation of aromatic hydrocarbons, such as benzene, toluene, xylenes, trimethyl-benzenes, and diethenyl-benzenes, results in the formation of mercapturic acids, relatively less toxic, water soluble, polar compounds, which are readily excreted in urine at physiologic pH.[11] Therefore, individuals with null or mutant genotypes are less capable of detoxifying cytotoxic substrates to protect their own tissues against oxidative damage.[12]

Given the fact that null genotypes (null GSTT1 and null GSTT1/GSTM1 genotypes) were significantly more prevalent among the cases, it would be reasonable and plausible to assume that the observed kidney dysfunction among this group, as reflected in abnormal KFTs, is very likely to be due to this genetic defect, resulting in increased vulnerability and susceptibility to nephrotoxic properties of benzene, toluene, ethyl-benzene and xylenes compounds, compared with their referent counterparts, carrying positive GSTT1 genotypes.

This conclusion is not inconsistent with the notion that changes in molecular weight alter the degree of susceptibility. Association of a null genotype with susceptibility to nephrotoxic properties of a chemical and changes in the parameters of renal function are likely to be due to changes in the level and quality of protein function. How the changes of polymorphism at the DNA level alter the function at the protein level was not the objective of this study and requires additional proteomics studies. This study sought changes at the DNA level, while investigation on molecular weight changes examine these variations at protein level. Changes in the polymorphism may be associated with changes in protein and molecular weight. The underlined mechanisms of these changes need to be investigated in future studies.

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The authors report no conflicts of interest.
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