

THE EFFECT OF RELEVANT GENOTYPES ON HEMOGLOBIN ADDUCTS OF ACRYLAMIDE AND GLYCIDAMIDE IN WORKERS EXPOSED TO ACRYLAMIDE

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Background and Aims: Acrylamide (AA) is an industrial chemical widely used in industries and also an environmental chemical found in tobacco smoke and food. It is classified as a probable human carcinogen (Group 2A) by the IARC. AA undergoes metabolism to glycidamide (GA). Both AA and GA react with hemoglobin (Hb) to form adducts (AA-Hb and GA-Hb), and these adducts are considered as biomarkers for long-term AA exposures. This study elucidates associations between AA- and GA-Hb adducts as well as their ratio with genetic polymorphisms *CYP2E1*, *mEH* (in exon 3 and exon 4), *GSTT1*, and *GSTM1*, involved in the activation and detoxification of AA-associated adducts.

Methods: Fifty-one AA-exposed workers and 34 controls were recruited and provided a post-shift blood sample for this study. Personal air sampling was performed for the exposed workers. AA- and GA-Hb were determined simultaneously using isotope-dilution liquid chromatography-electrospray ionization/tandem mass spectrometry (LC-ESI-MS/MS). *CYP2E1*, *mEH* (in exon 3 and exon 4), *GSTT1*, and *GSTM1* were analyzed using polymerase chain reaction.

Results: Our results reveal that AA personal exposures ranged from 4.37×10^{-3} to $113.61 \mu\text{g}/\text{m}^3$ with a mean at $15.36 \mu\text{g}/\text{m}^3$. The AA- and GA-Hb levels in the exposed group significantly exceed those in controls. The ratio of GA-Hb/AA-Hb, potentially reflecting the proportion of AA metabolized to GA, was calculated with a mean of 0.27 and in the range of 0.13-0.45. Multivariate regression analysis demonstrate that *GSTM1* genotypes significantly modify the formation of GA-Hb and the GA-Hb/AA-Hb ratio, polymorphism of exon 4 of *mEH* were all significantly associated with AA-Hb, GA-Hb levels and the GA-Hb/AA-Hb ratio after adjustment for AA exposures.

Conclusions: These results suggest that *GSTM1* and/or *mEH* associated with the formation of blood AA-Hb and GA-Hb. Further studies may be needed to cast light on the roles of both enzymes in AA metabolism.