Correlation Between the Urine Profile of 4-(Methylnitrosamino)- 1-(3-Pyridyl)-1-Butanone Metabolites and 7-Methylguanine in Urothelial Carcinoma Patients.

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摘要

Abstract

A major carcinogen, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), is present in cigarette smoke and its metabolite, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), is used as an exposure biomarker for environmental tobacco smoke (ETS). This metabolite (NNAL) can be either detoxified into glucuronidated NNAL (NNAL-Gluc) or activated into an unstable reactive metabolite that methylates DNA along with formation of 4-hydroxy-4-(3-pyridyl)-butyric acid [hydroxy acid (HA)]. Therefore, the carcinogenic risk associated with ETS exposure is greatly modulated by individual variations in metabolic activation and detoxification capabilities. In this study, we defined the urinary HA/total NNAL [HA/total NNAL] ratio as the activation index and NNAL-Gluc/free NNAL [(total NNAL-free NNAL)/free NNAL] ratio as the detoxification index of NNK. The major methylated DNA adduct N7-methylguanine (N7-MeG), considered as the carcinogenic biomarker for cigarette smoking, was excreted in urine. The objective of this study was to investigate the effects of these metabolic indexes of NNK on N7-MeG urinary excretion in a population of urothelial carcinoma patients. Urinary levels of total NNAL (free NNAL plus NNAL-Gluc), free NNAL, HA, and N7-MeG were positively correlated with smoking. Furthermore, activation index and detoxification index correlated positively and negatively with N7-MeG levels, respectively. Our results suggest that these metabolic indices may represent the phenotype of individual metabolism capability and modulate the carcinogenic risk of ETS exposure. (Cancer Epidemiol Biomarkers Prev 2008;17(12):3390–5)