Sulfotransferase 1A1 polymorphism, cigarette smoking, and colorectal adenomas

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Background: Sulfonate conjugation plays an important role in the metabolism of endogenous and exogenous compounds, including steroid hormones and carcinogens. Of a super family of sulfotransferases (SULTs), SULT1A1 is one of the most important members due to the wide distribution and abundance. Although sulfonation is generally regarded as a detoxification pathway, SULT1A1 is involved in the bioactivation of potential procarcinogens, including polycyclic aromatic hydrocarbons and arylamines contained in tobacco smoke. A functional polymorphism is recently known in exon 7 of the SULT1A1 gene. The polymorphism of Arg213His (G638A) affects the activity of the enzyme. The enzyme activity was shown to be substantially lower in individuals with the His213His genotype compared with the other genotypes. Few studies have addressed the effect modification of SULT1A1 Arg213His polymorphism on the relation between cigarette smoking and colorectal cancer and adenomas, reporting inconsistent results.

Purpose: The present study aims to clarify the effect modification of SULT1A1 Arg213His polymorphism on the association between cigarette smoking and colorectal adenomas.

Methods: Study subjects were 455 cases of colorectal adenomas and 1052 controls with normal colonoscopy among male officials in the Self Defense Forces (SDF) who received a pre-retirement health examination at the SDF Fukuoka Hospital or Kumamoto Hospital during the period from January 1997 to March 2001. Genotyping was performed by the PCR-RFLP method. A self-administered questionnaire was used to ascertain smoking habit, alcohol use, and other lifestyle factors. Total exposure to cigarette smoking was expressed as cigarette-years, which were calculated by multiplying the average number of cigarettes per day by the total years of smoking, and was categorized into 0, 1-399, 400-799, and 800+ cigarette-years. Odds ratio (OR) and 95% confidence interval (CI) were estimated by logistic regression analysis. Statistical adjustment was made for smoking, alcohol use, physical activity, body mass index, and others in examining the relation between the SULT1A1 polymorphism and colorectal adenomas. In the analysis on the interaction between the SULT1A1 polymorphism and cigarette smoking, the categories of 400-799 and 800+ cigarette-years were combined. Statistical assessment of the interaction was done by likelihood ratio test, comparing models with and without interaction terms.

Results: The SULT 1A1 polymorphism was unrelated to colorectal adenomas; crude OR (95% CI) for Arg/Arg, Arg/His, and His/His genotypes were 1.0 (referent), 1.0 (0.8-1.3), and 1.0 (CI 0.4-2.5), respectively. The corresponding adjusted OR (95% CI) were 1.0 (referent), 0.9 (0.7-1.7), and 1.0 (0.4-2.5), respectively. In the study population, cigarette smoking was positively related to the prevalence odds of colorectal adenoma as reported previously. The adjusted OR (95% CI) for 0, 1-399, and 400+ cigarette-years in the Arg/Arg genotype were 1.0 (referent), 1.0 (0.6-1.5) and 1.9 (1.4-2.6), and the OR (95% CI) for 0, 1-399, and 400+ cigarette-years in the Arg/His and His/His genotypes combined were 0.6 (0.3-1.1), 1.5 (0.8-2.8), and 1.9 (1.2-2.8), respectively. P value for the interaction was 0.12.

Conclusions: SULT 1A1 Arg213His polymorphism was unrelated to colorectal adenomas. Individuals with the 213His allele seemed to have an increased risk when the exposure to smoking was moderate, suggesting an effect modification of the 213His allele on the relation between smoking and colorectal adenomas.