RESEARCH COMMUNICATION

GSTM1, GSTT1 and CYP1A1 Polymorphisms and Risk of Oral Cancer: a Case-control Study in Jakarta, Indonesia

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Abstract

Purpose: to investigate genetic polymorphisms in GSTM1, GSTT1 and CYP1A1 and the association with the risk of oral cancer in the Jakarta population. Method: A total of 81 cases and 162 controls matched for age and sex were selected from 5 hospitals in Jakarta. Sociodemographic data using questionnaires were obtained and peripheral blood samples were collected with informed consent for PCR-RFLP assay. Conditional logistic regression analysis was performed to obtain the association between the risk of oral cancer and GSTM1, GSTT1 and CYP1A1 polymorphisms. Results: GSTM1 and GSTT1 null were slightly overrepresented among cases (60.5% and 45.7% respectively) compared to controls (55.6% and 41.4% respectively), but no statistically significant differences were observed. In contrast, the distribution of CYP1A1 polymorphism was higher among controls compared to cases (52.5% versus 42.4%). The odds ratio of null GSTM1 and GSTT1 genotypes was slightly higher compared to wild type genotypes (OR 1.19, 95% CI 0.70-2.02 and OR 1.19, 95% CI 0.72-2.05 respectively). Furthermore, the presence of CYP1A1 polymorphism did not increase the risk of oral cancer (OR 0.70, 95% 0.39-1.25). Conclusion: Genetic polymorphisms of GSTM1, GSTT1 and CYP1A1 may not be risk factors for oral cancer in the Jakarta population.

Key Words: Oral cancer risk - metabolizing enzyme polymorphisms - Jakarta, Indonesia

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Introduction

Oral cancer is one of the sixth most common cancers worldwide (Stewart et al., 2003a). Tobacco exposure and alcohol drinking have been established as major risk factors of oral cancer in most of countries in the world (Stewart et al., 2003b). In addition, betel quid chewing is also associated with the disease in some countries, such as India and Taiwan (Znaor et al., 2003; Jacob et al., 2004; Yang et al., 2005). Despite the risk of tobacco exposure, alcohol drinking and quid chewing, the majority of the patients who smoke or chew tobacco do not get cancer suggesting that factors that influence carcinogen-exposed individuals in developing malignancies may thus involve a combination of exposure and genetic polymorphisms in genes that may modulate their capacity in metabolizing the carcinogens mentioned above (Rebeck, 1997; Nair et al., 1999; Sreekleha et al., 2001).

Most carcinogens are not biologically active when they enter the body. They need to be converted into biologically active forms before they can interact with host DNA to cause mutations. Numerous carcinogens present in tobacco are metabolized by various enzymes, namely, metabolic activation by phase I (Cytochrome P450/CYP) and detoxification by phase II enzymes (glutathione S-transferase/GSTs) (Lazarus et al., 2000). Phase I (CYP) monooxygenases metabolism involves an initial oxidation of most endogenous chemicals (e.g. hormones and fatty acids) and exogenous chemicals (e.g. polyaromatic hydrocarbons/PAHs, aromatic amines and mycotoxins).

Two polymorphic sites, a T to C transition, 1194 bp downstream of exon 7, generating a new MspI cleavage site and the closely linked exon 7, A to G transition (isoleucine-valine, ile:val) polymorphism, are associated with an increase in CYP1A1 enzymatic activity towards benzo[alpha]pyrene (Park et al., 1997) and higher inducibility or enhanced catalytic activity of the valine-type CYP1A1 enzyme (Hayashi et al., 1991). This metabolic activation step is followed by phase II metabolism, which frequently involves detoxifying carcinogenic metabolites which is catalyzed by glutathione S-transferases (GSTs). This enzyme also plays an important role in determining an individual’s ability to metabolize various carcinogens particularly benzo[a]pyrene. In humans, based on their primary structures, GSTs are divided into seven families/classes: α (alpha), μ (mu), π (pi), τ (theta), ϕ (sigma), ω

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