Cytochrome P450 2E1 polymorphism and nasopharyngeal carcinoma development in Thailand: a correlative study

ABSTRACT

Though our finding was not statistically significant due to the moderate sample size of the study, similarity to the study in Taiwan with only a slight loss in precision was demonstrated. The higher RR found for the same genotype in distinct populations confirmed that CYP2E1 is one of several NPC susceptibility genes and that the RsaI minus variant is one mutation that affects phenotype.

INTRODUCTION

Background Nasopharyngeal carcinoma (NPC) is a rare tumor in most parts of the world, with annual age-standardized incidence rates typically below 1 per 100,000 people/year in both sexes. The tumor occurs most often in Southern Chinese who reside in Guangdong Province, at an incidence rate 30-50 per 100,000 people/year, in contrast with <1 per 100,000 people/year in white Europeans. The disease also occurs at moderate frequencies (3-10 per 100,000 people/year) in several non-Chinese ethnic groups such as Malay, Thai and Vietnamese. Numerous factors, both environmental and genetic, have been associated with the risk of developing NPC. The environmental factors include infection with the Epstein-Barr virus (EBV), as well as frequent consumption of high levels of nitrosamine from preserved food such as salted fish. In addition, host factors also play a major role in NPC development. Unique alleles of the human leukocyte antigen (HLA) and cytochrome P450 2E1 (CYP2E1) have been shown to be associated with high relative risk in several Asian ethnic groups, including the Chinese in Taiwan. CYP2E1, an enzyme involved in the metabolic activation of procarcinogens into reactive intermediates capable of forming adducts and damaging DNA, is believed to play an essential role in chemical carcinogenesis. Nitrosamine is a substrate of CYP2E1. It is believed that nitrosamine, once activated can lead to the development of numerous cancers. Studies have also demonstrated that CYP2E1 is expressed in the nasal epithelium of human. Evidence from previous epidemiological studies has suggested that salted fish is a food preferred by Chinese people and contains nitrosamines and nitrosamine precursors. Therefore, CYP2E1 is believed to render the nasopharyngeal epithelium susceptible to NPC development. A previous study in Taiwan employed a PCR-RFLP (polymerase chain reaction-restriction fragment length polymorphism) assay using the restriction enzyme RsaI in order to compare wild-type (+/+) and variant forms (-/-) of the CYP2E1 gene between NPC patients and the general population. The variant form of contains CYP2E1 polymorphic mutations in the distal 5'-flanking region of the gene, causing a marked difference in its transcriptional activity, as shown by CAT (chloramphenicol acetyltransferase). The Taiwanese association study showed that individuals homozygous for the variant allele (-/-) were at an increased risk for NPC development (relative risk [RR] = 2.6; 95% confidence interval [CI] = 1.2-5.7). There are many Chinese people who have immigrated and permanently lived in Thailand for 2 to 3 generations, resulting in a mixed population of Thai and Chinese people. From clinical observation, we had observed at least one-third of NPC patients were Chinese in origin. Since the susceptibility of CYP2E1 gene to develop NPC had only been reported from Chinese people in Taiwan, it was decided to investigate whether this allele played the same role in other populations. Therefore, we studied the correlation of the polymorphism of the CYP2E1 gene with NPC in Thai and

Chinese populations in Thailand.

CONCLUSION

Result of the reported crude odds ratio is 2.19 [95%CI = 0.62-8.68]. If the result is adjusted odds ratio, it will be 2.39 [95%CI = 0.72-7.89], which is closer to the Taiwanese odds ratio of 2.6, with only a slight loss in precision. Thus, this study confirmed a previous study in Taiwan that CYP2E1 appears to be one of a number of NPC susceptibility genes and the RsaI minus variant is not just a polymorphism but directly influences the development of the phenotype.