ABSTRACT

This thesis describes the association of twelve important single nucleotide polymorphisms from four detoxification genes (CYP1A1, CYP2E1, EPHX1 and NAT2) with oral cancer in the South Indian population. The subjects included 157 histopathologically confirmed of oral cancer patients and 132 control individuals who reported the absences of personal history of cancer. The genotyping was done by TaqMan allelic discrimination. The associations between genotypes, alleles and haplotypes of the polymorphic sites and oral cancer were then analyzed using a case-control study. The strength of the association between gene variants and oral cancer was estimated using the logistic regression. The genotype frequencies of all polymorphic SNPs were consistent with Hardy-Weinberg equilibrium in the control group.

The CYP1A1-Thr461Asn and CYP2E1-V179I loci are not polymorphic in the present study, whereas rs3813867 and rs2031920 are co-inherited. All the polymorphisms studied in EPHX1 and NAT2 genes were polymorphic in both cases and controls. For all the genes, there were no significant differences in genotype or haplotype frequencies between controls and cases with oral cancer. Of the EPHX1, NAT2 gene polymorphisms studied, two were in strong linkage disequilibrium and form 1 haplotype block in the respective genes.
The overall acetylator phenotypes, showed statistically significant association, in particular, rapid acetylator genotypes, to oral cancer risk. Lack of a significant association between detoxification gene polymorphisms and oral cancer in the present study might be explained by the substantially lower frequencies of these alleles. Further, the results are discussed in the light of detoxification of carcinogens found in tobacco smoke and alcohol.