Study of the Association of Genetic Polymorphisms in Biotransformation Genes (CYP1A1, GST, EPHX1) and Tumor-Suppressor Gene (p53 codon72) with the Susceptibility to Adult Acute Myeloid Leukemia

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Abstract

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Keywords: Polymorphism; Acute Myeloid Leukemia.

Introduction

Acute myeloid leukemia (AML) is the most common acute leukemia in adults with median incidence of 2.4 cases per 100,000 individuals.Biotransformation plays a crucial role in carcinogenic activity and many genetic polymorphisms in xenobiotic metabolizing enzymes have been associated with an increased risk of developing AML. Tumour Suppressor Gene acts as protective gene as it controls and monitor the cell growth and apoptosis. Genetic polymorphisms in drug metabolizing enzymes are extremely common but very few studies have investigated influence of GSTM1 and GSTT1-null polymorphisms, EPHX1 and CYP polymorphisms on risk of developing adult AML.

Material & methods

The study was conducted on 70 patients (46 males, 24 females; range 18-85 with median age 32 years). Primers for PCR were designed and standardized using gradient PCR and by taking annealing temperature ± 5°C of the Tm of primers. PCR and RFLP were used to study polymorphisms in Biotransformation Genes and Tumor-Suppressor Gene. All statistical analyses were performed with SPSS, version 11.5. Chi-square test was done to calculate P-value and to find association between adult AML and genetic polymorphisms in CYP1A1, GST, EPHX1 and p53 codon72 genes. P-value of <0.05 was considered statistically significant.

Results

Frequency distribution of GSTM1 null genotype was 33% and 49% whereas 19% and 30% for GSTT1 null genotype in AML patients and controls respectively. GSTT1 null genotype conferred a marginally significant 2.0 fold reduction in risk of AML relative to presence of the GSTM1 gene (OR=0.50, 95%CI: 0.25-0.98, p= 0.06). Frequency of EPHX1 Exon 3 and exon 4 variant genotypes were marginally different in cases versus controls. Protective effect of the Tyr113His genotype of EPHX1 gene against AML lacked a statistical significance. There was no significant difference in distribution of CYP1A12A variant genotype in cases and controls (9% and 7%). Frequency of p53 codon 72 polymorphism for Arg/Arg, Arg/Pro and Pro/Pro genotype was 31%,50%,19% respectively in cases while 25%, 57%, 18% respectively in controls. This distribution also showed no significant statistical differences between AML cases and controls ($\div^2$ =0.97, p =0.08).

Conclusion

Present study indicates lack of association of EPHX1, CYP1A1 and p53 with risk of adult AML. On the other hand GSTT1 deletion seems to play protective role. The present results suggest that further studies on multiple gene-gene interaction may provide better insight into the complex etiology of AML.