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Meeting abstract

Polymorphisms of the *thiopurine methyl transferase gene* in healthy and acute lymphoblastic leukemia mestizos

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Background

Polymorphisms at the thiopurine S-methyltransferase coding gene (*TPMT*) determine enzyme activity and as a consequence the development of toxicity to thiopurines

Materials and methods

A total of 108 DNA samples from volunteer donors and 39 from patients with acute lymphoblastic leukemia (ALL) were analyzed. Genomic DNA from peripheral blood leukocytes was isolated by standard methods. Known (wild type and polymorphic) sequenced PCR fragments of the *TPMT* gene were used as controls. TPMT gene fragments were amplified for exons 5, 7 and 10. PCR products were then analyzed by denaturating high performance liquid chromatography (DHPLC) for the most frequent mutant *TPMT* alleles, according to the method developed by Schaeffeler et al. on an analysis system from Transgenomics.

Results

No elution profiles at the DHPLC analysis were different to those already reported. The frequency of gene polymorphisms was 53.7% in healthy and 38.4% in the ALL population. However, only 17.6% of all polymorphisms found are considered as functional, being the most frequent the *3A (n = 13, 8.8%), followed by *3B (n = 5, 3.47%), *3C (n = 5, 4.6%) and *2 (n = 3, 2. 7%).

Conclusion

DHPLC is a highly sensitive, rapid and efficient method to identify relevant *TPMT* gene mutations which allows the screening for genetic variability in the *TPMT* gene. This is the first analysis of the polymorphisms at this gene in a Mestizos population. The frequency of known silent polymorphisms was higher than those reported in other regions worldwide, but although the frequency of functional polymorphism in healthy population is within the range found in other reports, the frequency of such polymorphism was higher in the patients. All together, the routine typing of *TMPT* polymorphisms in the patients with ALL is being set in our Institution.

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