Genotypic and Computational Analysis of Missense Mutations of Thiopurine S-methyltransferase in Patients with Acute Lymphocytic Leukemia.

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INTRODUCTION: Thiopurine methyltransferase (TPMT) catalyzes an step of thiopurines metabolism, agent used in acute lymphocytic leukemia (ALL) treatment. The TPMT shows genetic polymorphisms that alter their activity, and may hinder the effectiveness of the treatment. **OBJECTIVE:** Investigate the presence of the main TPMT mutant alleles in patients diagnosed with ALL and search structural changes through molecular dynamics simulations of protein containing the detected TPMT polymorphisms. **MATERIALS AND METHODS:** After obtaining consent of 55 patients Mossoró and region, we used multiplex PCR to identify the presence of main mutant alleles TPMT (TPMT*2, TPMT*3A, TPMT*3B and TPMT*3C) and analyzed the occurrence of adverse effects these patients the maintenance phase of treatment using the CTCAE v.3.0 NCI. Then we assess structural changes in the protein derived of these mutations in GROMACS. This study was approved by the Ethics Committee of the State University of Rio Grande do Norte under the 097/11 protocol number. **RESULTS**: Six of the 55 patients had heterozygous genotypes, four had TPMT*3A genotype and two TPMT*2 genotype, with allele frequencies of 3.64 and 1.82, respectively. Mucositis, leukopenia and neutropenia were the most common adverse reactions in these patients. The variants TPMT*2 and TPMT*3A showed difference in RMSD compared to native. Radius of giration differed only in TPMT*3A. The RMSF of TPMT*2 and TPMT*3A differed around the positions 35 and 60, respectively. **CONCLUSION:** Genotype and structural changes TPMT variants were analyzed in Mossoro and region. These structural modifications aid in the understanding of the occurrence of major adverse effects in patients with allelic variants. This knowledge contributes to the search for a more effective treatment.

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