ONCODAILY MEDICAL JOURNAL

abstract

The Role of TPMT and NUDT-15 Genetic Polymorphisms in 6-Mercaptopurine Dose Tolerability among Pediatric B-Cell ALL Patients in Saudi Arabia

Walid Ballourah, Abdul Ali Peer-Zada, Mohammed F Essa, Saad Al Daama, Ibrahim Al Ghemlas, Abeer Ali, Farah Malaeb, Khawar Siddiqui, Yasser Borai, Wasil Jastaniah

doi.org/10.69690/ODMJ-018-0425-2276

SIOP ASIA 2025
SAUDI ARABIA

ONCODAILY MEDICAL JOURNAL

SIOP ASIA 2025 SAUDI ARABIA

The Role of TPMT and NUDT-15 Genetic Polymorphisms in 6-Mercaptopurine Dose Tolerability among Pediatric B-Cell ALL Patients in Saudi Arabia

Author: *Walid Ballourah [1], Abdul Ali Peer-Zada, Mohammed F Essa, Saad Al Daama, Ibrahim Al Ghemlas, Abeer Ali, Farah Malaeb, Khawar Siddiqui, Yasser Borai, Wasil Jastaniah*

Affiliation: *[1] King Faisal Specialist Hospital and Research Center - Riyadh, Saudi Arabia*
DOI: *https://doi.org/10.69690/ODMJ-018-0425-2276*

Introduction: 6-MP is an essential antimetabolite used during the maintenance phase of acute lymphoblastic leukemia (ALL) therapy. Children from various regions, including Saudi Arabia, have been reported to exhibit lower dose tolerance for 6-MP. The (COG) protocols standardize the 6-MP starting dose at 75 mg/m2/day. This study investigates the impact of (TPMT) and (NUDT-15) polymorphisms on drug dose tolerability in children with B-cell ALL in Saudi Arabia.

Methodology: We prospectively assessed 146 pediatric ALL patients treated on COG-adapted protocols from six centers across Saudi Arabia, focusing on 82 with available DNA samples. Genetic sequencing of four TPMT and two NUDT15 variant alleles was performed using Sanger sequencing. The relationship between these genetic polymorphisms and 6-MP dose tolerability was analyzed.

Results: Among patients with intronic TPMT variant allele (Type A, rs2518463), 56 of 81 (69.1%) were heterozygous, requiring a median 6-MP dose reduction of 43.1%, whereas 30.9% with negative polymorphism needed a 29.7% reduction (P=0.894). TPMT variant allele (Type B, rs2842934) was present in 76 of 81 (93.8%) patients; 56.8% were homozygous, necessitating a 46.7% reduction, and 37% were heterozygous, needing a 33.3% reduction (P=0.687).

For the TPMT allele (Type C, rs6921269), 2 of 82 (2.4%) patients were heterozygous with a reduction of 45.1%, compared to 42.9% in those negative for Type C (P=0.717). Two patients with Type D required a median dose reduction of 3.2% vs. 43.3% in Type D negatives. Notably, two patients exhibited heterozygous NUDT15 variants (g.8153C>T; rs116855232) requiring a 19% reduction. Above 60% dose reduction correlated significantly with the presence of multiple SNPs (P=0.042).

Conclusion: Significant 6-MP dose reductions are required for this cohort. TPMT Type B rs2842934 is the predominant allele, differing significantly in frequency from other populations. The sample size may limit statistical correlation establishment. A lower starting dose of 6-MP is suggested.