The influence of thiopurine methyltransferase gene polymorphism on Egyptian children with acute lymphoblastic leukaemia

Azza A.G Tantawy[1], Fatma S.E. Ebeid[1], Amira A.M Adly[1], Eman El-Ghoroury [2], Mai Mostafa[1]
[1]Paediatric Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[2]Department of Clinical Pathology, National Research Center, Cairo, Egypt

Background: Thiopurine methyltransferase (TPMT) gene polymorphism regulates thiopurine therapeutic efficacy and toxicity. *Aim*: Determine the influence of TPMT gene polymorphism in Egyptian children with acute lymphoblastic leukaemia (ALL). *Methods*: Sixty-four patients with ALL, T lineage (27%) and pre-B phenotype (73%), who were treated with BFM 90 or CCG 1991 standard risk protocol, and who also experienced myelosuppression toxicity and required interruption and/or modification of thiopurine chemotherapy were recruited over a one-year period. Thirty-two patients were on maintenance and another thirty-two were finished their chemotherapy. Seventy healthy age- and sex-matched children served as controls. They subjected to clinical assessment, haematological panel investigations and TPMT gene polymorphism for G238C, G460A and A719G alleles assessment using PCR followed by RFLP analysis. *Results*: Although none of the studied patients had the mutant TPMT variant alleles, myelosuppression toxicity in form of different degree of neutropenia was detected in all patients. As result of myelosuppression toxicity, most of patients need 6-MP dose modification either once (53.1%), twice (15.6%), or ≥ three times (25.1%) during their maintenance course. Patients required stopping 6-MP for less than a week (62.5%), up to 2 weeks (28.1%), or > 2 weeks (6.3%). Patients also developed infection that mostly (71%) necessitating hospitalization. *Conclusion:* None of the studied G238C, G460A or A719G TPMT variant alleles was detected. Infections and febrile neutropenia were common causes of 6PM dose modification and interruption.