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Effect of Glutathione S-transferase mu 1 (*GSTM1*) gene polymorphism on chronic myeloid leukemia risk and Imatinib treatment response

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Abstract

Glutathione S-transferases (GSTs) gene polymorphisms were demonstrated to be associated with inter-individual variability of Imatinib mesylate (IM) response for chronic myeloid leukemia (CML) patients in a few studies; however, the results have been inconclusive. The aim of this study was to assess the role of such GSTs gene polymorphisms (*GSTT1* and *GSTM1*) in relation to IM treatment outcome in 96 Syrian CML in chronic phase (CP) patients. Screening of GSTM1 and GSTT1 genotypes (null or present of these genes) was determined by multiplex polymerase chain reaction. Our results revealed that a GSTM1 null genotype frequency was significantly higher in CML patients than control (reference group) (OR = 2.12, 95% CI: 1.24–3.7; p = 0.007) while the GSTT1 null had no significant effect on CML development (OR = 1.54, 95% CI: 0.83–2.9; p = 0.19). Dual GSTM1 and GSTT1 null were associated with the risk of CML development (OR = 3.6, 95% CI: 1.37–9.3; p = 0.01). The GSTM1 null significantly increased the risk of minimal cytogenetic response (p = 0.001). The similar trend was observed in patients with GSTT1 present/GSTM1 null genotypes (p = 0.009). The highest number of patients with minimal cytogenetic response was in the group treated with 400 mg of IM, while 600 and 800 mg of IM significantly decreased this frequency. Our results highlight the significance of *GSTM1* null alone, or in combination with the *GSTT1* gene null, significantly increased the likelihood of IM failure in the CML patients studied. Especially patients with minimal cytogenetic response and *GSTM1* null suffered from IM treatment failure in case of low dosage IM.

Abbreviations

ABL1, c-abl proto-oncogene 1 gene;
BCR, breakpoint cluster region gene;
CML, chronic myeloid leukemia;
CP, chronic phase;
CCgR, complete cytogenetic response;
CHR, complete hematologic response;
ELN, European LeukemiaNet;
GSTs, Glutathione S-transferases gene;
IM, Imatinib mesylate;
MDR1, multi-drug resistance gene;
PCyR, partial cytogenetic response;
Ph, Philadelphia chromosome;
PCR, polymerase chain reaction

Keywords

Chronic myeloid leukemia; Imatinib; GSTT1; GSTM1; Polymorphisms; Drug resistance