Glutathione S-Transferase polymorphisms does not impact busulfan clearancein patients undergoing hematopoietic stem cell transplantation

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Busulfan (Bu) is a vital drug in most of the preparative regimens prior to Hematopoietic Stem Cell Transplantation (HSCT). This study aims to assess the role of GST genetic variants in affecting the clearance of Bu in patients undergoing allogeneic HSCT.

Methods: This single center retrospective cohort study included 135 adult and pediatric patients who received IV Bu prior to their HSCT at Sultan Qaboos University Hospital (SQUH) in Oman from January 2003- October 2016. Patient's Bu clearance was calculated using Trapezoidal Method for drug exposure. Genotyping was done using Capillary Electrophoresis for GSTM1 and GSTT1 (insertion or deletion) and DNA sequencing for GSTA1 (C-69G, A-513G, G-1142C) and GSTP1 (A313G). Busulfan clearance was compared between genotypes using two sample t-test (if normally distributed) or Mann-Whitney test (if not normally distributed). Ethical approval was obtained from the Medical Research Ethics Committee at Sultan Qaboos University College of Medicine and Health Sciences.

Results: We included 135 patients, of which 63 were males and 72 were females. The median age of the studied population was 14 year (IQR: 5-24). The mean Bu clearance in our population was 3.7 ± 0.98 ml/min/kg. The frequency of GSTM1 and GSTT1 deletions in our population was 41% and 16%, while the frequency of the double insertion of GSTM1 and GSTT1 was 50%. The frequency of the wild type, heterozygous and homozygous genotypes of GSTA1 was 38%, 48% and 14% respectively while it was 0%, 4% and 96 respectively for A-513G, and 42%, 41% and 17% respectively for G-1142C. The wild type, heterozygous and homozygous genotype frequency for the locus A313G of GSTP1was; 47%, 40% and 13%; respectively. GSTM1 and GSTT1 deletion were not found to have an effect on Busulfan clearance (p values were 0.23 and 0.09; respectively). GSTP1 SNP A313G had no effect on Busulfan clearance (p = 0.984). All tested locations of GSTA1 SNPs (-69, -513, and -1142) had no effect on Busulfan clearance (p values were 0.315, 0.268, and 0.264, respectively).

Conclusions: Polymorphism of GST (GSTA1, GSTM1, GSTT1, and GSTP1) did not influence Busulfan clearance in our population. This may be explained by the low power due to small differences in clearance or by the differential impact of GST polymorphism in genetically different populations.