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Evaluating the over-time prognostic performance of biomarkers for cancer prognoses using time-dependent receiver operating characteristic (ROC) curve

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P-glycoprotein (PGp) encoded by the Multi-drug-resistance1(MDR1) gene is a member of the ATP-binding cassette (ABC) transporter family, drug transporting proteins involved in the bioavailability and pharmacokinetics of various drugs. Cancer chemotherapy drugs are characterized by narrow therapeutic windows with significant intra- and inter-patient variability in therapeutic and toxic effects. Temozolamide is a target for Pgp mediated chemo resistance. Thus, genotyping for MDR1 polymorphisms may become an important tool in predicting individual susceptibility to toxicity and developing drug resistance. In this prospective study, genetic polymorphism of MDR1 C3435T, C1236T were studied in 70 malignant Glioma patients undergoing chemo -radiation therapy with temozolamide drug and 100 normal controls using PCR-RFLP method . Plasma levels of Temozolamide were also calculated using reversed phase HPLC method. MDR1 (C1236T) polymorphism showed significant genotypic as well as allelic association with Glioma patients and controls ($P<0.05$). The average concentration of Temozolomide was found lesser (0.0326 ± 0.004 mcg/ml) in mutant genotype pattern when compared with wild type genotype (1.45 ± 0.32 mcg/ml). Our results suggest that genetic polymorphism of MDR1 does influence the metabolism and therapeutic outcome of Temozolamide in Glioma patients. Thus utilization of pharmacogenetic testing for the identification of different MDR1 alleles in patients may provide a useful tool for optimizing therapy with drugs that are substrates of P-gp.

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