



quetiapine, clozapine, olanzapine, chlorpromazine etc., are substrates of P-gp at the BBB having weak to moderate degree of affinity for the P-gp efflux transporter. Most of them are weak inhibitors of P-gp including thioxanthene derivative. Moreover the three major Single Nucleotide Polymorphisms (SNPs) of ABCB1 at C3435T, G2677T, and C1236T have been associated with efflux pump efficiency and with predicting tolerability of antipsychotic drugs in addition to the disease and drugs itself. So that concomitant administration of agents, that modulate ABC efflux transporter at BBB, with antipsychotic will be one possible way to overcome the pharmaco-resistant schizophrenia.

However, taking all findings into consideration published observations, even when made with the same probe drug and in the same racial group, is controversial. There are multiple possible explanations for these discordant results include differential experimental conditions, such as probe drug used, applied dose, steady-state versus single dose pharmacokinetics, small sample sizes, sample selection, or genetically heterogeneity due to ethnical diverse populations.

In order to determine conclusive result and the actual impact of all ABC efflux transporter on the schizophrenia and its treatment; multicenter (i.e., multiethnic), large sample size, multi-dose, long term cohort and well standardized study should be conducted to optimize its usefulness in individualized pharmacotherapy of drug resistant schizophrenia. And also identification of genetic variants and the complex regulatory pathways involved in P-gp modulation should be well elucidated in future. P-gp transport screening and its polymorphism has to be incorporated into the drug discovery process as recently recommended by the FDA.

In general, the role of P-gp in pharmaco-resistant schizophrenia was under studied even though majority of antipsychotic drugs are substrate for this efflux transporter. As a result, great focus should be given to P-gp efflux transporter at BBB in future if it is necessary to tackle drug resistant schizophrenia.

