CHAPTER 9

RECOMMENDATIONS

On the basis of the findings of this research, the following are recommended,

(i) Pharmacogenetic studies of schizophrenia need to collect data on pertinent clinical predictors. They should aim to develop combined clinical and pharmacogenetic association models. When we enthusiastically pursue our research for the promise of new discoveries, we should not overlook the inherent clinical heterogeneity of schizophrenia.

(ii) There is a need for reliable consensus research criteria to define treatment responses for future pharmacogenetic studies of schizophrenia. Such consensus criteria should go beyond a narrow focus on positive psychotic symptoms to incorporate global assessments of outcome, including cognition, functional disability and quality of life. Once a consensus on the domains of schizophrenia to be assessed and on the assessment instruments is reached, future pharmacogenetic studies of schizophrenia should employ such consensus criteria a priori to define treatment outcomes.

(iii) Routine screening for *CYP1A2* gene Single Nucleotide Polymorphisms (**1C, *1D, *1E* and **1F*) prior to starting clozapine is currently unwarranted.

(iv) Smoking is a potentially modifiable risk factor for non-response to clozapine. Nicotine deaddiction should be advised for all smoking patients with Treatment-resistant schizophrenia to augment their response to clozapine.

(v) Because of high inter-individual variability of serum clozapine levels, routine therapeutic drug monitoring of clozapine is desired in all clinical settings.

(vi) Clinical psychiatrists, working in the settings where routine therapeutic drug monitoring of clozapine is not feasible, may consider using our non-parametric equation during clozapine dose adjustments.

(vii) Minimum target oral dose for clozapine should be 250 mg/day for the patients with treatment-resistant schizophrenia, unless the patients develop intolerable adverse effects on lower doses.

(viii) If patients, who are on maintenance treatment with clozapine, report serum clozapine levels above 500ng/ml, appropriate dose reductions or adjustment of co-medications should be considered to reduce the risk of clozapine related seizures.

(ix) Clinical psychiatrists need to consider the influence of caffeinated beverages on serum clozapine levels of their patients. The patients should be advised to inform their treating psychiatrists, when they make any abrupt changes in their caffeine habits.