Model-Guided Antipsychotic Dose Reduction in Schizophrenia: A Single-Blind Randomized Controlled Trial

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Schizophrenia is a chronic psychiatric illness that generally requires long-term antipsychotic treatment. On the other hand, antipsychotics are associated with a variety of dose-related serious adverse events. Therefore, it is critically important to minimize exposure to these drugs and to identify the lowest effective dose for each individual patient. In reality, patients with schizophrenia as well as their psychiatrists are frequently hesitant to reduce the antipsychotic dose in fear of relapse, even when it exceeds the therapeutic threshold. To overcome such dilemmas, we developed models to individually calculate an oral dose that corresponds to a given target dopamine D_2 receptor occupancy. In this 52-week single-blind randomized controlled trial, 35 clinically stable patients with schizophrenia receiving either risperidone or olanzapine monotherapy were randomly assigned to dose-reduction group (n=17) or dose-maintenance group (n=18). In the former group, baseline doses were reduced to the doses corresponding to 65% D_2 occupancy (the lower end of therapeutic window) at trough that were calculated from randomly collected plasma concentrations, using our models. A total of 25 subjects completed all study procedures: 12 patients (70.5%) in the dose-reduction group and 13 patients (72.2%) in the dose-maintenance group, without any statistically significant difference. There were no significant differences in score changes in the Positive and Negative Syndrome Scale (p=0.983) nor Global Assessment Functioning (p=0.141) between the two groups. With regard to extrapyramidal symptoms, Abnormal Involuntary Movement Scale score reduction was significantly greater in the dose-reduction group than in the dose-maintenance group (p=0.025). In conclusion, the model-guided antipsychotic dose reduction strategy seems feasible in the maintenance treatment of schizophrenia. The preliminary findings in the present study should be confirmed in future studies through double-blind, larger samples and longer follow-up periods.