Using Bayesian Modeling to Optimize Antipsychotic Dosage in Clinical Practice

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Abstract

Aim A robust and user-friendly software tool was developed for the prediction of dopamine D2 receptor occupancy (RO) in patients with schizophrenia treated with either olanzapine or risperidone. This tool can facilitate clinician exploration of the impact of treatment strategies on RO using sparse plasma concentration measurements. Methods Previously developed population pharmacokinetic (PPK) models for olanzapine and risperidone were combined with a PD model for D2 receptor occupancy (RO) and implemented in the R programming language. MAP Bayesian estimation was used to provide predictions of plasma concentration and receptor occupancy and based on sparse PK measurements. Results The average (standard deviation) response times of the tools were 2.8 (3.1) and 5.3 (4.3) seconds for olanzapine and risperidone, respectively. The mean error (95% confidence interval) and root mean squared error (RMSE, 95% CI) of predicted versus observed concentrations were 3.73 ng/mL (-2.42 – 9.87) and 10.816 (6.71 – 14.93) for olanzapine, and 0.46 ng/mL (-4.56 – 5.47) and 6.68 (3.57 – 9.78) for risperidone and its active metabolite (9-OH risperidone). Mean error and RMSE of RO were -1.47% (-4.65 – 1.69) and 5.80 (3.89 – 7.72) for olanzapine and -0.91% (-7.68 – 5.85) and 8.87 (4.56 – 13.17) for risperidone. Conclusion Treatment of schizophrenia with antipsychotics offers unique challenges and requires careful monitoring to establish the optimal dosing regimen. Our monitoring software predicts RO in a reliable and accurate form.

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