

Antipsychotic Drug Stability in Serum and Plasma Patient Samples

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Background - Therapeutic drug monitoring (TDM) of antipsychotic blood levels is strongly recommended (clozapine and olanzapine) and recommended (risperidone, aripiprazole, and quetiapine) by the AGNP Consensus Guidelines for Therapeutic Drug Monitoring in Neuropsychopharmacology. To ensure accurate concentration determinations for effective TDM, it is crucial to understand both the stability of the drug in various sample types as well as any differences between the sample types. In this study, we investigated the stability and equivalence of clozapine, olanzapine, risperidone, aripiprazole, and quetiapine in serum and plasma (K₂EDTA) samples from patients undergoing antipsychotic treatment. Methods - Matched serum and plasma samples from patients taking clozapine, olanzapine, risperidone, aripiprazole, or quetiapine were collected according to an IRB-approved protocol. Drug concentrations were quantified using CE marked and Health Canada licensed immunoassays for the measurement of clozapine (also FDA-cleared), olanzapine, total risperidone/paliperidone, total aripiprazole, and quetiapine. Samples were stored refrigerated (4°C), at ambient room temperature (ART, 25°C), and frozen (-80°C). At each timepoint, six replicates of each sample were measured using the immunoassays and averaged. The percent deviation from their Day 0 average concentration was used to assess stability. Results – Equivalent results between serum and plasma were obtained for each patient, as the percent deviation between Day 0 values was $\pm 9\%$, except olanzapine which showed differences of up to $\pm 15\%$. Average bias between serum and plasma was $\leq -5\%$ (olanzapine: -9%). All drugs were stable ($\pm 15\%$ deviation; olanzapine $\pm 23\%$) in serum and in plasma for 7 days refrigerated and at ART, and for >8 months frozen. Conclusions - This study demonstrated that serum or plasma samples from patients taking the antipsychotic drugs clozapine, risperidone, aripiprazole, olanzapine, or quetiapine may be used for effective TDM as they have sufficient stability and show equivalent results. Key Words - antipsychotics, immunoassay, stability, psychiatry