

Inter- and Intraindividual Variation of Methylphenidate Concentrations in Serum and Saliva of Patients with Attention-Deficit/Hyperactivity Disorder.

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Abstract

Background

Therapeutic drug monitoring (TDM) is becoming increasingly important in psychiatric therapy; especially in children. However, for several reasons, it cannot yet be implemented as a daily routine in clinical or outpatient settings. To evaluate new, non-invasive procedures; blood and saliva (oral fluid) samples were collected from patients with attention-deficit/hyperactivity disorder (ADHD) who were also being administered methylphenidate (MPH). The study's main purposes were to correlate MPH concentrations in serum and saliva between subjects; and to analyze intraindividual variation of serum concentration.

Methods

Thirty-six ADHD patients (27 children and 9 adults) on methylphenidate medication were included for drug analysis. MPH and its major metabolite ritalinic acid (RA) were quantified using LC-MS/MS measurements. The following correlations were investigated: 1) between drug concentrations in serum and saliva, and 2) between pH value and saliva to serum concentration ratio. Furthermore, the mean intraindividual MPH-concentration fluctuation in saliva under constant frame conditions was analyzed.

Results

After quantification, MPH concentrations were approximately 5 times higher in the saliva than in the serum, while the concentrations of RA were much lower in saliva. We found significant correlations between concentrations of MPH in serum and saliva ($r=0.51$, $p<0.05$). Saliva MPH measures, compared to serum, were pH-dependent ($r=-0.56$, $p<0.01$). Daily coefficient of variance of saliva concentration in children taking constant medication was 27.3% (11%-42%), while the coefficient of variance for the ratio of saliva to serum was 122% (2%-2060%).

Conclusions

Our data indicates that the interindividual variation in saliva to serum concentrations is rather high, while the intraindividual variation is fairly low, as already shown in the literature for repeated citalopram serum measurements. Saliva may well serve as an alternative matrix for TDM of MPH in ADHD patients, especially for follow-up examinations. Future research should focus on analyzing the relationship between drug levels in saliva and clinical effects; as well as on understanding the mechanisms that generate saliva drug concentrations. These are essential steps prior to potential clinical use.