Poster

[P26-2] P26-2: Central nervous system drugs (1)

Chair: Atsushi Yonezawa, Japan

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[P26-2-4] Clinical validation of a dried blood spot method for determination of risperidone, aripiprazole, pipamperone and their major metabolites

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Background

Risperidone, aripiprazole and pipamperone are the three most frequently prescribed antipsychotic drugs in children in the Netherlands. Therapeutic Drug Monitoring (TDM) might reduce the side effects and improve patient outcome. The Dried Blood Spot (DBS) method offers a minimally invasive and patient friendly sampling method for TDM, especially suitable for TDM in children. The aim of this study was to validate the use of the DBS method for risperidone, aripiprazole, pipamperone and its major metabolites 9-OH risperidone and dehydroaropiprazole in a clinical setting.

Methods

Paired DBS and serum samples were obtained from adult patients treated with one of the drugs under study. Samples were analysed by a previously validated UHPLC-MS/MS method. Agreement between two methods was evaluated using Deming Regression and Bland-Altman plots. Estimated Plasma Concentrations (EPC) were calculated from DBS concentrations. Sensitivity was calculated by dividing the number of identical interpretations ('<LLOQ', 'below, within and above therapeutic range', and '>ULOQ') by the total number of interpretations.

Results

Mean plasma levels were 8.5 g/l for risperidone (n=26), 33.2 g/l for 9-OH risperidone (n=26), 156.1 g/l for aripiprazole (n=14), 60.5 g/l for dehydro-aripiprazole (n=14) and 103.0 g/l for pipamperone (n=16). With Deming regression analysis, for all analytes after correction to EPC, the 95% confidence interval (CI) of the slope included 1 and the 95% CI of the Y-intercept included 0. Bland-Altman analysis showed the following mean bias (SD): risperidone 0.1 g/l (3.9), 9-OH risperidone -1.0 g/l (16.5), aripiprazole 0.0 g/l (36.3), dehydroaripiprazole 0.0 g/l (15.3), pipamperone 0.0 (42.9). As can be seen a large SD was found. However, the sensitivity of the EPCs for clinical interpretation was good with 97% for risperidone, 98% for 9-OH risperidone, 97% for aripiprazole, 99% for dehydroaripiprazole, and 91% for pipamperone.

Conclusions

Our Deming regression and sensitivity analysis demonstrate that DBS is a valid alternative for conventional venous sampling. However, this is the first study in which Bland Altman plots are added to the interpretation of DBS and plasma level comparison for antipsychotics. As can be seen, the deviation is quite large and more patients might be needed to yield a smaller variance in bias.