Analytical challenges in dried blood spot and plasma sampling for therapeutic drug monitoring of antiepileptic drugs

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Antiepileptic drugs need to be monitored individually by therapeutic drug monitoring to find the balance between efficacy and adverse reactions. Carbamazepine, lamotrigine and valproic acid, are antiepileptics commonly used in monotherapy or in combination in treatment of epilepsy in children and adults.

Carbamazepine, lamotrigine and valproic acid

An LC-MS/MS multi-method for three antiepileptics in dried blood spot matrix was developed. The method is currently used in a clinical study to evaluate the possibility of using home sampling in therapeutic drug monitoring.

Results
Calibration curves were linear in the range 0.16-50 µg/mL for carbamazepine and lamotrigine and 5-300 µg/mL for valproic acid.

Valproic acid, detected in negative mode, showed low sensitivity due to high background noise on different instruments. On Waters, Xevo sensitivity was increased although the baseline was high (Fig. 1).

There were no useful quantifiable fragments for valproic acid and subsequently it had to be run in pseudo ms/ms-mode.

Results for valproic acid indicated that the impact of hematocrit on blood spot sampling volume was marginal in a normal hematocrit range (30-50%) (Fig 2), while DBS concentrations versus plasma concentrations were more affected by difference in hematocrit, due to the low blood-plasma ratio of valproic acid (0.64) (Fig 3).

Dried blood spots as matrix for therapeutic drug monitoring may require different therapeutic range due to analyte blood-plasma ratio. Although there are analytical challenges, dried blood spots have shown a great potential for home sampling in therapeutic drug monitoring.

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