Symposium

[S-14] S-14: Dried blood spot analysis: Are we ready for implementation?

Chairs: Christophe Stove, Belgium / Hiroyuki Yasui, Japan
Wed. Sep 27, 2017 10:30 AM - 12:00 PM Main Hall (1F)

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[S-14-3] Development of a liquid chromatography tandem mass spectrometric method for quantification of mycophenolic acid and its glucuronides in dried blood spot samples

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Keywords: dried blood spot, LC/ESI-MS/MS, mycophenolic acid, therapeutic drug monitoring

Background

Personalized immunosuppressive therapy, including accurate drug dosing based on drug blood level, leads to better clinical outcomes, specifically in regard to avoidance of drug-induced adverse effects and maintenance of efficacy. Mycophenolic acid (MPA) is used as an immunosuppressant in transplantation of various solid organs. Dried blood spot (DBS) sampling is a microsampling technique which has several advantages; easy sample corrections by the patients themselves, minimal invasiveness, and small blood volume. These characteristics are favorable for patients and therefore suitable for therapeutic drug monitoring of MPA. The aim of this study was to develop a method for quantification of MPA and its metabolites, mycophenolic acid 7-O-glucuronide (MPAG) and mycophenolic acid acyl glucuronide (AcMPAG), in DBS samples, using liquid chromatography/electrospray ionization tandem mass spectrometry (LC/ESI-MS/MS).

Methods

For sample preparation, a microwave-drying approach was used to deactivate enzymes and reduce drying time. Blood volume was calculated in a DBS disk of 3-mm diameter. Surrogate matrix calibration curves were evaluated. Concentrations of analytes in plasma from patients receiving mycophenolate mofetil were compared to DBS samples after hematocrit correction.

Results

The method yielded good recoveries of MPA, MPAG, and AcMPAG (90.3–104.2%). Blood volume in the disk was calculated as 3.0 ±0.2 L. Linearity over concentration ranges of 0.1–30 g/mL (MPA), 0.1–200 g/mL (MPAG), and 0.125–10 g/mL (AcMPAG) were obtained with r20.999. Slope and quantitative values did not differ significantly between the authentic calibration curve and surrogate matrix calibration curves. Intra-day and inter-day variation were less than 14.6%, and accuracy was within ±11.9%. Good correlations were obtained between plasma concentrations and DBS concentrations after hematocrit correction.

Conclusions

We developed and validated an LC/ESI-MS/MS method for analysis of MPA in DBS samples. The method is

useful for monitoring MPA blood level.