Poster

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

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[P26-2-6] Simultaneous quantification of perampanel and nine newer antiepileptic drugs in human serum using ultra performance liquid chromatography mass spectrometry detection

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Background

Recently, novel antiepileptic drugs including perampanel have been used in clinical situation. For routine therapeutic drug monitoring of newer antiepileptic drugs, simultaneous method using ultra performance liquid chromatography with mass spectrometry (UPLC-MS) was developed in order to quantify serum concentration of clobazam, N-desmethylclobazam, gabapentin, lacosamide, lamotrigine, levetiracetam, perampanel, rufinamide, topiramate and zonisamide.

Methods

A serum aliquot was deproteinized by addition methanol which contained roscovitine as an internal standard. After centrifugation, supernatant was diluted with water and was injected onto the ACQUITY UPLC System (Waters). The separation was conducted on a ACQUITY UPLC BEH C18 Column (Waters) with a gradient mobile phase of 10mM ammonium acetate containing 0.1% formic acid and methanol with a flow rate of 0.4 mL/min and a total runtime of 9.5 min. Antiepileptic drugs and the internal standard were detected with ACQUITY QDa Detector (Waters) using positive ion electrospray ionization. In order to compare between the described UPLC-MS method and currently used methods, the serum concentration of clinical samples was measured by both methods for clobazam, N-desmethylclobazam, lamotrigine, levetiracetam, topiramate and zonisamide, respectively.

Results

All antiepileptic drugs and the internal standard were detected and quantified without endogenous interferences. The calibration curves were linear over the therapeutic range of concentrations, and the determination coefficient (R^2) of all calibration curves was more than 0.99. The accuracy of intra- and inter-assay at the lower limit of quantification samples was within ±20%, and the accuracy of intra- and inter-assay at the other quality control samples were within ±15%. The precision of intra- and the inter-assay was less than 15%. Mean recoveries ranged from 86.1% to 97.7% and coefficients of variations of the matrix factor value were less than 15%. No carryover was detected in a blank sample injected after the highest standard sample. A good correlation between the developed UPLC-MS method and routinely used method was observed for all tested drugs.

Conclusions

The method described here was suitable for routine therapeutic drug monitoring of newer antiepileptic drugs.