Symposium

[S-12] S-12: TDM for central nervous system drugs

Chairs: Kiyofumi Yamada, Japan / Philip Nicholaou Patsalos, UK

Tue. Sep 26, 2017 10:30 AM - 12:00 PM Room E (1F)

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[S-12-2] Validation of a high-throughput method for the quantitation of Pregabalin in plasma using ultra-fast SPE-MS/MS

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Background

Pregabalin (Lyrica) is an anticonvulsant used to treat partial seizures in patients and is a more potent successor to gabapentin. It is also commonly used in the treatment of neuropathic pain and fibromyalgia. Quantitation of pregabalin in serum can be used by physicians to assess compliance and may be clinically useful in patients with renal failure. Therapeutic and toxic ranges are not well defined; however, therapeutic concentrations have been reported to be from 2-5 mcg/mL, while toxicity may occur at concentrations greater than 10 g/mL. We present a rapid method for the quantification of pregabalin in plasma using an Ultra-fast SPE-MS/MS.

Methods

Calibration standards, quality controls, and patient samples (50l) are mixed with 200 L internal standard (0.4 g/mL pregabalin-$^{13}C_3$ in acetonitrile). Precipitated proteins are removed by centrifugation and the supernatant is further diluted with mobile phase 1 (10 mM ammonium acetate, 0.1% formic acid, and 0.01% TFA in water), and 10 L is injected. Sample analysis was performed at a rate of less than 10 seconds per sample using a Rapidfire 365 system coupled to an Agilent 6495 MS/MS using electrospray ionization in positive ion mode. Concentrations were calculated based on a five point linear standard curve weighted $1/x^2$ curve fit.

Results

The assay was linear from 0.1 - 25.0 g/mL with a limit of detection of 0.01 g/mL. The average (n=5) linear regression demonstrated the following: slope= 0.9949; r^2= 0.9972; and intercept= -0.0719. With-in (n=20) and between-run (n=20) precision CVs were less than or equal to 10% across the analytical range. Absence of interferences from the top 25 prescribed drugs or common drugs of abuse was observed. Minimal ion suppression or enhancement due to the matrix effect was observed. No significant carryover was seen following a sample containing 50 g/mL. 35 patient samples were cross validated with a reference method, and the linear regression demonstrated the following: slope= 0.9299; r^2= 0.9775; and intercept= 0.0349.

Conclusions

An accurate and precise method to quantitate pregabalin in plasma with Ultra-fast SPE-MS/MS and cycle times <10 seconds per sample was developed.