Introduction

Background: Gabapentin concentrations in serum can be used as an aid in the therapeutic management of patients treated with gabapentin (Gabapentin Withdrawal). Placebos are anti-epileptic drugs indicated as adjunctive therapy in the treatment of partial seizures, and without secondary generalization, in patients over 12 years of age with epilepsy. The assay is also indicated as adjunctive therapy in the treatment of partial seizures in pediatric patients 2-12 years. It is also indicated for the management of postherpetic neuralgia in adults. Overall, in patients under therapeutic doses, serum gabapentin concentrations occur mostly in the order of 2.0-10 µg/mL. Neurontin is mostly in the order of 2-20 µg/mL (P.N. Patsalos et al. 2008. Epilepsia 49:1239-1276).

Methods

The ARK Gabapentin assay is a homogeneous enzyme immunoassay for quantifying gabapentin in human serum or plasma. The assay was evaluated on the Roche/Hitachi 917 automated clinical chemistry analyzer. The ARK Gabapentin Assay was calibrated using a six point calibration curve (0 to 40 µg/mL) where increasing reaction rate observed. Correlation studies were performed using CLSI/NCCLS Protocol EP9-A2. Results from the ARK Gabapentin Assay on the Roche/Hitachi 917 system were compared with results from LC-MS/MS. Gabapentin concentrations by LC-MS/MS ranged 1.0 to 39.0 µg/mL. ARK gabapentin values were supplemented with known limited amounts of gabapentin and assayed 40 times (5 runs, 8 days). Mean percent recovery: 100.9 ± 7.6 % (range 98.5% to 103.7%), and the average percentage recovery was 100.9 ± 7.6 % (98.5% to 103.7%). The amount of gabapentin observed was within 10% of the nominal values from 2.0 to 40.0 µg/mL. Limit of Quantitation (LOQ) of the ARK Gabapentin Assay was 0.07 µg/mL (2.5 µg/mL), 4.0% CV (8.0 µg/mL), and 6.3% CV (20.0 µg/mL). Limit of Quantitation was evaluated according to CLSI/NCCLS EP17-A. Pooled human serum controls of gabapentin were supplemented with known limited amounts of gabapentin and assayed 40 times (5 runs, 8 days). Mean determinations of gabapentin, standard deviation (SD) for within-run, between-run and coefficients of variation (%CV) were calculated. Full calibration, the ARK Gabapentin Calibrators (0.00, 1.50, 4.00, 10.00, 20.00, and 40.00 µg/mL) were calibrated using a full calibration (6-point) procedure. To perform a precision study, a target concentration and the percentage recovery was calculated. The amount of gabapentin recovered from nominal ranged from 98.5% to 103.7%, and the average percentage recovery was 100.9 ± 7.6 % (98.5% to 103.7%). The amount of gabapentin observed was within 10% of the nominal values from 2.0 to 40.0 µg/mL. Method comparison of Gabapentin Assay, along with a serum control of gabapentin. Measurement of gabapentin resulted in 95.8% recovery in the presence of interfering substances in the concentrations used.

Precision

Precision was determined as described in CLSI/NELSON Protocol EP1-A2. In level control and three patient pools containing gabapentin were assayed for 30 days. Mean determinations of gabapentin, standard deviation (SD) for within-run, between-run and coefficients of variation (%CV) were calculated. Full precision assays ranged from 0.96 to 7.05% at all levels tested.

Endogenous Interference

Interference studies were conducted using CLSI/NELSON Protocol EP1-A2 as a guideline. Clinically high concentrations of the following potentially interfering substances in serum with known levels of gabapentin (approximately 2 and 20 µg/mL) were evaluated. Each sample was assayed using the ARK Gabapentin Assay, along with a serum control of gabapentin. Measurement of gabapentin resulted in 95.8% recovery in the presence of interfering substances in the concentrations used.

Specificity

A high concentration of each compound was spiked into normal human serum with known levels of gabapentin (approximately 2 and 20 µg/mL) and assayed along with a serum control of gabapentin. Measurement of gabapentin resulted in 95.8% recovery in the presence of interfering compounds at the levels tested. The following compounds did not interfere with the measurement of gabapentin at the levels tested:

- Acetylsalicylic acid
- Acetazolamide
- Acidic amino acids (L-Tryptophan, L-Lysine)
- Aminoglycosides (Gentamicin, Neomycin
- Angiotensin I and II
- Beta-lactam antibiotics (Piperacillin, Benzylpenicillin)
- Beta-lactamase inhibitors (Clavulanic acid, Sulbactam)
- Biguanides (Metformin, Phenformin)
- Blood urea nitrogen
- L-glutamine
- L-lysine
- L-threonine
- Lithium carbonate
- L-tyrosine
- Mannitol
- Methicillin
- Mesalazine
- Methotrexate
- Penicillin V
- Phenytoin
- Prednisone
- Ranitidine
- Theophylline
- Uric Acid
- Zonisamide

Conclusions

Performance of the ARK Gabapentin Assay was demonstrated on the Roche Hitachi 917 system. Performance of the assay showed good precision, accuracy, specificity and linearity with excellent correlation to CLSI EP9-A2. The ARK Gabapentin reagents, calibrators and controls are provided in liquid form ready-to-use.

INTENDED USE

The ARK Gabapentin Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of gabapentin in human serum or plasma on automated clinical chemistry analyzers. Gabapentin concentrations can be used as an aid in the management of patients treated with gabapentin.

ASSAY RANGE

The range of the assay is 0.05 to 40.0 µg/mL. Report results below the range as 0.05 µg/mL. The ARK Gabapentin Assay is intended for use in the detection of gabapentin in plasma or serum in the range of 0.05 to 40.0 µg/mL. Use the analyzer-specific upper LOQ established in your laboratory.

Regulatory Status - USA

FDA cleared under 510(k) guidance.

ARK Gabapentin Assay - Healthcare Controls

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<th>Compound</th>
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