Poster

[P25-4] P25-4: Anti-infective drugs (4): Vancomycin

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[P25-4-9] HPLC method for determination of vancomycin in cerebrospinal fluid

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Backround

Vancomycin as a large glycopeptide compound used to treat a number of bacterial infections. Penetration of vancomycin into the cerebrospinal fluid (CSF) could be different. The CSF levels achieved by intrathecal administrations are variable, and therapeutic drug levels in the CSF should be monitored. Objective of this study was to evaluate a new HPLC metod for determination of vancomycin and its crystaline degradation products in cerebrospinal fluid in patients with infectious meningitis.

Methods

We developed a new HPLC method with UV detection for the determination of vancomycin and 2 isomers, CDP-1-M (major) and CDP-1-m (minor). The separation was accomplished on a Zorbax SB-Aq, 250x4.6 mm, 5 m column at 21 ˚C. The mobile phase components A and B consisted of phosphate buffer-acetonitrile-methanol (91:5:4, v/v/v) and buffer-acetonitrile-methanol (84:8:8, v/v/v) respectively. Separation were accomplished using the gradinet conditions. The detection was performed at 210 nm. 20 μl of internal standard (cefazolin) was added to 200 μl of CSF, and solid phase extraction was used (Sep-Pak, 500 mg, Waters). We measured patient samples from 6 patients with infectious meningitis at intervals 0.25,0.5,1,3,5,8,12,24,48, 48.5, 49 hours.

Results

A linear relationship between CSF concentration and peak area was obtained for all three substances with correlation coefficient r^2=0.99995 for vancomycin and r^2=0.99995 for CDP-1-M and r^2=0.99994 for CDP-1-m. The intra and interday accuracy and precision were evaluated on two QC samples by multiple analysis and coefficients of variation were less than 6.7%. Mean recoveries of the corresponding compounds were between 100.2% and 102%. Limit of quantification was found at 0.39 mg/L for vancomycin, 0.10 mg/L for CDP-1-M and 0.11 mg/L for CDP-1-m. Each patient with infectious meningitis received 20 mg of vancomycin per day by intrathecal administration. The maximum average concentration of vancomycin was reached during the first 15 minutes (727.6 ±208.8 mg/L), than the gradual decrease of vancomycin active form during 24 hours was observed up to 13.7 ±15.2 mg/L. CDP-1-M and CDP-1-m were not detected.

Conclusions

We evaluated and validated a new HPLC method for determination of vancomycin in CSF.

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