Poster

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

Chair: Noboru Okamura, Japan

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[P25-4-8] Therapeutic drug monitoring of vancomycin based on an HPLC method

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Background

Vancomycin, the first-line antibiotic for the management of MRSA infection, should be routinely monitored to maintain the concentration within the range of 10-20 g/ml. This study was performed to develop an HPLC method for determination of vancomycin in human plasma and apply this method to clinical therapeutic monitoring of vancomycin.

Methods

HPLC separation of vancomycin was successfully achieved using a Shimadzu ®INERSIL ODS C_{18} reversed phase column (250 mm ×4.6 mm, i.d.; 5 m) heated at 30 ºC under an isocratic mobile phase consisting of acetonitrile: 0.05 M potassium dihydrogen phosphate at pH 3.33 (9:91, v/v) and ultra-violet detection was set at 280 nm. Extraction of vancomycin was completed using 35 % perchloric acid plus acetonitrile, followed by adding a neutralizing agent (1.4 g K_2CO_3 and 0.65 g KCL dissolved in 5 ml deionized water) to improve the stability and quality of sample for analysis and extend column life. The method was validated according to the guideline published by FDA and in comparison with FPIA method. This validated method was applied to therapeutic drug monitoring (TDM) of vancomycin.

Results

The developed method, without requirement of internal standard, was highly selective with few interferences in the clinical TDM of vancomycin. Good linearities (r^2 >0.99) were achieved for the concentration range of 5–100 g/mL with the detection limit of 5 g/mL. The intra- and inter-day inaccuracies and imprecisions were less than 10 % with extraction recoveries of more than 95 %. The stability studies, including working solution stability (4 ºC, 60 d), whole blood stability (room temperature and 4 ºC, 6 h and 24 h), Freeze and Thaw Stability(-70 ºC, three cycles), bench-top stability (room temperature, 6 h), short-term stability (4 ºC, 7 d) and long-term stability (-70 ºC, 90 d), were completed and met the requirements of guideline. The correlation between this HPLC method and FPIA was y (FPIA) = 0.8624x (HPLC) + 2.154, r = 0.938. We applied this method to monitor the vancomycin concentrations in the samples from 19 patients and conduct individualized drug administration. Although the dosage regimen was either 1 g Q12 h or 0.5 g Q12 h, the patients aged over 60 years old had slightly higher concentrations (14.02±4.42 g/mL) than the patients aged between 18 and 60 years old (11.37±5.26 g/mL), suggesting elder patients should be carefully monitored when administered vancomycin. Furthermore, gender had a significant impact on the trough concentrations of vancomycin (16.97 ±2.51 *vs* 10.32 ±3.31 g/ml, $P<0.05$).

Conclusions

We have successfully developed and validated an economical, simple, stable and selective HPLC method to

perform TDM of vancomycin. This method has been successfully used to monitor the vancomycin concentrations of patients. However, more factors should be considered and more efforts paid to realize individualized administration of vancomycin.