Analysis of Pharmacokinetic parameters for assessement of dextromethorphan metabolic phenotype

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Abstract

In this study, the metabolic ratios of dextromethorphan to dextrorphan (DM/DX) in plasma were calculated at steady state after administering 2 dosage forms (Medicon) and Detusiv) of DM with different release rates. The urinary metabolic ratio for each subject was also determined based on the total drug concentration in the urine. An analysis of pharmacokinetic parameters for determining the DM metabolic phenotype was conducted. Results demonstrate that double logarithmic correlations between the metabolic ratios based on pharmacokinetic parameters of either AUC(0-tau,ss), C(max,ss), C(min,ss), or C(ave,ss) for Medicon and Detusiv and the urinary metabolic ratios were all significant. Probit plots of the metabolic ratios based on these pharmacokinetic parameters revealed 2 clusters of distribution, representing extensive and intermediate metabolizers. An antimode of 2.0 for total drug based on these pharmacokinetic parameters was determined and correspondingly referred to an antimode of 0.02 for the urinary metabolic ratio to delineate extensive and intermediate metabolizers. This model was also verified to be appropriate when using total plasma concentrations of DM and DX at any time during the period of the dosing interval at steady state to calculate the metabolic ratio for identifying extensive and intermediate metabolizers. Therefore, the metabolic ratio based on the pharmacokinetic parameters of either AUC(0-tau,ss), C(max,ss), C(min,ss), or C(ave,ss) and plasma concentrations of DM and DX in a single blood sample at steady state are proposed as an alternative way to identify phenotypes of CYP2D6.