Population pharmacokinetic model of methotrexate in Korean population

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Objectives: Methotrexate is a drug for treatment of cancers and autoimmune diseases. To our knowledge, population pharmacokinetic (PK) models have been built in Chinese and Western populations but there was no such model in Koreans. Our study aims to develop a population PK model of methotrexate in Korean population.

Methods: PK data were acquired from electronic medical records in Severance Hospital from 2005 January to 2016 January. Data obtained later than 120 hr post-dose, obtained from intrathecal injection, or without duration information were excluded. A total of 191 patients and 2,112 samples were used for the analysis. Patients had diseases including leukemia, lymphoma and etc. Weight was incorporated into PK model parameters using theory-based allometry and inter-occasional variability was also allowed. Model building was carried out using NONMEM ver 7.3.

Results: Two compartment model with first order elimination was chosen for the basic structural model, yielding parameter estimates of 270.6L for central volume of distribution (Vc), 104.6L for peripheral volume of distribution (Vp), 35.29L/hr for clearance (CL) and 1.463L/hr for intercompartmental clearance (Q). The inter-individual variability (CV%) of CL was 30.6% and the inter-occasional variabilities (CV%) were 169.5% in Vc, 301% in Vp, 163.9% in CL and 337.6% in Q. The residual error was chosen to be proportional error, with CV of 45.5%. The model adequately described the time course of observed concentrations.

Conclusions: In this work, we presented a basic structural model of methotrexate PK in Korean population. In next analysis, parameter-covariate relationships will be incorporated into the model.