Population Pharmacokinetic of Carbamazepine in Iranian Epileptic and Manic Patients.

A.H. Mohammadpour(1), S. Rezaee(2), S. Sadray(3), P. Ghaeli(4**)**

(1)Department of Pharmacodynamy and Toxicology ,School of Pharmacy, Mashad University of Medical Science, ,Mashad, Iran (2).Department of Pharmaceutics, Ahwaz Univerity of Medical Science, Ahwaz, Iran. (3)Department of Pharmaceutics, Tehran Univerity of Medical Science, Tehran, Iran (4)Department of Pharmacotherapy, Tehran Univerity of Medical Science, Tehran, Iran

Objectives: The aim of the present study was to develop a population pharmacokinetic model of carbamazepine from routine therapeutic drug monitoring data

Methods: Steady-state carbamazepine plasma concentrations in 126 epileptic and manic patients determined by HPLC method. Non-linear mixed effect method was used to construct population pharmacokinetic model of carbamazepine using WinNonMix software. After deriving the base model, influence of various covariates upon pharmacokinetic parameters of carbamazepine were assessed. Age, total body weight, sex, creatinine clearance, carbamazepine dosage, disease and concurrent medication were the fixed effects (covariates) tested simultaneously for their influence on the carbamazepine clearance in the regression model

Results:A one-compartment model was fitted to the data using nonlinear mixed effects modeling.In initial screening of covariate model, we found that carbamazepine clearance were significantly more in manic patients than in epileptic subjects (0.128 ± 0.016 L/kg/hr vs 0.112 ± 0.0147 L/kg/hr, P<0.00l). The only covariate which had significant influence on pharmacokinetics of carbamazepine in this population was the type of disorder; finally, this covariate entered in final model according to the following equation. CI = 0.099 [1+ (0.149 ± Disease)].The corresponding interindividual variability in clearance was described by using an exponential' .model and the residual error (including intraindividual variability, model misspecification and assay error) was described by using a simple model. The ω2 and σ2 values in final model were 0.0147 and 0.02 respectively. The carbamazepine clearance value in was 0.104 ± 0.001 L/kg/hr.

Conclusions: The model can be used for estimation of carbamazepine CL/F in individual patients in the postautoinduction phase and for selection of optimum dosing regimen in routine patient care.