Poster

[P27-9] P27-9: Pharmacokinetics and PK/PD
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[P27-9-4] Population pharmacokinetics of arginine glutamate in healthy Chinese volunteers

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Background
The pharmacokinetic (PK) properties of the combined using of arginine and glutamine is not well understood. The aim of this study was to develop population pharmacokinetic (PPK) models of arginine and glutamatein in healthy Chinese volunteers after intravenous injection and evaluate the variability among different individuals and the influence of individual factors on the PK of arginine and glutamate.

Methods
Plasma concentration data and demographic characteristics were collected from 24 healthy Chinese volunteers. Subjects were administered arginine glutamate in a single dose of 10 g or 20 g, or multiple doses of 20 g once a day for 4 days. Plasma concentrations of arginine and glutamate were quantified using a validated HPLC-MS/MS method. Two nonlinear mixed-effect models were developed using NONMEM$^{®}$ software to describe the pharmacokinetic properties of arginine and glutamate and assess the relevant parameters as well as the inter- and intra-individual variability. The potential covariates were screened using stepwise approach and the stability and predictive capability of the models were performed using bootstrap and visual predictive check.

Results :
The concentration time curve of arginine and glutamate are best described by a first-order elimination two-compartment model and a nonlinear elimination one-compartment model, respectively. For the former model, the final estimation of total clearance (CL) for male and female, the apparent distribution volume of central compartment (V1), the inter-compartmental clearance (Q) and the apparent distribution volume of peripheral compartment (V2) are 50.7 L/h, 38.8 L/h, 20.9 L, 23.4 L/h, 42.3 L, respectively. For the latter model, the final estimation of maximum rate of elimination (Vmax), concentration at 50% Vmax (Km), the apparent distribution volume (V) for low dose and high dose are 18.8 mg/h, 77.2 mg/L, 23.1 L, 36.3 L, respectively.

Conclusions
Two nonlinear mixed-effect models were developed for arginine and glutamate in healthy Chinese volunteers. For arginine, males have significantly higher total clearance than females, the increasing in creatinine level significantly increases inter-compartmental clearance, the gain in weight weight significantly increases apparent distribution volume of peripheral compartment. For glutamate, subjects received high dose (20g) have significantly higher apparent distribution volume compared to the those received low dose

(10g).