INTRODUCTION

Protein-energy undernutrition (PEU) can seriously compromise the outcomes of other pathologies since pathophysiological derangements in patients with PEU have a profound impact on absorption, protein binding, metabolism and elimination of drugs.

The aim of this study was to perform a PK modelling to describe the behavior of taurine in well-nourished rats and analyze the influence of PEU on the PK parameters of taurine in undernourished rats.

RESULTS AND DISCUSSION

At the end of the adaptation period, all animals in PEU group were classified as light (19%), green (47%), light (6%) or severe (34%), undernourished depending on weight and albumin levels. 100% of WN animals were classified as well-nourished.

A two-compartment population pharmacokinetic model with zero order endogenous formation, passive absorption, first order kinetics distribution and nonlinear elimination with parallel Michaelis-Menten excretion and reabsorption processes best described taurine pharmacokinetics. When models were scaled for malnutrition, undernutrition acted as covariate reducing the Vmax of the active elimination process. Goodness of fit plots (GOFPP) showed reasonable good results.

In conclusion, the selected two-compartment model was statistically selected and the model accounted for 91% of the variability in the taurine plasma concentrations.

**Internal validation: VPC**

- The VPC of the selected model showed a good agreement between measured and predicted plasma concentrations of taurine.
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**MATHEMATICAL AND METHODS**

Wistar rats were randomly distributed in two groups: WN (well-nourished) and UN (undernourished) and were fed with different diets for 23-26 days. During this time, weight was recorded daily and serum albumin was registered weekly.

After this time, nutritional status was assessed and taurine was administered intravenously (IV) or orally (PO) to WN and UN rats at different doses: 1, 10, and 100 mg (N=68). Plasma samples were collected for taurine and analyzed by HPLC.

Population pharmacokinetic modelling was performed using nonlinear mixed effects software (NONMEM 7.0) with FO estimation. Several distribution and absorption models were explored in combination with dose and/or time covariate effects. Covariates such as nutritional status, serum albumin, body weight and score of undernutrition were used.

**CONCLUSIONS**

- Data analysis showed linear absorption and distribution, and non-linear elimination processes for taurine. Elimination of taurine was reduced 10% in undernourished animals, suggesting that the reabsorption process via the secretion transporter was modified in this group.
- PK modelling provides a useful tool to describe the levels of taurine and offers a robust method to understand the changes in PK occurred in undernourishment.

**REFERENCES**