POPULATION PHARMACOKINETICS OF ACETAMINOPHEN IN ACUTE OVERDOSED PATIENTS

TO DERIVE A NEW RISK METRIC FOR ANTIDOTE ADMINISTRATION

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**Background & Objective**

Interpretation of acetaminophen (APAP) plasma concentrations is the standard risk-stratification method used to determine the risk of hepatotoxicity in acute acetaminophen overdose and the need for the administration of the antidote.

The purpose of this study is to examine whether a better metric, such as time of maximum plasma APAP concentration (PAC) or area under the curve, can be used as tools to identify those at greatest risk of liver injury in whom antidotal therapy is required using population pharmacokinetic modeling.

Specific objectives of this presentation:
- To explore the acute overdosed patients data
- To develop a population pharmacokinetic (PK) model of APAP in acute overdosed patients.

**Methods**

- Data from Maryland Poison Center
  - 561 patients
  - Acute APAP overdose
  - Between 2 and 6 PAC
  - 7 Product Categories
  - Some dose information missing

- Exploration of data by product categories

- PK Model with APAP only data
  - Structural PK Model
  - Between-Subject Random Effects
  - Residual Error Terms

- PK Models by Product Categories

- PK Model all data
  - Base PK Model

- Adequacy of Structural and Residual error model was determined with goodness of fit plots

- Observations and Predicted Concentration vs Time for 3 Patients

**Results**

- Dose available 39%

**Discussion/Conclusions**

- Exploratory plots of dose normalized concentration profile by product showed no major trend between products.
- For the PK model build by product the parameter estimates were similar between each other. Thus all data were modeled together.
- The parameter estimates are similar to that reported for therapeutic levels.
- The base model adequately predict the individual concentrations.
- The model still need to be improved by evaluation of covariates, before to be used to identify a better metric to determine should and when an antidote be administered.

**References**

2. McNeil’s background package on acetaminophen