

Population pharmacokinetics of intravenous albuterol in children with status asthmaticus

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Objectives

To develop a pop-PK model of R-albuterol and S-albuterol for children suffering from status asthmaticus following continuous intravenous administration.

Methods

- 19 children at ICU included treated with iv albuterol based on clinical symptoms (0.1-10 µg/kg/min).
- Blood samples analysed for R- and S-albuterol using a validated LC/MS-MS method.
- Pop-PK analysis of log-transformed data using NONMEM 7.2 and FOCE with interaction.
- Covariates tested: bodyweight (7.8-70 kg), age (0.8-15.3 years), creatinine concentration (17-10 µmol/L), alanine transaminase (5-29 IU/L), urea (1.6-4.8 mmol/L).

Results

- High doses caused by inhalation of albuterol in combination with fingerprick sampling were removed, resulting in 111 samples.
- 2-compartment model with separated clearance for R- and S-albuterol (fig. 1, table I).
- Start concentration (mainly due to inhalation) was estimated for each patient.
- Allometric scaling for bodyweight (BW):

$$CL = CL_{70\text{ kg}} \times (BW/70)^{\text{exp}}$$

$$\text{exp} = 0.75 \text{ for clearance (CL) and intercompartmental clearance (Q) and } \text{exp} = 1 \text{ for the central (Vc) and peripheral (Vp) volumes of distribution.}$$
- No other significant covariates.
- Goodness-of-fit plots and NPDE are presented for R- and S-albuterol (fig. 2 and 3).

Conclusion

The pop-PK model of R- and S-albuterol has been developed. This model can be used to evaluate the correlation between PK parameters and effect using a pop-PK/PD model.

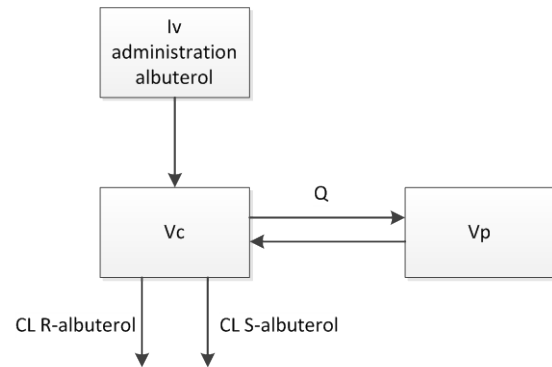


Figure 1: Compartments of the final model

Parameter	Estimation	IPV (%)
CL R-albuterol	16.3 L/h	41.8
CL S-albuterol	8.8 L/h	36.7
Vc	12.9 L	280
Vp	45.2 L	
Q	20.0 L/h	
Residual error	0.351	

Table I: Parameter estimations and interpatient variability (IPV)

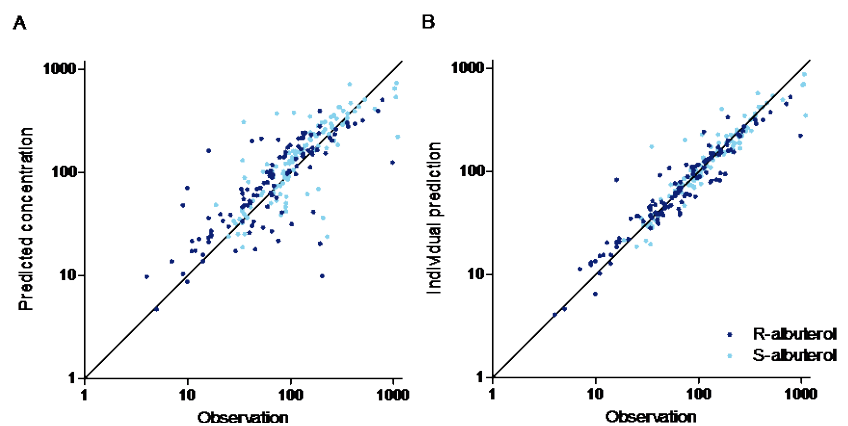


Figure 2: Observed vs predicted concentrations (A) and individual predictions (B)

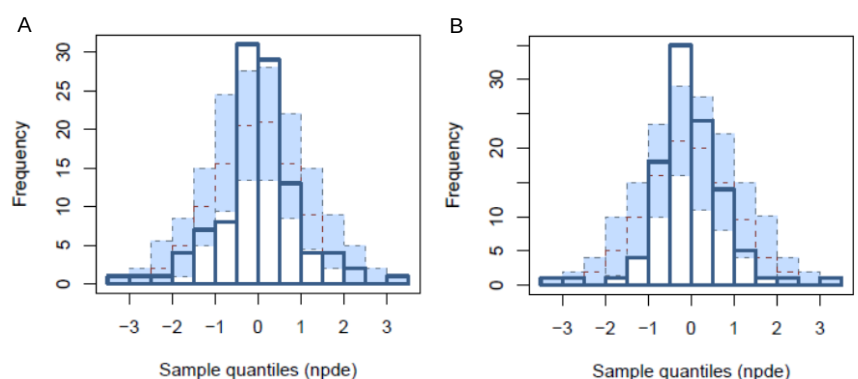


Figure 3: Normalised prediction distribution errors for R- (A) and S-albuterol (B)