Pharmacokinetics of intravenously administered and inhaled tobramycin and salbutamol in exhaled breath condensate

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Introduction

- Exhaled breath condensate (EBC) is a matrix from which compounds in expired air can potentially be measured
- EBC may be a promising technique to quantify the drug target concentrations in the lung
- The accuracy and sensitivity of EBC measurements on pharmacologicals has never been determined

Aim

Quantify the pharmacokinetic (PK) profile of salbutamol and tobramycin in exhaled breath condensate after intravenous or inhaled administration.

Methods

- An open-label, 4-way crossover study in 12 healthy male volunteers with the following doses:
  - Tobramycin 1 µg/kg I.V. in 30 minutes;
  - Tobramycin 170 mg inhalation;
  - Salbutamol 250/500 µg I.V. in 1-10 minutes; and,
  - Salbutamol 400 µg inhalation.
- 5 min EBC measurements were performed over a period of 7 (i.v. occasion) to 12 (inhalation occasion) hours after dosing.
- Samples were analysed on a LC-MS/MS system.

Results

- Tobramycin and salbutamol PK can be detected in EBC (**Fig. 1**).
- High levels of intra- and inter-individual variability in the EBC PK but not in the plasma PK (**Fig. 1 & 2**).
- Majority of EBC observations were < LLOD (**Fig. 3**) .
- No EBC concentrations after I.V. infusion were > LLOD.

Conclusions

- The application of EBC for the quantification of the pharmacokinetic profiles of drugs in the lung is possible but currently limited by the high variability.
- No environmental conditions have yet been identified that may be an explanatory variable for the intra-individual variability in the EBC observations in the current study.

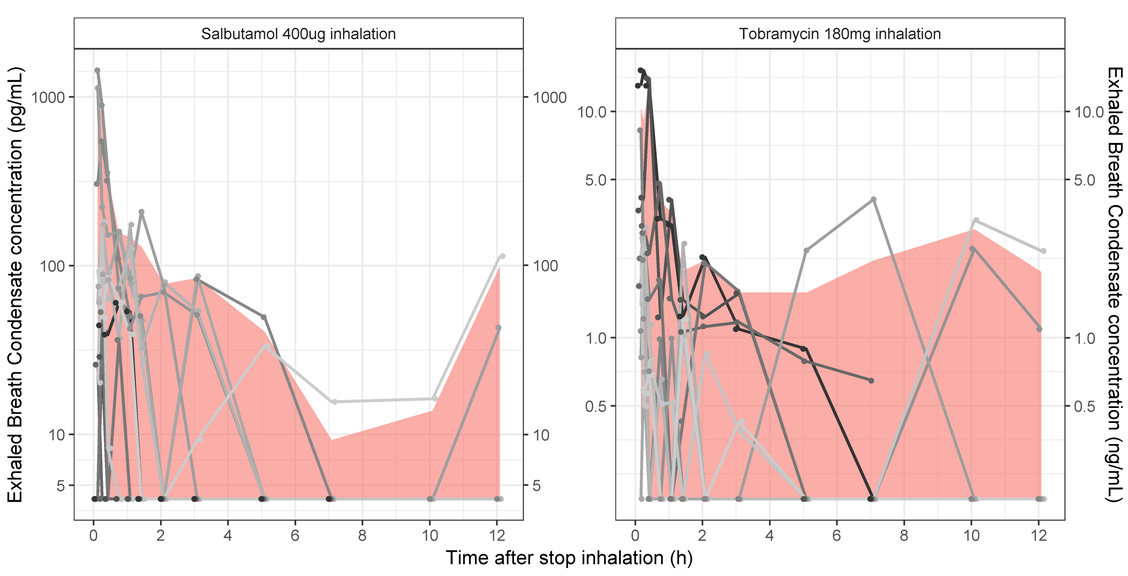

***Figure 1**: Pharmacokinetics of salbutamol and tobramycin in EBC after inhalation. Observations within the same individual are connected by lines. Red ribbon indicates 90% confidence interval of the observations. Data < LLOD were fixed to /2 the LLOD.*

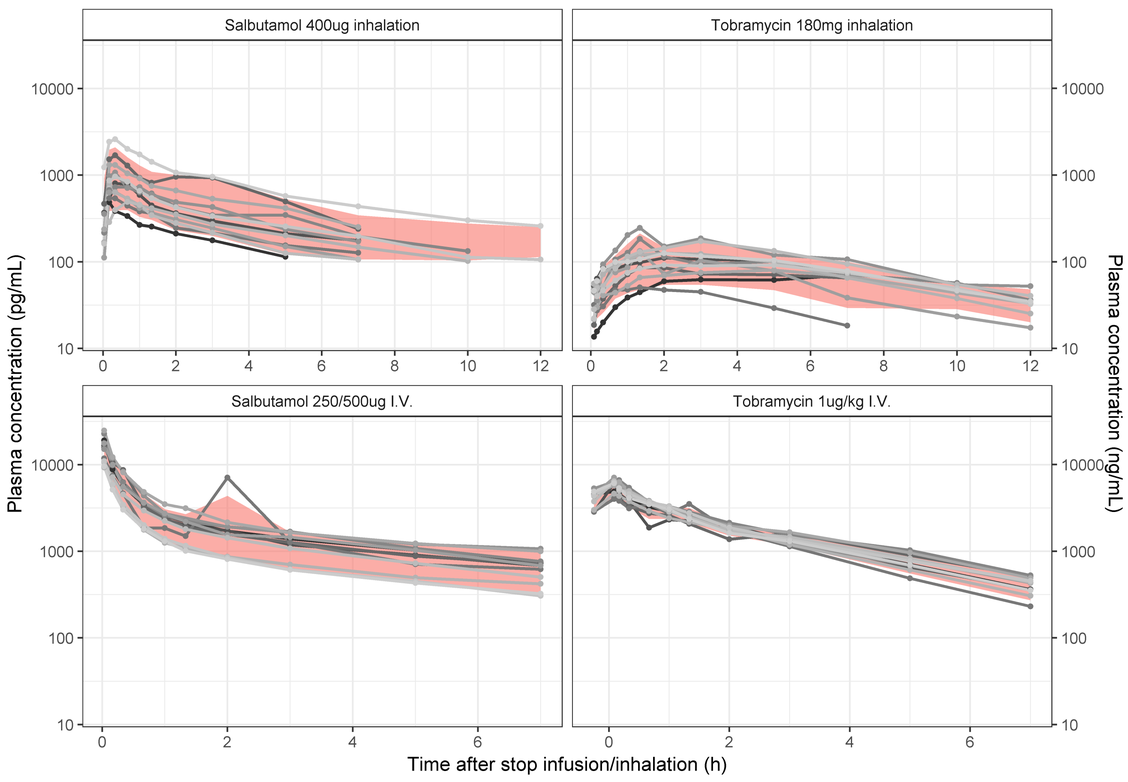

***Figure 2**: Pharmacokinetics of salbutamol and tobramycin in plasma after inhalation or I.V. administration. Observations within the same individual are connected by lines. Red ribbon indicates 90% confidence interval of the observations*

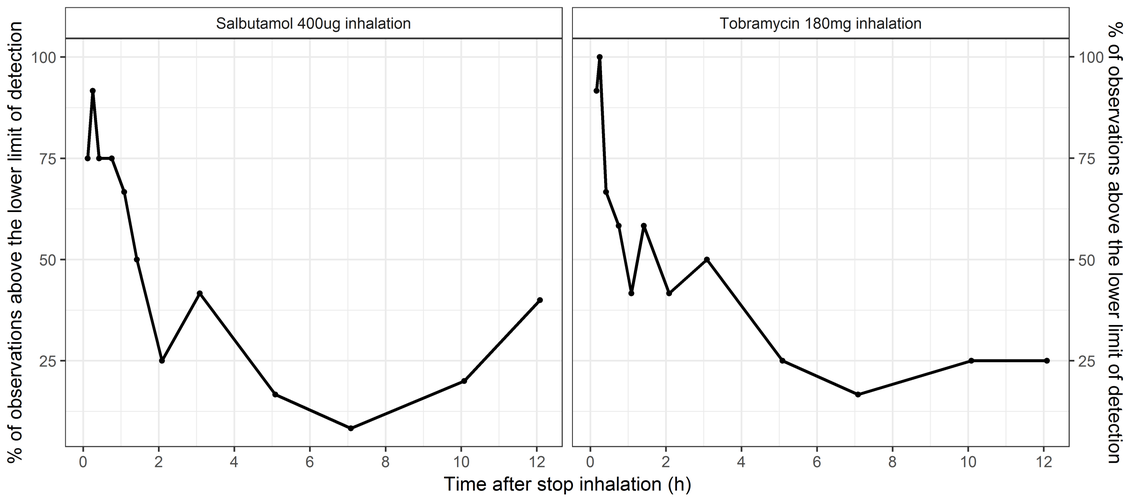

***Figure 3**: Percentage of observations in exhaled breath condensate below the lower limit of detection (LLOD) after inhalation of salbutamol or tobramycin*

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