

MEETING ABSTRACT

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# Characterization of colistin tissue pharmacokinetics by microdialysis

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## Background

Colistin is an important antimicrobial treatment option against multidrug-resistant Gram-negative bacteria. However, colistin is a large and chemically complex molecule and information on its ability to penetrate into tissues remains sparse. Thus, the present work investigated the ability of microdialysis ( $\mu$ D) to assess pharmacokinetics (PK) of colistin in the interstitium of soft tissues, i.e. at a potential site of infection.

## Methods

*In vitro*: Colistin recovery for linear CMA 66  $\mu$ D probes with a molecular weight cut-off of 100 kDa was assessed through forward and reverse  $\mu$ D for different colistin concentrations. *In vivo*: Three male healthy volunteers received a single intravenous dose of 2.5 million international units of the inactive prodrug colistin methanesulfonate. Colistin concentrations in plasma and in  $\mu$ D samples obtained from two probes inserted into subcutaneous adipose tissue of the thigh were determined. Retrodialysis was used for probe calibration. In both settings,  $\mu$ D was performed with and without addition of albumin to perfusion solutions and colistin was quantified by liquid chromatography/tandem mass spectrometry (LC-MS/MS).

## Results

*In vitro*, colistin recovery was constant over time and showed mean recovery values of  $52 \pm 3$  and  $71 \pm 8\%$  for forward and reverse  $\mu$ D, respectively. *In vivo*, recovery of colistin was  $43 \pm 15\%$ . In both settings, colistin recovery was not improved by addition of albumin to  $\mu$ D perfusion solutions. Due to small volumes, reliable quantification of

colistin was not possible in some  $\mu$ D samples, yet maximum concentrations in adipose tissue were relatively high ( $0.76 \pm 0.21 \mu\text{g/mL}$ ) compared with those in plasma ( $1.2 \pm 0.43 \mu\text{g/mL}$ ) attesting for extra-vascular distribution.

## Conclusions

The present data demonstrate the feasibility of  $\mu$ D for evaluation of colistin tissue pharmacokinetics and show opportunities for optimization of experimental setting.

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