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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 (μD) 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 μD probes with a molecular weight cut-off of 100 kDa was assessed through forward and reverse μD 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 μD samples obtained from two probes inserted into subcutaneous adipose tissue of the thigh were determined. Retrodialysis was used for probe calibration. In both settings, μD 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 ± 3 and 71 ± 8% for forward and reverse μD, respectively. *In vivo*, recovery of colistin was 43 ± 15%. In both settings, colistin recovery was not improved by addition of albumin to μD perfusion solutions. Due to small volumes, reliable quantification of colistin was not possible in some μD samples, yet maximum concentrations in adipose tissue were relatively high (0.76 ± 0.21 μg/mL) compared with those in plasma (1.2 ± 0.43 μg/mL) attesting for extra-vascular distribution.

Conclusions

The present data demonstrate the feasibility of μD for evaluation of colistin tissue pharmacokinetics and show opportunities for optimization of experimental setting.

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