Poster

# [P25-5] P25-5: Anti-infective drugs (5)

Chair: Paula Schaiquevich, Argentina

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## [P25-5-4] Pharmacokinetics of intrathecal administration of vancomycin in patients with infectious meningitis

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### Background

*Gram-positive* bacteria, mostly *Staphylococcus spp.,* cause the majority of meningitis cases in neurosurgery. Because of poor blood-brain barrier permeability, intrathecal administration of vancomycin is becoming common. The vancomycin cerebrospinal fluid (CSF) “trough” concentration 15-20 mg/l and $AUC_{0-24}$/MIC 400 have proven as good treatment success predictors. This study describes pharmacokinetics of combined intravenous and intrathecal vancomycin in context of interpatient variability, risk of neurotoxicity and reliability to achieve recommended target.

### Patients and methods:

CSF and plasma vancomycin concentration were determined by validated HPLC assay with UV detection. Six patients with staphylococcal meningitis (4 females, 2 males), median age 53 (±10 years), weight 70 (±21.3 kg) and GFR 100 (±59.4 ml/min) received 20 mg of intrathecal vancomycin every 24h. Five patients concomitantly used 2g of intravenous vancomycin administered as continual infusion. CSF samples were obtained by lumbar or ventricular drainage at 0, 0.25, 0.5, 1, 3, 5, 8, 12, 24h after the first dose, before the third (48h) and 0.5 and 1h after (48.5, 49h). Plasma vancomycin concentrations were collected 24h after beginning of continuous infusion. Vancomycin concentration/time profile data were used to calculate PK/PD target and individual pharmacokinetic parameters.

### Results

The CSF peak concentration at 0.25h was 727 (±208.8 mg/L) and decreased to 7.8 (±15.2 mg/L) at 24h. $C_{min}$ before the third dose was 10.0 (±11.4 mg/l). Four of six patients (67%) did not attain CSF target trough vancomycin concentration (15-20 mg/l) neither before second nor third dose. The median $AUC_{0-24h}$ was 1911.3 (±603.5 mg*h/L) and T1/2 was 3.9 (±1.5h). Microbiological liquor sterility time ranged from 24h to 120h after the first intrathecal application. MICs for six isolated staphylococci were between 0.5 -1.5 mg/l. Median vancomycin plasma concentrations 24h after starting of continual infusion were 12.1 (± 4.4 mg/l). An increased risk of neurotoxicity wasn’t observed.

### Conclusions

Results suggest that to achieve the desired PK/PD objectives and reduce CSF sterility time, 10 mg of intrathecal vancomycin every 12h would be optimal. However, larger samples are required to reach definitive conclusions. Therapeutic drug monitoring is essential to maintain target CSF levels.

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