THERAPEUTIC DRUG MONITORING OF GENTAMICIN AFTER **PRE-DIALYSIS ADMINISTRATION**

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Background and importance

Due to the increase of multidrug-resistant Gram-negative bacteria, aminoglycoside therapy is frequently essential, and its management is especially problematic in dialysis patients.

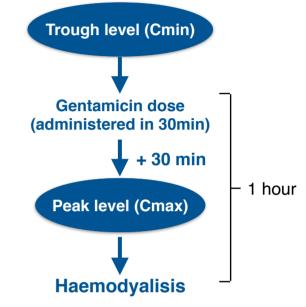
Aim and objective

To calculate the mean gentamicin dose required to optimise pharmacokinetic/pharmacodynamic (PK/PD) parameters in intermittent haemodialysis patients to determine an initial dosing protocol.

Material and methods

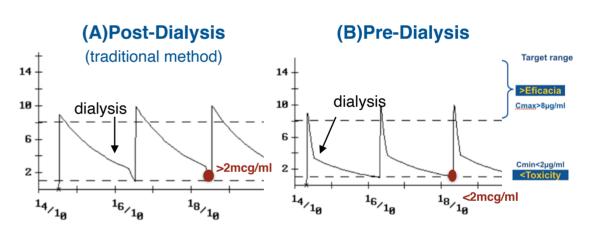
Retrospective observational study (January 2009-April 2020), including patients treated with gentamicin on a 4-hour haemodialysis programme 3 times per week.

Gentamicin concentration was analysed by chemiluminescence(CMIA). The estimation of kinetic parameters was performed by Bayesian methods with a single-compartment population model implemented in the Abbottbase-Pharmacokinetic System. Dialysis was introduced into the model as a disposition factor that increases drug clearance only during the 4 hours of dialysis. Data were evaluated using chi-square test. Significance was designated at p<0.05.

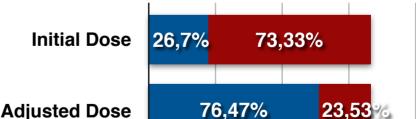


Results

Population	19 patients
Median age	66 (45-80) years
Median weight	67,89 (44-89) Kg
Haematocrit	29,6% (22-38%)
Dialysers	9 FX80 7 FX10 3 other dialysers
Mean Filtration Rate	2200ml/h
Treatment duration	17 (4-47) days
Initial mean dose	2.35±0.52mg/kg
Vd	0.33±0.1L/kg
inter dialysis Cl	0.46±0.16 L/h
t _{1/2}	33.65±17.29 h



Drug concentration-time profiles of individual patients administered gentamicin (A) post dialysis dosing or (B) 1 hour before hemodialysis.





Adjusted Dose



Klebsiella pneumoniae (KPC)

- SSTI
- UTI
- Bacteriaemia
- Pneumoniae
- Endocarditis

0 60 90 120 30 Optimal levels (Cmin<2mcg/ml; Cmax>8mcg/ml)

Non-optimal levels

Conclusions

To optimise the PK/PD parameters of gentamicin in patients undergoing haemodialysis, an initial dose of **2.5mg/kg one hour** pre-dialysis is proposed, without the need for loading doses.

Reference

O'Shea S. et al. "Aminoglycosides in Hemodialysis Patients: Is the Current Practice of Post Dialysis Dosing Appropriate?". Editorials (2009). Teigen MMB. et al. Dosing of Gentamicin in Patients With End-Stage Renal Disease Receiving Hemodialysis". Journal of Clinical Pharmacology, 2006;46:1259-1267 (2006).