INTRODUCTION & BACKGROUND

Aminoglycoside Dosing
- Pharmacokinetic (PK) literature in intermittent hemodialysis (IHD) is outdated - current practice employs more efficient IHD modalities.
- Efficacy is obtained by maximizing the peak serum concentration (C_{max}) to minimum inhibitory concentration (MIC) ratio.
- Toxicity (nephrotoxicity) is thought to be related to body exposure as measured by the area under the serum concentration versus time curve (AUC).

Nontuberculous mycobacterium (NTM)
- Amikacin is one of the most active parenteral agents against Gram-negative bacilli and NTM isolates, including multidrug-resistant NTM.
- ATS/IDSA guidelines recommend targeting peak levels in the low-20 mg/L range[3].
- Current amikacin dosing recommendations for IHD patients (3.5 mg/kg given 30-60 minutes at the end of IHD) is unlikely to obtain target peak levels for serious infections including NTM, and may even lead to relatively high AUCs and toxicity.

Optimizing Pharmacokinetic/Pharmacodynamic (PK/PD) Principles
- Augmented dosing strategies (“high-dose” or “once daily”) emphasize optimizing PK/PD and show similar, or less nephrotoxicity.
- Goal: to maximize efficacy and minimize toxicity.
- Renal dysfunction patients were excluded from these studies.

Experts have suggested that the ideal time to administer aminoglycosides in IHD patients is before the start of each IHD session. However, high-dose pre-IHD aminoglycoside dosing is uncommon since literature (clinical, PK/PD) supporting this practice is lacking.

METHODS

Dosing: Amikacin 7mg/kg (rounded to nearest 50mg) was administered 4 hours before start of IHD dissolved in 100 mL D5W or NS, infused over 30 mins.

Hemodialysis: IHD filter used in patients was Fx3000 Hellenic ( Fresenius Medical Care). Blood flow rate = 250-300 ml/min; Dialyate flow rate = 500 ml/min; Ultrafiltration coefficient (UFR) = 75.

Therapeutic Drug Monitoring: amikacin levels were drawn as follows:
- 4 pre-IHD (C_{pre-IHD} “pre-IHD”)
- post-IHD (C_{post-IHD} “post-IHimports”)
- pre-dose administration, pre-IHD (C_{pre-IHD} “true trough”)
- pharmacokinetic analysis assumed one compartment, linear kinetics

CONCLUSION

- Administration of pre-IHD IV amikacin at 7mg/kg achieved guideline-recommended C_{max} levels in two cases of NTM peritonitis.
- Amikacin clearance with current IHD modalities was much more efficient than prior reports, while high-dose, pre-IHD dosing strategy successfully improved pharmacokinetic parameters (allowing high C_{max} while decreasing overall amikacin exposure on non-IHD days).
- We suggest consideration of pre-IHD IV amikacin to optimize PK/PD for IHD patients who require high-dose therapy for serious infections.