Aminoglycoside prescribing advice for Cardiff and Vale NHS Trust Nephrology and Transplant Directorate

This guidance has been developed by pharmacy, microbiology and nephrology, predominantly in response to clinical incidents related to gentamicin for haemodialysis patients. It is also relevant for other aminoglycosides, such as amikacin, and aminoglycoside prescribing for other renal patients.

Haemodialysis patients
Avoid aminoglycosides
Peritoneal Dialysis patients
Avoid aminoglycosides
Chronic Kidney Disease (CKD) Stage 5, Stage 4 (eGFR <30ml/min) or progressive Stage 3 (eGFR 60-30ml/min), Renal Transplant and Acute Renal Failure patients
Avoid aminoglycosides or prescribe with extreme caution

Rationale: General considerations

High risk of nephrotoxicity causing:
Loss of residual renal function in dialysis patients (especially important in peritoneal dialysis)
Progression of CKD or acute on CKD
Damage to renal transplant
Delayed recovery from acute renal failure
High risk of ototoxicity
Even when prescribed optimally, there is a high risk of toxicity, excessive dosing or even sub-therapeutic dosing:
Aminoglycosides have virtually 100% excretion in the urine as unchanged drug
Aminoglycoside clearance approximates to creatinine clearance so these agents accumulate in renal impairment (eg dialysis patients have eGFR of <10ml/min for drug dosing purposes)
Aminoglycoside dosing is complicated by considerable inter- and intra-patient variability in drug pharmacokinetics (for example related to patient's fluid status and the drug volume of distribution)
Aminoglycoside dosing in renal impairment results in high and prolonged trough drug levels increasing risk of toxicity (particularly in anuric patients)
Aminoglycoside dosing in renal impairment results in low peak drug levels which reduces efficacy
Therapeutic Drug Monitoring is logistically extremely difficult and prone to errors and confusion, particularly for haemodialysis patients

Rationale: Specific considerations by renal patient group

Haemodialysis patients
Unlikely to have sufficient residual renal function to excrete significant aminoglycoside between haemodialysis sessions so drug levels remain elevated
Haemodialysis does remove a significant amount of aminoglycoside from the circulation but there is no data as yet to accurately quantify this effect with haemodialysis using high flux membranes
Following haemodialysis drug levels increase as the drug redistributes from tissues (rebound effect)
Drug levels therefore should only be taken around 2 hours after haemodialysis as this is the only time that patient may have a suitable trough level to interpret
Drug levels must be interpreted before further doses are prescribed
Peritoneal Dialysis patients
Peritoneal dialysis does not remove a significant amount of aminoglycoside from the circulation
Intraperitoneal aminoglycosides are absorbed systemically so the same prescribing advice applies
Chronic Kidney Disease (CKD) Stage 5, Stage 4(eGFR <30ml/min) or progressive Stage 3 (eGFR 60-30ml/min), Renal Transplant and Acute Renal Failure patients
Prescribing aminoglycosides is particularly difficult in patients with unstable renal function

Exceptions

One off, small doses (eg gentamicin 80mg or 2mg/kg) are acceptable as prophylaxis pre surgical procedure if required
Haemodialysis line locks containing gentamicin are acceptable
Multiple doses only prescribed under strict microbiology recommendation dictated by culture and sensitivities (not as empirical cover, eg for neutropenic fever)
Seek advice from microbiology on alternative antibiotics
If multiple doses indicated:
- Stop aminoglycoside if patient exhibits signs of nephrotoxicity or ototoxicity
- Keep course length to a minimum to reduce cumulative toxicity risk

Therapeutic Drug Monitoring

If a course of an aminoglycoside is indicated, then timing of monitoring and target drug levels should be in line with recommendations for once daily aminoglycoside dosing regimens:
- ⁎Trough (pre-dose) levels indicate toxicity risk so must guide dosing
- ⁎Peak (approx 1 hour post dose) levels are not required

For example:
- ⁎Gentamicin trough levels should be < 1mg/L
- ⁎Amikacin trough levels should be < 5mg/L

Earlier and more frequent monitoring compared to non-renal patients:
- Seek advice from renal pharmacist
- Check first trough level at 24 hours post first dose and await levels before prescribing subsequent doses
- Daily trough levels usually required and further doses only prescribed once the levels have been appropriately interpreted

For haemodialysis patients, monitoring must tie in with dialysis sessions and requires advice from renal pharmacist (see above)
Specific dosing advice is not provided in this guidance as it is important to individualise the dose regimen for a renal patient - seek advice from a renal pharmacist

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