The Leeds Teaching Hospitals NHS
NHS Trust

Amikacin Therapeutic Drug Monitoring

Interpretive notes – antibiotic assays Version 2, February 2009.

These notes are not a comprehensive review of the subject and should only be used as a guide to decision making. If discussion is desired, please contact the duty microbiologist

General response to an assay result

- **Does this patient still need to be on antibiotic(s)?**
- **If yes: are they currently on the most appropriate one(s)?**
- **Can they be switched to a suitable alternative: eg a narrower spectrum / less toxic &/or an oral agent?**
- **If this agent is still indicated: how does this specific result influence patient management?**
- **Was the assay taken at an appropriate time in relation to the dose?**
- **Is the level in the desired therapeutic range – or too low or too high?**
- **What dosing adjustment, if any, is required?**
- **Is there any evidence of toxicity?**

The answer to these questions may be assisted by the information given below.

Amikacin

Preferred assay(s):

- For multi-dose therapeutic regimens: Take a trough level prior to administering the dose, then take a further level at **one hour** post-dose

Normal range:

- For multi-dose therapeutic regimens: Pre-dose <10 mg/l; post-dose 20-30 mg/l

Dose by slow intravenous injection or infusion (as recommended in the BNF):

- For multi-dose therapeutic regimens in adults: 15mg/kg daily in two divided doses, increasing to 22.5mg/kg daily in three divided doses in severe infections; maximum 1.5g daily for up to 10 days (max. cumulative dose 15g).
- For multi-dose therapeutic regimens in children: 15mg/kg daily in two divided doses.
- For multi-dose therapeutic regimens in neonates: 10mg/kg loading dose then 15mg/kg daily in two divided doses.

Target organisms:

- Multi-resistant gram-negative bacilli, such as coliforms and *Pseudomonas aeruginosa* (notably if resistant to gentamicin / tobramycin)
- Multi-drug-resistant *Mycobacterium tuberculosis* (MDR TB) and some atypical mycobacteria e.g. *M. abscessus*

Therapeutic issues:

- Amikacin works most effectively the higher the concentration of the drug exceeds the MIC of the target organism: the higher the peak, the greater the bactericidal activity.
- Amikacin MICs for susceptible coliforms and *P. aeruginosa* are usually less than 8mg/l. Therefore achieving a peak between 20-30mg/l will be significantly in excess of this.

Toxicity issues:

- Like gentamicin, amikacin is nephrotoxic (increased creatinine) and ototoxic (deafness and vestibulitis). See gentamicin section for further details.

Specific response to an amikacin assay result:

Always interpret the result in the light of the patient's clinical condition and available culture and sensitivity results.

- Trough level in the normal range:
    - Ensure the patient is responding clinically. Please discuss with the duty microbiologist if further guidance required on a case-by-case basis.

- Trough level too high:
    - Check when the assay was taken in relation to the amikacin dose – high levels can result from levels being taken shortly after a dose (i.e. they are not true trough levels).

- Check where the blood sample was taken from – falsely high levels can be obtained from samples taken from the same line that the drug was given through.
- Check the patient's renal function. An increase in trough level may coincide with decreased creatinine clearance.
- If the high trough level appears genuine, consider reducing the dose frequency (and the total dose). Final action dependent on post-dose level also.

- Post-dose level in the normal range:

  - Ensure the patient is responding clinically. Please discuss with the duty microbiologist if further guidance required on a case-by-case basis.

- Post-dose level too high:

  - Check when the assay was taken in relation to the amikacin dose – high levels can result from being taken too soon after a dose (i.e. they are not true one-hour post-dose levels).
  - Check where the blood sample was taken from – falsely high levels can be obtained from samples taken from the same line that the drug was given through.
  - Check the patient's renal function. An increase in post-dose level may coincide with decreased creatinine clearance.
  - If the high post-dose level appears genuine, consider reducing the dose (and the dose frequency). Final action dependent on trough level also.

- Post-dose level too low:

  - Check to ensure that previous dose(s) have been given as prescribed
  - If the low post-dose level appears genuine, consider increasing the dose and/or the dose frequency if clinically appropriate. Final action dependent on trough level also.

Frequency of testing:

- For multi-dose regimens levels should normally be checked around one of the 3rd, 4th or 5th doses after commencement. This should also be the case after any dose adjustment.
- In patients with satisfactory clinical response and stable renal function, retesting should not need to be any more frequent than twice-weekly.
- In patients with unstable renal function and/or uncertain clinical response, testing may be more frequent.