Gentamicin Prescribing

*With Dr Kate Clezy, Infectious Diseases Physician at Prince of Wales Hospital*

**Introduction**
This podcast aims to cover the basics of gentamicin prescribing.

**Case** - You are a JMO working in orthopedics. A 75 year old female develops urosepsis post-operatively and you are considering prescribing some ampicillin and gentamicin. You have checked that she is not allergic to gentamicin.

1. **What additional information would you like to obtain from the history and examination?**
   - Whether the patient is taking any other nephrotoxins
   - Past or family history of adverse effects from aminoglycoside use, such as ototoxicity

2. **What is the mechanism of action of aminoglycosides?**
   - Aminoglycosides are bactericidal antibiotics that inhibit protein synthesis through binding to the 30s subunit of the ribosome of the bacteria. This leads to the incorrect insertion of amino acids into the peptide chain, and if the peptide chain is in the cell membrane, it no longer functions correctly and the cells will not divide properly, ultimately resulting in the death of organism.

3. **How do you give gentamicin, parenterally or orally?**
   - It is usually given parenterally
   - It can be given intramuscularly
   - It can be nebulised in cystic fibrosis patients with pseudomonas bronchiectasis
   - It can be given orally, for local effects on the gut

4. **What is gentamicin’s spectrum of action?**
   - It works very well against gram negatives organisms and pseudomonas
   - Therefore, gentamicin is good for gut related conditions and urinary tract related infections
   - For example, *E coli, Proteus, Klebsiella pneumoniae*

5. **What investigation/s would you perform before giving gentamicin?**
   - It is important to know the creatinine clearance which can be calculated from the serum creatinine
   - In this case, it would also be important to do blood cultures before commencing the patient on antibiotic therapy

6. **What factors are used to determine the dose of gentamicin?**
   - The initial dose is 4-7mg/kg of the ideal body weight
   - In patients who are septic, usually a higher dose (7mg/kg) is given due to the altered volume distribution
• Other groups that require dosing adjustment includes patients on renal placement therapy, and patients with ascites or burns. It would also be advisable in these groups to seek the opinion of a pharmacist
• Patients with creatinine clearance of less than 40ml/min and over the age of 80 should be dosed with caution, and have their renal function monitored closely

7. Where should gentamicin be charted in the medication chart?
• The variable dosing section of the medication chart so that the team will regularly review the indication for dosing

8. Is there a particular time of the day that the gentamicin should be charted?
• If it is empirical therapy, as in this case, the patient will usually receive 3 doses (0, 24, 48hrs) or for a maximum of 48 hours. The time of dosing would not matter as you will not have to test the level
• With directed therapy however, the trough level of gentamicin needs to be monitored. The gentamicin should be charted so that the trough level coincides with the time of routine blood collection

9. Why are gentamicin and ampicillin used in combination in patient’s with urosepsis?
• Gentamicin provides cover for most of the gram negative bacteria but ampicillin broadens the coverage to gram positive organisms. The two drugs also work synergistically to combat enterococcus

10. What are the adverse effects associated with gentamicin?
• Ototoxicity
  o Can present with hearing loss, tinnitus, or vestibular toxicity
  o Affects 1% of patient
  o Rate of complication is unpredictable, but generally more common with cumulative dosing
• Nephrotoxicity
  o More common with cumulative dosing
  o Causes proximal tubule damage which is reversible if detected early
  o The rate of toxicity is not related to trough level
• Neuromuscular blockade leading to respiratory depression

11. What are the risk factors that predispose patients to developing side effects from gentamicin?
• Familial toxicity secondary to gentamicin use
• Pre-existing tinnitus, significant hearing loss, or vestibular dysfunction (because it may worsen their pre-existing condition and it is difficult to determine the magnitude of contribution of gentamicin to their adverse effect)
• Concurrent nephrotoxic drugs
• Recent anaesthesia

12. What other drugs or medical condition contraindicate the use of gentamicin?
• Neuromuscular blockades, such as suxamethonium. Gentamicin can potentiate the action of these drugs and enhance neuromuscular blockade
• Magnesium sulfate → neuromuscular blockade
• Nephrotoxins → additive toxicity to the kidneys
• Myasthenia Gravis
13. **What are the advantages of using gentamicin over ceftriaxone?**
   - It is rapidly bactericidal
   - There is lower rates of resistance for urinary pathogens
   - It is associated with a low rate of Clostridium difficile
   - Gives a broader cover of urinary organisms, and also covers pseudomonas which ceftriaxone does not

14. **What other drugs or condition contraindicate the use of gentamicin?**
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   - Magnesium sulfate $\rightarrow$ neuromuscular blockade
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   - Myasthenia Gravis

15. **At what time should gentamicin levels be taken?**
   - Empirical dosing does not require monitoring serum gentamicin level
   - Depends on the condition and dosing schedule
   - Should consult the hospital pharmacist

16. **What should a junior doctor do if the level returns elevated?**
   - Seek senior advice

**Take home messages**
   - Gentamicin is an excellent drug for the treatment of gram negative sepsis
   - It needs to be dosed according to the patient’s ideal body weight
   - If patient is dosed for over 48 hours, please ask senior clinician and pharmacist for advice regarding monitoring