Once Daily Gentamicin: Administration and Monitoring in Adults

September 2018

Gloucestershire Hospitals NHS Foundation Trust
Objective:
Policy for the administration and monitoring of once-daily gentamicin at Gloucestershire Hospitals NHS Foundation Trust (GHNHSFT).

Background/policy statement:
Gentamicin is the aminoglycoside of choice at GHNHSFT due to its lower cost and suitability for most infections requiring treatment with an aminoglycoside. Tobramycin and amikacin are normally reserved for treatment of infections that require treatment with an aminoglycoside antibiotic where the causative organism is resistant to gentamicin, or on the advice of a Consultant Microbiologist, or specialist physician (eg Respiratory Consultant). Tobramycin is the preferred aminoglycoside for treatment of respiratory tract Pseudomonas species infections.

Aminoglycoside antibiotics such as gentamicin must be administered parenterally as they are poorly absorbed from the GI tract. In general, once-daily administration is now recommended in most clinical situations. Once daily gentamicin is:

- As effective as multiple dosing regimes
- Less toxic (less nephrotoxicity & ototoxicity)
- More convenient to administer and monitor
- More economical

The usual maximum duration for a course of once daily gentamicin is one week.

The policy is for the use of gentamicin for the treatment of infection only. Guidance on gentamicin dosing and use for surgical prophylaxis can be found in individual surgical prophylaxis guidelines on the GHNHSFT Intranet Antimicrobial Resources pages.

Cautions and contraindications:
The guidance does not apply to gentamicin use in the following:

- synergistic treatment of endocarditis (where some treatment regimens use twice daily or thrice daily dosing) or Staphylococcal bone infection
- patients treated in Renal units or receiving haemodialysis or haemofiltration
- major burns (>20% total body surface area)
- ascites
- age < 16 years
- cystic fibrosis (where higher doses of aminoglycosides are normally required)
- Gentamicin should not be used in:
  
- Myeloma patients
- Myasthenia gravis
- Patients allergic (hypersensitive) to gentamicin
Cautions:

Cautions to gentamicin therapy:

- Patients with decompensated liver disease - aminoglycosides are associated with an increased risk of renal failure.
- Concurrent administration of neurotoxic and / or nephrotoxic agents increases the risk of gentamicin toxicity. Review therapy and consider amending or withholding nephrotoxic drugs during gentamicin treatment. Avoid co-administration with the following where possible:
  - neuromuscular blockers
  - other potentially nephrotoxic (e.g. NSAIDs and ACE Inhibitors) or ototoxic drugs
  - potent diuretics
  - other aminoglycosides

This list is not exhaustive – consult the Summary of Product Characteristics (eSPC) for a full list (www.medicines.org.uk)

- Chronic Kidney Disease (CKD) Stage 4 or more, known or suspected acute kidney injury (AKI) in the previous 48 hours (50% increase in baseline serum creatinine or oliguria > 6 hours). If gentamicin is clinically indicated, give one dose as per guidance and check with ward pharmacist or senior clinician before giving a second dose. Gentamicin should be used with caution in patients with renal impairment. See page 6 for dosage recommendations in renal impairment.

- Patients with auditory or vestibular dysfunction. Ototoxicity secondary to gentamicin is independent of drug concentration. It is suggested by any of the following: new tinnitus, dizziness, poor balance, hearing loss or oscillating vision. Toxicity is associated with prolonged aminoglycoside use (usually > 10 days but may be > 72 hours) and is secondary to drug accumulation within the inner ear. Stop treatment if ototoxicity is suspected and refer to microbiologist or antimicrobial pharmacist for advice on alternative therapy. If gentamicin continues for >7 days, consider referring to Audiology for assessment
Dosage:

Give 3-5mg/kg* (3mg in patients >65 years of age) once daily as an intravenous infusion in 100mls of dextrose 5% or sodium chloride 0.9% over 60 minutes. Round dose up or down to the nearest 40mg.

*Use ideal body weight (IBW) rather than actual body weight (ABW) because gentamicin distributes poorly in fat. For obese patients (BMI >30 or >120% of ideal body weight) it is recommended that the dose is calculated using the patient’s obese dosing body weight (ODBW):

Obese dosing body weight (ODBW) = IBW + 0.4 (ABW - IBW)

To calculate ideal body weight, use the following equation:

Ideal body weight (Male) = 50kg + (2.3kg x height in inches over 5 feet)
Ideal body weight (Female) = 45.5kg + (2.3kg x height in inches over 5 feet)

When to give the dose

The first dose of gentamicin may be given at any time of day (i.e. as soon as the first dose is needed).

Subsequent doses should be moved to a time that is convenient for both the patient (i.e. not overnight) and the Chemical Pathology Department for the purposes of monitoring gentamicin levels (i.e. no samples for gentamicin levels should be sent for testing between 11pm and 6am).

Evening dosing is preferred. To facilitate this, the second dose may be given 18 to 36 hours after the first dose provided that the first gentamicin level is within the recommended range (see monitoring/interpretation below) and the patient’s renal function has not changed significantly.

Monitoring:

A post-dose level is required. A single serum sample should be obtained 12 to 18 hours after the dose and sent to CHEMICAL PATHOLOGY. As there is flexibility about the timing of the sampling a time which is convenient for the patient and the laboratory should be chosen.

Samples should not be collected or sent for testing between 11pm and 6am.

Blood sample forms must include the following information:

- Date and time of last dose
- Date and time of blood sample taken
- Dose or dose per kg used (e.g. 5mg/kg)
- Dosing regimen (e.g. daily dosing)

Target serum concentration for once-daily gentamicin:

12 hours post dose = <2mg/L
18 hours post dose = <1mg/L
Interpretation:

Take gentamicin level 12-18 hours after the first dose. Plot the result of the gentamicin level on the graph below to decide if the level is safe (recommended range), intermediate or potentially toxic.

![Graph of Gentamicin levels](image)

**Safe:** If the serum gentamicin level is ≤ 2mg/l after 12 hours and ≤1mg/l after 18 hours it is safe to give the next dose on time (same dose).

**Intermediate:** If the level falls in the intermediate area a dose reduction needs to be made, this reduced dose can be given when the next dose is due. Dose reduction to a new dose will be required as per this equation:

\[
\text{New Dose} = \frac{\text{Previous daily dose} \times \text{Target serum value}}{\text{Actual serum level}}
\]

Serum gentamicin levels should be rechecked 12 to 18 hours after the new revised dose has been administered.

**Potentially toxic:** Omit the next dose if the level is in the potentially toxic area. Consider whether it is safe to continue ongoing gentamicin in the near future or whether alternative antibiotic treatment (specifically for Gram negative cover) is required. Discuss with Microbiology if necessary.

If gentamicin levels are within the recommended range with normal renal function then monitor levels and U&Es twice weekly.

Caution must be used when using this graph to interpret levels taken from patients with renal dysfunction, as their concentration-time-curve may be different.
Dose adjustment for impaired renal function

Cockroft-Gault equation for estimating creatinine clearance:

\[
\text{Creatinine Clearance (GFR)} = \frac{(140 - \text{Age}) \times \text{Weight (Kg)} \times F}{\text{Serum Creatinine (µmol/litre)}}
\]

Where F = 1.23 (For Men)  
1.04 (For Women)

Dose adjustment recommendations:

<table>
<thead>
<tr>
<th>GFR (ml/min)</th>
<th>Dose</th>
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<tbody>
<tr>
<td>30-70</td>
<td>3-5mg/kg once-daily</td>
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<tr>
<td>10-30</td>
<td>2-3mg/kg once-daily</td>
</tr>
<tr>
<td>5-10</td>
<td>2mg/kg every 48 to 72 hours according to levels</td>
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Always keep in mind that the potential nephrotoxicity of gentamicin may worsen residual renal function.

NB  
Please note that the maximum dose in patients >65 years of age, regardless of renal function, is 3mg/kg.

For further advice or clarification please contact:

<table>
<thead>
<tr>
<th>Microbiology:</th>
<th>CGH ext. 4430</th>
<th>GRH ext. 5054</th>
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<tr>
<td>Medicines Information:</td>
<td>CGH ext. 3030</td>
<td>GRH ext. 6108</td>
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Selected References:

**Authorisation** | **Name and Position** | **Date Approved** |
--- | --- | --- |
Responsible Authors | Delyth Ahearne  
Antimicrobial Pharmacist  
Dr Robert Jackson  
Consultant Microbiologist | 26<sup>th</sup> September 2018 |
Policy Sponsor | Dr. Alan Lees  
Consultant Microbiologist  
Lead Consultant for Antimicrobial Stewardship | |
Assured by | Trust Policy Group | |

**Consideration at authorised groups (e.g. Board, Board sub committees, Policy Group, Clinical policies Sub Group, Departmental meetings etc)**

| Name of Group | Minute details | Date considered |
--- | --- | --- |
Antimicrobial Stewardship Committee Antibiotic Policy Review Sub-group |  | 26<sup>th</sup> September 2018 |