GENTAMICIN

01. Assay Details

CH Labs Test Reference Guide

02. Therapeutic Range

1. A 24-hour AUC of 70-100 mg/L.hr if using the target-AUC method (100 mg/L.hr if severe infection)
2. A 24-hour trough concentration of <0.5 mg/L if the AUC method not available

How well established:

Results from early studies in serious Gram-negative infections suggested that when using 6-12 hourly dosing, peak and trough concentrations should be 6-10 mg/L and <2 mg/L respectively. In the 1990's, evidence became available from animal and human studies that once-daily is generally preferable to multiple daily administration. Over 30 clinical studies and at least 9 meta-analyses have now shown that once-daily administration is more effective than multiple-daily dosing and results in less nephrotoxicity. There is no significant difference in incidence of ototoxicity. Methodology for monitoring concentrations with once-daily administration is debated. In Christchurch, a target 24-hour area-under-the-concentration-time-curve (AUC) method has been developed as above with a target range of 70-100 mg/L.hr which is the AUC range expected with doses of 5-7 mg/kg/day in patients with normal renal function and average population values for volume of distribution and clearance. Although there is a sound theoretical basis for the target-AUC method of monitoring, the method has not been compared with other methods. A retrospective analysis of 100 patients treated using the target-AUC method suggested that the method was practical, more appropriate than aiming for a trough concentration, and toxicity was not greater than expected.

03. Pharmacokinetics

F: 0	**Vd** (L/kg): 0.27 (0.24-0.33)	**Cl** (L/h/kg): 0.06 (0.04-0.12)	**t½:** 2.5 (1.5-4) hours
Fe: >0.9	**Elimination route:** Renal		
CYP: Nil		**Protein binding:** <0.1	

F = Bioavailability, Vd = volume of distribution, Cl = clearance, t½ = terminal half-life of elimination, Fe = fraction excreted unchanged in the urine, CYP = cytochrome P450 enzyme/s
Other PK data: Nil

04. Indications

1. Gram-negative bacterial infection - including Pseudomonas, Proteus, Serratia, Klebsiella, E.coli
2. Gram-positive Staphylococcus infections

3. Infections of bone, respiratory tract, skin, soft tissue, abdomen, urinary tract, and endocarditis, and septicaemia

05. Loading Dose

3-7 mg/kg lean body weight according to the Table

Cal. CrCl (ml/min)	Dose in mg/kg	Time of second blood sample (hours)
>66	5-7 }depending on the	6-14
55-66	5-6 }severity of infection	8-16
41-54	5	10-18
31-40	4	12-20
20-30	3	14-22
<20	consider using another antibiotic	

$$\text{CrCl(ml/min)} = \frac{(140 - \text{age}) \times \text{lean body weight (kg)}}{\text{plasma creatinine (mmol/L)} \times 800} \quad (\times 0.85 \text{ if female})$$

lean body weight (kg) males = 50kg + 0.9kg for each cm > 150cm in height
lean body weight (kg) females = 45kg + 0.9kg for each cm > 150cm in height

Give the dose once-daily by IV infusion over 30 minutes in 100 ml saline.
Record the exact times of starting and finishing the infusion
Take 2 blood samples at 30 minutes after the end of the infusion and at between 6 and 22 hours after the infusion depending on renal function as in the Table
Record the exact time of blood samples
Contact the ward pharmacist or Clinical Pharmacology (Ext 80900) during normal working hours, with the concentration results to get a dose prediction for the next dose

06. Maintenance Dose

Adjust the dose according to the calculated AUC as above aiming for an AUC between 70 and 100 mg/L.hr depending on the severity of infection.

07. Notes on Administration

Give the dose once-daily by IV infusion over 30 minutes in 100 ml saline

08. When to Monitor

Refer to Loading Dose above. Repeat the 30 minute and 6-22 hour post-infusion blood samples every 3 days or prn depending on the clinical situation.

09. Dose Individualisation

Adjust the dose according to the calculated AUC as above aiming for an AUC between 70 and 100 mg/L.hr depending on the severity of infection.

10. Adverse Effects

>10%
CNS: vertigo, ataxia
ENT: ototoxicity

1-10%
DERM: pruritus, rash
ENT: ototoxicity
RENAL: nephrotoxicity

<1%
CNS: drowsiness, headache, pseudotumour cerebri, neuromuscular blockade - in patients with a coexisting abnormality of neuromuscular transmission, tremors, muscle cramps, weakness
DERM: photosensitivity, erythema
GI: anorexia, nausea, vomiting, weight loss, increased salivation, enterocolitis
HAEM: granulocytopenia, agranulocytosis, thrombocytopenia
LIVER: elevated LFTs
LOCAL: burning, stinging
RESP: dyspnoea

11. Drug Interactions

Increased nephrotoxicity can occur with concurrent:
diuretics, cephalosporins, piperacillin, clindamycin, amphotericin B, vancomycin, cisplatin, calcium channel blockers, NSAIDs, radiocontrast agents

Increased ototoxicity can occur with concurrent:
diuretics, other ototoxic agents

Neuromuscular blockade can be aggravated with other neuromuscular blocking agents

12. Factors that may give a False Assay Result

Nil known.

13. Overdose

TOXINZ

14. Dialysability

This is of questionable value.
Haemodialysis is preferred over peritoneal dialysis

15. Comments

Nil.

16. Key References

1. Barclay ML, Begg EJ. Aminoglycoside toxicity and relation to dose regimen. Adverse Drug React Toxicol Rev 1994, 13(4): 207-234.
2. Barclay ML, Kirkpatrick CMJ, Begg EJ. Once daily aminoglycoside therapy; Is it less toxic than multiple daily doses and how should it be monitored? Clin Pharmacokinet 1999, 36(2): 89-98.
3. Drug Information Handbook.
4. PML

17. Author/Date

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