Guidelines on the use of 'extended interval' Aminoglycoside (gentamicin and tobramycin) therapy

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

This guideline covers the prescribing and monitoring of gentamicin for all patients (except neonates) prescribed gentamicin (there are exclusions see page 1)

This guideline is for use by the following staff groups:
All qualified healthcare professionals involved in prescribing, administering or monitoring gentamicin.

Lead Clinician(s)

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Extension approved on:	6th December 2017
Review Date: This is the most current document and is to be used until a revised version is available	7th September 2018

Key amendments to this Document:

Date	Amendment	By:
11.05.06	Approved by Clinical Effectiveness Committee	
July 2010	Change of dosing regimen for gentamicin to 5 mg/kg and switch to use of Urban and Craig nomogram for monitoring levels	See list
September 2010	Approved by Medicines Safety Committee	
July 2012	Reviewed –Change in author job title	K Hinton
July 2014	Document extended for 3 months	Dr Catterall
November 2014	Document extended for 1 month	Dr Catterall
June 2015	Document extended for 6 months whilst it is in the review process	Dr Catterall
November 2015	Document extended for 12 months as per TMC paper approved on 22nd July 2015	TMC
Oct 16	Further extension as per TMC paper approved on 22nd	TMC

	July 2015	
November 2017	Document extended for three months whilst document under review	TLG
December 2017	Sentence added in at the request of the Coroner	
December 2017	Document extended for 3 months as per TLG recommendation	TLG
March 2018	Document extended for 3 months as approved by TLG	TLG
June 2018	Document extended for 3 months as per TLG recommendation	TLG

Guidelines on 'Extended Interval' Gentamicin Regime

Introduction

Gentamicin is an aminoglycoside antibiotic which is bactericidal and active against some Gram-positive and many Gram-negative organisms. It is not absorbed from the gut and must therefore be given by injection for systemic infections. Gentamicin is potentially toxic, so serum monitoring is important to avoid both excessive and sub-therapeutic concentrations, thus preventing toxicity and ensuring efficacy. Traditionally gentamicin has been administered two to three times a day, but the 'extended interval' regimen described in this guideline has been shown to be safe, effective and more convenient (although some indications are excluded due to insufficient evidence, see below).

Aminoglycoside therapy (bnf section 5.1.4)

Gentamicin / tobramycin

- Broad spectrum agents
- Good Gram negative activity
- Nephro- and oto-toxic
- Synergy with penicillins
- Amikacin and tobramycin should be reserved for specific indications (e.g. cystic fibrosis)
- May be given by multiple or single daily dose

Guideline

Giving gentamicin as a single large dose, rather than using the traditional two or three times per day regimes, offers several definite advantages. These include:

- Reduced staff time in preparing and administering the drug
- Reduced drug wastage
- Timing of dose less critical (as giving the dose an hour or two early or late makes much less difference to potential toxicity than with a multiple daily dose regime)
- Dose more likely to be optimal according to pharmacodynamic principles
- Reduced staff time in taking blood for levels
- Reduced laboratory costs in measuring levels
- Once daily administration is at least as safe as multiple daily dose regimens

Exclusions to this regime: (use multiple daily dosage)

- Treatment of endocarditis
- Pregnancy
- Ascites
- Major burns (>20%)
- Amputees
- Cystic fibrosis

- Neonates (refer to Trust guideline WAHT-NEO-XXX)
- Renal impairment (CrCl <40ml/minute using the Cockcroft-Gault equations) if necessary, discuss with microbiologist or clinical pharmacist.

Procedure for giving and monitoring extended interval gentamicin regime:

1. **Obtain weight of patient in kilograms.**

Dosing weight in obesity (i.e. >20% above ideal body weight) Use ideal body weight	
For adults	Calculate ideal body weight (IBW) which can be calculated by: Men (IBW): 50kg + (2.3kg x number of inches over 5foot) Women (IBW): 45kg + (2.3kg x number of inches over 5foot) For patient's < 5foot, use IBW = 45kg (women) or 50kg (men)
For children	Use the mean weight for age listed at the back to the BNF

2. **Ensure the patient's renal function is sufficient for the use of extended interval gentamicin.**

For adults, calculate creatinine clearance using the Cockcroft-Gault equations shown below. (must be >40ml/min for use of 'EI' gentamicin) Alternatively go to the pharmacy intranet web-page information for prescribers to access a link on how to calculate this.

Men: $CrCl = 1.23 \times \frac{(140 - age) \times weight\ (kg)}{Serum\ creatinine}$ Women: $CrCl = 1.04 \times \frac{(140 - age) \times weight\ (kg)}{Serum\ creatinine}$

For children with renal impairment use of 'EI' gentamicin must be discussed with the microbiologist.

3. **Calculate dose (gentamicin or tobramycin) = 5mg/kg (adjusting for obesity as detailed above)**

MAXIMUM DOSE IS 560mg. NB the dosage intervals are changed and NOT the dose.

In a minority of cases, patients may require a higher dosage (7mg/kg) e.g. in Pseudomonas sp. infection but this will be on the specific recommendation of a microbiologist. For these patients, the Urban-Craig nomogram *must* not be used – follow advice from the microbiologist.

Do not give more than one dose in 24 hours unless on the specific recommendation of a microbiologist or clinical pharmacist.

Dilute each dose in 100ml sodium chloride 0.9% and give over 60 minutes.

Monitoring - Adults

- **Important** - record time at which first dose given (start of infusion)

- Take a 5 ml blood sample in a gold-topped Vacutainer tube at a convenient time between **6 to 14 hours after the start of the infusion**. The sample should be sent to Biochemistry using the antibiotic assay request cards (blue for gentamicin) **stating the times at which the dose was given and the blood sample taken**, as soon as possible/immediately after collection. N.B. Interpretation of the level is impossible if the times requested as above are not known.

- **Continue to give further doses of gentamicin as prescribed until this result is known, unless there are concerns regarding renal function e.g. reduced urine output or raised serum creatinine.**

- If the renal function is stable (monitoring serum creatinine and urine output) the level need only be checked twice per week. If the renal function deteriorates the level must be checked more frequently; if you are unsure please discuss with the ward pharmacist or duty consultant microbiologist.

- Information required on the request form for aminoglycoside levels:
  - patient details
  - drug given, dose and dosage interval
  - time last dose given
  - time blood sample taken (trough or peak or 'EI')

- If plasma gentamicin concentration is not known*, as a guide*, until a level is correctly determined, interval of 'EI' gentamicin dosing is:
  every 24hours CrCl ≥60ml/minute
  every 36hours CrCl 40-59ml/minute

- When the result is obtained, plot it on the **Urban-Craig aminoglycoside nomogram** (see below). This will indicate the optimal dose interval. If the value lies on the line, use the longer interval. If you are unsure please discuss with the ward pharmacist or duty consultant microbiologist. If the level falls above the 48 hour dosing line then use of extended interval gentamicin MUST be discussed with the duty consultant microbiologist or pharmacist.

- Aminoglycoside therapy should be reviewed after three days and continuation of therapy discussed with a consultant microbiologist if prolonged therapy is considered necessary.

Monitoring – Children

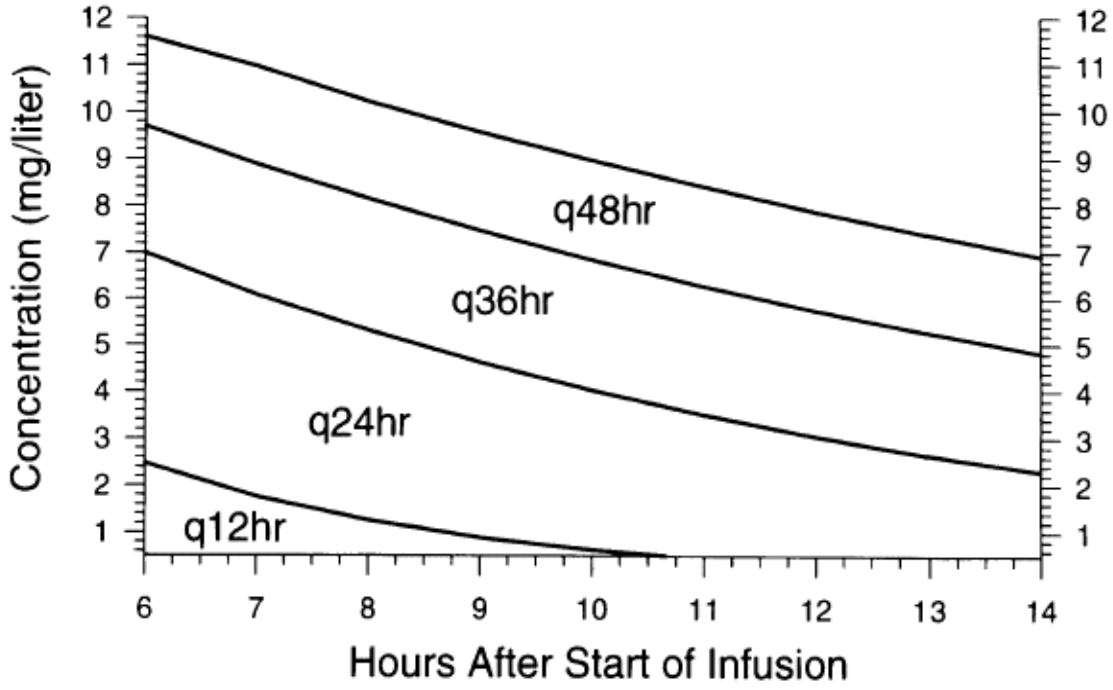
- The nomogram used for adult serum level interpretation is not validated for use in children. Therefore a pre-dose level (i.e. a level taken 23 hours or more after the dose) should be taken and further doses given if this is <1 mg/L

- Aminoglycoside therapy should be reviewed after three days and continuation of therapy discussed with a consultant microbiologist if prolonged therapy is considered necessary.

Monitoring – Critical Care patients receiving haemofiltration

- Check pre-dose level (i.e. a level taken 23 hours or more after the dose) and only give repeat dose when plasma concentration is <1 mg/L.

Urban & Craig nomogram for 5mg/Kg IBW gentamicin dosing*



*Urban-Craig nomogram only to be used for adult patients.

Monitoring Tool

Following the introduction of this guideline an audit will be carried out within one year by Pharmacy/Microbiology to monitor compliance

STANDARDS	%	CLINICAL EXCEPTIONS
All prescriptions for 'EI' gentamicin will be prescribed and monitored according to this guideline	100	See Exclusions

References

1. The British Medical Association and The Royal Pharmaceutical Society of Great Britain. British National Formulary, No. 59: March 2010. The Bath Press, Bath.
2. Cockcroft D, Gault MD. Nephron, 16:31-41, 1976
3. Urban AW, Craig WA. Daily dosage of Aminoglycosides. Current Clinical Topics in Infectious Diseases Vol 17, JS Remington & MN Swartz, Eds. Blackwell Science, Malden, MA, 1997
4. Trissel LA. Handbook on Injectable Drugs, 11th Edition (2001). American Society of Health-System Pharmacists, Bethesda, USA

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