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Aminoglycosides: Recommendations for use, dosing and monitoring

Clinical Guideline

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Contents

Aminoglycosides: Recommendations for use, dosing and monitoring Clinical Guideline

1. Introduction

This guideline has been developed by the SA expert Advisory Group on Antimicrobial Resistance (SAAGAR) to assist clinicians to safely manage aminoglycoside therapy. The guideline focuses on the indications for use of aminoglycosides and provides recommendations on dosing and treatment duration, contraindications and precautions, therapeutic drug monitoring and clinical monitoring.

This guideline **does not** provide guidance on the following (seek specialist advice):

- use of gentamicin in surgical prophylaxis (refer to SA Health Surgical Antibiotic Prophylaxis Clinical Guideline)
- use of tobramycin in respiratory infections
- use of amikacin in mycobacterial infections
- use of aminoglycoside for patients on dialysis
- use of aminoglycosides for neonates (refer to South Australian Neonatal Medication Guidelines – Gentamicin)
- use of tobramycin in paediatrics

2. Background

Aminoglycosides are bactericidal antibiotics used to treat infections caused by aerobic Gram-negative organisms. Gentamicin, tobramycin and amikacin are registered for parenteral use in Australia.[1]

Empiric short-term use of aminoglycoside antibiotics is potentially lifesaving but prolonged or inappropriate use can cause harm, including auditory, vestibular and renal toxicity. Empiric therapy with aminoglycosides should be limited to 48 hours.[2] If greater than 48 hours of therapy is anticipated, therapeutic drug monitoring (TDM) is recommended to ensure adequate dosing and clearance in addition to audiometric and vestibular testing to monitor for ototoxicity.[3,4] Renal function should be monitored throughout the course.

3. Definitions and acronyms

ABW	Actual Body Weight
AdjBW	Adjusted Body Weight
AUC	Area-Under-the curve (plasma concentration vs time)
BMI	Body Mass Index
CrCl	Creatinine Clearance
IBW	Ideal body weight
ID	Infectious Diseases
IE	Infective Endocarditis
IV	Intravenous
MIC	Minimum inhibitory concentration

SAAGAR South Australian expert Advisory Group on Antimicrobial Resistance
TDM Therapeutic Drug Monitoring

4. Principles of the standards

The following National Safety and Quality Health Service Standards[5] apply:

Standard 1 – Governance for Safety and Quality in Health Care
Create integrated governance systems that maintain and improve the reliability and quality of patient care, as well as improve patient outcomes.

Standard 3 – Preventing & Controlling Healthcare-Associated Infection
Improve infection prevention and control measures to help prevent infections, and the spread of antimicrobial resistance through the appropriate prescribing and use of antimicrobials

Standard 4 – Medication Safety
Ensure competent clinicians safely prescribe, dispense and administer appropriate medicines to informed patients and carers.

5. General guidance

5.1. Indications for aminoglycosides

Empirical therapy

Aminoglycosides are valuable first-line agents for short-term empirical treatment of suspected Gram-negative infections, pending the outcome of microbiological investigations.

Empirical therapy with aminoglycosides is recommended for a limited course only. In most instances, no further aminoglycoside doses should be given beyond 48 hours (i.e. a maximum of three empirical doses at 0, 24 and 48 hours). If further antimicrobial therapy is required, an appropriate alternative IV or oral agent based on the susceptibility testing should be commenced. If ongoing aminoglycoside therapy is thought clinically necessary, seek Infectious Diseases (ID)/Microbiology advice.

Specific guidance on the dose and dosing interval of gentamicin for empiric therapy according to the patient's age, weight and renal function are provided in **Appendix 1**. Dosing of gentamicin for the empirical treatment of infective endocarditis is outlined in **Appendix 2**.

Directed therapy

In a limited number of circumstances, aminoglycosides are indicated for directed therapy. These include, but are not restricted to:

> infections when resistance to other safer antimicrobials is known or expected;
> combination therapy for serious *Pseudomonas aeruginosa* infections and brucellosis;
> low doses of gentamicin as synergistic treatment for endocarditis (see **Appendix 2**);
> amikacin for central nervous system *Nocardia* spp. infection;and/or
> amikacin for mycobacterial infection including *M.abscessus complex and M. avium*

complex (MAC) and *M. tuberculosis*in the setting of drug-resistant infection.

Routine use of aminoglycosides is NOT recommended for:

> *Staphylococcus aureus* bacteraemia and endocarditis;
> Gram-negative infections with endogenous resistance including *Stenotrophomonas maltophilia* and *Burkholderia cepacia;*
> Routine use prior to urinary catheter insertion; and/or
> Intra-abdominal infection for greater than 3 days.[2]

5.2 Contraindications and precautions

Contraindications

Aminoglycosides are contraindicated in patients who:

> have a history of aminoglycoside-induced vestibular or auditory toxicity;
> have experienced a serious hypersensitivity reaction to an aminoglycoside; and/or
> have myasthenia gravis.[2]

Precautions

Aminoglycosides should not generally be used in patients with a **high risk of ototoxicity** such as:

> a pre-existing significant auditory impairment;
> a pre-existing vestibular condition (vertigo, dizziness, balance problems);[6]
> a family history (first-degree relative) of auditory toxicity caused by an aminoglycoside or a maternal relative with deafness due to mitochondrial mutation A1555G;[7]

A **single dose** of an aminoglycoside can be used in patients:

> with chronically impaired renal function (adults with a creatinine clearance less than 40 mL/minute and children with an estimated glomerular filtration rate less than 50 mL/minute/1.73 m^2)
> with rapidly deteriorating renal function unrelated to sepsis
> who are frail and elderly (e.g. 80 years or older)[2]

Pregnancy & Breastfeeding

Gentamicin, amikacin and tobramycin rapidly crosses the placenta into the foetal circulation and amniotic fluid.[8,9] Aminoglycosides are classified as category D in pregnancy by the Therapeutic Goods Administration (TGA), however this is based on small animal studies of nephrotoxicity.

Larger studies where gentamicin was administered in pregnancy, including randomised trials, showed no increased incidence in adverse events to pregnant patients nor to their foetuses.[10] Despite the TGA classification, gentamicin has been used safely in pregnant woman to treat serious infections such as sepsis and acute pyelonephritis under specialist advice.[8] Careful dosing and monitoring is required to ensure efficacy and avoid toxicity.

Small amounts of gentamicin, amikacin and tobramycin are excreted into breast milk.[8,11] All three aminoglycosides are poorly absorbed orally however variable gastrointestinal

maturation in the neonate may result in some oral absorption from breast milk. Gentamicin is considered safe to use in breastfeeding patients.[8,12]

5.3 Risk assessment and clinical monitoring of patients on aminoglycosides

Nephrotoxicity

Aminoglycoside-induced nephrotoxicity is usually associated with pre-existing renal impairment and prolonged treatment courses (longer than 5 to 7 days). It is generally reversible. Prior to commencing an aminoglycoside, serum creatinine should be checked and renal function (creatinine clearance) estimated. If the patient is acutely unwell it is appropriate to administer an initial empirical dose without ascertaining renal function.

Repeat dosing of aminoglycosides in patients with renal impairment (clearance less than 40 mL/minute and children with estimated glomerular filtration rate less than 50 mL/minute/1.73 m^2) should be administered with caution and requires close monitoring. Refer to Appendix 1 for dosing guidelines.

If therapy is ongoing, monitor renal function at least twice each week OR daily if renal function is unstable or there is concomitant use of other nephrotoxic agents.

Ototoxicity

Ototoxicity secondary to aminoglycoside use is directly related to the duration of treatment and can occur in patients with normal renal function and with serum drug levels within the target range.[6] Ototoxicity refers to both cochlear (hearing loss, tinnitus, feeling of fullness within the ear) and vestibular (nausea, vomiting, vertigo, lack of balance) toxicities. In some cases ototoxicity may be irreversible and result in permanent hearing loss.

All patients initiated on an aminoglycoside should be reviewed for their risk of ototoxicity **before** treatment begins (refer to contraindications and precautions above). If the patient is at high risk of ototoxicity, alternative antibiotics should be considered (seek ID/Microbiology advice).

Audiometric testing

> Referral for **baseline** high-frequency audiometry testing should be considered for all patients where treatment is likely to continue for 5 days or more. Testing should ideally be conducted prior to initiation of treatment however baseline testing should not delay therapy. Repeat testing between days 5 and 10 of therapy and then every 1 to 2 weeks thereafter.

Vestibular function testing

> The 3-step bedside exam for vestibular toxicity is recommended to be performed at least weekly during therapy (see Appendix 3).[13]

> Formal vestibular function monitoring by the audiology department should occur:

- If during the course the patient has any signs or symptoms of ototoxicity such as hearing loss, tinnitus, aural fullness, oscillopsia or blurred vision during head movement, gait ataxia, or imbalance
- At the mid-point of the treatment course for extended therapy (3-6 months)

Following completion of the course, clinicians should liaise with the audiology department to determine a plan for further formal testing, noting that signs of audio-vestibular toxicity may appear several months after treatment has been stopped.

SAAGAR notes that high-frequency audiometric and formal vestibular function testing is not widely available at all sites, however arrangements for testing should be made if therapy is prolonged. Refer to **Appendix 3** for further information.

Patient education and monitoring

> Patients and/or guardians/carers should be informed about the potential adverse effects of aminoglycosides and this should be documented in the medical record
> Consider providing the patient with an aminoglycoside consumer information sheet (see example in **Appendix 4**)
> Nursing staff and patients should document any signs of ototoxicity exhibited by the patient in the medical record and report symptoms to treating medical staff

If audio-vestibular toxicity is suspected during therapy, stop the aminoglycoside and seek advice from ID/Microbiology.

5.4 Therapeutic drug monitoring (TDM) for aminoglycosides

(for recommendations on TDM for infective endocarditis, see Appendix 2)

Therapeutic drug monitoring (TDM) for aminoglycosides is recommended following the FIRST dose if:

> greater than 48 hours of therapy is anticipated
> the patient's renal function is changing rapidly or substantially (e.g. critically ill patients with sepsis or patients with suspected acute renal failure)
> the patient has altered pharmacokinetics (refer to **Appendix 1** for a list of such patients)

Measure the plasma concentration every 48 hours, or more frequently for patients with unstable or impaired renal function. TDM should also be repeated after a dose adjustment.

Provide the following information with the pathology request to enable accurate TDM interpretation:

> dose administered
> infusion start and finish times
> time the concentration(s) was taken

TDM interpretation – Area under the concentration-time curve (AUC)

Aminoglycoside antibiotics are concentration-dependent, meaning a higher antibiotic concentration (Cmax) to minimum inhibitory concentration (MIC) ratio (Cmax:MIC) will exhibit a greater antimicrobial activity. Recent data however, have suggested that the AUC_{0-24}/MIC ratio is a better predictor of aminoglycoside efficacy while a high Cmin and AUC exposure over days has been associated with ototoxicity and nephrotoxicity.[14]

For Gram-negative organisms, the targets conventionally used for gentamicin are: [2,14]

- AUC_{0-24}/MIC of 80 to 100 mg.hr/L (MIC ≤ 1 mg/L assumed)
- Cmin (trough) – less than 1 mg/L

It is important to recognise the inherent imprecision of MIC measurement and the high degree of variability between MIC testing methods.[15] For extended courses, consider requesting the MIC of the pathogen and, if more than 1 mg/L, adjust the AUC accordingly (seek expert advice).

TDM interpretation – dose optimisation

It is recommended computerised dose optimisation software is utilised for TDM as this accounts for individual variation in aminoglycoside pharmacokinetics.[16] Examples of such programs include DoseMe, TDMx, TCI Works, SeBA-GEN, RxKinetics and ALLADDIN.

The optimal sampling time points for most computerised methods requiring two measurements are:

- 30 minutes after the completion of the infusion
- 6 to 8 hours after the dose

Programs that use population pharmacokinetic models and Bayesian predictive models may only require one plasma concentration measurement.
Where a software program is unavailable, manual calculation of the AUC can be undertaken. This requires at least two serum concentrations per dosing (with preferred sampling times, one approximately 30 minutes after the end of the infusion and another at a later time (6-22 hours) depending on renal function.[17]

TDM is a tool to assist with optimal dosage determination and should always be used by a clinician experienced with the software. It should also be considered critically in the context of the patient's clinical situation.

A workflow practice for TDM should be developed. This should include consideration of practical dosing and blood sampling strategies to support good patient care and accurate dose prediction.

- Regional and smaller hospitals should liaise with a tertiary referral centre to develop a system to manage patients requiring directed therapy with aminoglycosides. Options include remote clinical supervision (for example, by contacting metropolitan pharmacy departments or pharmacologists to assist with TDM), access to ID/clinical microbiology advice, or training and supervision of local staff.
- Regional and smaller hospitals should consider the availability of laboratory services that can provide timely aminoglycoside blood level results before commencing directed therapy. If delays in receiving timely results are likely to occur, a switch to alternative therapy should be made. In general, a switch to third-generation cephalosporins (as aminoglycoside substitute) should be avoided. Alternatively, consider transferring the patient to a larger hospital with daily pathology services.

5.5 Recommendations for the safe and effective use of aminoglycosides in South Australian hospitals

Practices of aminoglycoside prescribing and monitoring should be regularly reviewed and updated. The following information should be available to medical, nursing and pharmacy staff:

- methods of identifying patients who have been prescribed an aminoglycoside

- timing of aminoglycoside dosing and infusion duration
- support for aminoglycoside dosing and monitoring (protocol development and maintenance, pharmacy staffing, phlebotomy, pathology and audiology services).
- Strategies to eliminate unnecessarily long courses of aminoglycoside therapy should be in place:
    - gentamicin use as part of triple antibiotic therapy following intra-abdominal surgery should not continue for more than 48 hours
    - prescribe gentamicin within the variable dose section of the patient's national inpatient medication chart OR enter an automatic stop date in the electronic medication record
    - education of medical staff regarding estimating renal function and weight-based dose adjustment for empiric aminoglycoside therapy
    - Infectious diseases/clinical microbiologist and/or clinical pharmacist review/advice for patients on an aminoglycoside for more than 48 hours.
- Use of potential aminoglycoside substitutes, particularly third-generation cephalosporins, should be considered **only** when narrow-spectrum antibiotics are not an option.

6. Safety, quality and risk management

National Safety and Quality Health Service Standards

National Standard 1 Clinical Governance	National Standard 2 Partnering with Consumers	National Standard 3 Preventing & Controlling Healthcare-Associated Infection	National Standard 4 Medication Safety	National Standard 5 Comprehensive Care	National Standard 6 Communicating for Safety	National Standard 7 Blood Management	National Standard 8 Recognising & Responding to Acute Deterioration
☒	☐	☒	☒	☐	☐	☐	☐

7. Appendices

Appendix 1 – Gentamicin dosing and monitoring guidelines
Appendix 2 – Aminoglycosides for the treatment of infective endocarditis
Appendix 3 – Audiometric and vestibular function testing
Appendix 4 – Example consumer information sheet for aminoglycosides

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9. Document Ownership & History

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01/05/17	V2.1	SA Safety and Quality Strategic Governance Committee	Minor update
01/06/16	V2.0	SA Safety and Quality Strategic Governance Committee	Updated references and added appendices
01/05/16	V1.1	SA Safety and Quality Strategic Governance Committee	Amended department name to 'Department for Health and Ageing'.
01/03/11	V1.0	SA Safety and Quality Strategic Governance Committee	Original approved version.

Appendix 1 – Gentamicin dosing and monitoring guidelines

(For dosing information for tobramycin and amikacin, consult the current version of *Therapeutic Guidelines: Antibiotic*[18]*)*

TABLE 1: Review gentamicin contraindications and precautions prior to prescribing	
CONTRAINDICATIONS	
> History of aminoglycoside-induced vestibular or auditory toxicity > Serious hypersensitivity reaction to an aminoglycoside	> Myasthenia gravis
PRECAUTIONS - OTOTOXICITY Aminoglycosides should **not generally** be used in these patients due to a high risk of ototoxicity	
> Pre-existing significant auditory impairment > Pre-existing vestibular condition (vertigo, dizziness, balance problems) > Family history (first-degree relative) of auditory toxicity caused by an aminoglycoside or a maternal relative with deafness due to mitochondrial mutation A1555G	
PRECAUTIONS – NEPHROTOXICITY Consider alternative agent(s) if appropriate. A **single dose** of gentamicin can be used in patients:	
> With chronically impaired renal function (adults with a CrCl < 40 mL/minute and children with an eGFR < 50 mL/minute/1.73 m^2) > With rapidly deteriorating renal function unrelated to sepsis > Who are frail and elderly (80 years or older) Review patient's medication history and assess appropriateness of coadministration with other nephrotoxic medications (e.g. non-steroidal anti-inflammatory drugs)	
PRECAUTIONS - PATIENTS WITH ALTERED PHARMACOKINETICS **e.g. increased clearance, altered drug distribution** Modified / higher doses may be required with increased monitoring - Seek advice for ongoing dosing	
> Critically ill patients with severe sepsis or septic shock > Patients with severe burns > Patients with ascites > Morbidly obese patients	> Patients receiving renal replacement therapy > Patients with cystic fibrosis > Pregnant women > Patients treated with chemotherapy that causes kidney dysfunction (e.g. cisplatin)

TABLE 2: Estimate renal function (where possible prior to the first dose, do not delay treatment in acutely unwell patients)	
Measure weight and height and calculate creatinine clearance	
SAAGAR recommends using the Cockcroft-Gault equation (adults) or Modified Schwartz formula (children) to estimate renal function. If using the eGFR (CKD-EPI) routinely reported in pathology results, adjustment is needed for patients with extremes of body size. To do this, multiply the eGFR by the patient's body surface area (in m^2) and divide by 1.73 m^2	
CAUTION - Renal function estimates can be unreliable in the following situations. Therapeutic drug monitoring from the first dose is recommended. **Patients with unstable creatinine concentrations**	
> Pregnant women > Patients with acute renal failure > Patients with serious co-morbidities (e.g. in intensive care)	> Patients with febrile neutropenia > Renal dialysis patients
Patients with extremes in muscle mass and diet	
> Amputees / paraplegics > Cachectic / malnourished patients > Patients taking creatine dietary supplements	> Obese patients > Vegetarian / low meat diets > Muscle wasting / neuromuscular disorders

TABLE 3: Monitoring (refer to 5.4 TDM for aminoglycosides for more information)
Monitor renal function daily if unstable or there is concomitant use of nephrotoxic agents Monitor renal function at least twice each week if therapy is ongoing
Perform TDM following the FIRST dose if > 48 hours of therapy is anticipated OR patient's renal function is changing rapidly or substantially OR the patient has altered pharmacokinetics. Measure plasma concentration every 48 hours, or more frequently if renal function unstable or after dose adjustment.
Perform beside vestibular function testing at least once a week if therapy is ongoing

Arrange for baseline audiometric testing if treatment duration is likely to be > 5 days and repeat between days 5 and 10 of therapy and every 1 to 2 weeks during treatment

TABLE 4: Empiric gentamicin dosing recommendations for ADULTS [1]

Use ideal body weight (IBW) or actual body weight (ABW), whichever is less

For obese patients (BMI 30-35 kg/m^2) use adjusted body weight[#] (AdjBW) up to 100 kg

For BMI ≥ 35 kg/m^2, seek expert advice

Creatinine Clearance (CrCl)	Dose ^		Dose Frequency	Maximum number of empirical doses
	Noncritically ill (max dose 500mg)	Critically ill (max dose 700mg)		
more than 60 mL/min	4 to 5 mg/kg	7 mg/kg	24-hourly	3 doses (at 0, 24 and 48 hours)
40 to 60 mL/min	4 to 5 mg/kg	5 mg/kg	36-hourly	2 doses (at 0 and 36 hours)
less than 40 mL/min	4 mg/kg	4 mg/kg	Single dose, then seek expert advice for subsequent dosing or selection of alternative antibiotic	

^ Round dose to the nearest multiple of 40 mg

[#] Adjusted body weight (AdjBW) = IBW + [0.4 x (Actual Body Weight – IBW)]

TABLE 5: Ideal body weight (IBW) estimation

Height (cm)	Height (feet/inches)	IBW (kg) Male	IBW (kg) Female
155	5'1"	53	48
160	5'3"	57	53
165	5'5"	62	57
170	5'7"	66	62
175	5'9"	71	66
180	5'11"	76	71
185	6'1"	80	76
190	6'3"	85	80
195	6'4"	89	84

IBW (female) = 45.5 kg + 0.9 kg per cm over 152cm
IBW (male) = 50 kg + 0.9 kg per cm over 152cm

TABLE 6: Empiric gentamicin dosing recommendations for CHILDREN [1]

For children with impaired renal function (eGFR < 50 mL/minute/1.73 m^2) give a single dose only, then seek expert advice

Age	Gentamicin Dose[#]	Dosing frequency	Maximum number of empirical doses
Children 1 month to younger than 10 years	7.5 mg/kg[^] up to 320mg[†]	24-hourly	3 doses (at 0, 24 and 48 hours)
Children 10 years and older	6 mg/kg[^] up to 560mg[†] 7 mg/kg for children with septic shock or requiring intensive care support[^†]	24-hourly	3 doses (at 0, 24 and 48 hours)

[^] Use actual body weight. For obese children, use adjusted body weight (AdjBW).

AdjBW = IBW + [0.4 x (ABW – IBW)]

[#] For treatment beyond 48 hours therapy, seek advice from Infectious Diseases

[†] The dose cap does not apply to children with septic shock or requiring intensive care support

Appendix 2 – Aminoglycosides for the treatment of infective endocarditis

Empirical gentamicin therapy for treating infective endocarditis

Gentamicin is used for the empirical treatment of infective endocarditis to cover the possibility of Gram-negative sepsis pending blood culture results. In most cases dosing is as for non-critically ill patients (see Appendix 1) however higher doses may be recommended for critically ill patients provided there is no pre-existing renal impairment. Therapeutic drug monitoring (TDM) should occur from the first dose using the AUC method.

Directed synergistic gentamicin therapy for treating infective endocarditis

In directed therapy, aminoglycosides given in combination with cell wall inhibitors (i.e. beta-lactams and glycopeptides) provide synergistic bactericidal activity to help shorten the duration of therapy and eradicate highly resistant organisms.

In confirmed streptococcal or enterococcal infective endocarditis, the usual dose of gentamicin is 1mg/kg IV 8-hourly (adults and children >1month). In patients with renal impairment (CrCl < 60 mL/min), 12-hourly dosing may be considered.

Despite limited evidence, some international guidelines endorse gentamicin 3 mg/kg IV once daily for directed synergistic dosing, based on the possibility of a lower risk of nephrotoxicity and simplified administration regimen.[19] There is a paucity of strong evidence to support this practice – seek advice from ID/Microbiology.

Therapeutic drug monitoring (TDM) in infective endocarditis

Empirical therapy

Standard TDM should occur from the first dose using the AUC method.

Directed therapy

Multiple-daily dosing regimens are associated with a higher risk of nephrotoxicity and duration of therapy for confirmed streptococcal or enterococcal endocarditis may need to be continued for 2 or more weeks.[20]

For directed therapy with a multiple-daily dosing regimen, the AUC approach to monitoring aminoglycoside plasma concentrations is not required. A trough (pre-dose) concentration is recommended to ensure the gentamicin concentration is detectable for efficacy but not elevated.[2]

- Check the trough level 24 hours after the start of treatment
- Aim for a trough concentration of 0.5 to 1 mg/L
- Monitor renal function and trough serum gentamicin concentrations at least twice a week, or daily in patients with impaired or unstable renal function

If renal function is deteriorating substantially, consideration should be given to stopping gentamicin—seek advice from ID/Microbiology.

Appendix 3 – Audiometric and vestibular function testing

All patients at high risk of ototoxicity **or** where treatment is likely to continue for 5 days or more should have high-frequency audiometric testing **and** vestibular function testing.

Patients should be informed about the potential adverse effects of aminoglycosides and this should be documented in the medical record. Consider providing the patient with an aminoglycoside consumer information sheet (see example in Appendix 4).

Ask the patient regularly about gait ataxia, balance problems, hearing loss or blurred vision during head movement, and inform them to report immediately if they occur.

If audio-vestibular toxicity is suspected during therapy, stop the aminoglycoside and seek expert advice.

Audiometric Testing

High-frequency audiometry tests involve exposing the patient to a range of sound frequencies and may be used to detect hearing loss in the high tone range (> 4,000 Hz). It is most accurate if baseline results are available to enable comparison with previous hearing capability therefore it is important to identify early if a patient is likely to require prolonged aminoglycoside therapy. Audiometric testing should be repeated between days 5 and 10 of therapy, and repeated every 1 to 2 weeks during treatment.

Vestibular Function Testing

Formal vestibular function monitoring by the audiology department should occur:

- If the patient has any signs or symptoms of ototoxicity such as hearing loss, tinnitus, aural fullness, oscillopsia or blurred vision during head movement, gait ataxia or imbalance
- At the mid-point of the treatment course for extended therapy (3-6 months)

A three-step bedside exam for vestibular toxicity should be performed weekly during therapy. This is described in detail here and includes:

1. **Dynamic visual acuity (DVA) test** to establish if the patient has early oscillopsia
   - Patient is asked to read a visual acuity chart (e.g. Snellen) at rest and during passive sinusoidal head rotation at 2 Hz. A drop of more than two lines of acuity suggests vestibular hypofunction.

2. **Head impulse test (HIT)** to check vestibulo-ocular reflex
   - The examiner holds the patient's head in his/her hands, facing them. The patient is asked to fix vision on the examiner's nose and then the patient's head is turned from side to side.
   - The patient should be able to maintain fixation on a single point with smooth eye movements (no corrective saccades observed).

3. **Romberg test on foam rubber** to test vestibulospinal reflexes for patients who can stand
   - Firm surface: The patient stands with their feet together. Steady balance should be maintained for 15 seconds. Test with eyes open and closed.
   - Foam surface: Repeat above steps on foam surface.
   - Patients who have bilateral vestibulopathy should have a negative Romberg test on a firm surface and positive results on a foam surface.

Appendix 4 – Example consumer information sheet

Aminoglycosides

(Gentamicin, tobramycin & amikacin)

You have been prescribed an antibiotic that is part of a group of antibiotics called aminoglycosides. Aminoglycosides work by stopping bacteria from growing and by killing them. They are usually used to treat serious infections for which other medicines may not work. This includes infections in:

- your chest (including your lungs)
- your urinary tract (kidneys or bladder)
- your heart (sometimes called endocarditis)
- your blood (sometimes called bacteraemia or septicaemia).

Aminoglycosides can treat other types of infection not mentioned here.

Your doctor will be able to tell you about the infection that you are being treated for.

This medicine will be given to you as an injection into a muscle or into a vein.

Side effects

Like all medicines, aminoglycosides can cause **some** side effects. If they occur, most are likely to be minor or temporary. There are some side effects that are more serious, but these are less common. Many patients do not experience any side effects at all.

One of the more serious side effects of these medicines is damage to the ear, which can result in problems with hearing and balance. It can occur at any time during your treatment but is more likely to happen if you receive treatment for more than 5 days. Your doctor will monitor your progress; this may involve some blood tests and hearing tests.

Tell a doctor/nurse immediately if you notice any of the following:

- hearing problems, ringing in the ears, feeling of fullness in the ears
- blurred vision or vision that seems to 'jump' during head movement
- problems with balance or feeling unsteady on your feet.

If you want to know more about the possible side effects of aminoglycosides, please ask your doctor or pharmacist.

For more information

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