Gentamycin: Uses, MOA, Dosage, Side effects

Gentamicin is an aminoglycoside antibiotic that is usually used in combination to treat severe systemic infections that are due to sensitive Gram-negative and other organisms.

They include biliary tract infections, brucellosis, endometritis, gastroenteritis, cystic fibrosis as well as prophylaxis of surgical infections and the treatment of immunocompromised patients in intensive care.

Like other aminoglycosides, gentamicin synergizes with penicillins in killing Streptococcus faecalis in endocarditis.

Gentamicin sometimes can be used alone but usually in combination with other antibiotics such as penicillins or cephalosporins

Gentamicin is often used synergistically in combination with a-lactam antibiotics or vancomycin for serious infections that require broad coverage.

Aminoglycosides induce the binding of “wrong” t-RNA-AA complexes, resulting in the synthesis of false proteins. Aminoglycosides are bactericidal.

Aminoglycoside antibiotics consist of glycoside-linked amino-sugars. They contain numerous hydroxyl groups and amino groups that can bind protons. Hence, these compounds are highly polar, poorly membrane permeable, and not absorbed enterally.

Aminoglycosides gain access to the bacterial interior by the use of bacterial transport systems. In the kidney, they enter the cells of the proximal tubules via an uptake system for oligopeptide

Mechanism of Action:

- Binds **irreversibly to the 30S ribosomal subunit**
- Inhibits **initiation complex formation**
- Induces **misreading of mRNA** , producing abnormal or nonfunctional proteins
- Ultimately **bactericidal**
- Requires **oxygen-dependent transport** into bacteria, hence **ineffective against anaerobes**

Spectrum of Activity

- **Primarily active against Gram-negative aerobes**
- Limited Gram-positive activity; used **synergistically with ?-lactams** for serious Gram-positive infections (e.g., *Enterococcus faecalis* in endocarditis)

Indications

Used **alone** or in **combination therapy** for severe systemic infections:

- **Sepsis** and **bacteremia**
- **Endocarditis** (with penicillin or vancomycin)
- **Intra-abdominal infections** (e.g., peritonitis)
- **Complicated urinary tract infections (UTIs)** (not for uncomplicated UTI)
- **Bone and joint infections** (e.g., osteomyelitis)
- **Skin and soft tissue infections** (e.g., infected burns, cellulitis)
- **Pneumonia** (typically nosocomial, in combination)
- **Eye infections** (topical drops)

Pharmacokinetics

- **Route of Administration:**
  - **Intramuscular (IM)** or **intravenous (IV)**
  - **Topical** for ocular infections
- **Absorption:** Poor oral absorption
- **Distribution:**
  - Poor **CSF penetration**
  - Low protein binding (~30%)
- **Excretion:**
  - **Renal (unchanged)**
  - Adjust dose in **renal impairment**
- **Half-life:** Prolonged in neonates and renal dysfunction

Dosing

- **Standard dose:** 3–5 mg/kg/day divided every 8 hours (q8h)
- **Extended interval dosing** (once daily) may reduce toxicity

Mechanism of Resistance

- **Plasmid-mediated enzymatic inactivation**
- **Altered ribosomal binding site**
- **Decreased drug uptake** or **efflux**

Side Effects (Dose & Duration Dependent)

1. Nephrotoxicity

- Accumulates in **renal proximal tubules**
- Often **reversible**
- Risk ? in elderly, dehydration, renal disease

2. Ototoxicity

- Damage to **cochlear** (hearing loss) and **vestibular** (balance) systems

- **Irreversible**
- Symptoms: tinnitus, vertigo, hearing loss
- Risk ? with prolonged use or high serum levels

3. Neuromuscular Blockade

- Rare, can cause **respiratory paralysis**
- Risk ? with **anesthetics or neuromuscular blockers**
- Antidotes: **Calcium gluconate, Neostigmine**

4. Others

- Hypomagnesemia (prolonged use)
- Antibiotic-associated colitis (e.g., *C. difficile*)
- Stomatitis, nausea, vomiting
- Rash and hypersensitivity reactions

Contraindications

- Known hypersensitivity to gentamicin or other aminoglycosides
- **Myasthenia gravis** (can worsen symptoms)
- **Pregnancy** (Category D: potential for fetal ototoxicity)
- Use cautiously in:
  - **Parkinsonism**
  - **Premature neonates** (immature renal function)
  - Patients receiving **loop diuretics** (e.g., furosemide)

Drug Interactions

- **? Nephrotoxicity:**
  - Other aminoglycosides
  - Vancomycin
  - Amphotericin B
  - Cisplatin, Cyclosporine
- **? Ototoxicity:**
  - Loop diuretics (e.g., furosemide, ethacrynic acid)
- **? Neuromuscular blockade:**
  - Non-depolarizing neuromuscular blockers

Monitoring Parameters

- **Serum gentamicin levels:**
  - **Trough** (<2 µg/mL) before next dose
  - **Peak** (4–10 µg/mL) after administration
- Monitor **renal function** (BUN, creatinine)
- Watch for signs of **ototoxicity** and **neuromuscular weakness**

Toxicity and Overdose

- Serum levels >12 µg/mL increase toxicity risk
- **Treatment:**
  - **Hemodialysis** or **peritoneal dialysis**
  - **Stop drug immediately**
  - Monitor hearing and renal function

High-Yield Points

- **Not effective against anaerobes**
- Used synergistically with **?-lactams or vancomycin**
- **Narrow therapeutic index** – serum level monitoring critical
- **Nephrotoxicity and ototoxicity** are the most dangerous adverse effects
- **Extended interval dosing** may reduce toxicity
- Avoid in pregnancy unless life-saving