Aminoglycosides

Many aminoglycosides are bactericidal agents that are commonly used in clinical practice. These antibiotics function by inhibiting protein synthesis through various mechanisms. They irreversibly bind to the 30S ribosomal subunit in bacteria to inhibit formation of the initiation complex and interfere with the mRNA proofreading process. They can also inhibit translocation of peptidyl tRNA. There is evidence that they can also disrupt bacterial cell membranes. Common aminoglycoside antibiotics include gentamicin, neomycin, amikacin, tobramycin, and streptomycin. Aminoglycosides are used to treat many forms of infections caused by gram-negative aerobes, such as pseudomonas, enterobacter, and even mycobacteria. The most common use resides in empirical treatment of serious septicemia, GI infections, UTIs, and hospital-acquired pneumonia. Aminoglycosides require oxygen for uptake by bacteria and, therefore, do not work well against anaerobic bacterial infections. Aminoglycosides can cause many side effects, especially nephrotoxicity and ototoxicity, which is why their use is limited. It causes nephrotoxicity because it inhibits protein synthesis in renal cells and can lead to acute tubular necrosis and renal failure. The renal side effect is especially common when aminoglycosides are given together with cephalosporins, and ototoxicity is especially common when given at the same time as loop diuretics. Since these antibiotics are classified as teratogens, they should be avoided in pregnant patients. Additionally, aminoglycosides can block neuromuscular junctions by inhibiting the release of acetylcholine at the presynaptic nerve terminal; therefore, they are contraindicated in patients with myasthenia gravis. This neuromuscular blockade can lead to respiratory paralysis, requiring supportive care. Resistance to aminoglycosides develops due to certain transferase enzymes that inactivate the drug. These transferases alter the structure of aminoglycosides through various chemical reactions such as acetylation, adenylation, or phosphorylation.

PLAY PICMONIC

Drug Names

Gentamicin
Magenta-gentleman-mouse
This aminoglycoside antibiotic is used for gram-negative infections such as Pseudomonas and Proteus but not for Neisseria or Legionella. It can cause ototoxicity and nephrotoxicity, which limits its use clinically. It is not given orally due to its lack of absorption from the small intestine. It is often used to coat surgical implants and tools. It is also often used in combination with beta-lactams for empiric treatment of neonatal sepsis, especially for suspected gram-negative pathogens.

Neomycin for Bowel Surgery Prep
Neon-mouse Performing Bowel-bowl Surgery
Neomycin is a popular topical aminoglycoside antibiotic. It is highly ototoxic and nephrotoxic and subsequently is not used as a systemic treatment. Since the intestine does not absorb it, it is used as a second-line agent (after rifaximin) to treat hepatic encephalopathy by eliminating ammonia-producing bacteria in the intestine. It is also used to reduce the risk of infection during intestinal surgery by eliminating intestinal bacteria.

Amikacin
Moccasin
This aminoglycoside is mainly used for Pseudomonas, Enterobacter, and Serratia infections, but like the other aminoglycosides, it can cause nephrotoxicity and ototoxicity. This drug cannot be given orally, and dosing should be carefully monitored in patients with renal failure. It is often used in combination with beta-lactams for empiric treatment of neonatal sepsis, especially for suspected Gram-negative pathogens.

Tobramycin
Cobra-mouse
Tobramycin is another aminoglycoside antibiotic used for gram-negative infections. It is better than gentamicin when it comes to treating pseudomonal infections of the lung, so it is used in cystic fibrosis patients during pseudomonal infections. It also cannot be given orally but has a special application as an ophthalmic solution (Tobrex) for bacterial conjunctivitis. Just like other aminoglycosides, tobramycin also causes ototoxicity and nephrotoxicity.

Streptomycin
Stripper-mouse
Streptomycin was the first aminoglycoside discovered and was used for Mycobacterium tuberculosis infections. This antibiotic is now occasionally used for endocarditis, Yersinia pestis infestation, and tuberculosis. Just like other aminoglycosides, streptomycin also causes ototoxicity and nephrotoxicity. Its use has significantly declined due to resistance and the availability of better alternatives.

Mechanism of Action

Bactericidal

Bacteria-sliders

Unlike bacteriostatic agents, which simply stop bacteria from reproducing, bactericidal agents actually cause bacterial cell death. Aminoglycosides bind the ribosomal subunit of bacteria and cause misreading of mRNA during protein synthesis. The production of nonfunctional proteins disrupts cell membrane integrity and key metabolic processes. They do not directly affect DNA replication, but inhibiting proper protein synthesis impairs bacterial growth and division. A higher concentration of medication leads to quicker eradication of the infection.

Inhibit Formation of Initiation Complex

Inhibiting-chains on Initiation-screen Complex-building

Aminoglycosides bind to the 30S prokaryotic ribosomal subunit and inhibit bacterial protein synthesis. This is performed by inhibiting the formation of the initiation complex required to translate bacterial mRNA.

Cause Misreading of mRNA

Misread Mail-(RNA)-rhino

Aminoglycosides bind to the 30S prokaryotic ribosomal subunit and are known to interfere with the proofreading process, increasing the error rate during synthesis and misreading of bacterial mRNA. This commonly leads to premature termination of protein synthesis.

Indications

Require O2 for Uptake

O2-tank Uptake-tube

Aminoglycosides require oxygen for uptake into the bacterial organism. They are ineffective against anaerobic bacteria because they require oxygen-dependent transport to enter bacterial cells. Anaerobic bacteria lack the oxygen-dependent transport system required for aminoglycoside uptake.

Gram-Negative Rod Infections

Graham-cracker Negative-devil-with-rod

Aminoglycosides are typically used for aerobic gram-negative rod infections, including Pseudomonas and Enterobacter. The most frequent use of these antibiotics includes empiric therapy for serious infections, including septicemia, complicated intra-abdominal infections, UTIs, and nosocomial URIs. Gentamicin or amikacin is used in combination with ampicillin in neonates due to coverage of E. coli, Klebsiella, and Listeria monocytogenes.

Synergistic with B-Lactam Antibiotics

(B lac) Black Beta-fish

Aminoglycosides are sometimes used in conjunction with beta-lactam antibiotics in streptococcal infections due to their synergistic effects, especially in the treatment of endocarditis. One of the most frequently used combinations is ampicillin and gentamicin.