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 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 a teratogen, they should be avoided in pregnant patients.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 it is not used 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 heat stable and is often used to coat surgical implants and tools.

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 it is not absorbed by the intestine, it has been incorporated 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.

Tobramycin

Cobra-mouse

This is another aminoglycoside antibiotic used for gram negative infections. It is better than gentamicin when it comes to treating pseudomonal infections of the lung. 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

This 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.

Mechanism of Action

Bactericidal

Bacteria-sliders

Unlike bacteriostatic agents, which simply stop bacteria from reproducing, bactericidal agents actually cause active bacterial cell death.

Inhibit Formation of Initiation Complex

Inhibiting-chains on Initiation-engine

Aminoglycosides bind to the 30S prokaryotic ribosomal subunit and inhibit bacterial protein synthesis. This is performed by inhibiting 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.

Require O2 for Uptake

Oxygen-mask from O2-tank

Aminoglycosides require oxygen for uptake into the bacterial organism. As such, these antibiotics are ineffective against anaerobes, which do not require oxygen for proliferation.

Resistance

Resistance by Transferase Enzymes

Tied-up by Transformer wearing Resistance-bandana

Enzymatic modification by transferase enzymes is the most common mechanism of aminoglycoside resistance. The genes encoding for these modifying enzymes are typically found on plasmids and transposons. There are three types of aminoglycoside modifying enzymes, including acetyltransferases, phosphotransferases and adenyltransferases.

Acetylation

A-seagull

Acetylation refers to the transfer of an acetyl group on an amino group and this form of enzymatic modification can lead to aminoglycoside resistance.

Phosphorylation

Phosphate-P

Phosphotransferases catalyze ATP-dependent phosphorylation of a hydroxyl group and this form of enzymatic modification can lead to aminoglycoside resistance.

Adenylation

Add (+) signs

Adenyltransferases catalyze ATP-dependent adenylation of hydroxyl groups and this form of enzymatic modification can lead to aminoglycoside resistance.

Indications

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 include empiric therapy for serious infections, including septicemia, complicated intra-abdominal infections, UTIs, and nosocomial URIs.

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.

Side Effects

Nephrotoxicity Especially When Used with Cephalosporins

Kidney with Toxic-green-glow held by Chef-spore-head

Cephalosporins and aminoglycosides demonstrate a synergistic nephrotoxic interaction when used in conjunction. Therefore, this drug combination should be avoided unless clinically required and kidney function should be monitored throughout the treatment course.

Ototoxicity Especially When Used with Loop Diuretics

Ear with Toxic-green-glow from Launching Loop-hen Die-rocket

Aminoglycosides and loop diuretics, like furosemide, demonstrate a synergistic ototoxic interaction when used in conjunction. Therefore, this drug combination should be avoided when possible.

Teratogen

Tarantula-gem

Aminoglycosides are known teratogens and are in pregnancy category D, meaning there is positive evidence of human fetal risk based on data from studies in humans. Teratogens are agents that cause a defect or malformation in the development of the embryo or fetus. Aminoglycosides are especially associated with causing hearing deficits.