MISCELLANEOUS ANTIBIOTICS

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NEWER ANTIBIOTICS

ANTIBIOTICS INHIBITING CELL WALL SYNTHESIS

GLYCOPEPTIDES-VANCOMYCIN, TECOPLANIN

LIPOPEPTIDE-DAPTOMYCIN

POLYPEPTIDE-BACITRACIN

FOSFOMYCIN-a phosphonic acid derivative

CYCLOSERINE-an analogue of D-alanine

NEWER ANTIBIOTICS

OXAZOLIDINONES-LINEZOLID, RADEZOLID
TOREZOLID
STREPTOGRAMINS-PRISTINAMYCIN
POLYMYXIN-B AND COLISTIN
MUPIROCIN
FUSIDIC ACID

VANCOMYCIN

Vancomycin is obtained from streptococcus orientalis.

It inhibits gram-positive bacterial cell wall synthesis by complexing with D-alanyl D-alanine portion of the terminal end of peptidogycan pentapeptide
It also damages the cell membrane and alters cytoplasmic membrane permeability→ bactericidal
Vancomycin is active against aerobic and anerobic gram positive species- streptococcus, staphylococcus(MRSA) enterococcus, corynebacterium diptheriae

VANCOMYCIN

MRSA, staph. Epidermidis infections –parentral vancomycin
Staph. Enterocolitis and Endocarditis
Enterococcal endocarditis-vancomycin+gentamycin
Pseudomembranous enterocolitis(PMC) when C. difficile colitis is not responding to metronidazole
P/K-given orally,
preferred route of administration IV 1g BD

VANCOMYCIN

Red neck syndrome –due to histamine release
Minor events-ototoxicity, nephrotoxicity, reversible neutropenia, eosinophilia, chills and fever

Second generation glycopeptides- TELAVANCIN, DALBAVANCIN AND ORITAVANCIN

Telavancin exhibits rapid bactericidal activity
$T_{1/2}$ -8hrs, more potent than vancomycin against MRSA

Dalbavancin $T_{1/2}$ -6-11 hrs –once weeky for skin and soft tissue infection caused by MRSA
Oritavancin inhibits transglycosylation and transpeptidation process during cell wall synthesis for vancomycin-resistant staphylococci and enterococci

Teicoplanin and Ramoplanin

MOA- similar to vancomycin
More active than vancomycin against enterococci but equally effective against MRSA
It is used as prophylaxis against endocarditis, peritonitis (associated with continued peritoneal dialysis and to treat PMC or infections in immunocompromised patients
Can be given IV/IM (less chances of tissue necrosis)
$T_{1/2}$ is 50hrs
Dose-400mg→200mg/day

Miscellaneous group

Daptomycin –is a new lipopeptide antibacterial drug
It is used for IV treatment of complicated gram-positive infections of skin and soft tissue infections
MRSA and Enterococci-Daptomycin+ Gentamycin

Bacitracin is a mixture of polypeptide-antibiotics produced by bacillus subtilis.
It is primarily a topical antibiotic
It is highly active against staphylococcus aureus
PMC associated with clostridium

Fosfomycin

It is a phosphonic acid derivative
It is bactericidal against a range of gram positive and gram negetive bacteria including staph.aureus
Is demonstrates synergistic effects when combined with pencillins, cephalosporins, aminoglycosides or fluroquinolones
UTI- single 3g dose
P/K-orally and parenterally
Excreted unchanged in urine-90-95%
ADR-GIT distress, visual disturbances, asthma

Cycloserine

Second line anti-tubercular drug
Completely absorbed from GIT
Crosses blood brain barrier and placental barrier
Plasma $T_{1/2}$-10hrs
ADR-dose related CNS toxicity-headache, vertigo, tremors
Levocycloserine – under trial for Gaucher's disease

OXAZOLIDINONES

LINZOLID, RADEZOLID, TOREZOLID

Linezolid is totally synthetic antibiotic

Active against gram-positive organisms including staphylococci, streptococci, enterococci, gram-positive anaerobic cocci, and gram-positive rods such as Corynebacterium spp. and Listeria monocytogenes

MOA-it inhibits bacterial protein synthesis by binding to 50S ribosomal subunit near the interface with 30S. Thus the formation of initiation complex is prevented

OXAZOLIDINONES

This prevents the possibility of cross resistance
Spectrum-gram positive organisms only
USE-The drug is reserved for
Vancomycin resistant enterococcus faecium and MRSA-endocarditis, bacteremia, nosocomial and community acquired pneumonia caused by staph. Aureus
P/K-oral bioavailability is 100%
-food does not interfere with absorption
metabolised in liver and excreted in urine
plasma T1/2 of 4-6hrs
Post antibiotic effect- 1.5hrs

OXAZOLIDINONES

ADR- Myelosuppression, including anemia, leukopenia, pancytopenia, and reversible thrombocytopenia

reversible neutropenia

reversible optic neuropathy

Drug interaction- linezolid is reversible inhibitor of MAO enzyme and may lead to **cheese reaction** with food containing tyramine

It may also precipitate **serotonin syndrome –** confusion, hypertension, seizures, tachycardia, muscle rigidity

Streptogramins -pristinamycin

Obtained from Streptomyces pristinaespiralis
Pristinamycin available for oral administration
It is a synergistic combination of streptogramin-B(quinupristin) and streptogramin-A (dalfopristin) in a 30:70 ratio respectively, they bind to 50s and 70s ribosome and prevent the extrusion of newly synthesised peptide chain from ribosome
Spectrum is similar to vancomycin and linezolid
Used for vancomycin resistant enterococcus faecium and skin infections of staph.aureus, Nosocomial Pneumonia
P/K-the combination is rapidly metabolized by nonenzymatic reactions to active metabolites
ADR-pain at site of infusion-related arthralgia-myalgia syndrome

Polymyxins-B and Colistin

Peptide antibiotics are very toxic
Colistin is polymyxin E –
Colistin sulphate for oral use and colistimethate sodium for parenteral use
Polymyxin-B and colistin(polymyxin-E) function as cationic detergents and disrupt the bacterial cell membrane osmotic integrity by displacing Ca+ and Mg from membrane lipid phosphates
It is remarkably effective against pseudomonas aeruginosa
ADR-neurotoxicity-parasthesia, ataxia and slurred speech
neprotoxicity-hematuria, proteinuria and tubular necrosis

Mupirocin

Mupirocin inhibits bacterial RNA and protein synthesis
Binds to isoleucyl-t-RNA synthetase
This prevents incorporation of isoleucine into the bacterial protein synthesis. It inhibits bacterial protein synthesis, but by elongation of peptide chain
Antibacterial spectrum for mupirocin includes staphylococci and streptococci

Aminocyclitols (Spectinomycin)

Aminocyclitols (Spectinomycin)-is an antibiotic produced by Streptomyces spectabilis.

MOA-It selectively inhibits protein synthesis in gram-negative bacteria. The antibiotic binds to and acts on the 30S ribosomal subunit. Its action is similar to that of the aminoglycosides, but spectinomycin is not bactericidal and does not cause misreading of messenger RNA.

Use

Its only therapeutic use is in the treatment of gonorrhea caused by strains resistant to first-line drugs

ADR-urticaria, chills, fever

Resistance-Bacterial resistance may be mediated by mutations in the 16S ribosomal RNA or by modification of the drug by adenylyl transferase

FUCIDIC ACID

It interferes with protein synthesis, but by interfering with peptide chain(elongation factor-G)
It is particularly active against penicillinase-producing staphylococcus aureus, corynebacterium and clostridium.
It is highly lipid soluble agent which readily penetrates the skin
It is used for boils impetigo and pyoderma

Lincosamides

Lincomycin Clindamycin

Antibacterial spectrum: lincosamides are active against staphylococci, gram-positive and gram-negative anaerobes, including Bacteroides fragilis.

Mechanism
Binding to 50s ribosome subunit and inhibiting protein synthesis
Pharmacokinetics
Absorbed well, Penetrate well into most tissues including Bone but not CSF.
About 90% protein-bound
Excretion via the liver, bile, and urine

Resistance

- Alteration of 50s ribosomal subunit by adenine methylation
- Chromosomal mutation of 50s ribosomal protein
- Drug inactivation

Dose -150-300mg every 6th hourly

Lincosamides-Therapeutic uses

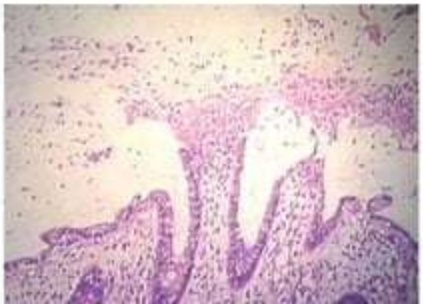
1. Severe anaerobic infection
2. Acute or chronical suppurative osteomylitis , arthritis caused by susceptive organisms especially Staphylococci aureus
   aerobic G+ cocci infection
3. Combination with pyrimethamine for AIDS-related toxoplasmosis (600, 75)
4. Combination with primaquine for AIDS-related pneumocystis carinii pneumonia

Adverse reactions

Gastrointestinal effects: severe diarrhea and pseudomembranous enterocolitis caused by Clostridium difficile

Higher IV dose –neuromuscular blockade

Other :Impaired liver function , neutropenia, hypersensitivity



Ketolides

TELITHROMYCIN, CETHROMYCIN
Telithromycin is semisynthetic derivative of erythomycin
Tighter binding to ribosomes
Decreased incidence of resistance
Longer post antibiotic effect
T1/2- 13hrs
Has activity against erythromycin resistant G+ve cocci
Mainly for macrolide resistant CAP, chronic bronchitis
Dose -800mg OD for 10 days

Ketolides – Cethromycin

- More potent than telithromycin
- Used against macrolide resistant Streptococci and Enterococci

Resistance -Ribosomal modification via inducible or constitutive methylation .

Ribosomal modification via point mutation- H.pylori

Drug efflux- S.pyogenes

Adverse reactions

Diarrhea, nausea

Drug interaction

Prolonged QT interval (cisapride, terfenadine)

Increased blood levels of theophylline, midazolam