Cell wall synthesis inhibitors

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Vancomycin

- Vancomycin naturally produced by *Streptococcus orientalis* and *Amycolatopsis orientalis*.
- Vancomycin after binding with D-ala-D-ala and inhibit bacterial cell wall synthesis by inhibiting the enzyme peptidoglycan synthetase/ transglycosylase which is responsible for translocation of precursors (polypeptide layer) across the cytoplasmic membrane to incorporate these in growing chain of peptidoglycan. This inhibit in further elongation of peptidoglycan and cross linking.

Vancomycin…….

- Resistant strains of Enterococci do modification in D-ala-D-ala binding site. These bacteria replace terminal D-ala with D-lactate.
- Similarly resistant strains of Staphylococci develop false D-ala binding site that result in resistance against vancomycin.
- Active against gram (+) bacteria particularly *Staphylococcus aureus*. But this drug is less active than penicillin in dividing cells of sensitive strains of Staphylococci.

Vancomycin…..

- Poorly absorbed from GIT. Orally used in antibiotic associated enterocollitus caused by *Clostridium difficile*.
- Normally given through intravenous infusion,
- Widely distributed including upto 30% in CSF.
- 90% of the drug excreted through GFR. In anephric patient half life may exceed upto 10days.

Vancomycin……

- Bactericidal effect appear at 0.5 to 10mcg/ml.
- Parenterally used in sepsis caused by methicillin-resistant strains of Staphylococci (MRSA).
- Vancomycin+ gentamycin/streptomycin combination is effective against *Enterococcus faecium* and *Enterococcus faecalis in patients who are allergic to Penicillin*.

Vancomycin……

- Vancomycin +ceftriaxone is effective in meningitis caused by Penicillin resistant strains of Pneumococci.
- Parenteral dose is 1g every 12 hourly.
- Dose in antibiotic-associated collitus is 0.125-0.25 g every 6 hourly. In resistant strains, Metronidazole 300mg 3-4 times a day is given along with Vancomycin.
- ADR: Chills and fever, Redman/redneck syndrome, nephrotoxicity.

Fosfomycin

- Fosfomycin inhibit very early step of bacterial cell wall synthesis .
- Drug is actively transported into the bacterial cell by glycerophosphate or glucose-6-phosphate transport system.
- Resistance develop due to inadequate transport of drug.
- Fosfomycin inhibit peptidoglycan synthesis by covalently binding to the cysteine residue of cytoplasmic enzyme enol pyruvate transferase and block the addition of phosphoenol pyruvate to UDP-N-acetyl glucosamine which then ultimately converted to UDP-N-acetyl muramic acid.

Fosfomycin

- Oral bioavailability is 40%. Half life is 4 hour.
- Effective against both gram (+) and gram (-) bacteria.
- Single 3 g dose for lower UTI infection in women.
- Also be effective in bacterial diarrhea.
- Fosfomycin is safe to be used in pregnancy.
- ADR: headache, pharyngitis, dizziness etc

Cycloserine

- Cycloserine is an analogue of D-alanine and inhibit cell wall synthesis by blocking alanine racemase enzyme which is responsible for incorporation of D-alanine in the penta/poly-peptide chain of the peptidoglycan.
- Used in tuberculosis caused by Mycobacterium tuberculosis. Dose is 0.5 to 1.0g in two or 3 divided doses.
- ADR: Headache, tremor, acute psychosis and convulsion