Macrolides and Quinolones

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Macrolides

Macrolides

- Mechanism of action

Binds to bacterial ribosomes and interferes with protein synthesis

Macrolides

- Erythromycin
- Clarithromycin
- Azithromycin

Erythromycin

- T1/2- 2-4h
- Effective against gram positive organisms
- Spectrum similar to penicillin

Pharmacokinetics

- Absorption – erythromycin estolate well absorbed even in the presence of food
- Hydrolysis of erythromycin estolate releases active erythromycin ---- diffuses readily into tissues
- Elimination –bile and feaces

Erythromycin-indications

- Effective alternative –penicillin allergy
- *Mycoplasma pneumoniae* infections
- *Legionella* infections
- Diptheria
- Pertussis
- Chlamydial infections

Erythromycin dose

- 250mg-500mg six hourly

Adverse effects

- GI disturbances-Nausea /diarrhea- frequent
- Cholestatic hepatitis-with estolate preparation

Interactions

- Inhibit cytochrome P 450
- Inhibit inactivation of certain drugs-ex-digoxin,warfarin,theophilline ,carbamezapine
- Increases concentration of erythromycin with co administed azoles, CCB,protease inhibitors

Clarithromycin

- Similar spectrum to erythromycin (gram positives) and more effective against *H influenzae.*
- *Twice daily dosing*
- *GI side effects rare*

Clarithromycin

- Rapidly absorbed
- 60% of dose inactivated by metabolism , rest excreted in urine
- Used for atypical pneumonias/soft tissue infections
- Effective against *Mycobacterium avium intracellulare* in HIV patients

Azithromycin

- Additional gram negative activity
- Little less effective against gram positives than erthromycin
- Excreted in bile CI in liver failure
- Gastrointestinal side effects less

Quinolones

- Inhibits DNA synthesis by promoting cleavage of bacterial DNA in the DNA enzyme complex of DNA gyrase and type IV topoisomerase

Quinolones

- Concentration dependant killing
- Bactericidal

Pharmacokinetics

- Well absorbed following oral administration
- Serum drug levels following oral absorption are comparable to those with IV dosing

(this allows early transition to oral following IV therapy)

Cations like iron, calcium significantly reduces absorption

- T1/2- 1.5-16 h –allows bd dosing
- Elimination –renal/bile
- Tissue penetration generally high but not well concentrated in CSF
- Liver enzyme inhibiting properties –inc concentration of Warfarin/theophylline

Drugs

- Ciprofloxacin
- Norfloxacin
- Ofloxacin
- Nalidixic acid
- Levofloxacin
- Moxifloxacin

Spectrum

- Good gram negative coverage
- *Pseudomonas aeruginosa*
- *Legionella pneumophila*
- *Mycobacteria*
- Chlamydial and mycoplasma infections
- Less active against gram positives and anaerobes

Uses

- Urinary tract infections
- Prostatitis
- Travellers' diarrhea
- Skin and soft tissue infections
- Pneumonias
- Infective exacerbations in cystic fibrosis

Adverse effects

- Gastrointestinal disturbances
- Rashes
- Dizziness/headache
- Reversible arthropathy in immature animals
- Achillies tendon rupture –mainly elderly/on steroids
- QT prolongation in ECG

Ciprofloxacin

- Widely used for urinary,GI,respiratory and soft tissue infections

Levafloxacin

- has greater activity against pneumococci
- for respiratory and urinary infections

Moxifloxacin

- strong gram positive and antianerobic activity
- weak against pseudomonas
- Causes QT prolongation
- CI in heart failure and rhythm abnormalities

Norfloxacin

- Used in the treatment and as prophylactic treatment for recurrent UTI
- Used for Spontaneous bacterial Peritonitis prophylaxis in patients with cirrhosis
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Nalidixic acid

- 1st Quinolone
- Effective for UTI as concentrated in urine but little systemic activity(urinary antiseptic)
- Also used as prophylactic agent for recurrent UTI
- Can precipitate hemolysis in G6PD deficiency