Aminoglycosides
&
tetracyclines

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Outline -

- Aminoglycosides
- Tetracyclines

- MOA
- Pharmaco kinetics/dynamics
- Antibacterial spectrum
- ADR

Aminoglycosides

Mechanism of action

- Streptomycin was the first aminoglycoside came in to clinical use.
- Interferes with bacterial protein synthesis.
- Binds to ribosomes resulting in incorrect amino acid sequences entering to peptide chains
- Resulting abnormal proteins are fatal to the microbes

Aminoglycosides cont.-

- Bactericidal
- Water soluble
- Do not cross membranes easily.
- Not absorbed sufficiently to be effective orally.
- Needs I.V or I.M administration
- Oral use is only for topical effect e.g. Neomycin in hepatic encephalopathy
- Neomycin is also used as a topical therapy in dermatology

Pharmacokinetics

- T I/2 is 2-5 hours
- Eliminated unchanged by glomerular filtration
- Dose reduction necessary in renal impairment
- Needs monitoring of plasma concentrations even if the renal functions are normal
- Trough levels are associated with adverse effects

Anti bacterial activity

- Staphylococcus
- Aerobic gram (-) ve bacteriae including pseudomonas

Clinical indications for the use of aminoglycosides

- Septicaemia
- Endocarditis
- Abdominal sepsis. Peritonitis, cholecystitis
- Pyelonephritis & other severe UTI
- Tuberculosis (streptomycin)
- Topical application Neomycin Skin, Hepatic encephalopathy

Adverse effects

- Ototoxicity.
  - Both auditory and vestibular damage may occur
- Nephrotoxicity.
  - dose related
  - usually reversible.
- Impair neuromuscular transmission.
  - Worsens myasthenia
- Rashes

Individual aminoglycosides

- Gentamicin
- Netilmicin - same spectrum of action, but more resistant to aminoglycoside inactivating enzymes
- Amikacin- do
- Streptomycin
- Neomycin

Gentamicin

- Usually combined with a another antibiotic due to poor penetration
- Not used as a single agent against Staph aureus
- Especially useful in endocarditis in combination with a penicillin, synergistic effect
- creams ointments and solutions are used topically in skin and ear infections
- IV or IM use in severe infections

Streptomycin

- Second line treatment in tuberculosis
- Also used in some non tuberculous infections
  - Plague
  - Tularemia
  - Brucellosis

How to reduce toxicity

- Monitor levels
- Take precautions in the elderly and patients already on other nephron-toxins and people with impaired renal function
- Monitor renal functions daily
- Single daily dose.

Tetracyclines

Mode of action

- Interferes with protein synthesis
- Bacteriostatic
- Broad spectrum antibiotics

Pharmacokinetics

- Most tetracyclines are only partially absorbed
- Mainly excreted unchanged in urine
- Doxycycline is safe in renal impairment

Uses

- Chlamydia/ Mycoplasma infections
- Non specific urethritis / PID
- Rickettsia. Typhus
- Cholera
- Acne. Inhibits sebum secretion
- Acute exacerbations of chronic bronchitis
- Local application skin ointment

- Use is now limited partly due to increasing bacterial resistance.

Adverse effects

- Heart burn, Gastric irritation
- Diarrhoea
- Sore mouth
- Discoloration of teeth
- Photosensitivity

Contraindications

- Pregnancy
- Children

Interactions

- Absorption is affected by
  - dairy products
  - Antacids
  - Iron preparations

Individual tetracyclines

- Tetracycline
  - t ½ - 6 hours
  - Administered 6 hrly
- Doxycycline
  - t ½ - 16 hours
  - Administered once a day