

AMINOGLYCOSIDE ANTI BIOTICS:

→ Amino group + Amino sugar

→ These are group of natural & semisynthetic Antibiotics having polybasic Amino group. linked to two or more Aminosugar.

CLASSIFICATION:

SYSTEMIC AMINOGLYCOSIDES

- streptomycin (1st mem)
- Gentamicin
- Kanamycin
- Tobramycin
- Amikacin
- Sisomicin
- Netilmicin

TOPICAL AMINOGLYCOSIDES

- Neomycin
- Framycetin

SOURCE:

Natural:

Aminoglycosides with names ending with
- MYCIN - obtained from genus streptomyces
eg: streptomycin, Tobramycin

GENIN - obtained from genus micromonospora
eg: Gentamicin, Kanamycin

Synthetic

eg: Netilmicin

Common properties

- All exhibit ototoxicity & nephrotoxicity
- Active against Aerobes gram -ve bacilli & not Anaerobes
- excreted unchanged
- interfere in b/c protein synthesis - bactericidal

NOTE:

- Parenteral
- small vol
- low PPB
- Renal excretion.

→ used with other Antibiotics.

Q/O pregnancy

- do not penetrate CSF
- highly polar, antitoxin

THROMBIN
→ HACEOLAS

MODE OF ACTION:

- Inhibit protein synthesis

SPECTRUM

- Mainly against gram -ve aerobic bacilli
- E. coli, Proteus, Klebsiella, Shigella
- Pseudomonas
- Mycobacterium Tuberculosis
- not used for Anaerobes & G+ve cocci

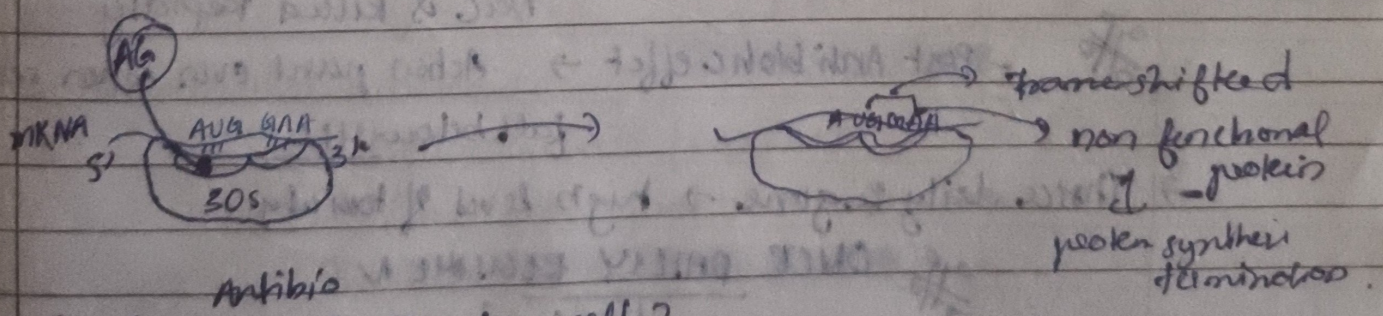
AMIKACIN HAS WIDEST ANTIBAC SPECTRUM.

CLINICAL USES:

- Infective endocarditis
 - Pneumonia
 - Sepsis
 - T.B., Meningitis, Pelvic infection, etc.
 - Gonorrhea, Pelvic infection, etc.
 - Plague, Tularemia.
- used in combination

MECHANISM OF ACTION:

- Bacteriocidal.
- bind to 30S subunit.
- misreading of genetic code
- non-functional group
- protein synthesis termination



How does it enter the bac. cell?

- They enter the bac. cell through porin & reach the periplasmic space
- then they pass through cytoplasm

ECM
PS
ICM

→ energy dependent phase 1 (EDP₁)

proton pumps → oxygen dependent

ie, only Active against Aerobes.

Enter inside cell via O₂ dependent process.

- Inhibitors of bacterial cell wall like β lactam Antibiotics (like penicillin & cephalosporins) enhance entry of Aminoglycosides & potentiate their action.

DRUG SYNERGISM

Step 2 → Bact. Protein synthesis Inhibition.



Mixing of codon incorporates wrong AA
Premature chain termination & blocks further translation

MECHANISM OF RESISTANCE:

- phosphorylation / Adenylation or Acetylation of the drug
- ↓ Affinity to Ribosomal Protein
- Impaired transport of the drug.

NOTE:

→ concentration dependent killing → Higher the Plasma conc, more of bac. is killed Rapidly.

☞ Post Antibiotic effect → Action persist even when serum conc falls below MIC

→ Thrice daily regime → high level of toxicity

☞ ONCE DAILY REGIMEN

- less nephrotoxic
- less ototoxic

ADR:

1) OTOTOXICITY:

- dose-limiting adverse effect
- Irreversible

→ vestibular

→ cochlear

} toxicity

→ Hearing loss

→ due to villous damage re, Ab accumulation in perilymph & endolymph of inner ear

- High pitched tinnitus - 1st symp
- Auditory impairment
- Detected on Audiometric examination

→ Risk is

→ elderly people

→ Repeated course of AC

→ preexisting Auditory impairment

MOST OTOTOXIC DRUGS

→ Neomycin

→ Kanamycin

→ Amikacin

vestibulotoxic DRUGS

→ Gentamicin

→ Streptomycin

least toxic - Neomycin

→ Reduced by $-Ca^{2+}$ supplements

→ Abg⁺ con is renal CO₂ H₂O → bicarbonate
concentrable

2) NEPHROTOXICITY:

→ Reversible impairment occurs who receive drug 7-10 days

NEOMYCIN (highest)

TOBRAMYCIN

BIENTAMYCIN

AMIKACIN

} most nephrotoxic

Streptomycin - least nephrotoxic

NOTE

→ Abg⁺ inhibit the release of Acetylcholine from motor nerve

3) → neuromuscular blockade:

→ Displacing Ca^{2+} from NMJ

→ Blocking post synaptic NMJ Receptor

→ Inhibiting Ca^{2+} release from Ach.

Myasthenia gravis not used

Other effect

→ Rare hypersensitivity Rx

→ Skin Rash

→ eosinophilic, fever, Angioedema

4) Hypersensitivity of pregnancy

PRECAUTIONS:

- Avoid during → pregnancy
- Caution use of Muscle Relaxant in pts using Aminoglycosides
- Caution use in elderly & with renal damage
- use of other nephrotoxic drug.

GENTAMYCIN:

- Most commonly used, broad spectrum
- Use → urologic, gram -ve infection, UTI, prostheses, klebsiella, wounds & burns etc.

AMIKACIN

- wide spectrum
- Resistant to Aminoglycoside inactivating enzyme

NEOHYCLIN: topical & oral Administration:

resorption of bowell & hepatic enterophlogia

